Caloric Restriction

► Slow-Ageing Diets

Cambodia Aging Survey

► Cambodia Elderly Survey

Cambodia Elderly Survey

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Synonyms

Cambodia aging survey; Health and retirement studies series; Health and retirement study; Survey on older adults; Surveys for aging studies

Overview

The Survey of Elderly in Cambodia (SEC), conducted in 2004, involved data collection from a representative sample of 1,273 adults aged 60 and older living in Cambodia. It was supported by grants from the National Institute on Aging and from UNFPA Cambodia. The data collection and subsequent analyses was led by Dr. John Knodel at University of Michigan and Dr. Zachary Zimmer currently at Mount Saint Vincent University in Canada. The lead researchers were assisted by Kiry Souvan Kim and Sina Puch of the Department of Sociology at the Royal University of Phnom Penh. Until the time of the survey, relatively little if any systematic data had been collected on Cambodia's older population. Consequently, one chief purpose of the survey was to provide a basic but comprehensive cross-sectional demographic, social, economic, and health profile of Cambodia's older population. This profile was published in a report commissioned by UNFPA Cambodia (Knodel et al. 2005).

Study Details

While the SEC questionnaire included a number of standard survey components that tend to be the focus of general studies of older-aged populations, such as those that garner information on household composition, socioeconomic standing, and physical well-being, older Cambodians at the time were dealing with some unique circumstances, and efforts were taken to include survey questions to cover topics that were distinctive to this population. First, older-aged Cambodians lived through an exceptionally traumatic period of history during their earlier adult years. They were all survivors of

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the Khmer Rouge takeover in 1975 and the Khmer Rouge rule that lasted until 1979. During that period of upheaval, political violence, severe food shortages, and lack of medical care resulted in an estimated 1.5–2 million deaths constituting as much as a fourth of the total population (Heuveline 1998; Kiernan 2003). Many of those who died were the sons, daughters, and spouses of the older-aged population. Some questions on the SEC were included to capture the impact of the dramatic political history that may have influenced the lives of older Cambodians. Second, although declining, Cambodia was experiencing the highest AIDS prevalence rates in Asia. Adult AIDS prevalence peaked at 3% in 1997 (UNAIDS 2006). Many who were infected and died were adult sons and daughters of the older population, and older persons were frequently primary caregivers for their HIV-infected children. Some questions on the SEC were meant to assess the influence of illness and death of adult children and awareness and knowledge of older persons regarding AIDS, especially as related to caregiving to HIV-infected persons.

Methods

The SEC sample came from the six most populous provinces of Cambodia, which combined included more than 50% of the national population. These were, in the order of population size: Kampong Cham, Kandal, Phnom Penh, Prey Veng, Battambang, and Takeo. Sampling was conducted by a multistage cluster proportionate to size design that involved stratified selection in the following manner: selection of districts within provinces, selection of communes within districts, selection of villages (PSUs) within communes, selection of two adjacent enumeration areas (EAs) within villages, random selection of 25 households within the 2 EAs, and selection of one older person within households. (Due to its smaller geographic size, in Phnom Penh, the sampling began at the stage of selecting villages). The sample was drawn with the assistance of staff at the National Institute of Statistics (NIS). NIS also provided staff who enumerated households that contained an older person within EAs, working from maps that were hand-drawn during the 1998 Cambodian Census.

Fieldwork took place in three stages; the first was in April 2004 with data collection in Phnom Penh. The second was in July and August 2004 with data collection in five provinces. The third was supplemental fieldwork undertaken in August and September 2004, again in Phnom Penh. The final sample included 800 respondents from rural areas in the 5 provinces and 473 from the city of Phnom Penh. This meant that Phnom Penh was oversampled, which was done to increase the number of urban residents in the survey. The overall response rate was 91.5%; 84.6% in Phnom Penh, and 97.9% in the other 5 provinces.

The final dataset includes weights that can be used to make the sample representative of the population 60 and older in Cambodia at the time of the survey. Weighted statistics indicated that the basic characteristics of the sample, such as age, sex, and marital status distributions, resembled closely characteristics of those aged 60+ from previous nationally based enumerations such as those collected by the 1998 Cambodian Census and the 1999 Socioeconomic Survey.

Selected Findings

Results from the SEC are available in the main report (Knodel et al. 2005) as well as in several academic papers published by the lead researchers and colleagues. Some of the more interesting findings follow. The Cambodian older-aged population in 2004 had an unusual sex ratio favoring females, a function of high mortality rates of males during the Khmer Rouge period. As a result, a large proportion of older Cambodian households were female headed. The Cambodian population of older adults in 2004 was found on average to be living with very low socioeconomic conditions. For instance, they were characterized as having minimal wealth, with a substantial proportion living in poverty, and very few having any schooling or literacy. Schooling levels and literacy rates were however much higher for males versus females; about 28% of males were totally illiterate compared to about 80% of females (Knodel et al. 2005). The health status of older Cambodians was found to be, on average, much worse than other populations of older persons in the region. For instance, the prevalence of disability as measured by Activities of Daily Living was found to be as much as twice as high as that found in surveys in Myanmar, Indonesia, Philippines, and Thailand (Zimmer 2006). Older-aged parents in Cambodia were found to commonly play a key role in the care of their grown sons and daughters living with AIDS; however, knowledge of HIV/AIDS was found to be relatively low while willingness to care for their ailing children was found to be strongly related to knowledge (Knodel and Zimmer 2007). A large percentage, about 43%, of older Cambodians were found to have experienced the death of a child during the 4-year Khmer Rouge period (Zimmer et al. 2006). Moreover, a large majority of these deaths were reported to have been caused by violence. While these events are no doubt traumatic, the analyses could not find much association between deaths of children during the Khmer Rouge period and living arrangements, levels of support or economic well-being at the time of the survey.

Conclusion

SEC notwithstanding, Cambodia's older population remains understudied with no national representative surveys focused on them having taken place since SEC. SEC data remain available for academic analysis. Interested parties should contact Dr. Zachary Zimmer at Mount Saint Vincent University in Canada for information on accessing the data.

Cross-References

▶ Chinese Longitudinal Healthy Longevity Survey (CLHLS)
▶ Indonesia Family Life Survey
▶ Malaysia Ageing and Retirement Survey
▶ Myanmar Aging Survey
▶ National Survey of Older Persons in Thailand

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Cancer

▶ Cell Damage and Transformation in Aging

Cancer Assessment

▶ Cancer Diagnosis

Cancer Detection

▶ Cancer Screening

Cancer Diagnosis

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Synonyms

Cancer assessment; Cancer screening; Early detection of cancer; Early diagnosis of cancer

Definition

Methods to identify and characterize cancer in the early stages of disease and predict tumor behavior.

Overview

Advanced age is an important risk factor for cancers. Due to demographic and epidemiological transitions, the number of older people worldwide is increasing rapidly. In the next two decades, the absolute number of people aged 65 and older will double, leading to more number of new cases of cancer in this population. In 2035, the number of new cases will approach 14 million and will concern all world regions with a greatest relative increase in Middle East and North Africa (157%). By 2035, older adults will represent 58% of the total cancer incidence burden and over two-thirds of all cases will be diagnosed in northern America, Europe, Oceania, and China (Pilleron et al. 2019). This relentless increase needs to be anticipated and the question of the care of older patients addressed properly (Smith et al. 2009). In the last decade, tremendous progress and efforts have been made to adapt treatment strategies in older patients. Screening tools for frailty, geriatric assessment, and specific guidelines were designed to help practitioners in the decision-making process and guide treatment (Mohile et al. 2018; Hurria et al. 2015). Enrollment of older patients in clinical trials and dedicated clinical trials have also increased in the last years (Le Saux et al. 2016; Hurria et al. 2014). However, data available in older patients is mostly extracted from subgroup analyses which prevent from drawing any generalized conclusions.

Key Research Findings

Patterns of Cancer Diagnosis in Older Patients

A common misconception among the general population and some practitioners is that all cancers grow slowly in older patients. The prognosis of cancers is related to the histology and molecular subtype as well as the host. Modifications of metabolism and functional reserves with aging may lead to general symptoms rather than organ-related symptoms. Thus, older patients often have atypical or occult disease presentation such as lack of a fever during infection. Nonspecific symptoms such as delirium, falls, and reduced intake of food and/or fluids may be the only presentation related to a wide range of diseases. These symptoms could be interpreted as normal aging and be neglected either by patients or physicians.

Cancer may also be difficult to investigate in older individuals due to comorbidities, particularly dementia, and could lead to delayed diagnosis (Havlik et al. 1994). Several studies notably in breast cancer patients showed that older patients are at risk of delayed diagnosis (Yancik et al. 1989; Gershenson et al. 1993; Freyer et al. 2006; Wildiers et al. 2009). In breast cancer patients, 52% of patients >75 years of age had a metastatic disease at diagnosis compared with 39% of patients between 65 and 74 years old ($p < 0.0001$) Freyer et al. (2006). This phenomenon also affects men with 4% of patients diagnosed with distant metastases of prostate cancer in <75 years of age compared to 12% in ≥75 years of age (Hu et al. 2017). This proportion increased between 2004 and 2013 (6.6% vs 12%; $p < 0.01$) according to the Surveillance Epidemiology and End Results (SEER) database. The main reasons for delayed diagnosis are lack of knowledge of the symptoms; neglect clinical signs of the disease by patient or physician;

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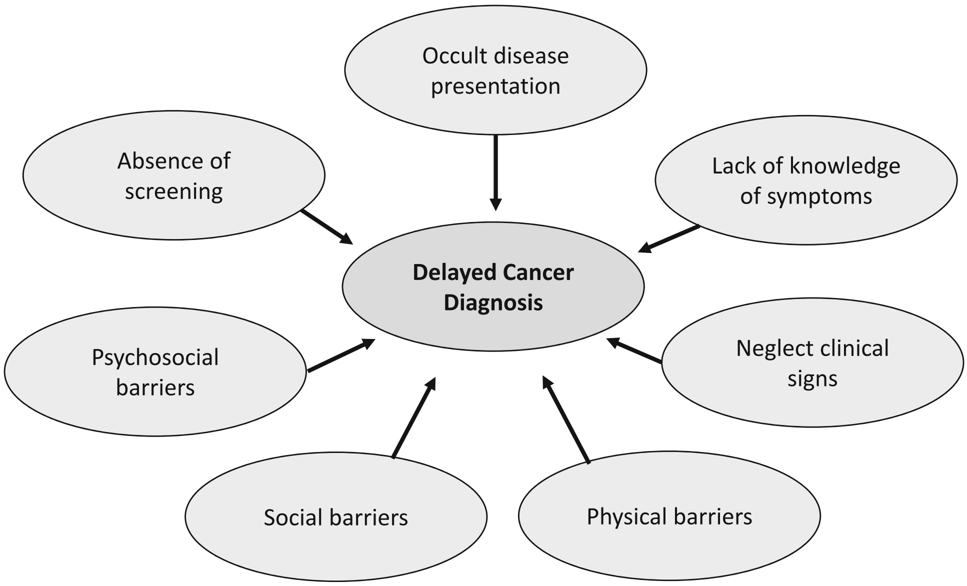

Cancer Diagnosis, Fig. 1 Potential causes of delayed cancer diagnosis in older individuals

perception of personal risk of cancer; physical, social, and psychological barriers; and absence of screening (Ramirez et al. 1999; Macleod et al. 2009; Burgess et al. 2006) (Fig. 1). Women over 65 years old are less likely to look for medical help for any breast symptoms and are more likely to have concerns about disfigurement and the financial consequences of seeking help (Grunfeld et al. 2003). Older patients are less likely to be fully investigated, that is, have a tissue diagnosis or staging investigations (Turner et al. 1999; Higton et al. 2010). This may be due to the higher prevalence of functional limitations and geriatric syndromes in older cancer patients (Mohile et al. 2009).

Older age is associated with poorer outcome in patients with cancer. In the EUROCARE-5 study, 5-year relative survival for adults with cancer diagnosed in 2000–2007 was lower in older patients ($\geq$75 years old) across all tumor types (stomach, colon, rectal, lung, skin melanoma, breast, ovarian, prostate, kidney, and Non-Hodgkin lymphoma) (De Angelis et al. 2014). In breast cancer patients, the 5-year survival rate was 85% in women aged 65 to 74 and 72% in women $\geq$75 years old. This rate was 78% in men aged 65 to 74 with prostate cancer and 52% in men $\geq$75 years old. Survival disparities by age are an important concern and may be explained by later stage at diagnosis but also under or over treatment. Clinicians are uncertain about the tolerability and benefit of cancer treatments (Giovanazzi-Bannon et al. 1994; Chen et al. 2003). Older patients receive less chemotherapy or aggressive treatments than recommended by clinical practice guidelines (Bonadonna and Valagussa 1981; Berry et al. 2013; Hurria et al. 2008; Mandelblatt et al. 2010; Schrag et al. 2001; Cress et al. 2003; Gupta and Lamont 2004). However, due to heterogeneity of older patients defining clear guidelines according to functional status is challenging. Dedicated clinical trials are needed to improve our knowledge and establish robust guidelines for everyday clinical practice.

Impact of Cancer Diagnosis

Disclosure on cancer diagnosis is crucial for patients with cancer and clinicians. It may improve treatment decisions, adherence, patient-physician relationship, and quality of life at terminal stage (Kumar and Temel 2013). There is some evidence that physicians fail to inform patients and more often in older patients (Mosconi et al. 1991; Thomsen et al. 1993). However, most older people would like to be told if they developed cancer and would like their families to be informed (Ajaj et al. 2001). This contrasts with physicians and family perception who are reluctant to give full disclosure (Kawakami et al. 2001; Elkin et al. 2007; Cavanna et al. 2009). In a French prospective cohort survey of individuals aged 70 and older as-yet untreated, reasons for not reporting complete information were carcinoma of unknown primary (CUP), lung cancer (OR = 7.7, 95% CI = 2.7–21.7), two or more major comorbidities (Cumulative Illness Rating Scale for Geriatrics grade 3 or 4 CIRS-G) (OR = 2.7, 95%CI = 1.3–5.9), and Mini Mental State Examination (MMSE) less than 23 (OR = 1.95, 95%CI = 1.9–22.7) (Kempf et al. 2016). The large majority of patients reported complete information on cancer diagnosis and treatment (89%). This proportion may vary according to race, education and income, different geographical areas, and culture (Hagerty et al. 2005; Dein 2004). In a similar Italian study, 34% of the 622 patients received only partial or no information on diagnosis and prognosis (Repetto et al. 2009). The main factors associated with better information were educational level, geographical area, ECOG PS, and number of family members (Repetto et al. 2009). Stage of disease was not correlated with the level of information. Knowing the diagnosis and taking part in the management plan is an essential right for the patient. Thus physicians have a legal and ethical responsibility to provide adequate information to the patient for processing the information and make appropriate decisions. However, some studies showed that older patients may prefer to receive less information than younger individuals especially on diagnosis, seriousness of the disease, treatment options, and possible side effects (Giacalone et al. 2007). They grew up at a time when medicine was paternalistic and did not take patient's opinion into account. It might impact the level of information they need. Older patients want to be informed but differently from younger patients (Chouliara et al. 2004). They are more afraid of recovery but are not interested in how to deal with the disease on daily basis (Giacalone et al. 2007; Chouliara et al. 2004). They are also less likely to seek information on their own particularly from the Internet (2% vs 25% in the younger group) (Giacalone et al. 2007). Cancer is still considered in many societies as an "incurable disease." Many older patients think that the diagnosis of cancer is associated with death. They prefer to limit their information to maintain hope and manage fear. The information should be tailored to what older patient want to know and are able to receive. Therefore, it is essential to assess the needs of each patient at all phases of the disease.

Coping strategies might differ between younger and older patients. Previous studies showed that the emotional impact of cancer diagnosis was greater among younger patients, older patients showing more passive resignation, hopelessness, or denial (Hughes et al. 2009; Hernández et al. 2009; Vos and de Haes 2007). However, younger patients have more psychological resources than older patients to fight and cope with this period (Scholl et al. 2015). Knowing the diagnosis of cancer is not associated with increased risk of depression (Silay et al. 2015). Depressed mood may be the first symptom of a medical condition and is usually associated with functional disability and multiple illnesses (Polsky et al. 2005).

Prospects

Cancer diagnosis is a major issue in older patients. With the interruption of screening and misconceptions, patients are diagnosed at a later stage. Health authorities and scientific societies should work together to improve information among the general older population. Several initiatives have been made such as awareness raising campaign worldwide. In France, the French society of geriatric oncology (SoFOG) launched an awareness campaign targeting the general population through general practitioners called "There is no age limit to be treated for cancer." Many efforts have been made in the last decade and should be carried on.

Robust networks could also be created involving cancer specialist, primary care physicians, healthcare professionals, and patients to improve delay in diagnosis and treatment access. Geriatricians should be involved sooner to improve older patients care.

Summary

Cancer is associated with older age. In the next decades, the number of older patients with cancer will increase drastically leaving physicians with multiple challenges. Patterns of cancer diagnosis vary in older patients, and common misconceptions such as slower growth still exist in the general and medical community. Balancing risk and benefit is sometimes difficult in such a heterogeneous population. However, assessment of frailty with the help of a geriatrician may guide decisions on an individual level. In the next years efforts should be made to improve information and older patients care.

Cross-References

▶ Aging and Cancer
▶ Aging and Cancer: Concepts and Prospects
▶ Cancer Screening
▶ Geriatric Assessment for Older Adults with Cancer
▶ Geriatric Interventions

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Cancer Screening

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Synonyms

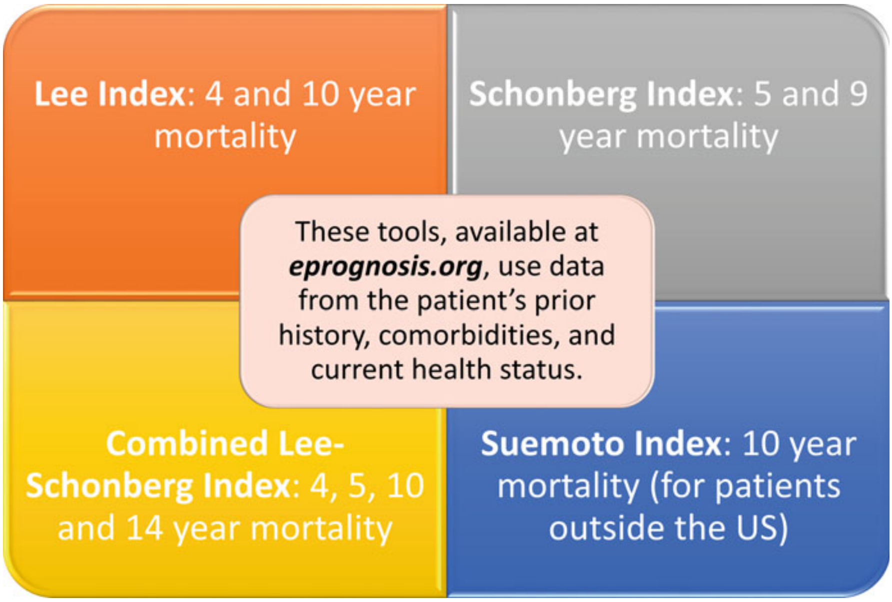
Cancer testing; Cancer detection; Cancer diagnosis; Genetic testing for cancer

Definition

Cancer screening refers to the identification of subclinical disease in a population through rapid and easy examinations and/or tests. The design and implementation of cancer screening requires the creation of mechanisms for systematic follow-up of individuals with abnormal results, a robust participation of the target population (at least 70%), and the infrastructure to offer the test and to further investigate and/or treat any abnormal findings (World Health Organization 2018; Maxim et al. 2014).

Overview

In 2018, the four most common malignancies among people aged ≥65 years worldwide were those of the lung, colon, prostate, and breast, all of which are susceptible to screening (Ferlay et al. 2018). Ideally, detecting (and treating) cancer at an early stage should lead to a reduction in mortality. However, most randomized controlled trials (RCT) of screening strategies have included mostly younger individuals, and the benefit of these



Cancer Screening, Fig. 1 Selected life expectancy estimation tools

interventions in older adults is not completely known (Kotwal and Schonberg 2017). Moreover, screening may derive in short- or long-term harm to patients.

Since some older adults may not live long enough to achieve the potential benefits of screening, predicted life expectancy should be incorporated in screening decisions. Unfortunately, up to 55% of patients with limited life expectancy received inappropriate cancer screening in the USA between 2000 and 2010 (Royce et al. 2014). A practical way of estimating life expectancy is the use of online calculators (Fig. 1). Calculating 5- and 10-year life expectancy is useful when considering screening, due to the lag time to benefit of interventions (Lee et al. 2013).

Key Research Findings

Lung Cancer

Lung cancer is the most common cancer and is a leading cause of cancer-related mortality among older adults globally, with over one million deaths per year in people aged ≥65 years (Ferlay et al. 2018). Although initial trials of screening with chest x-rays failed to decrease lung cancer-related mortality, the advent of low-dose computed tomography (LDCT) led to profound changes in lung cancer screening guidelines (Kotwal and Schonberg 2017). The US National Lung Screening Trial (NLST) demonstrated that, among patients who were at high risk for lung cancer, such as current smokers aged 55–74 years with a history of cigarette smoking of ≥30 pack-years or former smokers quitting within the previous 15 years, screening with annual LDCT reduced the rate of death from any cause by 6.7%, with a 20% reduction in lung cancer mortality (NLST 2011). These findings were mimicked by the European NELSON trial, in which screening smokers aged 50–75 years with LDCT reduced lung cancer mortality by 26% (De Koning et al. 2018).

Upper age limits for screening differ according to guidelines (Table 1). While some recommend continuing to screen until age 80 (Kotwal and Schonberg 2017), others suggest that stopping at age 77 would be more appropriate, since this better reflects the oldest age of participants in NLST at the end of the screening period (Mazzone et al. 2018). Regardless of age, the

Cancer Screening, Table 1 Selected international recommendations for cancer screening

	Breast cancer		Cervical cancer	Colorectal cancer		Lung cancer		Prostate cancer	
	Age-specific recommendation	Suggested method	Age-specific recommendation	Age-specific recommendation	Suggested method	Age-specific recommendation	Suggested method	Age-specific recommendation	Suggested method
NHS (UK)	Screening for women 50–71, extending to age 73 is being studied. Women over 71 can choose to continue screening	Mammography every 3 years	Women ≥65 years should not be tested for cervical cancer unless they have a recent abnormal test	Patients aged 65 to 74 regularly screened. Patients aged ≥75 may obtain a home test kit	FOBT every 2 years	The United Kingdom does not currently have a national screening program for lung cancer		The United Kingdom does not currently have a national screening program for prostate cancer	
INCA (France)	Screening for women aged 50 to 74	Mammography every 2 years	Screening recommended up to age 65	Regular screening until age 74. Screening stopped at age 75	FOBT every 2 years	France does not currently have a national screening program for lung cancer		France does not currently have a national screening program for prostate cancer	
USPSTF (USA)	Screening women aged 50–74 recommended Current evidence is insufficient for women ≥75	Mammography every 2 years	Screening should be ceased in women ≥65 years who have had adequate prior screening and are not otherwise at high risk	Continue regular screening until age 75. Individualize decisions in adults aged 76–85 years depending on health status and comorbidity	FOBT **or** endoscopic methods	Screening until age 80 if 30 pack-year smoking history and current smoker or quit within the past 15 years. Discontinue in case of health problems limiting life expectancy	Yearly LDCT	Individual decision between ages 55–69. Do not screen adults aged ≥70	PSA-based screening, no interval specified

(continued)

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Cancer Screening, Table 1 (continued)

	Breast cancer		Cervical cancer	Colorectal cancer		Lung cancer		Prostate cancer	
	Age-specific recommendation	Suggested method	Age-specific recommendation	Age-specific recommendation	Suggested method	Age-specific recommendation	Suggested method	Age-specific recommendation	Suggested method
ACS (USA)	Screen women aged ≥ 55. Continue as long as a woman is in good health and is expected to live 10 more years or longer	Mammography every 1–2 years	Women ≥ 65 years who have had regular cervical cancer testing in the past 10 years with normal results should not be tested for cervical cancer	Regular screening until age 75. Discuss risks and benefits between age 76 and 85. Stop screening at age 85	FOBT every 1 to 3 years **or** endoscopic methods	Screening until age 74 if fairly good health and currently smoking (at least 30 pack-year) or quit smoking in the past 15 years	Yearly LDCT	Informed decision beginning at age 50 in men with at least a 10-year life expectancy. No recommendation on when to stop	PSA every 1–2 years

Abbreviations: *NHS* National Health Service, *INCA Institut National du Cancer*, *USPSTF* United States Preventive Services Task Force, *ACS* American Cancer Society, *FOBT* Fecal occult blood test, *LDCT* low-dose computed tomography. (Data obtained online from: NHS Screening, (https://www.nhs.uk/conditions/nhs-screening/); INCA *Dépistage et detection précoce*, (https://www.e-cancer.fr/Professionnels-de-sante/Depistage-et-detection-precoce); USPSTF Published Recommendations, (https://www.uspreventiveservicestaskforce.org/BrowseRec/Index); and ACS Guidelines for the Early Detection of Cancer (https://www.cancer.org/healthy/find-cancer-early/cancer-screening-guidelines/american-cancer-society-guidelines-for-the-early-detection-of-cancer.html)) patient's functional status should be taken into account before undergoing screening, and LDCT should not be performed in patients with comorbidities that adversely influence their tolerance to further evaluations or treatment, or in those with limited life expectancy (Kotwal and Schonberg 2017; Mazzone et al. 2018).

Colorectal Cancer

Colorectal cancer (CRC) is the fourth most common cancer and the third cause of cancer-related deaths among older adults worldwide (Ferlay et al. 2018). CRC screening aims to reduce its incidence and mortality by detecting precancerous adenomas, as well as through the early detection of malignant lesions. Various techniques have been proposed, including stool-based tests, endoscopic evaluations, and radiographic assessments. Both stool-based (guaiac testing and fecal immunochemical test [FIT]) and endoscopic (sigmoidoscopy and colonoscopy) tests have shown reductions in CRC-related mortality, while only endoscopic screening has shown a reduction in incidence (Lauby-Secretan et al. 2018).

Although the mortality reduction of CRC screening seems to be maintained in those aged 65–74 years, evidence of benefit is lacking among those aged ≥75 (Schonberg et al. 2015). A meta-analysis of four trials of CRC screening using flexible sigmoidoscopy found it took 9.4 years (95% CI 7.6–11.3) to observe an absolute risk reduction of one CRC-related death per 1000 screenings. Therefore, it seems appropriate to conclude that patients with an estimated life expectancy of <10 years derive limited benefit from screening (Tang et al. 2015). Additionally, the incidence of screening-related complications, such as perforation, increases with age (Schonberg et al. 2015). Current recommendations for CRC screening suggest taking into account both age and life expectancy when discussing the benefits and risks of both stool-based and/or endoscopic techniques (Table 1).

Although a personalized approach aimed at avoiding low-value CRC screening has been suggested, many older adults refuse screening cessation and are skeptical about physicians' abilities to predict CRC risk and life expectancy (Piper et al. 2018) A useful tool to inform discussions is the *ePrognosis* Colorectal Screening Survey (http://cancerscreening.eprognosis.org/screening/) which provides tailored screening recommendations, highlighting benefits and risks.

Prostate Cancer

Prostate-specific antigen (PSA) was introduced as a screening test for prostate cancer (PC) in the 1990s. PC screening is controversial, since none of the screening trials have shown benefits in all-cause mortality. These studies included men aged up to 74 years, with about 13% aged >70, and only one trial reported a benefit in PC-specific mortality (one death averted per 781 men screened) after 13 years of follow-up (Schröder et al. 2014).

In the PLCO trial, annual screening led to an increase in PC incidence, particularly of Gleason 2–6 tumors, for which the benefit of treatment is questionable (Pinsky et al. 2018). In the PIVOT trial of radical prostatectomy vs. observation, no reduction in all-cause or PC-specific mortality was seen over a 12-year period, with subgroup analyses showing no benefit of treatment in low-risk tumors (Wilt et al. 2012). This information supports utilizing life expectancy to determine screening, since patients with limited life expectancy most likely would not derive benefits from active treatment.

Patients should be informed about potential harms of screening arising from diagnostic biopsies (bleeding, infection, hospital admission) and from subsequent treatment (erectile dysfunction, urinary incontinence, dysuria, diarrhea, rectal bleeding). In light of the controversies regarding PC screening, guidelines vary between recommending shared decision-making to not recommending screening at all (Table 1).

Breast Cancer

Breast cancer (BC) incidence and mortality increase with age. Half of newly diagnosed women with BC are ≥60 years old, and a fifth are ≥70 (Ferlay et al. 2018). Screening mammography aims at reducing BC mortality by detecting small, node-negative tumors. A meta-analysis including 11 RCTs suggested that screening mammography leads to a 20% reduction in BC-related deaths. However, those studies included few women aged ≥68 years, and information regarding the benefit of screening in this population is limited (Independent UK Panel 2012). Two RCTs of screening mammography including women up to 69 (Swedish Malmo trial) and 74 years (Swedish Two-County trial) concluded that screening might be effective at least until age 69 (Harris and Leininger 1995). Data from RCTs and observational studies shows a risk reduction in BC-related deaths from 31% to 25% among women aged 60–69 years. On the other hand, the number needed to screen to prevent one additional BC death or advanced BC among women aged ≥74 years is considered high, and thus this age group is not included in most BC screening guidelines (Nelson et al. 2016) (Table 1).

When recommending BC screening, healthcare workers need to be aware that, among older women with limited life expectancy, the benefit of screening mammography may decrease, while the risk of harms may increase. One such harm is overdiagnosis, or the detection of tumors that would have not carried a risk of death if left undetected, which has been calculated from 11% to 19% (Independent UK Panel 2012). Additionally, screening might lead to false-positive recalls and biopsies, which increase costs, cause emotional distress, and negatively impact the quality of life of older women (Lee et al. 2018; Euhus et al. 2019). Therefore, screening strategies should balance benefits and harms, taking into account each patient's individual preferences.

Cervical Cancer

Cervical cancer is a late occurring consequence of infection with high-risk types of human papilloma virus (HPV). About 50% of new cases are diagnosed in women who never had a screening test, while >80% of cervical cancer-associated mortality occurs in the developing world. In high-income countries, the age-specific incidence of cervical cancer shows a bipolar pattern, with the highest rates found between ages 45 and 65. Although this pattern is likely an artifact, older adults account for a considerable proportion of patients with cervical cancer, whose diagnosis is often delayed due to the heterogeneity of their characteristics (Sharma et al. 2012).

Organized screening with cervical cytology decreases the risk of invasive cervical cancer and cervical cancer-associated mortality, and RCTs suggest that HPV-based screening may provide even better outcomes through improved detection of premalignant disease (Melnikow et al. 2018). However, screening is linked to increased false-positive results leading to unnecessary diagnostic and treatment procedures. Other associated harms include discomfort, psychosocial consequences, and financial burden related to further procedures (Melnikow et al. 2018). For older adults, guidelines recommend stopping testing after age 65, as long as adequate prior screening took place (Table 1).

Although most cervical cancer screening strategies generate extra costs, HPV testing every 5–10 years seems cost-saving, as well as the most efficient strategy, generating better survival at lower cost (Barré et al. 2017) However, current cervical cancer screening practices are frequently inefficient due to variable screening rates and over- and undertreatment among women with abnormal results (Kim et al. 2015).

Future Directions of Research

One of the highest priorities for research in cancer screening among older adults is the improvement of shared decision-making for screening cessation, as well as the development of age-tailored screening strategies aimed at decreasing overdiagnosis. As a general rule, screening should be stopped when its harms outweigh its benefits, taking into account not only chronological age but also overall health status and comorbidity. Simulations have found that, for persons with no, mild, moderate, and severe comorbid conditions, stopping breast, colorectal, and prostate cancer screening at ages 76, 74, 72 and 66 years, respectively, resulted in a risk-benefit relationship similar to average-health persons (Lansdorp-Vogelaar et al. 2014). Stopping cancer screening might be a difficult personal choice. However, older adults may be more likely to stop screening when they have a trusting relationship with their physician. Additionally, although patients support using their age and health status to individualize screening choices, they may not completely understand or accept the utilization of predicted life expectancy as a factor to stop screening (Schoenborn et al. 2017). For some patients, the use of visual decision aids before or during screening discussions may be adequate, and decision aids have been found to decrease PSA screening by 12% (Stacey et al. 2017).

A survey conducted among patients and caregivers by the Detecting Cancer Early Priority Setting Partnership of the James Lind Alliance identified the top ten research priority questions for cancer screening (Baldrick et al. 2019). These included the design of blood tests to identify multiple cancers, the use of genetic testing to identify at-risk populations, the use of big data to identify patients who might be experiencing early symptoms of cancer, and the creation of integrated screening systems across healthcare sectors and professionals (Baldrick et al. 2019). Importantly, none of the identified priorities focused on the strategies to limit screening in populations with limited life expectancy and/or comorbidities, on the study of the benefit of cancer screening in older populations, or on avoiding the risk of overdiagnosis.

Another potentially attractive strategy for improving the yield of screening strategies and reducing overdiagnosis is the utilization of artificial intelligence (AI). A recent study showed that an AI system outperformed human experts for the detection of malignant mammographic abnormalities, with a significant reduction in both false-positive and false-negative findings (McKinney et al. 2020). Although these findings are provocative, it is important to highlight that, before novel strategies are adopted, these should be tested in RCT powered to show either a cancer-specific or overall survival benefit (Welch and Black 1997).

Summary

Discussions regarding the appropriateness of screening among older adults will increase as the population ages. Using life expectancy information and shared decision-making tools to supplement current guidelines may help in selecting those patients most likely to benefit, while protecting others from harm and overdiagnosis.

Cross-References

▶ Aging and Cancer
▶ Aging and Cancer: Concepts and Prospects
▶ Cancer Diagnosis
▶ Epidemiology, Aging, and Cancer
▶ Prehabilitation in older adults with cancer
▶ Rehabilitation in older adults with cancer
▶ Tumors: Breast
▶ Tumors: Colorectal
▶ Tumors: Gastrointestinal Cancers
▶ Tumors: Gynecology
▶ Tumors: Non-small Cell Lung Cancer
▶ Tumors: Urologic Cancer

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Cancer Testing

► Cancer Screening

Cancer Trial Design

► Clinical Trial Design for Older Cancer Patients

Cancer-Related Cognitive Impairment

► Cognitive Disorders in Older Patients with Cancer

Candidate-Gene Studies

► Genetic Control of Aging

Carbon Footprint

► Gray Consumption

Cardiac Decompensation

► Heart Failure

Cardiac Failure

► Heart Failure

Cardiac Insufficiency

► Heart Failure

Cardiodilatin

► Atrial Natriuretic Peptide

Cardiogeriatrics

► Vascular Diseases of Ageing

Cardiovascular Diseases

► Hypertensive Cardiovascular Diseases

Cardiovascular Diseases of Ageing

► Vascular Diseases of Ageing

Cardiovascular Diseases of Old Age

► Vascular Diseases of Ageing

Cardiovascular Reactivity

► Cardiovascular Response

Cardiovascular Response

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Synonyms

Cardiovascular reactivity

Definition

The cardiovascular response is one of the behaviors that influence the cardiovascular function when the components of cardiovascular system interact to adjust to a variety of stimuli, which tend to disturb normal homeostasis in individuals.

Overview

The cardiovascular system consists of the heart, the blood vessels, and the lymphatics.

The heart is composed of two pumps in series; between these pumps is the pulmonary circulation which oxygenates the blood. Generally, several key variables and indexes were used to assess or determine cardiovascular response, such as arterial blood pressure, cardiac output, total peripheral resistance, heart rate, and so on (Yuenyongchaiwat 2017). Cardiac output, usually expressed in liters per minute, is the product of the stroke volume (amount of blood ejected per contraction) and the heart rate. The heart rate and the contractile properties of the heart are neurogenically controlled by both vagal and sympathetic influences (Nobrega et al. 2014).

Several mechanisms are involved in cardiovascular response to stimuli that threaten the brain and heart and other vital organs' oxygen supply. One is the autonomic nervous system (Mitchell 2017), comprised of sympathetic and parasympathetic divisions which supply innervation of glands, heart, and blood vessels; another one is humoral stress hormone system that originates in the kidney (Frank et al. 2003); central nervous system (CNS) is more speculative than that of the peripheral nervous system in cardiovascular response, due to technical issues (Nobrega et al. 2014). The best-understood function of the CNS is the neuroendocrine system regulated by the hypothalamic-pituitary axis.

The cardiovascular responses to stimuli include physical stress, mental stress, thermal pain, emotional stimuli, cutaneous and visceral stimuli, auditory stimuli, and age. Later, several modifiers of cardiovascular response are discussed including age, sex, diet, training, and drugs (β-receptor blocker, remifentanil). Finally, cardiovascular response to aging is further discussed as cardiovascular diseases are one of the most important issues in elderly population (Williamson et al. 2016; Menotti et al. 2019).

Key Research Findings

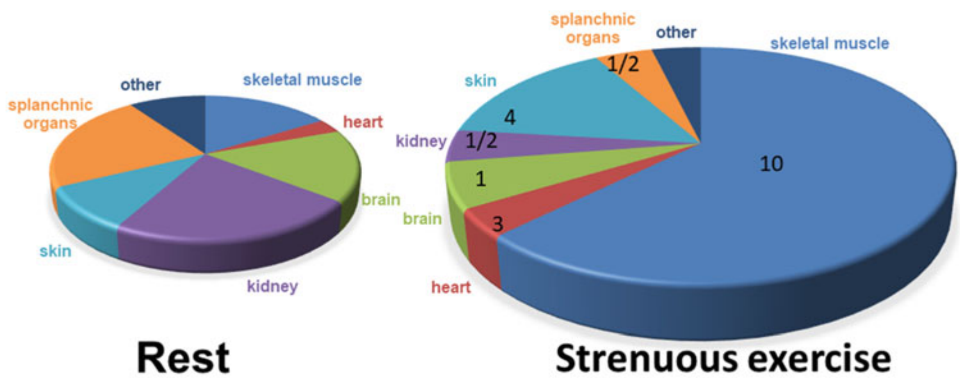
Physical Stress

The primary goal of cardiovascular response to physical stress is to provide adequate tissue perfusion throughout the body and guarantee enough blood flow to the important tissues, such as the brain and heart (Nobrega et al. 2014). Here arterial baroreceptor reflex and renal fluid balance mechanisms are always involved in the response (Takahashi and Naruse 2016). The cardiovascular response is formed in the primary disturbance and compensatory responses that are triggered by the primary disturbances.

The respiratory activity during the stimulation of physical stress can have major effects on venous return and cardiac output; the periodic changes of intrathoracic pressure in a respiratory cycle lead to venous return, increased inspiration, and decreased expiration (Javorka et al. 2018). Because of these cyclic changes in intrathoracic pressure, normal breathing is associated with transient changes in heart rate, cardiac output, and arterial pressure. This is also referred to as the respiratory pump during exercise. An example of the response to respiratory activity is the Valsalva maneuver (Sabatier et al. 2012; Pstras et al. 2017), which is a forced expiration against a closed glottis usually performed by individuals. Another key effect of the physical stress is gravity, as the pressures and blood volume distribution change in different body positions; here the skeletal muscle contraction, known as skeletal pump, plays an important role in the adaption of stress (Gocentas et al. 2005). In pathological situations, the response is more complicated and difficult to determine.

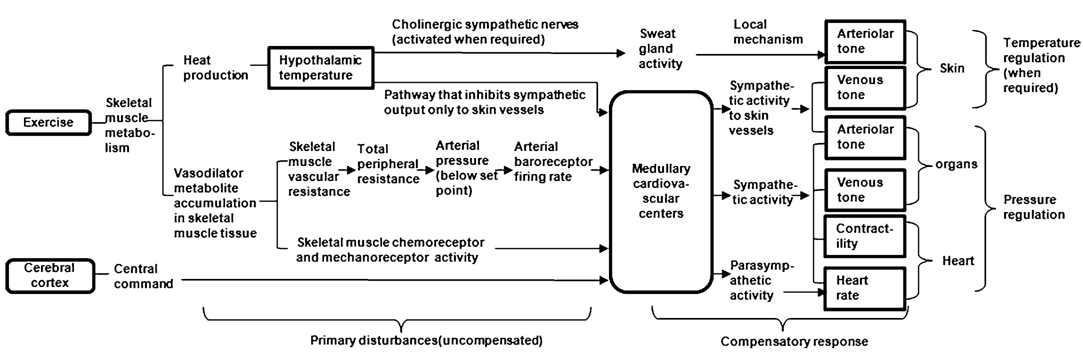
Cardiovascular response to acute exercise depends on several factors including the type of exercise (Navare and Thompson 2003), the intensity, duration of the exercise, the age of the individual, and the level of "fitness" of the individual (Piepoli 2000). The example is typical of cardiovascular alterations that might occur in a normal, untrained, middle-aged adult doing a dynamic-type exercise, shown in Fig. 1. The main mechanisms of the response to physical stress are shown in Fig. 2 (the respiratory and skeletal pumps that participate in the cardiovascular response to dynamic exercise are not shown).

As for chronic exercise, physical training or "conditioning" produces substantial beneficial effects on the cardiovascular system (Lavie et al. 2015). Similarly, the response depends on the type of exercise, the intensity, duration of the training period, the age of the individual, and his or her original level of fitness on the cardiovascular system. Cardiovascular alterations seen at rest associated with conditioning may include decreases in heart rate, increases in cardiac stroke volume, and decreases in arterial blood pressure. The chronic exercise can lead to significant increase in circulating blood volume, eccentric cardiac



	Cardiac output	Heart rate	Ejection fraction	Arterial pressure	Central venous pressure
Rest	6L/min	70 beats/min	60%	120/80mmHg	2mmHg
Strenuous exercise	18L/min	160 beats/min	80%	150/80mmHg	2mmHg

Cardiovascular Response, Fig. 1 Changes in cardiovascular variables with strenuous exercise. (Modified from Cardiovascular Physiology 9th edition, 2018, David E. Mohrman and Lois Jane Heller)



Cardiovascular Response, Fig. 2 Cardiovascular mechanisms involved during exercise. (Modified from Cardiovascular Physiology 9th edition, 2018, David E. Mohrman and Lois Jane Heller) hypertrophy. It is clear that exercise and physical conditioning can significantly reduce the incidence and mortality of cardiovascular disease (Liu et al. 2019).

Mental Stress

A study claimed the increased cardiovascular response to mental stress in labile hypertension and also in some normotensive subjects with a genetic risk for hypertension (Falkner et al. 1979). A meta-analysis including a total of 175 stress responsivity and cardiovascular risk status-related associations showed that greater cardiovascular responses to laboratory mental stress were associated with poor subsequent cardiovascular risk status (Chida and Steptoe 2010). The overall meta-analyses showed that a greater reactivity to and poor recovery from stress were associated longitudinally with poor cardiovascular status. Notably, incident hypertension and increased carotid intima-media thickness were more consistently predicted by greater stress reactivity and poor stress recovery, respectively, whereas both factors were associated with higher future systolic and diastolic blood pressures. This meta-analysis suggests that a greater response to acute mental stress has an adverse effect on future cardiovascular risk status (Chida and Steptoe 2010). Sub-analyses showed that associations between the greater stress reactivity and future cardiovascular risk status seemed to be more pronounced in men. The most consistent cardiovascular outcomes related to greater stress reactivity were incident hypertension and higher systolic and diastolic blood pressure (BP). Systolic and diastolic blood pressure reactivity are the cardiovascular response predictors of poor cardiovascular outcomes.

Unconscious Stress

Stress-related cognitive processes may occur outside of awareness, here referred to as unconscious stress, and affect one's physiological state (van der Ploeg et al. 2017). Evidence supporting this idea would provide necessary clarification of the relationship between psychological stress and cardiovascular health problems. The findings indicate that cardiovascular activity changed according to the hypothesized pattern: a higher mean arterial pressure and total peripheral resistance and a lower heart rate variability in the threat condition compared with the neutral condition were found with practically meaningful effect sizes. Changes in cardiovascular activity were not moderated by trait worry or resting heart rate variability (van der Ploeg et al. 2017).

Thermal Pain

Thermal pain, including both heat and cold stimuli, also triggers cardiovascular response such as increased heart rate and blood pressure. Research showed that heat, as well as cold, produced a stable elevation of BP. However, BP was higher with a cold stimulus than in the presence of heat; heart rate was also increased during thermal pain, both heat and cold, but the two tests differed with respect to the time course of responses. It also pointed out that individual sensitivity and adaptability to tonic thermal pain is related to the intensity of initial pain rating and the latency to peak pain but not to cardiovascular responses (Devoize et al. 2016). The cardiovascular response could be less of sensitivity to cold stimuli in patients with hypnotic-focused analgesia (Casiglia et al. 2007).

Emotional Stimuli

In daily life, emotional stimuli can be roughly divided into positive and negative ones. It is possible that positive and negative emotions could occur at the same time in stressful situations, and, in fact, this is what happens. It has been believed that the sensitivity of the behavioral inhibition system (BIS) is the predictor of an individual's negative emotional stresses in stressful situations, regardless of the nature of stressors. The results consider the activity of the behavioral inhibition system to be associated with heart diseases and believe this to be due to the creation of negative emotions and increased activity of the sympathetic system (Brenner et al. 2005; De Gucht 2002; Gray 2010). One recent study showed that BIS patients achieved higher scores in diastolic blood pressure and heart rate in comparison with behavioral activation system patients (BAS) after presenting stressful stimuli. Also, BAS patients achieved lower scores in systolic blood pressure and heart rate in comparison with BIS patients after presenting pleasant stimuli (Taban Sadeghi et al. 2013).

Cutaneous and Visceral Stimuli

A recent study showed that a high thoracic or cervical spinal cord injury interrupts supraspinal vasomotor pathways and results in disordered hemodynamics (Partida et al. 2016). As a result of the reduced sympathetic activity, patients with spinal cord injury may experience hypotension, cardiac dysrhythmias, and hypothermia post-injury (Partida et al. 2016). In some situation like irritable bowel syndrome, cardiovascular autonomic function can also be impaired (Waring et al. 2004).

Auditory Stimuli

The evoked cardiac response and event-related potentials to auditory stimuli may result from intensity and cognitive load effects (Lawrence and Barry 2009). As for young boys with fragile X syndrome (FXS), older boys with FXS display increased cardiac reactivity to auditory input than younger boys with FXS that distinguishes them from typically developing controls (Roberts et al. 2013).

Age

Age is demonstrated to be the most important factor in cardiovascular health (North and Sinclair 2012). The prevalence of all cardiovascular diseases (CVD) such as hypertension, coronary heart disease (CHD), heart failure (HF), and stroke is increased with the age over 65 years especially 80 years (Heidenreich et al. 2011). According to the prediction, the costs of CHD and HF will increase over 200% by 2030 (Heidenreich et al. 2011). A better understanding of clinical aspects of age-associated cardiovascular responses and their mechanisms helps us to get medical care timely.

The elevated systolic blood pressure and the broadening pulse pressure are the most obvious cardiovascular responses in older persons. Increased arterial stiffness is related to systolic hypertension. In the aortic wall, the fracture and calcification of elastic fibers, deposition of collagen fibers, amyloid deposition, and migration/proliferation of vascular smooth muscle cells (VSMC) promote the progression of aortic sclerosis. During aging, the cellular environment becomes more pro-inflammatory. Some cytokines and elastases such as transforming growth factor (TGF-β), matrix metalloproteinases (MMP), and cysteine proteinases help to the accumulation of collagen and depletion of elastin (Zieman et al. 2005). These reduce the central arterial distensibility and elevate the pulse wave velocity, and then the systolic pressure rises. The diastolic pressure of older people is usually reduced, and the pulse pressure is increased with aging. Increased pulse pressure reflects the depression of vessel adaptability and can be an independent risk factor for stroke, MI, and HF (Franklin et al. 1999).

Another feature of aging-associated cardiovascular response is the development of myocardial ischemia. The decrease of diastolic blood pressure reduces the perfusion of the coronary artery during diastolic phase. Elevated systolic blood pressure increases cardiac afterload, which increases oxygen demand. As the cardiac afterload increases, the myocardium gradually thickens, and oxygen consumption is further increased. The disrupted oxygen balance promotes the occurrence and development of myocardial ischemia. What's more, the incidence of coronary atherosclerosis gradually increases with aging, which limits the blood supply to the heart. Chronic hypertension affects the myocardial microvascular system in addition to the remodeling of the aorta. Under chronic hypertension, myocardial arterioles thicken, and the vasomotor function is damaged, which further impedes left ventricular perfusion.

Drug therapy is proved to be effective in reducing stroke and total mortality (Staessen et al. 2000). Recent studies show the effectiveness of low-sodium diet in controlling systolic hypertension in older persons (Cook et al. 2016). Diastolic pressure less than 70 mm Hg was related to the increased risk of cardiovascular outcomes in patients with hypertension and coronary artery disease. Routine antihypertension should be taken with caution (Vidal-Petiot et al. 2016). However, the lower-blood pressure treatments has been confirmed to be relatively safe and effective in older persons with diastolic blood pressure ≥70 mmHg (Beckett et al. 2008; Williamson et al. 2016). Clinicians should make individualized treatments according to the conditions of coronary artery heart disease, side effects of drug, and other factors (Fuster 2016).

Future Directions of Research

Future research may focus more on the cardiovascular response to lipid-lowering agents like statins. Lipoprotein(a) might be a useful biomarker that has a causal link to atherosclerosis and associated with cholesterol-lowering response and cardiovascular risk (Akyea et al. 2019; Willeit et al. 2018). Taking account of the LDL-cholesterol response to statins would greatly improve individual management, cost-effectiveness, and the population impact of statins (Soran et al. 2014). A clinical trial pointed out that ApoB and ApoB:ApoA-I ratios were only marginally better than LDLC:HDLC in predicting cardiovascular risk in type 2 diabetes (Charlton-Menys et al. 2009). More effective biomarkers in the future related to statins therapy should be expected.

The impact of age is also a hot topic because of the aging population. Advanced age has been found to be associated with greater rise in blood pressure pulsatility and diminished cardiac reserve during isometric handgrip exercise (Cauwenberghs et al. 2020). Perhaps the poor response due to the impaired vascular function should be paid more attention to in aged people (Thanassoulis et al. 2012).

Mental stress may also be more focused on as it increases in modern society. Augmented systolic blood pressure responses to mental arithmetic were associated with increased future systolic blood pressure, and cardiovascular reactivity remains a prediction of future blood pressure and may play a role in the development of hypertension and cardiovascular disease (Yuenyongchaiwat 2017). Future studies should pay more attention to patients with diseases such as mild cognitive impairment as it affects the cardiovascular response to mental stress (Henley et al. 2018).

Finally, sex difference may be another attractive topic as most of the researches focus on men. Exercise training in women with cardiovascular disease displays a different training response, even when accounting for age, height, and lean muscle mass compared with men. Improve referral, enrolment, and adherence to exercise training in women may improve the admission, adherence, and outcome of exercise-based cardiac rehabilitation (Witvrouwen et al. 2019).

Summary

The cardiovascular response can be tested and determined to all kinds of stimuli in complicated situations including physiology and pathophysiology. Many factors, including age, sex, and drugs, may modify the intensity of response and, therefore, influence the outcomes. Age is both a modifier of response and a key factor in the development of cardiovascular disease. Early intervention of diet and drug may be considered in future management of cardiovascular diseases.

Cross-References

▶ Atherosclerosis
▶ Cardiovascular System
▶ Cholesterol Levels
▶ Circulatory System
▶ Heart Failure
▶ Hypertension
▶ Hypertensive Cardiovascular Diseases
▶ Ischemic Attack
▶ Ischemic Heart Disease
▶ Myocardial Infarction
▶ Stroke

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Cardiovascular Stroke

► Myocardial Infarction

Cardiovascular System

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Synonyms

Blood vascular system; Circulatory system; Heart and vasculature

Definition

Anatomically, the cardiovascular system is made up of heart and blood vessels. This complex transport system ensures the maintenance of blood circulation in the human body by essentially making two loops: pulmonary circulation, through which deoxygenated blood gets oxygenated, and the systemic circulation, through which the rest of the body receives oxygenated blood.

Overview

The cardiovascular system includes all the blood vessels present throughout the body and the heart, which pumps blood to the entire body. This system transports oxygen, nutrients, and hormones to each cell of the body and removes metabolic wastes such as carbon dioxide, nitrogenous wastes, etc. This system also protects the body against foreign microbes and toxins by transporting white blood cells, antibodies, and complement proteins. It also helps in maintaining homeostasis, pH, and body temperature. In addition to blood transport, the cardiovascular system acts as an important component to other body systems such as the respiratory system, digestive system, renal, and urinary system.

Blood vessels consist of arteries, veins, and capillaries. Arteries are thick walled elastic tubes that transport oxygen-rich blood away from heart to the tissues present throughout the body. Arteries divide and re-divide into very thin walled microscopic capillaries in tissues, large enough to allow only one blood cell to pass through at a time. Nutrients and wastes can diffuse through theses extremely thin walls into or out of the cells. Capillaries rejoin to form veins which are relatively thick walled than arteries that collect and return deoxygenated blood to heart. Metabolic wastes or by-products are filtered through lungs and kidneys. Nutrients from ingested food are absorbed in small intestine and supplied to liver before their transport to other parts of the body. CO_2 is discarded, and oxygen is absorbed during circulation of blood through lungs. Metabolic heat is dissipated by blood through skin by radiation or sweat evaporation.

The heart consists of two pumps, each includes two chambers: an atrium and a ventricle. Deoxygenated blood from the body is received in right side of the heart and pumped to lungs under low pressure to get oxygenated and get rid of CO_2. Oxygenated blood is returned to the left side of the heart from where it is pumped to the entire body at relatively high pressure. A remarkable balance is achieved through sensors which detect flow changes, pressure, fluid composition, temperature, etc. (See ▶ "Circulatory System").

Aging of the cardiovascular system is the biological phenomenon which is the result of the gradual accumulation of cellular, tissue, or organ damage leading to the decline in anatomy and physiology. Aging is not the sole cause of cardiovascular disease (CVD) but it itself contributes to the manifestation of disease and designated as one of the major or primary risk factors associated with CVD. The population of the modern world is aging. More than 20% of the population is aged 65 or more in Europe and North America, and by 2030, about one fifth of the world population will be aged 65 or older. More than half deaths related to cardiovascular disease develop in people aged 65–74 years. Annually, about one third of the deaths around the world and USA are caused by heart disease and it is the most common cause of deaths in China. By 2020, cardiovascular diseases are expected to become the leading cause of mortality and disability (WHO 1997; Zhao et al. 2014).

With increasing age, several structural changes occur in the heart and blood vessels such as vascular stiffening, ventricular wall thickening, and fibrosis, resulting in diastolic dysfunction, increase in afterload, and heart failure. Decreased arterial elasticity is characterized by the loss of elastin and increased collagen. Cardiovascular calcification also contributes to the loss of elasticity leading to high blood pressure. The valves of the heart become less flexible resulting in blood turbulence. End systolic and diastolic volumes, contractility, systolic contraction, and diastolic relaxation duration changes with advanced aging of heart. Endothelial and vascular smooth muscle cells (VSMCs) show key structural and functional changes at the cellular and mitochondrial level to promote cardiovascular diseases. Various mechanisms, including endothelial dysfunction, mitochondrial, oxidative stress, chromatin remodeling, and genomic instability, are implicated in aging of cardiovascular system. The changes in vascular physiology must be differentiated from pathology, however, the changes taking place as aging consequences set the stage for diseases associated with cardiovascular system such as hypertension, heart failure, and so on.

Cardiovascular performance is capable of remaining excellent in the absence of disease throughout life. However, in normal cardiovascular aging, cardiovascular reserve is decreased due to changes in structure and function of cardiovascular system associated with age. Life-style-related risk factors such as excessive calorie consumption, compromised metabolism, smoking, and lack of exercise accelerates age-related cardiovascular changes. Therefore, with advancing age, the prevalence and incidence of CVD increase rapidly at the age of 45 in men and at 55 in women (Lloyd-Jones et al. 2010). Various genetic, environmental, and lifestyle factors are responsible to accelerate cardiovascular changes with age, which associates advanced age with prevalence of heart and brain failure. Therefore, even though aging does not cause CVD itself, however, it decreases the threshold for manifestation of CVD.

Key Research Findings

Various progressive structural and functional changes occur below the clinical threshold of disease recognition, as a part of normal aging of cardiovascular system. These changes range from changes in molecules to cells to arterial tissue, the blood, and neural factors that are responsible for modulation of molecules, cells, and tissues.

Arterial Changes

With increasing age, there is a progressive decrease in central arterial distensibility and increase in stiffness of arterial wall, resulting in increased pulse wave velocity (PWV), early return of reflection wave during systolic ejection leading to increased systolic blood pressure, decreased diastolic pressure, and increased pulse pressure. These age-associated changes are physiologic but can become pathophysiologic. Chronic increased pressure can be transmitted to brain and kidney causing injury or failure of these vital organs.

There is huge gap in the knowledge between the events taking place under microscope and the events that can be measured in vivo. Various characteristic changes occur in medial layer of arterial wall including fragmentation of elastic fibers, increased collagen deposition, calcification, migration, and proliferation of vascular smooth muscle cells (VSMCs). Complex mechanisms and factors contribute to arterial remodeling (van Varik et al. 2012). Several mechanical and humoral factors stimulate the pro-inflammatory microenvironment and low-grade inflammation to drive the age-associated structural and physiological arterial remodeling at cellular and matrix level. In aged arteries, changes in signaling system including angiotensin II (Ang II) signaling driving chronic pro-inflammatory profile to occur. Downstream signaling of Ang II and secretion from VSMCs in aged arteries is increased leading to increased VSMCs proliferation, migration, senescence, and extracellular matrix deposition. Enhanced Ang II signaling leads to disrupted endothelium, medial intima thickening, fibrosis, calcification, elastin disruption, and matrix modification, ultimately manifesting a clinical phenotype. The body responds to chronic stress by adrenergic signaling, which in turn cause increased activation of renin-angiotensin-aldosterone-endothelin signaling, a response mechanism against chronic stress executed by endothelial and VSMCs shifting their phenotype to produce of inflammatory cytokines. Ang II receptor-associated protein (AGTRAP) and Sirtuin 1 (SIRT1) are negative regulators of angiotensin signaling. Their decreased expression leads to age-associated pro-inflammation and arterial remodeling (Lakatta 2015). The extent of activation of these events leading to structural and functional changes is debatable.

Aged vessels act as fertile soil for cardiovascular disease manifestations (See ► "Vascular Diseases of Ageing"). In animal models, it has been shown that pro-inflammatory profile of diseased arterial wall was like age-associated Ang II-mediated profile (Wang et al. 2014). Moreover, as Ang II signaling and calorie restriction (CR) are associated to longevity; therefore, we can say that arterial wall changes associated with advanced age, and hypertension, atherosclerosis, and diabetes associated changes complement each other at cellular and molecular level.

Cardiac Changes

With advanced age, increased myocyte size and increased vascular impedance results in increased left ventricular wall (LV) thickness. With increase in LV wall tension, cardiac muscarinic receptors (which regulate heart rate and electrical conduction) density and function is reduced resulting in resting cardiovascular physiology decline including peak cardiac reserve function as well as peak oxygen consumption. Aging in healthy persons show some substantial changes in peak cardiac reserve capacity such as heartbeat rate acceleration and blood ejection from left ventricle are compromised. Multiple factors are responsible for decreased peak heart rate with age, including impaired sinoatrial pacemaker cell function, impaired ventricular myocyte contractility, and increased mismatch in arterial-ventricular load. All these changes interfere with contractility and ejection of blood by myocyte (Strait and Lakatta 2012).

During stress, sympathetic stimulation of cardiovascular system modulates heart rate, LV contractility, and arterial afterload that diminish with aging. Reduction in beta-adrenergic (β-adrenergic) signaling with aging links the age-associated impaired CV reserve with impaired brain-heart communication, that is associated with increased plasma levels of neurotransmitters such as epinephrine and norepinephrine in older persons (Fleg and Strait 2012).

Ventricular cells in aged heart work on the borderline of disease. Upon careful inspection of aging heart, myocyte enlargement is associated with a change in gene expression, Ca^{2+} homeostasis, regulatory protein expression, impaired response to acute stress, increased chronic stress markers, altered membrane lipid composition, increased reactive oxygen species (ROS), increased cell death, and decreased cell replacement (Sheydina et al. 2011). In aging and chronic myocardial overload rat models, similar altered cellular RNA expressions are observed (Meerson et al. 1978). Like aged arteries, renin-angiotensin (RAS) is responsible for Ang II-mediated pro-inflammatory profile in older hearts. Evidence suggests the role of RAS in cardiac hypertrophy (Piratello et al. 2010). Most of the age-associated alterations present pathophysiology of CVD. These factors can be modified by changes in lifestyle such as diet, exercise, and also through drugs such as Ang II targeting drugs.

Cellular Renewal in Cardiomyocytes and Nonmyocytes

In adult cardiomyocytes, replicative and reparative potential decreases with age and factors including telomeres, genetics, and epigenetics give insights into this decline. Proliferation of mammalian cardiomyocytes is very important in developmental stage during formation and growth of heart. This proliferative potential is lost shortly after birth, while neonatal mammalian heart retains the capacity of regeneration owing to the differences in the transcriptional and epigenetic profiles (Quaife-Ryan et al. 2017). Factors promoting cell division are downregulated and cell proliferation inhibitory factors are upregulated (Foglia and Poss 2016). Although low turnover rate of cardiomyocytes is important for cardiac structure and function, decreased cardio-myogenesis may be linked to the decline in cardiomyocytes and cardiac physiology. Viral-based introduction of telomerase reverse transcriptase (TERT) in mice cardiac muscle rescued telomere length and promoted cardiac myocyte survival but could not increase cardiomyogenesis (Oh et al. 2001). The area of cardiomyogenesis remains open for active research and debate.

Noncardiomyocyte cells including endothelial, pericytes, smooth muscle, immune, neuronal, and fibroblast cells give insights into the mechanisms involved in cardiac development and aging. Vascular cells include VSMCs, endothelial cells, and pericytes. Vascular renewal is important after cardiac injury, and vascular cells have potential to proliferate in vitro and in vivo after injury. Fibroblasts, pericytes, and mesenchymal cells form the interstitial cells population and are important in tissue homeostasis. They proliferate and secrete extracellular matrix after cardiac injury. Stiffer left ventricle in older individuals is a consequence of extracellular matrix remodeling and collagen deposition by dysfunctional fibroblasts (Trial et al. 2016).

Cardiac progenitor cells (CPCs) are population of cardiac interstitial cells which have limited reparative potential after cardiac injuries. CPCs number is maintained, and upon some pathological stimuli they migrate towards the site of injury. The isolation of this cell population, genetic engineering to enhance their repair function and transfer to animal models shows their potential benefit in cell therapy (Mohsin et al. 2012). Function of endothelial progenitor cells (EPCs) is also affected by age. The age-related decline in function is related to cell proliferation factors deprivation, oxidative stress, and senescence; however, through anti-aging strategies like exercise and serum factors, this decline can be countered (Hoetzer et al. 2007; Zhu et al. 2009). Neovascularization is impaired with aging-associated inability of vascular progenitor cells to replenish the vascular system.

Cellular Senescence in Cardiomyocytes and Nonmyocytes

Senescence is a cell cycle arrest, due to stress induced by reactive oxygen species (ROS)/inflammation induced telomere shortening, DNA damage, ploidy, and other molecular changes mediated by p53-p21 pathway (See ► "Cell Senescence"). Senescence-associated secretory phenotype (SASP) acts in a paracrine manner resulting neighboring cells' senescence or repair after damage (Demaria et al. 2014). Age-related accumulation of senescent cardiomyocytes affects cardiac function and promotes chronic inflammation leading to loss of cardiomyocytes. In a human centenarians' population study, inflammation was found as a better predictor of successful aging compared to telomere length (Arai et al. 2015). Cardiac research is directed towards antagonizing cardiomyocyte senescence to avoid the decline in cardiac structure and physiology.

Nonmyocytes such as vascular and interstitial cardiac cell senescence display SASP, inflammation, telomere shortening, and senescence markers. Aging-associated accumulation of senescent cells, calcification, inflammation, and collagen deposition results in disease manifestation of cardiovascular system (See ► "Cellular Aging/Senescence"). Senescent fibroblasts and CPCs result in poor remodeling of aged heart. Youthful characteristics can be restored by genetic reprogramming such as reprogramming of induced pluripotent stem cells (iPCs) restored youthful characteristics in aged mice and human somatic cells (Cheng et al. 2017). The therapy has its challenges; however, iPCs from aged systems can be insightful models to study aging characteristics.

Molecular and Cellular Mechanisms

Oxidative stress. In animals and humans, reactive oxygen species (ROS) produced by oxidates of NADPH (reduced nicotinamide adenine dinucleotide phosphate) and mitochondria contribute to age-associated endothelial dysfunction and arterial stiffening. Most pronounced effect of oxidative stress is impaired nitric oxide (NO) bioavailability which affects endothelial mediated vasodilation, leading to cardiovascular and cerebrovascular diseases. NO inactivation activates inflammatory pathways like NF-kB (molecular factor kappa-light-chain enhancer of activated B cells) resulting in pro-inflammatory phenotype in aged human vasculature (Donato et al. 2007). Oxidative stress-associated activation of matrix metalloproteinases (MMPs) leads to arterial stiffness and even impairs cerebral circulations with aging (Toth et al. 2015).

Mitochondrial dysfunction. There is marked increase in mitochondrial dysfunction with age and it plays regulatory role in aging process and life span (Schriner et al. 2005). mtROS (mitochondrial ROS), impaired electron transport chain (ETC), inhibition of mitochondrial biogenesis, impaired mitochondrial pathways (e.g., $p66^{Shc}$, Nrf2), and inhibition of mitochondrial enzymes negatively affect cellular energetics of arteries and capillaries. mtROS is linked to NF-kB and MMP activation in endothelial and VSMCs leading to inflammation and activation of Bcl-2 (B-cell lymphoma 2) dependent pathway resulting apoptosis (Mills et al. 2016; Rice et al. 2006; Ungvari et al. 2011a). Increased mitochondrial DNA (mtDNA) damage and decline in NAD^+ availability leads to low activity of Sirtuin enzymes which control mitochondrial metabolism and biogenesis (Mills et al. 2016). This contributes to dysfunctional mitochondria in aged vasculature.

Impaired response to molecular stress. There is a marked difference in vasculature response to molecular stress induced by ROS in aged cells compared to young cells. Young endothelial and VSMCs attenuate ROS stress by a redox sensitive transcription factor Nrf2 (nuclear factor-like 2) which regulates ROS detoxifying enzymes. Aging-related Nrf2 dysfunction may contribute to low resilience of vasculature against oxidative stress (Ungvari et al. 2011b).

Impaired proteostasis. Chaperones, the process of autophagy, and proteasomes are important components of proteostasis which manages synthesis, folding, and degradation of proteins. Age-related dysregulation of these components is related to decline in vascular health (Kaushik and Cuervo 2015).

Apoptosis. Age-related increased apoptosis of endothelial cells due to decreased NO bioavailability, upregulated TNF-α (tumor necrosis factor alpha), and mtROS contribute to cardiovascular aging phenotypes. Upregulation of programmed cell death (apoptosis, necroptosis) and their relationship to vascular disease has been shown in monkeys and mice (Asai et al. 2000; Wang et al. 2015).

Dysregulated nutrient sensing. mTOR (mammalian target of rapamycin), AMPK (AMP-activated protein kinase), and sirtuins are conserved nutrient sensing pathways. Inhibition of mTOR has been shown to increase life span and reverse age-associated vascular dysfunction in old mice models (Lesniewski et al. 2017). There is growing evidence of role of mTOR in cardiovascular and cerebrovascular dysfunction; however, definitive role of mTOR in vascular aging is yet to be established. AMPK and sirtuins are shown to be elevated in longevity enhancing interventions such as calorie restriction (CR). Sirtuins play important role in vascular cell protection. Sirtuin enzymes are NAD^+ (nicotinamide adenine dinucleotide) dependent and their levels decline with age, making them a promising target for antiaging drugs. Age-related inactivation of AMPK cause vascular dysfunction in old mice, while its reactivation showed beneficial effects (Lesniewski et al. 2012).

Genome instability. There is no clear evidence for the causal role of genome instability in normal vascular aging. In some studies, inefficient DNA damage repair (DDR) system in endothelial cells has shown impaired vascular function upon severe DNA damage. Mouse models with defective DDR systems and spindle assembly checkpoints (to promote aneuploidy) have shown endothelial and vascular dysfunction in addition to severe kidney, bone marrow, and neurological phenotypes (Durik et al. 2012; Matsumoto et al. 2007). Contribution of these pathways in normal aging is yet to be discovered.

Epigenetics. Epigenetic changes, e.g., DNA methylation and post-translational histone modifications of genes related to vascular aging is an area of great interest. Many chromatin remodeling factors and miRNAs show altered expression in aging. Long non-coding RNAs also mediate senescence regulation (Gupta et al. 2014). Studies are needed to understand the mechanisms of epigenetic changes in developing age-related cardiovascular pathologies.

Genetics. Genetics play an important role in the variance of human age. Conclusive causal relationship between genetics, human longevity, and cardiac aging has not been established yet. Mutations in genes, e.g., *LMNA* and *WRN* genes, are associated with diseases like Progeria and Werner syndrome which predispose patients to accelerated aging and CVD. Genome-wide association studies (GWAS) can be used to identify genes and pathways associated with longevity and late onset of cardiovascular disease. *APOE* and *FOXO3* have been identified as longevity associated genes. GWAS of Han Chinese centenarians identified 11 independent longevity associated loci including two novel loci, one nearest to *IL6* gene. Integrated analysis also indicated four pathways (carbohydrate metabolism, immune response, MAPK, and calcium signaling) highly associated with longevity in HAN Chinese (Zeng et al. 2016). Genetic overlap exists between longevity trait and age-related phenotypes, e.g., coronary artery disease (CAD). Genome-wide screening revealed *NEXN*, *SCML4,* and *THSD7A* genes as susceptibility genes for CAD in HAN Chinese (Li et al. 2018; Wu et al. 2013). Moreover, genetic variants of *TFP1* and *LRP6* genes are found to be associated with CAD and familial normolipidemic CAD (Guo et al. 2016; Zhao et al. 2017). It can be presumed that good genes or variants contribute to longevity, while bad genes or variants predispose an individual to disease.

Examples of Applications

Cardiovascular aging starts very early in the life and lifelong exposure to suboptimal external and internal risk factors contribute to the aging process and development of disease. Billions of dollars are spent every year on treatment of highly prevalent cardiovascular diseases like stroke, heart disease, hypertension, and so on. Cardiovascular aging is modulated at cellular level by many external factors such as air pollution, life style, exercise, and even psychological stress. Air pollution is linked to increased cardiovascular disease risk by promoting inflammation and oxidative stress leading to telomere shortening (Martens and Nawrot 2016). Calorie restriction, intermittent diurnal rhythm, and feeding with specific micro and macronutrients have beneficial effects for cardiovascular disease and accumulation of molecular damage prevention. Nondietary interventions such as physical activity, mindfulness, and CR mimetic drugs can promote cardiovascular health.

Calorie restriction (CR) is the most robust intervention to increase lifespan and delay age-associated diseases in invertebrates and vertebrates including mammals. Atherosclerosis mouse models have shown resistance to atherosclerosis upon calorie restriction even when fed on atherogenic diet (Guo et al. 2002). Rhesus monkeys on CR diet showed reduction in cardiometabolic risk factors. CR rodents have decreased intima media thickness, improved LV function, and improved heart function. Long-term CR without malnutrition in humans have beneficial effects on CVD risk factors including serum levels of cholesterol, triglycerides, glucose, blood pressure, etc. (Fontana et al. 2004; Stein et al. 2012). Molecular and cellular mechanisms underlying these effects may include inflammation prevention, improved nutrient sensing (IGF, mTOR pathways), low oxidative stress-induced DNA damage, decreased activation of sympathetic and angiotensin system, and improved autophagy and proteostasis. Delay in age-related DNA methylation was observed in mice and rhesus monkeys showing the role of epigenetic modulation by CR (Maegawa et al. 2017). Similarly, intermittent fasting and meal timings also effect cardiovascular metabolic health and can extend mice lifespan by 30% (Mattson et al. 2017). Mutation in mice circadian clock gene caused obesity (Liu et al. 2014). Moreover, *Drosophila* circadian clock genes were found to be associated with beneficial effects of CR (Gill et al. 2015). Effects of fasting include improved insulin sensitivity, decreased inflammation and oxidative stress, and improved mitochondrial function. Cardiometabolic health in humans is affected by eating patterns by modulating several energy sensing pathways, e.g., AMPK, AKT1-mTOR and, CREB (cAMP response element-binding protein) which control metabolism and circadian clock targets (Fontana 2018).

Exercise confers profound effects on cardiovascular system at cellular and systemic levels and is positively associated with improved cardiac health and leukocyte telomere length (LTL), a molecular marker of vascular aging (Edwards and Loprinzi 2017). Acute exercise activates MAPK signaling and telomere protective genes to protect telomeres. In mice and humans, protective effects of exercise and running are associated with increased telomerase activity, decreased telomere erosion, decreased expression of senescence markers, and activated IGF-I signaling (Ludlow et al. 2017). Experimental data have shown positive correlation of exercise with improved cardiovascular and metabolic health including mitochondrial biogenesis, calorie consumption, improved insulin sensitivity, glucose tolerance, and reduced systolic blood pressure. The anti-inflammatory and antioxidant actions of exercise protect against endothelial dysfunction and arterial stiffening. Collectively, beneficial effects of exercise work at molecular and cellular level to ensure youthful phenotype and delay aging (Gude et al. 2018). Similarly, social and psychological environmental stress also increases the risk of cardiovascular disease. Exercises such as yoga, meditation, and repetitive prayer can help relieve the mental stress and alleviate aging and cardiac diseases. Relaxation exercises can affect processes like telomere maintenance, metabolism, and expression of inflammation stress-associated genes (Krishna et al. 2015). Sleep deprivation, psychological stress, and disruption of circadian rhythm molecular clock in murine models lead to vascular senescence and cardiomyopathy (Alibhai et al. 2017). Therefore, everyday behavior, lifestyle, and environment can influence cardiovascular health at organismal and cellular level.

Many available pharmacological interventions (aspirin, angiotensin converting enzyme inhibitors, fish oil, statins, and antidiabetic drugs) target CVDs by prevention of cardiovascular risk factors (hypertension, circulatory metabolic biomarkers). CR has shown to affect lifespan reproducibly leading to development of calorie restriction mimetics and other pharmacological interventions. Conventionally, these interventions target molecular and cellular pathways responsible for development of aging or diseased phenotypes. Experimental data shows the potential of some traditional cardiovascular drugs to extend lifespan in addition to counter disease. Previously, aspirin showed the potential to increase median lifespan in male mice (Strong et al. 2008). Rapamycin, a drug which target nutrient sensing pathway mTOR, extended mean and maximal lifespan of mice of both genders (Miller et al. 2014). Acarbose, which is an antidiabetic drug, has shown to increase median and maximum lifespan in both genders of mice by increasing mtTORC2 (mTOR complex 2) activity in liver (Harrison et al. 2014). Metaformin, another drug, which targets AMPK and mTOR activities, could not extend life span, but in combination with rapamycin strongly extended lifespan. Nordihydroguairetic acid, 17 α-Oestradiol, and protandim (a plant derived nutraceutical) also extended median lifespan in only male mice. Resveratrol, a Sirt1 and AMPK activator, showed positive effects in lifespan extension of yeasts and worms but its results are controversial in flies, mice, and humans (Alfaras et al. 2016; Nadon et al. 2016). Tissue culture and animal studies results cannot be translated entirely in humans. Although a significant progress has been achieved in understanding age-related changes in cardiovascular system, research efforts should be directed towards devising agents which can reduce the age-related implications before appearance of disease.

Future Directions of Research

Aging associated changes in the arteries and heart make aging an independent risk factor for cardiovascular diseases. These changes can be modified by lifestyle-related factors like exercise and dietary modification. Thus, understanding the cause of these changes and preventing these causes can be targeted for novel interventions to prevent or delay aged phenotype. In addition, limitation in translating the results of preclinical trials should also be acknowledged. Our current understanding of cardiovascular aging includes various cellular and molecular processes causing inflammation, telomere shortening, metabolic imbalance, impaired autophagy, mitochondrial dysfunction, and oxidative stress. Several animal models have been developed to study aging, CVDs, and health span. Telomere mouse models support the role of telomere maintenance in cardiovascular aging. Similarly, mouse models with gene mutations in *LMNA* gene provide insights into accelerated aging as in progeria syndrome. Some antiaging drugs are also used in mouse models to ablate senescent cells. These models are critical tools for understanding the mechanisms of aging and CVDs; therefore, further refinement and studies will be key for translational applications and progress towards clinical studies. Ongoing research is directed towards alleviating aging effects on cardiovascular aging based on targeting abovementioned processes, since dietary supplements, for example, sirtuin activators, have shown positive results in mice. Similarly, pharmacological interventions, including use of inhibitors or activators of metabolic or epigenetic factors, are an area of huge interest to mitigate age-related effects on cardiovascular system. Therefore, these lifestyle and pharmacological interventions might be used in the near future to prevent cardiovascular dysfunction and diseases. Moreover, advancement in molecular technologies, e.g., gene editing tools (CRISPR-Cas9) and iPSCs, promise their use in treating aging. However, before clinical application, unintended effects of these strategies must be addressed.

Summary

The world is aging. Age-related cardiovascular diseases are the leading cause of mortality worldwide. The cardiovascular system performs a vital role in the circulation of nutrients, removing wastes, and maintaining homeostasis in the body. Age-related changes in the heart and vessels, including arterial stiffness and decline in cardiac reserve, which promote cardiovascular dysfunction in the later age, are unavoidable. Thus, aged heart and arteries are vulnerable sites for the development of disease. Age may not cause cardiovascular disease directly but prognosis of CVDs worsens with age. Several external factors (environment, life style, mental health) and internal factors (telomere attrition, genetics, epigenetics, metabolism, apoptosis, autophagy, and senescence) contribute to the aging related changes in the heart and vessels. Changes in daily life habits (exercise, mindfulness, and avoid smoking) and dietary interventions (CR, intermittent fasting) are powerful interventions to slow or avoid buildup of molecular damage. Conventional strategies target cardiovascular risk factors. Instead of targeting single disease, targeting aging process has the potential to treat vascular and age-related diseases.

Cross-References

▶ Cardiovascular Diseases
▶ Cell Senescence
▶ Cellular Aging
▶ Circulatory System
▶ Vascular Diseases of Ageing

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Care Coordination

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Synonyms

Care management; Case management; Geriatric care coordination; Patient navigation; Population health

Definition

A systematic review of care coordination programs by the Agency for Healthcare Research and Quality synthesized over 40 definitions to define care coordination as: "*the deliberate organization of patient care activities between two or more participants (including the patient) involved in a patient's care to facilitate the appropriate delivery of health care services*" (McDonald et al. 2014, p. 6). The goal of geriatric care coordination is to help older adults and their families understand and navigate complex systems; facilitate interdisciplinary collaboration; create meaningful, patient-centered care plans; and monitor progress towards health goals.

Overview

Need

The aging U.S. population has an increasing number of chronic health conditions such as diabetes, hypertension, and heart disease (Sambamoorthi et al. 2016). Older adults also experience a variety of psychosocial barriers to health and wellness. While psychosocial needs and chronic health conditions often co-occur and can be mutually reinforcing, their care is fragmented across many healthcare and community-based providers. Care coordination addresses these challenges by connecting service delivery and sharing knowledge across disciplines and care settings.

Settings

Care coordination activities may be carried out from a variety of settings where older adults are already receiving services or care. Most programs are based in ambulatory healthcare settings, with staff operating from outpatient clinics or from a hub serving several clinics or a medical group. However, inpatient- and emergency department-based programs exist, while the growth of managed care has led many plans – including Medicare Advantage – to provide limited care coordination support to their patients. Finally, as awareness of social determinants of health grows, community-based organizations that already serve older adults are beginning to offer care coordination programs (Shier et al. 2013). These organizations might include senior housing programs, Area Agencies on Aging, senior centers, and other social service providers.

Professions Involved

The role of geriatric care coordinator may be performed by professionals with specialized training in working with older adults, including social workers, nurses, pharmacists, patient navigators, and community health workers. It is important to match care coordinator disciplines with patient needs. In most programs, an interdisciplinary approach is most effective, since older patients typically experience a combination of complex medical and social needs.

Key Research Findings

Care coordination programs vary significantly, though several key features are needed for a basic framework: (i) engagement – older adults and their caregivers must be meaningfully engaged in care coordination activities; (ii) comprehensive assessment; (iii) collaborative care planning, which includes patients' goals and preferences; and (iv) interdisciplinary care.

Patient Selection

Limited resources demand that care coordination services target appropriate patient populations. Targeting strategies abound, typically falling into one of three categories: (i) high-utilizing, costly patients (risk stratification); (ii) patients likely to become high-utilizers (predictive modeling); and (iii) disease-specific groups (e.g., diabetes, hypertension, mental health). Patients may be identified via direct referral, medical or social determinant risk screens, automatic electronic medical record reports, provider or insurance registry databases, or a combination of these.

Enabling Elements

To effectively integrate into usual care, care coordination programs must be approached systemically by creating customized workflows and protocols. Most programs are interdisciplinary in nature, so role clarity must be established and communicated to older patients and their caregivers. Additionally, information systems must be able to support program activities, particularly shared care plans and data collection for program evaluation.

Measurement

Various metrics have been used to study care coordination implementation and impact. Findings to date have largely focused on clinical and utilization outcomes (McDonald et al. 2014), including emergency department use, hospital readmissions, primary care engagement, and use of long-term support services. However, broadening the focus to include process and system-level measures, including quality of care, improved self-efficacy, patient satisfaction, cost impact, and other metrics can help create standard program development and evaluation approaches.

Prospects

Health care policy reform, particularly the national shift to value-based care, has prompted many health systems to include care coordination as part of regular patient care. The Center for Medicare and Medicaid Innovation (CMMI) has incentivized innovation in service delivery in order to test and disseminate a number of care coordination models targeting Medicare beneficiaries.

However, creating a business case for care coordination remains a challenge. Though care coordination may decrease costs by preventing unnecessary emergency department visits and hospital readmissions, it may also correct underuse and ensure timely access to care, potentially increasing costs in the short term (McWilliams 2016). To assist providers with this challenge, several fee-for-service billing codes are recognized by Medicare and commercial payers that allow for interdisciplinary team members and community-based organizations to participate in care coordination activities.

While payment reform has prompted growth in care coordination efforts, further work is needed to understand the mechanisms of its impact and to improve the sharing and security of health information. Effectively implementing interdisciplinary care teams for older adults calls for policymakers to address scope of practice and reimbursement challenges for social work, community health workers, and other professionals involved in care coordination. Meanwhile, continued innovations from health and community-based providers will continue to advance efforts to build coordinated care across the country.

Cross-References

- ▶ Aging Network
- ▶ Care Management
- ▶ Case Management
- ▶ Geriatric Social Workers
- ▶ Health Information Exchange
- ▶ Managed Care and Aging
- ▶ Person-Centered Care for Older Adults

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Care Costs

▶ Fee-for-Service

Care Decision-Making

▶ Preparation for Future Care: The Role of Family Caregivers

Care for Activities of Daily Living

▶ Personal Care

Care for the Aged

▶ Gerocomia in the History of Aging Care

Care for Veterans

▶ Veterans Care

Care Home Stories

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Definition

Care home stories are narratives – fictional or nonfictional – that represent spaces and places of long-term institutional care from various perspectives, thus reflecting, but also creating, cultural imaginations of the institution that often houses the oldest old. As Chivers and Kriebernegg argue in their edited collection *Care Home Stories: Aging, Disability, and Long-Term Residential Care*, "care home stories challenge stereotypes of institutional care for older adults, illustrate the changes that have occurred over time, and illuminate the continuities in the stories we tell about nursing homes" (2017, pp. 17–18).

Overview

Whether in a nursing home, care home, retirement home, assisted living, or other form, institutional care for older people offers a cultural repository for fears and hopes about an aging population. While people adamantly desire to age well at home, without making the "big move," (See ▶ "Aging in Place") as Anne Wyatt-Brown, Helen Q. Kivnick, and Ruth Ray Karpen call it (2016), to render their later years more manageable, and policy makers play to that desire, buoyed by how it offers them an opportunity to download the costs of care onto the family unit, the fact remains that many contemporary older persons will require institutional care. Enormous changes have occurred in how institutional care is structured, with models from the poor house through the hospital to the home and the hotel and the village. But the legacies of the poor house and the hospital persist, creating panicked views of the nursing home as a dreaded fate for people who may actually benefit from new living quarters in late life. Stories about the paradoxical nature of a space meant to be both hospital and home offer up critical tensions for examination by age studies scholars. In particular, Katherine Orellana points out that they can "reveal the role of contexts and the tension between these establishments [care homes] being people's homes, corporate endeavours, and working environments" (2019, p. 655).

Why Care?

While thinking about care might seem to limit what we imagine later life to be, the question especially of long-term care propels social and cultural meanings of population aging. When the popular press is overwhelmed by negative images of older people (See ► "Age Stereotypes"), it is not just evoking fear about what each person's fate might be – a deep fear of physical change that could bring pain and restriction to the activities of daily living, not to mention raising the specter of death. Beyond that, images of older adults overtaking youth – often pictured as a giant wave – are about dependency. The idea that younger generations will have to do the work of care and, worse yet, pay for care is a significant portion of what makes such demographic projections play apocalyptically. Thus, care is at the crux of age/ing studies. Changing the meaning of care stands to substantially change what it means to "age well," (See ► "Aging Well") and care home stories offer a creative and significant way to reorient thinking about care.

Why Home?

Home appears throughout understandings of long-term residential care as an unquestioned ideal. The notion that institutional settings are improved when they are homelike goes virtually unquestioned. Not only is that assumption worth up-ending, so too must be questioned whose home these spaces are meant to be "like." As Annmarie Adams and Sally Chivers point out in the context of design, "how to capture and conjure up an image of home to residents of various backgrounds" poses a "perennial challenge" (2015, p. 138). It is, perhaps, easier to pinpoint what is not homelike than to effectively describe let alone manifest homelikeness. Home is held up as an unquestioned good, particularly in policy documents that stress the widespread desire of people to age in place, meaning in their homes. But care home stories, in their multiplicity, show how home is a thorny concept that benefits from interdisciplinary and international scrutiny.

Why Stories?

In *The Truth about Stories*, Indigenous author Thomas King famously states, "The truth about stories is, that's all we are" (2003, p. 2). Yet care homes are not usually thought of as sites for *new* stories – instead the people who live within them are thought to be vessels for stories of a past from before they made the "big move." Care home stories put the key terms of "care" and "home" together because they offer a meaningful and aesthetic way to contain and revel in multiplicities. A story can offer a few vantage points without taking a side but a story can also effectively and convincingly play favorites. There is no need for objectivity but rather a helpful indulgence in productive subjectivities. There are new stories to tell regarding care home spaces about, with, and by the people who work, live, and visit them. Such stories are important, because, as Kathleen Woodward argues, "one of the most effective modes of advocating for changes in public policy is engaging people's understanding through stories and images" (2012, p. 17).

Key Research Findings

The need to tell and analyze care home stories intensifies due to the infiltration of neoliberal process into public institutions, including long-term residential care. Care home stories reflect the need to think about what values underlie the systems in which long-term residential care functions, beyond those that situate seniors in need of care as "customers" who contribute to or sap "financial" viability. Instead of aiming to grow one's care business to become number one, and instead of supporting the notion that public institutions ought to be run like businesses, care home stories facilitate a discussion about many different ways in which long-term residential care in late life could become something desirable rather than necessary.

Care home stories challenge the spatial separation of old age in that they counteract a decline narrative and argue for the inclusion and participation of old people. Cultural representations of age need not remain locked in primarily negative stereotypes and can do more than shallowly contradict them with empty positive visions. While representations of even the "fourth age" as a time of agency and self-determination are important because they contest the decline narrative of old age, care home stories can do even more. They can reveal the culturally constructed nature of the binary opposition of young and old. Care home stories express cultural assumptions – positive or negative – about aging and old age and, thus, about life itself. Care homes in such texts are always spatial metonymies that allow authors to talk about existential questions of life, offering them the opportunity to depict the ambiguities and ambivalences of our very existence.

Two aspects deserve to be highlighted with regard to care home stories: (a) the spatiality of aging and (b) the special quality fictional care home stories possess.

Spaces and Places of Care: The Spatiality of Aging

Rather than emphasizing how late life is a stage when time is running out, care home stories link the cultural construction of old age to questions of *space* and *place*: "Identities are spatialized, in that where we are says a lot about who we are," cultural geographer Glenda Laws notes (1997, p. 93). Care homes are not exempt from this observation: Age is defined by place, and where one is old matters. When care homes are represented in stories, such depictions usually place an emphasis on the fact that such a home is more than simply a building or residence. Rather, it is "a micro-complex of architectural, administrative, financial, clinical, familial, symbolic, and emotional interactions and power relations" (Katz 2005, p. 204). It is, in many ways, a world in itself where a seemingly homogeneous group of people is housed that shares two characteristics: being old and being in need of a certain amount of help in everyday life. The interplay of the interactions and power relations constitute the care home's social practices, which, in turn, create the specific place. The care home contributes to discourses on the aging body and individual. As Jaber Gubrium and James Holstein put it, the home serves as a "discursive anchor for the aging body [. . .]. We age bodily, in other words, as much because our bodies are discursively anchored by a particular institution, as because our bodies grow old" (1999, p. 537). The home shapes its residents' identities by providing a framework of signification and description (Gubrium and Holstein 1999). Care home stories foreground the constructedness of these discourses contributing to a larger understanding of the heterogeneity of late life.

Fictionality

Filmic and fictional representations of institutionalized eldercare are currently flourishing (Chivers 2003; Kriebernegg 2017; Kriebernegg 2020), reflecting the wide variety of caregiving models that range from prison-like, infantilizing, and even abusive "total institutions" (Goffman 1961, p. 14) to hotel-like retirement facilities with luxurious amenities and responsible caregivers. The threat of ending up as inmates of "'halfway houses' between society as we know it and the cemetery" (Garvin and Burger 1968, p. 11) has been mirrored in literary texts on both sides of the Atlantic since the late 1960s and has become increasingly common up until today. The care home novel/care home movie is a newly established category and comprises fictional works that are set in care homes or deal with the complex array of problems and feelings associated with moving oneself or relatives into a care-giving institution. They also give voice to caregivers (e.g., *A Sleep Full of Dreams* by Edna Alford (1981) or friends and family visiting their loved ones in a care home

(Nicholas Sparks, *The Notebook* (1996); Alice Munro, "The Bear Came Over the Mountain" (1999)). Yet, the "horrible home," with its parallels to the Gothic novel and the sublime, has become a predominant topos in literary texts. In such narratives, the care home always serves as a symbol, a pars pro toto, for the experience, fears, and uncertainties associated with being old and illustrates the marginalized social position of old age. May Sarton's novel *As We Are Now* (1973) is one of many literary examples that illustrate the fear, hopelessness, and despair commonly associated with nursing homes. Fiction and film that reflect the increasing variety of today's eldercare options, including its positive sides, have also begun to appear, for instance, the British movies about *The Best Exotic Marigold Hotel* (2011) which is based on Deborah Moggach's 2004 novel *These Foolish Things*, the film *Quartet* (2012), based on a play with the same title by Ronald Harwood (1999), or the French movie *Et Si On Vivait Tous Ensemble* (2011). Further examples that show various aspects of life in a care home are Paco Roca's *Arrugas* ("*Wrinkles*" Spain 2011), which is based on the graphic novel with the same title (2007), or Shani Mootoo's *Cereus Blooms at Night* (1996). Most importantly, all of these fictional representations also focus on the aspect of agency in old age, a dimension that crystallizes in the "care home escape narrative," (See ▶ "Aging and the Road Movie") e.g., *The Hundred-Year-Old Man Who Climbed Out of the Window and Disappeared* (Hundraåringen som klev ut genom fönstret och försvann) by Swedish author Jonas Jonasson (2009, the English version appeared in 2012). Other well-known examples are Canadian/American Sara Gruen's *Water for Elephants* (2006, movie adaptation Lawrence 2011), Oscar Casares' Mexican-American novel *Amigoland* (2009), Thom Fitzgerald's movie *Cloudburst* (2011) (See ▶ "Intersections of Race/Ethnicity and Age in Film and Literature"), or Canadian novelist Janet Hepburn's *Flee, Fly, Flown* (2013). An annotated bibliography of fictional texts about life in a care home has been compiled by Margaret Morganroth Gullette and can be found in *The Big Move* (Wyatt-Brown et al. 2016).

Summary

Care home stories link literary and narrative gerontology with new approaches used by cultural geographers to analyze how such narratives retell the institution as a textual space in which stereotypical notions of old age can be deconstructed. Defining old age as an uncanny and dangerous place also positions the care home as an uncanny site. Therefore, a re-imagination of care homes as sites of meaningful identity development in old age is crucial to be able to counteract ageism. Narrative representations of care homes can encourage readers and listeners to engage in such redefinitions because many such stories portray individuals who have the most important experiences at the latest stages of their lives, experiences which enable them to re-narrate their lives, and arrive at new and meaningful conclusions to their narratives despite, or perhaps even because of, their physical frailty. Similarly, care home stories can give center stage to persons working in care homes or visiting them, making their voices heard as well, bringing into visibility what Kathleen Woodward terms "a scandalous public secret of everyday life" (2012, p. 17).

Cross-References

▶ Aging and the Road Movie
▶ Decline and Progress Narrative
▶ Intersections of Race/Ethnicity and Age in Film and Literature
▶ Reifungsroman/Vollendungsroman/Bildungsroman
▶ Silvering Screen
▶ Television Series on Aging: Aging and Serial Narration

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Care Management

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C

Synonyms

Case management; Case/care manager; Geriatric care manager/management; Geriatric nurse care manager/management

Definition

Care management is the process of improving health and wellness for persons with complex or chronic health conditions. As opposed to case management (See ▶ "Case Management"), which is episodic and often short-term, care management is intended to provide comprehensive care over a period of several months or years. Geriatric care management is this process applied in the context of aging. A geriatric care manager works strictly with the older adult population and has specialized training in gerontology.

Overview

Geriatric care managers are knowledgeable about health, illness, families, finance, legal, and medical issues as well as the availability of and eligibility requirements for resources and social services in their community. Care coordination is the hallmark responsibility of geriatric care management and includes comprehensive assessment of care needs (See ▶ "Care Coordination") (Peikes et al. 2009; Taylor et al. 2013); development and monitoring of individualized care plans shared across care settings (Peikes et al. 2009; Taliani et al. 2013; Taylor et al. 2013); discussing and reviewing care plans with patients, families, and the care team (Moreo et al. 2014); collaboration with other clinicians across settings, conditions, and diseases (Taylor et al. 2013); facilitating care transitions from inpatient or acute care settings and implementing strategies to prevent readmission (Moreo et al. 2014); provision of patient education and training for self-management (Peikes et al. 2009; Taliani et al. 2013; Taylor et al. 2013; Tricco et al. 2014); the use of behavior change models (e.g., motivational interviewing) (Peikes et al. 2009); and connection to community resources and social services (Peikes et al. 2009; Taliani et al. 2013; Taylor et al. 2013; Tricco et al. 2014). The goals of care management are to improve the quality of patient care, decrease the cost of care, improve satisfaction in health care, and reduce fragmentation of care through the promotion of interdisciplinary collaboration and coordination of care (Parsons et al. 2012).

Geriatric care managers act as guide and liaison to advocate for older adults and those in a caregiving role for older persons, intervening in each phase of the chronic illness trajectory to address influential factors, prepare for future stages of illness, and assist individuals and families in attaining the highest quality of life and care possible. Geriatric care management may be fostered by various disciplines including mental health, physical and occupational therapy, gerontology, health education, nursing, clinical pharmacy, or social work. Geriatric care managers may hold a baccalaureate, master's, or Ph.D. degree in their field of study or may be certified after extensive experience working in care/case management through organizations including the National Academy of Certified Care Managers (CMC credential), the Commission for Case Manager Certification (CCM credential), and the National Association of Social Workers (C-ASWCM or C-SWCM credentials). Advanced certification is offered through the Aging Life Care Association (formerly National Association for Professional Geriatric Care Managers). Several higher education institutions including the University of Utah and University of Pennsylvania now offer nurse master's degrees in care management as well as certificates in care management and gerontology for health-care professionals (See ► "Gerontological Nursing").

Key Research Findings

Care becomes more complex for older adults as the number of providers who treat them increases. On average, Medicare beneficiaries were treated by 3.4 different clinicians during the year 2012 (Bynum et al. 2016). The more clinicians involved in the patient's care, the greater the opportunity for overuse and misuse of care, duplication of services, and exposure to communication-related risks and errors (Bynum et al. 2016). Additionally, health-care providers report increased difficulty caring for individuals with multiple chronic conditions citing poor care coordination as a major contributing factor to adverse health outcomes, leading to low satisfaction in caring for this population (Anderson 2010).

Older adults may access the services of a geriatric care manager privately in their community. Geriatric nurse care managers may be found imbedded in geriatric care clinics. Many health-care institutions now include registered nurse care managers in the outpatient setting as part of the primary care team and are commonly included when a primary care practice wishes to obtain special certification as a patient-centered medical home (PCMH). A high-performing team is now commonly recognized as an essential part of developing a more patient-centered, coordinated, and effective health-care system and requires shared goals, clear roles, mutual trust, effective communication, and measurable processes and outcomes (Mitchell et al. 2012). When primary care practices draw on the expertise of various team members, including care managers, patients are more likely to get the care they need (Schottenfeld et al. 2016).

Examples of Application

Chronic Care Management

Chronic care management (CCM) is a program offered under the Centers for Medicare and Medicaid Services (CMS) that provides non-face-to-face services to Medicare beneficiaries who have two or more chronic conditions expected to last at least 12 months or until death. Program benefits include additional help managing chronic conditions such as a comprehensive care plan, structured recording of patient information using certified electronic health record technology, 24/7 access and continuity of care, comprehensive care management, management of care transitions, and home- and community-based care coordination. CMS pays for CCM services separately under the Medicare fee-for-service program (US Department of Health and Human Services 2016a).

Transitional Care Management

Geriatric nurse care managers are frequently involved in another program under CMS called transitional care management (TCM). TCM services are offered when a beneficiary's care transitions from an acute care setting, such as the hospital or skilled nursing facility, to the community. Services include care coordination, education, assessment of treatment regimen adherence and medication management, identification of resources, and assistance in accessing needed care and services (US Department of Health and Human Services 2016b).

Summary

Care management is a growing and diverse field. Its purpose and goals help to facilitate comprehensive care for the complex older adult population. Assessment of health outcomes after participation in a geriatric care management program, specifically in a health-care setting, may lead to additional support from CMS through coverage of and increased reimbursement for services.

Cross-References

▶ Care Coordination
▶ Case Management
▶ Gerontological Nursing
▶ Managed Care and Aging

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Care Needs

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Synonyms

Needs of care; Needs of care services; Needs of care support

Definition

Care needs can be broadly conceptualized as rational drives for care services, including both the needs for health-care services and the needs for formal and informal long-term care assistance. Such needs are defined subjectively by people's own perception or objectively by experts of people's availability of assistance for their daily living, the affordability for services, their health status, and so on. In a narrow sense, care needs always refer to the subjective domain of needs (i.e., felt needs (expected, wanted, desired, or perceived needs) and expressed needs) for care assistance in either formal or informal form.

Overview

Multidimensionality of Care Needs

The multidimensionality of care needs can be understood starting from the dimensions of care and needs.

Dimension of Care

Care is about the assistance for the following items: cognition, communication, hearing, vision, mood, behavior, physical function, continence, health condition, oral status, nutritional status, dental status, skin condition, etc. With respect to the types of care, there are several ways to categorize it. First, according to the service providers, care can be categorized into informal care and formal care. The assistance from family members and other informal resources is regarded as informal care. This kind of assistance to a person living in the same household is for one or more of the following activities: cognition or emotion, communication, health care, housework, meal preparation, mobility, paperwork, property maintenance, self-care, and transport (Australian Bureau of Statistics 2003). The assistance from formal resources is regarded as formal care. This kind of assistance to a person in a different household relates to "everyday types of activities," without specific information on the activities (Australian Bureau of Statistics 2003). Second, care can be classified into tangible care and intangible care. Tangible care always refers to some instrumental (practical) assistance, and intangible care always refers to some emotional or informational assistance.

Dimension of Needs When discussing about needs, it could usually be defined by the discrepancies between the target situation and the actual situation, namely, what should be versus what is (Petersen and Alexander 2001). In regard to the conceptualization of needs, a wide array of frameworks can be proposed. Some frameworks put forward needs only by types (Bradshaw 1972; Petersen and Alexander 2001; Brill and Levine 2002), and the others presented needs by the hierarchy of different kinds of needs (Doyal and Gough 1991; Maslow 1954).

Needs Conceptualized in Types Bradshaw's (1972) "typology of needs", which is most widely used in categorizing needs, categorized needs into four types. First is felt needs, which can be measured by means of asking whether one is satisfied with his/her current situation. Felt needs are the psychological condition of wanting a certain gratification, usually some basic physiological needs. This type of needs is regarded as an inadequate measure of "real needs" because of individual's limited knowledge of the availability of services or assistance, as well as the inflation by those who ask for help without "really needing it." Second is expressed needs, which is defined as the felt needs expressed or demanded explicitly. Both felt needs and expressed needs are subjectively defined by people's own viewpoints of the availability of assistance for their daily living, the affordability for services, their health status, and so on. Third is normative needs, which are identified as need in any given situation by experts, professionals, administrators, or clinicians. Fourth is comparative needs, which are identified by way of comparing groups of people with similar comparable characteristics. Comparative needs are also defined by experts.

Moreover, Petersen and Alexander (2001) classified needs into four types, namely expected needs, expressed needs, extrapolated needs, and comparative needs. Brill and Levine (2002) suggested a framework of universal basic needs, including physical, intellectual, emotional, social and spiritual needs.

Needs Conceptualized in Hierarchy With respect to the hierarchy of needs, some researchers proposed their own classifications. Maslow (1954) theorized that needs can be categorized according to a "hierarchy," which is ranked into physiological needs (the lowest level of needs), security needs, love and belonging needs, esteem needs, and the needs for self-actualization (the highest level of needs). People satisfy the lower level of needs before "promoting" to the higher level of needs.

Moreover, Doyal and Gough (1991) categorized needs into two domains. The first domain is basic needs, including physical health and autonomy, which are regarded as an "optimum" level of needs and are the universal prerequisites for successful and, if necessary, critical participation in a social form of life (Castles et al. 2010; Doyal and Gough 1991). The second domain is intermediate needs, which involve the identification of those characteristics of need satisfiers which everywhere contribute to improved physical health and autonomy (Gough 1988, p. 54).

Measurement of Care Needs

Measurement of care needs can be made in both objective and subjective ways.

Objective Way of Measuring Care Needs

When assessing care needs by objective way, we usually adopt well-developed assessment tools to measure it from the following aspects: cognition, communication, hearing, vision, mood, behavior, physical function, continence, health condition, oral status, nutritional status, dental status, skin condition, etc.

Subjective Way of Measuring Care Needs

Expressed Needs of Long-Term Care (LTC) Mode When discussing about care needs, the care mode issue is bound to come up. The care mode may not only refer to the ones related to health care (i.e., primary care, secondary care, tertiary care, and home and community care) but also refer to the ones related to long-term care.

For LTC mode, it is usually categorized into informal care and formal care. Informal care, referring to family care, is mostly delivered by family members. Traditionally, older people across different cultures prefer to live at home and receive assistance from family members, neighbors, and friends instead of seeking help from formal care service institutes (Cantor 1989; Gott et al. 2004; Lou et al. 2011). As the most important primary group in society, family is the primary resource in providing both emotional and instrumental support for older adults. Even in the Western European countries, where family function is relatively weak, family still takes the most responsibility for caring older people. Formal care refers to institutional care (residential care) and home- and community-based care (HCBC). Institutional care could contribute to relieve family members' burden on elderly care and provide older people more intensive and professionalized care services. But, several problems of institutional care are also obvious, such as less opportunity of self-determination and lack of privacy and sense of belonging (Liu 1983). HCBC derives from the deinstitutionalization movement in the United Kingdom in the 1960s. Along with increasing frailty and incidence of chronic illnesses, older people would require more care assistance services, while, with an increasing number of women engaged in jobs and the changing family structure, the traditional family care function has been weakening, especially for instrumental care support. The traditional family-based elderly support system has been changing along with the changes of society, economy, and people's understanding of taking care of older people. In this situation, the importance of HCBC in LTC system has been further manifested. HCBC mode can satisfy older adults' willingness of being "aging in place" and meanwhile can liberate labor force of family members. For the past decades, studies from various countries have evidenced that HCBC can effectively prevent or delay institutionalization, improve the physical functions, and slow the decline in cognitive functioning of older people (Be'land et al. 2006; Mai and Eng 2007). For most developed countries, they have built up relatively advanced service delivery systems for older adults' formal care. For example, the percentage of older adults aged 65 or above receiving formal care services exceeded 15% in seven OECD countries in 2011, namely, Israel (22.1%), Switzerland (20.3%), the Netherlands (19.1%), New Zealand (17.6%), Norway (17.4%), Denmark (16.7%), and Sweden (16.3%, He et al. 2016). However, for the countries with underdevelopment of care system or with a more familistic culture (i.e., China), older adults expressed more needs on informal care (Fu et al. 2017).

Expressed Needs of the Intensity of Care Services The measurement of the intensity of care services involves several ways. Some researchers measure it by the types of care services needed by asking how many services they need by a yes or no question and then sum up in expressing the number of care services needed (Wee et al. 2014b) or whether or not they need a specific care service item (Hwang 2015). Additionally, some other researchers measure the expressed needs of the intensity of care services by asking the frequency they need a specific service item or a series of care services in a specified period of time (Coughlin et al. 1992).

Patterns of Expressed Needs for care services In addition to the LTC mode and the intensity of care services (types of care services and frequency of care services), another measurement is to categorize the homogeneous groups of people into distinct types of care service patterns, based on the differences in number and variation of care service items. This measurement has been used in a number of studies on the utilization of care services (Beeber et al. 2008; Igarashi et al. 2017; Lafortune et al. 2009).

For care service items, the list of care service items may refer to a wide range of care services in the international scene, only based on the provision of care services in the area (especially for some countries or regions at an early stage of care development) or just based on the items measuring older adults' functional ability (i.e., activities of daily living (ADLs) and instrumental activities of daily living (IADLs)).

Moreover, differences on the most needed care services may exist among countries/regions and among groups of older adults. For example, in the Netherlands, physical health treatment, household activities (domestic assistance), and mobility are the top three care services needed by frail older adults (Hoogendijk et al. 2014). In Hong Kong, making decision and planning ahead are most needed for older adults at the early or middle stages of dementia, and bathing is most needed for older adults at the late stages of dementia (Chung 2006). With respect to the most needed HCBC services, cleaning the house and shopping are the top two among frail older adults in Canada (Michel et al. 2011); taking dedication, managing money, and shopping are the top three among older adults with Alzheimer's disease in America (Li et al. 2012); and home maintenance, mobility, and mental health and social behavior/community living are the top three among older adults in Australia (Harrison et al. 2014). In regard to the most needed institutional care services, looking after the home, food, and physical health are the top three among older adults living in the institutions in Poland (Tobis et al. 2018); household activities, memory, and accommodation are the top three among older adults with dementia living in the institutions in the United Kingdom (Hancock et al. 2010). For the most needed health-care services, eyesight/hearing/communication, physical health, and mobility are the top three among older adults in Germany (Stein et al. 2019).

Key Research Findings

Along with the aging tendency all over the world, older adults' care needs issue has attracted increasing attention. On the studies of care needs, many scholars mainly focus on the influencing factors of care needs, the relationship between care needs and actual utilization, as well as the unmet needs of care services.

The Influencing Factors of Care Needs

The influencing factors of care needs have been widely examined in the existing literature. The Andersen model, developed in the late 1960s, was initially designed for discussing about health service utilization. Nowadays, it has become a widely used theoretical model for explaining or predicting care needs (Fu et al. 2017; Chung et al. 2008). Based on the Andersen model, the influencing factors can be categorized into predisposing characteristics (i.e., age, gender, marital status, and educational level), enabling factors (i.e., living arrangement, number of children, social support, and financial condition), and need factors (i.e., ADLs, IADLs, and number of chronic diseases).

The Relationship Between Care Needs and Actual Utilization

When discussing an individual's care needs, actual utilization cannot be excluded. Both care needs and actual utilization are important domains in terms of older adults' behaviors in care services. With respect to the objective aspect of care needs, a large number of studies have demonstrated the important role that care needs played in actual utilization of care (Alkhawaldeh et al. 2014; Beeber et al. 2008; Borowiak and Kostka 2013; Murphy et al. 2015; Wee et al. 2014a, b; Zielinski and Halling 2015).

When discussing the subjective aspect of care needs, care needs are an indication of readiness to perform a given behavior; nevertheless actual utilization is older people's observable response in a given situation with respect to care services or care mode. In the theory of planned behavior which was proposed by Ajzen (1985), intended use, which was regarded as an immediate antecedent of behavior, was found to be positively related to actual utilization, which was regarded as a behavior in response to a situation with respect to a target. The stronger the behavioral intention, the more likely an individual performs the actual behavior. The direction of this association ran from intended use to actual use. Moreover, the practice-oriented model, developed by Yeatts et al. (1992), further explained the barriers existing between care needs and actual utilization, including knowledge, access, and intent. Moreover, some empirical studies also helped to understand the relationship between care needs and actual utilization among other population groups (Ozegowski and Sundmacher 2014), while investigations were limited on whether an individual's interest in using services can serve as a factor affecting service utilization among older adults or their caregivers.

Unmet Needs of Care Services

Unmet care needs can be defined as the discrepancy between expressed needs and actual use of care services. It occurs when people are in need of help but the services are unavailable or insufficient. The studies on unmet care needs mainly include the consequences of unmet care needs and the influencing factors of unmet care needs.

Consequences of Unmet Care Needs

A number of the consequences of unmet care needs have been discussed in previous studies. For example, unmet care needs were found to be associated with increased risk for future hospitalization and increased risk for mortality (He et al. 2015). Moreover, several studies addressed the question of how unmet care needs were associated with the utilization of care services (Gaugler et al. 2006). Additionally, according to Pearline's stress Process Model (Pearlin et al. 1990), unmet needs could be regarded as one of the stressors of the outcomes of caregiver stress (i.e., depression, anxiety, cognitive disturbance).

Influencing Factors of Unmet Care Needs

The same factors that predispose one to need and use services appear to be factors in unmet needs (Williams et al. 1997). Among the existing studies addressing the influencing factors of unmet care needs, living alone, IADLs limitations, ADLs limitations, lack or withdrawal of informal support, cognition, gender, lack of awareness, reluctance, unavailability, and affordability of services, the relationship between caregiver and older adults, expectation to have access to care services were found to be related to unmet care needs (Desai et al. 2001. Casado et al. 2011; Zhu 2015).

Future Directions of Research

First, there is still much to explore about the impact of cultural values on care needs. Different core culture value and cultural environment may help to shape the care needs in different ways. Second, more empirical studies in the factors related to care needs among different groups are expected, so as to address discrepancies in existing research. For example, the gender disparities on health and socioeconomic status may gradually transfer into the difference in factors affecting care needs. However, the existing findings of gender difference on influencing factors of care needs lack of consistency (Chan 2014; Lum et al. 2016; Luppa et al. 2010). Moreover, although the influencing factors of care needs have been found to be different among age groups in several studies (Fu et al. 2017; Woo et al. 2000), the age-related differences in factors affecting care needs have yet to be empirically and fully explored (Wu et al. 2014). Furthermore, the "care needs" may not be confined to the older adults but also their family (spousal and children) caregivers. Therefore, the "caregivers' care needs," especially the family caregivers' care needs, is also a research area. However, limited studies addressed the difference in influencing factors between older adults and their informal caregivers and even among caregivers in different relationships with older care recipients (i.e., spouse caregiver vs. child caregiver, working caregiver vs. non-working caregiver). Both researchers and practitioners should be more sensitive to such group differences on the influencing factors of care needs. Third, more exploration is needed on how to measure the intensity of care needs in a more scientific way. The most popular way of measuring care needs is still counting the number of care service items needed or scoring the frequency of needing a specific service item or a series of care services in a specified period of time. A same hypothesis exists behind these two methods, which is all the care service items accounted for were with same weight in the care service system. It is necessary for future studies to continue studying about a more appropriate measurement of care needs when assessing the intensity of care needs.

Summary

Care needs can be broadly conceptualized as rational drives for care services and defined in both objective way and subjective way. In a narrow sense, care needs always refer to the subjective domain of needs (i.e., felt needs (expected, wanted, desired, or perceived needs) and expressed needs) for care assistance in either formal or informal form. The influencing factors of care needs, the relationship between care needs and care service utilization, as well as the unmet needs of care services are three key issues in this research area. Future studies are expected to have more exploration on addressing care needs issue from caregiver's perspective, the impact of culture values on care needs, the factors related to care needs among different groups, the measurement of care needs when assessing the intensity of care services, and so on.

Cross-Reference

▶ Adult Day Services
▶ Adult Protective Services
▶ Care Coordination
▶ Care Management
▶ Faith-Based Social Services
▶ Formal and Informal Care
▶ Home- and Community-Based Services
▶ Kin Availability
▶ Legal Services
▶ Mental Health Services

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▶ Personal Assistant Services
▶ Personal Care
▶ Preventive Care
▶ Quality of Care
▶ Respite Care
▶ Skilled Care
▶ Social Services Utilization
▶ Social Support
▶ Social Work

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Care Networks

► Self, Informal, and Formal Long-Term Care: The Interface

Care of Older Adults

► Formal and Informal Care

Care Pathways

▶ Self, Informal, and Formal Long-Term Care: The Interface

Care Planning

▶ Case Management

Care Satisfaction

▶ Quality of Care

Care Trajectories

▶ Self, Informal, and Formal Long-Term Care: The Interface

Care Transitions

▶ Self, Informal, and Formal Long-Term Care: The Interface

Care Transitions Planning

▶ Preparation for Future Care: The Role of Family Caregivers

Care Work

▶ Caregiving and Social Support: Similarities and Differences
▶ Self, Informal, and Formal Long-Term Care: The Interface

Career Choices and Ageism

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Definition and Overview

Ageism is a complex phenomenon that describes prejudice and discrimination against people because of their age. While ageism can manifest as positive stereotypes (e.g., access to benefits and privileges not granted to other age groups) (Levy and Macdonald 2016), negative attitudes and stereotypes about older adults and the aging process are far more prevalent (Kotter-Grühn and Hess 2012) (See ▶ "Age Stereotypes"). Compared to other forms of institutionalized discrimination, ageism receives significantly less scrutiny and criticism and is normed nearly to the point of invisibility through jokes, songs, birthday cards, and a widespread "anti-aging" industry (Palmore 2015; Gendron et al. 2017). The roots of ageism are complex and in part can be traced to a dominant but mistaken cultural understanding of aging as a sole process of disease and deterioration. This limited view of aging as synonymous with decline is often exacerbated in training and education programs that prepare professionals to work with older adults in all sectors including healthcare, social services, psychology, recreation, and leisure as well as business, finance, and industry professions (see ▶ "Aging Network"). Unchallenged ageism that perpetuates negative views of one's own aging and stereotypical, misinformed views of older adults creates barriers that influence career choice (See ▶ "Age Discrimination in the Workplace"). For example, the number of healthcare professionals who choose to specialize in geriatrics has been steadily declining during the last 20 years ("Geriatrics workforce by the numbers" 2017) (See ▶ "Ageism in Healthcare"). As well, there have been increasing reports of age discrimination in hiring, promotion, and recruitment practices that pose substantial challenges for older workers seeking employment (Griffin et al. 2016).

Key Research Findings

Research has shown that negative attitudes about one's own aging have been correlated with adverse health outcomes including a 7.5-year impact to longevity (Levy and Myers 2005), a cost of 63 billion dollars in healthcare expenditures (Levy et al. 2018; Slade et al. 2018), increased risk for chronic disease (Allen 2015), perceived ill health (Ramírez and Palacios-Espinosa 2016), and increased risk of biomarkers for Alzheimer's disease (Levy et al. 2016). Ageist attitudes toward older adults living in long-term care have also been shown to decrease their autonomy (Coudin and Alexopoulos 2010). Ageism also represents a critical workforce challenge, in that it may negatively impact job satisfaction and job retention among individuals working with older adults (Gendron et al. 2014). Perhaps most concerning of all, research has also shown that ageist attitudes are often unconsciously and unintentionally perpetuated even by those who choose to work with older adults (Gendron et al. 2017). Taken together, the research demonstrates compelling evidence that ageism can impact career choice and career commitment.

Examples of Application:

Ageism can impact career choice by both influencing reasons (e.g., disinterest) for choosing a career working with older adults and by discouraging older workers to seek employment. Frequently influencing reasons and cited barriers to choosing a career focused on older adults include: lower pay and perception of lower prestige (Album and Westin 2008), negative attitudes toward aging and older adults (Golden et al. 2014; Higashi et al. 2012), concerns about the capacity to be effective, and the complexity of geriatric care (Meiboom et al. 2015). Motivation for pursuing a career in aging is also influenced by personality factors, personal experiences with family and work experience as well as exposure within classroom settings (Moye et al. 2018). A study by Moye et al. (2018) reported that academic exposure such as mentorship, research, or coursework were catalysts that sparked interest in a career working with older adults. Counter to these findings, Higashi et al. (2012) reported that mentors and practitioners that display negative, and sometimes outright prejudicial, behaviors negatively affect the attitudes of less experienced professionals which can deter individuals from committing to a career with older adults.

Many older adults desire to continue or pursue employment during their later years. However, institutionalized ageism in the workplace, fueled by beliefs about the universal desire and benefit for retirement based solely on age, deters the hiring, promotion, and productivity of older workers. Stereotypes and generalizations about older workers, such as diminished performance or motivation, provoke concerns that influence hiring practices. However, research has found no evidence to support the accuracy of older worker stereotypes such as evidence of lower performance or shorter tenure (Posthuma and Campion 2009).

Future Directions of Research

Disrupting the cycle of ageism as it relates to career choice requires taking a multi-pronged approach that targets all levels of the ecological system. On an individual and microsystem level, research is needed to develop evidence-based mechanisms that raise awareness of the pervasive, hidden nature of ageism and provide interventions that change attitudes and behaviors. The PEACE (Positive Education about Aging and Contact Experiences) Model represents one promising practice for reducing ageism through education and positive contact with older adults (Levy 2016). Within the exosystem, research is needed to develop best practices for reducing discrimination within systems and organizations. Although research has identified some mechanisms for improvement, such as examining human resource practices, and increased intergenerational contact (See ► "Intergenerational Programs on Anti-Ageism"), limited research has developed an evidence-based approach to reduce age discrimination in employment practices (Truxillo et al. 2017). And finally within the macrosystem, research and advocacy efforts are needed to reframe our understanding of older adulthood from one as a singular process of decline to a more robust and accurate understanding of older adulthood as a process of dynamic change that includes purpose, opportunity, and development.

Summary

Ageism, as it relates to choice of career, impacts those in the process of determining a career path, those practicing in a profession focused on older adults, as well as those seeking employment later in life. Thus, ageism represents a systemic challenge that influences all levels of the ecological system. Future research must focus on the development of evidence-based practices and interventions to disrupt the pervasive, invisible, contagious, and systematic nature of ageism.

Cross-References

- ▶ Age Discrimination in the Workplace
- ▶ Age Stereotypes
- ▶ Ageism in Healthcare
- ▶ Anxiety About Aging
- ▶ Language and Communication Disorders
- ▶ Self-Reported Ageism

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Caregiver Credits

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Synonyms

Family service credit; Pension credits

Definition

Caregiving is an essential part of economic and social human life as well as a crucial component of individual well-being of the dependent. However, because it is usually provided by families on an unpaid basis, it may cause an opportunity cost for the caregiver. Clearly, during the caregiving period, caregiver has to stay out of the labor force and cannot make any contribution to his/her overall pension benefits. In order to compensate for this loss of contribution, caregiver credit programs are designed and implemented increasingly in many countries. In short, caregiver credits are provided to caregivers for the time they spent out of the workforce to provide care for a dependent such as children, older adults, or persons with disability.

Overview

Many people, to a great extent female people, undertake the work of caring for their loved dependents without getting paid for it. While this "invisible labor" is a significant component of social solidarity and cohesion, it also has negative impacts definitely on caregivers' potential earnings from the labor market.

In order to turn this invisible labor into visible labor, caregiver credit policy was introduced in many countries. Even though the first examples of these programs are possible to trace back to around 1945, the widespread implementation only started to gain currency around the 1980s. Jankowski (2011), in this sense, argues that the first wave of caregiver credit programs in modern sense started in Sweden (1970s), Germany (1986), Norway (1992), and Switzerland (1998), and the second wave went into effect in Luxembourg (2002), Austria (2005), and Finland (2005).

The coverage of these programs was extended gradually through subsequent social security reforms in order to, for instance, include not only women but also men as well. Even though a vast majority of these programs designed to cover only the childcare periods at first, they were extended to cover other dependent individuals, such as older or sick relatives, too (White-Means and Rubin 2008).

As regards the most recent past, caregiver credit programs have become almost universal across the countries of the Organisation for Economic Co-operation and Development (OECD) and also an essential part of their social security schemes (D'Addio and Whitehouse 2009). Today, as a result of this extension, many states in Europe implement advanced caregiver credit programs within their public pension programs.

As an advanced liberal welfare state, the United Kingdom, for instance, carries out a caregiver credit program for caregivers who provide care to a child with disabilities or adult for at least 35 h per week. Another important feature of this program is being based on the means-testing method. Thus, in order to get the credit, the person under care must be receiving government benefits that are less than a disability designation (Munnell and Eschtruth 2018).

Germany is another successful example of the caregiver credit program. In Germany, working less than 30 h a week is the first condition for a caregiver to be covered by the program. In addition to this first condition, a dependent person under care must receive benefits through the general social protection scheme. The exact amount of the credit is determined by the number of care hours per week and the level of nursing-care dependency. As an essential feature of this program, there is no time limit for receiving the credits. As long as the conditions are met, the caregiver continues getting the credits (Munnell and Eschtruth 2018).

In contrast with Europe, there is no such long caregiver credits history in the United States. A bill, titled the Social Security Caregiver Credit Act, was launched only in 2017. This Act was built on the need for improving the financial well-being of caregivers generally. The primary objective here was to compensate for the retirement security benefits loss of caregivers during their caring periods due to being out of working life. However, clearly, caregiver credits are added to the total career earnings while calculating future social security benefits thanks to the bill. Apart from the given benefit, the bill includes two essential supports for caregivers in the family, too. The first is to establish a social security credit to bolster the economic prospects of unpaid care and the second one is to provide caregivers with added retirement security (NAC 2017).

Rationale and Objectives of Caregiver Credits

In recent years, analysts and policymakers have directed increasing attention to caregiver credit programs. However, this attention needs to be accompanied by the concerns of long-term fiscal sustainability of social security schemes in general. In this sense, in order to integrate caregiver credit programs into this main concern of decreasing overall costs in social security schemes successfully, governments attempt to reduce benefits, such as changing the calculation techniques and, on the other hand, increasing revenues such as increasing the contribution rates. Therefore, caregiver credit programs may mean a gain in social security in such an era when there is considerable pressure to decrease the costs globally.

The widespread extension of caregiver credits in a brief time in almost all developed countries with a few exceptions only is the result of a number of factors. First of all, today's neoliberal climate and its pressures to limit overall social expenditures resulted in substantive reductions in social security benefits. This made it even more urgent to find new ways to protect caregivers. Second, an increasing number of countries started to connect pension benefits directly to the lifelong earnings in the framework of cost-cutting measures in free explicitly defined benefits programs. Some countries even introduced mandatory defined contribution programs under strict rules. As the third and the last one, many countries aimed at reconciling care duties with employment in the scope of the attempts to substitute for the institutionalized provisions with interpersonal and family-based measures which are believed to be cheaper (Jankowski 2011).

As one of the pioneering countries in caregiver credit programs, Canada implements it under income tax measures package. Caregiver credit program, in this sense, is intended to reduce caregivers' federal income taxes and other hidden and invisible costs of caregiving duty as well as provide overall relief. Even though it is well-planned, the caregiver credit program in Canada does not provide much money for the caregiver, and there are strict rules and preconditions to be entitled to. Thus, the Canadian government contributes to only a moderate level of the costs borne primarily by private households (Torjman 2011).

In general, the essential reasons of the design and implementation of these programs are to employ more family-friendly policies, reward the social contribution of caregivers, increase female employment, and, in some cases, encourage new births as a part of broad pronatalist policies (Amarante and Tenenbaum 2018). There are also some cases where caregiver credits are implemented implicitly when the pensions are universal and based, for example, on residency. Caregiver credits, however, are criticized particularly from the feminist perspective to some extent by some authors. According to this view, these credits encourage and reproduce already existing traditional gender roles and domestic responsibilities of women (Gilbert 2006). Therefore, caregiver credits may mean the isolation of women within the family and to exclude them from the public sphere as equal citizens as men.

In the broadest sense, caregiver credits are considered typical to and common in developed countries. While the primary objective does not change from country to country, their design and implementation may vary to a great extent due to the objectives they have. The primary objective of caregiver credit program is, in this sense, to compensate for career cuts for caregivers and prevent the possible welfare losses stemming from staying out of the workforce and, therefore, paying less contribution to the pension system during caregiving periods. In this way, it is aimed to provide them with a more comfortable retirement period, at least, in financial terms. As expected, pension loss is even higher mainly in the countries where pension benefits are causally related to the active working duration.

Governments may also seek to promote higher fertility rates, to encourage new mothers to return to the labor force by offering a bonus to working caregivers, or only to reward the provision of unpaid care through caregiver credit program. Another common feature of these programs is to link credits to parenthood only; being married is not a necessity (Munnell and Eschtruth 2018). This mix of objectives has led to a significant variation in the design of caregiver credit programs across the world.

Designing Caregiver Credit Programs

The success of a caregiver credit program depends mainly on how it is designed. In this sense, there are a number of crucial issues that must be addressed thoroughly while designing a program. The first one is determining the optimum number of years an individual will be eligible to receive the credits. The second is about the way of calculation of the exact amount of the credit. The third one includes the decision of who is eligible to receive the credits, such as a mother, a father, or both. The fourth addresses the option of whether the individual has to leave the labor force altogether to receive the credit. Countries with caregiver credits display a large variety regarding these crucial issues. This variation is, to a great extent, determined by the particular objectives that each program follows and designed for (Munnell and Eschtruth 2018; Jankowski 2011).

Even though countries share similar targets, such as provision domestic care for recipients and decreasing the overall cost of institutionalization for both families and governments, each of them develops its own rules and methods to determine who would be the recipients of caregiving programs. In the US practice, for instance, only the working individuals can benefit from the federal Care Tax Credit (DCTC) if they pay a caregiver for caring for their child or another dependent. There are also age and health conditions as such being either under 13 or physically or mentally incapable of self-care. The program requires the care recipient to live together with the dependent in the same residence as another eligibility criterion as well. Even though there is no explicit means-testing mechanism, the federal program gives priority to older individuals who suffer from the greatest socioeconomic destitution (James et al. 2016). As regards the implication in Canada, the three-tiered tax credits system for caregivers, which was criticized as being complicated to understand, were attempted to simplify in 2017 by integrating them under one new Canada Caregiver Credit scheme. According to the new system, the caregiver credit can be shared by multiple caregivers providing care for the same relative. Older adults with a disability cannot benefit from the new caregiver credit program unless they live together with their adult children (Wouters 2017).

While designing caregiver credit programs, there is always the risk of exploitation by ineligible individuals. Put clearly, under specific design and targeting failures, the credits may go to higher-income individuals, who can, in reality, afford without getting paid for significant periods and, therefore, are not eligible at all. On the other hand, individuals from lower-income groups, who need to integrate the caregiving with at least part-time work, may be out of the coverage. That would be the case for one of the narrowest forms of caregiver credits, whereby credits are awarded only to parents who leave the workforce entirely (Jankowski 2011).

Even though a caregiver credit program is designed successfully, this does not guarantee that it would be entirely successful. The way how it is administered is equally crucial in the success of the program as well. The most significant administration failure would be the misspecification of the people in real need of. Targeting mechanism and eligibility determination may be extremely complex issues of the administration process.

Enabling the program sustainable regarding funding includes another vital risk for the success of the entire program. Even though other risks are attempted to cope with through diverse ways by countries, this final risk is addressed by a similar response, which is based on paying for caregiver credits out of general budget or from tax revenues.

Future Directions of Research

Caregiving responsibilities have a significant social and economic impact on both men and women. However, there is still much unknown about them. The vast majority of researches, to this end, approach the concept from technical points such as design and implementation of programs, differences between country experiences and income loss due to either working less than usual, or leaving the labor force earlier to care a loved one (NAC 2017). The human rights perspective is, however, generally disregarded, or not considered sufficiently in studies. In-depth analyses and researches including mixed methods and relating caregiver credits to the right of social security as a fundamental human right are needed. The relationship between the satisfaction level of the caregiver and the well-being of the dependent needs to be further explored. Future qualitative research also should focus on the match between expectations and perceptions of both the caregiver and the dependent. This new area of research may contribute to other related subjects such as aging in place and/or successful aging as well.

Summary

Caregiver credits are designed to realize specific objectives, such as improving benefit adequacy by compensating the period spent out of work because of caregiving duties, promoting higher fertility rates, balancing family and working life, rewarding unpaid care, avoiding from the high costs of institutionalized caring services, encouraging returning to work as early as possible after giving a childbirth, etc. There are distinct reasons for the implementation of caregiver credit programs. However, it is possible to assert that these programs are, to a great extent, the products of the attempts of decreasing the overall generosity of public pension schemes and linking pension programs with workers' lifetime earnings in a far stronger way through social security reform packages. Moreover, keeping older adults out of nursing homes and encouraging various caring in-place policies instead are considered as good complements for existing reform packages aiming at reducing the costs of institutionalization. In the scope of this strategy, it is claimed that the required funds for credits can be met through the reduction of expenditures for nursing homes (White-Means and Rubin 2008).

Even though essential motivations and objectives are similar, caregiver credit programs are designed and implemented in multiple ways. The answer to the question of which objective will be referred to as the essential objective depends heavily on the unique conditions of the given country.

Cross-References

▶ Benefits of Caregiving
▶ Caregiver Interventions
▶ Employment and Caregiving
▶ Fee-for-Service
▶ Gender and Caring in Later Life
▶ Pension Systems

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Caregiver Distress

► Caregiver Stress

Caregiver Identity

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Synonyms

Caregiver identity theory; Caregiver role

Definition

A cognitive construction that develops when individuals characterize themselves as a caregiver to a family member or friend, normally for those in need of support due to chronic illness or disability. Caregiver role identities serve as interpretive frames and sets of standards used by individuals to make sense of personal experiences, actions, and emotions, as well as guide subsequent behavior.

Overview

Family caregiver identity research highlights the salience of socially informed, shared expectations about and interpretations of caregiving. Peoples' self-descriptions of themselves change through providing care over time; this process is influenced by gendered and culturally specific role expectations, as well as interactions with others who reinforce identities.

Key Research Findings

Family caregiver identity is distinct from the enactment of particular caregiving behaviors or role performance. Some individuals may begin expecting and thinking about caregiving long before the onset of objectively defined care (e.g., anticipatory caregiving, Sörensen 1998), and a caring identity may continue even after the last episode of caring, as when former or bereaved carers become advocates for other carers (Larkin 2009). Moreover, family members may provide care without self-identifying as carers; evidence suggests that some carers are uncomfortable with this identity (Henderson 2001; O'Connor 1999). For instance, in one survey of over 4000 older adults in the United States, 15% of respondents reported providing various activities typically associated with caregiving, yet did not self-identify as a caregiver in response to a targeted question (AARP Caregiver Identification Study 2001).

There is little empirical research that directly addresses family caregiver identity. In a recent review of research pertinent to caregiver identity and its development among those providing care for adults with chronic disease (Eifert et al. 2015), only 23 articles were identified. Summarizing this literature, the review authors identify several important influences on family caregiver identity development, including roles or responsibilities, familial ties and changes in relationships, and social influences (Eifert et al. 2015).

Most existing academic research applies a developmental or stage approach to caregiver identity, although emerging research also illustrates the variability and fluidity of caregiver self-identification (Hughes et al. 2013; O'Connor 2007). Considering developmental approaches, Montgomery and Kosloski's Caregiver Identity Theory (2013) provides a promising base for understanding how caregiver identities emerge over time. They propose that caregiver identities develop as family members reconcile what they are doing with their expectations and understandings of their role identity; the disparity between responsibilities and expectations can create dissonance and stress, and caregivers may be motivated to change their identities so as to address this disparity (Montgomery and Kosloski 2009). They add:

> Identity change [is] usually not a smooth, continuous process. Rather the assumption of a caregiver identity is an iterative process of change, which alternates between periods of relative stability wherein a role identity is maintained through small adjustments in behavior or perceptions, and periods when there are significant shifts in the caregiver's identity that are associated with the acceptance of new norms for behavior. (Montgomery and Kosloski 2013: 137)

In relation to the expectedness of caregiving, one recent Canadian study (Guberman et al. 2011, 2012) found that baby-boomer caregivers tended not to view caregiving as a natural part of the life course or normal familial roles. The authors conclude that in the context of North American social and cultural change, women in particular are also less likely than in the past to primarily self-identify in terms of traditional familial roles, and wish to maintain multiple identities (including caregiver) simultaneously. Other research indicates this phenomenon may be most salient in North American culture, for instance, in contrast to Japanese (Wallhagen and Yamamoto-Mitani 2006) and other ethno-cultural groups of carers (Martin 2000). Some suggest that when a person does not expect caregiving as a part of their normal life course, this is associated with higher perceived stress and burden and reduced satisfaction among those providing family care (Martin 2000; Kirsi et al. 2000). Complicating the interpretation of research findings, however, is an apparent lack of consensus in the literature about whether the perception of care for older family members as natural and expected facilitates or impedes self-identification as a caregiver.

Identities are social – people internally negotiate their own identities in ways that are informed by their social contexts, and identities can be supported or not (or even stigmatized) by external others (Carpentier 2012; O'Connor 2007). Indeed, "individuals may be unaware of the label but through interactions with others, they develop an awareness and eventual identity related to caregiving" (Eifert et al. 2015: 364). The now-classic work by Finch and Mason (1993) demonstrated how women making initial decisions to care often developed "caring" or "responsible" reputations that served to reinforce the tendency for them to be viewed by others as the appropriate caregiver in the family.

Sabat (2002, 2010) emphasizes that identity construction in persons with dementia and family caregivers is interdependent; caregiver identity development is shaped by and shapes relational connections between individuals, as roles and normative responsibilities in relation to one another change with the onset of illness and care provision (Eifert et al. 2015; Goldsteen et al. 2007; Hayes et al. 2009). In this process, gendered and culturally specific expectations that shape understandings in families of who should do what, and for whom, become salient (Eifert et al. 2015). If the other person in the relationship can no longer perform their role (e.g., as parent, spouse), this may also motivate identity shifts among caregivers (Eifert et al. 2015). Caregiver identity may also develop when family members develop an intense sense of responsibility vis a vis other network members, for instance, when they do not trust other family members or professionals to provide competent care (Goldsteen et al. 2007; Henderson 2001).

Caregiver identities can exist alongside other role identities in one individual, and caregiver activities can shape these other role identities in important ways (e.g., Calasanti and Bowen 2006; Heward et al. 2011). Yet Eifert et al. (2015) suggest that when care provision intensifies and leaves little time for other roles, previous self-identities are eroded, and caregiver identities may be developed to fill the void: “individuals do not just gain a new identity as a caregiver but see previous identities fade away or become less relevant because of caring responsibilities” (360). Building on early work on self-identity loss when intensively caring for persons with dementia (and subsequent risks to psychological wellbeing and self-esteem: Skaff and Pearlin 1992), scholars have examined how people might preserve or adjust self-identities during care provision (e.g., Perry 2002; Karner and Bobitt-Zeher 2005; Sabat 2010).

Many believe that caregivers should be encouraged to develop a caregiver identity, to facilitate their access to and use of supportive formal services (Andreasson et al. 2018). For example, this may help them recognize their own needs as independent from those of the care recipient (Dobrof and Ebenstein 2003; Harding and Higginson 2001; Henderson 2001; Paoletti 2002). However, the evidence is not entirely clear, since overly strong identification with a caregiver role might equally promote caregiver need minimization or suppression, for instance, as caregivers strive to protect the identity of the care recipient (Moore and Gillespie 2014).

Caregiver self-identification has also been suggested to promote an empowering “sense of belonging and connection to a broader community” (O’Connor 2007: 165) and potentially reduce caregiving stress (Montgomery and Kosloski 2009). In contrast, Sabat (2010) recommends that caregivers’ network members should reinforce their originally existing valued self-identities that have been threatened by the onset of care, preventing engulfment within a role that is arguably devalued within broader social structures. Recent work by Riley et al. (2018) further suggests a need to protect spousal caregivers’ preexisting relational identities with their partner. Moreover, when caregivers are prompted to adopt a caregiver identity (especially as a dominant role), this can involve difficult emotions (discomfort, ambivalence) and may entail emotion work especially for those who do not wish to self-identify (O’Connor 2007; Molyneaux et al. 2011). O’Connor (2007) also concludes that overly strong caregiver identification may inadvertently result in marginalizing or eroding the sense of identity of care recipients (see also Eifert et al. 2015).

Examples of Application

That many family caregivers do not self-identify is a methodological concern (since caregiving research tends to recruit self-identified caregivers), as well as a challenge for advocates for those who want to make unpaid work more visible and valued.

Ultimately however, academic and policy interest in caregiver identity has been driven by an interest in how identity might shape or contribute to caregiving behavior (Eifert et al. 2015). However, Caregiving Identity Theory proposes that behaviors or practices also shape identities (Montgomery and Kosloski 2009). Research in this area is also important because of concern for how caregiver identity may be connected to well-being and caregiver outcomes, whether through the stress generated when identities do not match behavior, or through unmet needs and problems accessing supportive services. Increasing concern with the latter has informed the development of caregiver assessment tools for use in clinical practice. These tools are in part intended to encourage caregivers if not to self-identify, to at least to recognize their own distinct role and needs. The use of one such tool, the USA-based TCARE protocol, led to lower identity discrepancy and stress burden in caregivers (Kwak et al. 2011). Other similar tools have had variable results, with more evaluations focusing more on the impact on professionals (Aoun et al. 2015; Keefe et al. 2008). More generally, however, existing research on caregiver self-identification points to the need for caregiver support programs to focus outreach efforts on those who may not self-define as caregivers, as well as those who do (Corden and Hirst 2011; Dobrof and Ebenstein 2003).

Future Directions of Research

There is much still unknown about caregiver identity development and how this varies over time and in relation to particular relationships, families, and societal contexts. In-depth and mixed-methods research into the processes and effects of self-identification in different groups is needed, so as to address discrepancies in existing research. Connections between self-identification, role expectedness, and caregiver satisfaction and well-being need to be further explored in ways that account for the simultaneous existence of other, potentially competing role identities among caregivers. Future qualitative research also should focus on how caregiver self-identification is expressed (or not) in talk about the entire life course. For instance, Miller et al. (2008) explored how caregivers drew on past parenting and intergenerational transmission narratives when interpreting their current caregiving identities. They also imbued their caregiver identities with a sense of competence derived from previous family and work experiences. Such meaning-making processes in relation to identity may provide insights into how best to support caregivers. In addition, more exploration is needed of how external others (especially health care practitioners) define and shape carers' identities in face-to-face interactions. Quantitative methods can also contribute to developing measures of carer role identification that would allow for testing links between identification, norms, care behaviors, and outcomes.

Summary

In contrast to research into caregiving role enactment, caregiver identity research focuses on what people think they should or should not (or will or will not) do for friends and family members in need of long-term support, and whether and how these expectations, internalized within particular role identities, shape caregiver interpretations of their experiences and their future well-being. Theoretically and practically, the issue of family caregiver identity is particularly complex and necessitates a considerable expansion of research in this area.

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Cross-References

► Caregivers' Outcomes
► Caregiving and Ethnicity
► Double-Duty and Triple-Duty Caregivers
► Former Caregivers
► Social Services Utilization

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Caregiver Identity Theory

► Caregiver Identity

Caregiver Interventions

► Interventions for Caregivers of Older Adults

Caregiver Planning

► Preparation for Future Care: The Role of Family Caregivers

Caregiver Preparedness

► Preparation for Future Care: The Role of Family Caregivers

Caregiver Psychological Stress

► Caregiver Stress

Caregiver Role

► Caregiver Identity

Caregiver Stress

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C

Synonyms

Caregiver distress; Caregiver psychological stress; Family caregiver stress; Informal caregiver stress

Definition

Caregiver stress is defined as a state of mental or emotional strain or tension resulting from demanding circumstances (Hunt 2003; Llanque et al. 2016; Pearlin et al. 1990).

Overview

Caregiving is often demanding and stressful. Caregivers are not only physically engaged in basic activities of daily living (ADLs) and instrumental activities of daily living (IADLs) but also psychologically troubled by care recipients' behavioral and emotional challenges. As their stress accumulates, caregivers become increasingly prone to physical and psychological consequences that can jeopardize the quality of care by, for example, diminishing their decision-making ability and capacity to handle emergencies. To date, researchers have identified, examined, and compared three types of caregivers (i.e., grandparent caregivers, adult–child caregivers, and spouse caregivers), as well as developed and implemented interventions, some involving technological assistance, to alleviate stress among caregivers and, in turn, contribute to the development of evidence-based interventions for caregiver stress.

Key Research Findings

Causes of Caregiver Stress

Factors of caregiver stress are often called "caregiving stressors." In general, stressors are the conditions, experiences, and activities that cause stress, and in caregiving contexts, stressors emerge as either primary or secondary stressors. Primary stressors arise from the delivery of direct care, which can involve providing assistance to care recipients with tasks that they can no longer perform independently; such tasks can include six ADLs (i.e., bathing, dressing, toileting, transferring, continence, feeding) and eight IADLs (i.e., ability to use telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medications, ability to handle finances) (Lawton and Brody 1969; Katz 1983). Having to perform those activities for care recipients can restrict the personal lives, social lives, and employment opportunities of caregivers. While delivering care, caregivers are sometimes troubled with care recipients' behavioral problems (e.g., verbal and physical aggression, agitation, hyperactivity, and aggression) and emotional problems (Wilks et al. 2011). By contrast, secondary stressors are associated with the cognitive evaluation of the demands of direct caregiving, feelings of uncertainty and overload, and the inadequacy of coping resources (Lou 2010; Pearlin et al. 1990).

Outcomes of Caregiver Stress

The stressors experienced by caregivers are multifaceted and have the potential to both positively and negatively affect their physical and psychological well-being in direct and indirect ways (Gaugler et al. 2009; Rivera 2009; Rowe et al. 2010). Developed in the early 1990s, Pearlin's stress process model (SPM) has been a dominant framework for examining outcomes of caregiver stress. According to the SPM, stress can cause severe consequences, including mental illness and poor well-being, if caregivers do not cope with it well (Hilgeman et al. 2009). Research on caregiving has highlighted several protective factors that moderate caregiver stress, including personal mastery, a sense of self-efficacy, and access to coping resources (Harmell et al. 2011).

Consequences of stress upon the physical well-being of caregivers include difficulties with sleeping (Rowe et al. 2010), cardiovascular disease (Haley et al. 2010), poor immune functioning (Lovell and Wetherell 2011), and even increased risk of death mortality (Fredman et al. 2010). Ample research has shown that caregivers are prone to experiencing fear, hopelessness, mood disturbances, depression, and anxiety (Lou et al. 2011; Markey 2015; Rivera 2009; Stenberg et al. 2010). Caregivers have also reported feeling socially isolated (Robison et al. 2009) (See "▶ Social Stress"), and several studies have shown that rates of depression and anxiety among caregivers are no less than and can even surpass those of care recipients (McLean et al. 2008; Rivera 2009). Empirical evidence has additionally revealed that depression among caregivers was an important predictor of poor quality of care, the abuse of older adults, and premature institutionalization (Gaugler et al. 2009; Wiglesworth et al. 2010).

Despite those potential difficulties, numerous caregivers have also reported personal growth and improved personal relationships with care recipients amid experiences with caregiver stress (Harmell et al. 2011; Lou et al. 2015; Mackenzie and Greenwood 2012). In a systematic review of literature addressing caregivers' experiences with stress in caregiving, Mackenzie and Greenwood (2012) identified a range of positive experiences in providing care for sufferers of stroke and other long-term illnesses, including a greater understanding of oneself, moments of joy, increased pride in personal capacity to navigate new crises, feelings of being appreciated, and increased self-esteem (See ▶ "Stress and Coping Among Older Adults"). Caregivers have also reported gains and rewards, such as being in good or better health, increased gratification, improved relationships with care recipients, and increased meaning and purpose in life (Harmell et al. 2011).

Caregiver Stress Among Different Types of Caregivers

Subgroup differences among caregivers, especially in terms of gender, relationship to care recipients, and diseases cared for, are significant factors of varying levels of caregiver stress (Liu and Lou 2017; Penning and Wu 2015; Pinquart and Sörensen 2011). In terms of gender, women experience more severe caregiver stress than men (Penning and Wu 2015), possibly because women tend to employ emotionally focused approaches in performing caregiving tasks, whereas men tend to employ strategic approaches (McDonnell and Ryan 2013).

In terms of relationship to care recipients, grandparent caregivers, adult–child caregivers, and spouse caregivers all experience a high level of depressive symptoms and unhappiness (Liu and Lou 2017). Among those types of caregivers, grandparent caregivers exhibit the greatest stress in terms of effects on physical health (Broussard 2010), whereas spouse caregivers experience the most emotional stress and financial problems (Pinquart and Sörensen 2011).

By type of disease cared for, caregivers of individuals with cancer, dementia, heart failure, and stroke tend to experience significant stress and poor quality of life (Collins and Swartz 2011). Those chronic conditions can prompt various disease-specific scenarios given the specific problems and targeted coping strategies associated with the conditions. (See ▶ "Caregiving Across Neurodegenerative Diseases") Moreover, most caregivers face difficulties with seeking disease-specific help and caregiving resources (Collins and Swartz 2011).

Interventions to Support Caregivers

Evidence-based practices have been developed to support caregivers, especially to reduce the caregiving burden or enhance the quality of life among caregivers, if not both. Disease-specific interventions focused on cancer, dementia, and stroke are more established than interventions for other conditions (See ▶ "Quality of Life"). The American Cancer Society provides various disease-specific programs to assist caregivers in reducing their stress and increasing their quality of life, including the Patient Navigator Program for personal cancer support and Reach to Recovery for breast cancer support (Collins and Swartz 2011). Similarly, the Alzheimer's Association provides various resources for care and a safety program for caregivers of individuals with dementia (Collins and Swartz 2011), while the National Stroke Association offers two disease-specific programs for caregivers of sufferers of stroke: the Stroke Center Network for rehabilitative stroke care and the Professional Society, which provides professional support and education (Collins and Swartz 2011). In the collaboration of health-care and social care resources, family-oriented care management has empowered families to provide support to relatives following their discharge as patients (Lou 2018). Because supporting caregivers in the community is a complex process, the ecological model of health behavior, a framework focusing on behavior that related to environmental and policy, with the influence of social and psychological aspects, is the most effective in changing behavior and behavior-specific cases (Sallis et al. 2015). It has recently been advocated to assist in identifying the risks and resilience of caregivers and further developed to reduce their specific types of caregiver stress (Capistrant 2016; Mullins et al. 2015).

Amid the rapid rise of technological advances, different types of technology-driven interventions using websites, virtual reality, and the Internet of Things have been integrated with health- and motion-monitoring devices in order to reduce caregiver stress (Godwin et al. 2013; Rghioui et al. 2014). Such interventions have even been identified as more effective than face-to-face interventions for reducing caregiver stress (Hu et al. 2014) and improving mental health status, self-efficacy, neuroticism, social support, and stress responses, especially those offered by the Caring for Me website (Marziali and Garcia 2011). Caregivers' perceived stress and stress-related symptoms decreased significantly as a result of using the iCare Stress Management program versus a traditional intervention (Kajiyama et al. 2013) (See ▶ "Technology and Telemedicine"). Similar tools have had similar results with caregivers of diverse demographic backgrounds (Lorig et al. 2012; Smith et al. 2012).

Future Directions for Research

Future research on caregiver stress should place greater emphasis on the positive consequences of stress, including resilience, positive growth, wisdom, and meaning making (See ▶ "Benefits of Caregiving"). New theoretical frameworks that extend the SPM should be developed and examined to understand, explain, and predict caregiver stress and its positive as well as negative consequences. More research comparing the effects of traditional and technology-driven interventions or integrated interventions on reducing caregivers' burden and enhancing their well-being is also encouraged.

Summary

Caregiver stress is unavoidable and demanding. Although caregiving stressors are multiple, the consequences of stress among caregivers can be positive and negative. Negative consequences include not only poor physical and mental health but also poor quality of care delivered and even abuse of care recipients, positive consequences, currently understudied, include personal growth, improved personal relationships with care recipients, and even new avenues for meaning making. To mitigate the negative consequences and promote the positive ones, evidence-based interventions have been developed that apply both traditional and technology-assisted means (See ▶ "Gerontechnology").

Cross-References

- ▶ Benefits of Caregiving
- ▶ Caregiving Across Neurodegenerative Diseases
- ▶ Care Needs
- ▶ Formal and Informal Care
- ▶ Gerontechnology
- ▶ Personal Care
- ▶ Primary Caregivers
- ▶ Quality of Care
- ▶ Quality of Life
- ▶ Resilience
- ▶ Social Stress
- ▶ Stress and Coping Among Older Adults
- ▶ Technology and Telemedicine

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Caregiver Support

► Interventions for Caregivers of Older Adults

Caregivers' Outcomes

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Synonyms

Caregiving providers; Caregiving role; Carers; Family caregiver

Definitions

Family caregiving refers to the efforts of family members to assist an individual with physical health and/or mental health problems and with difficulties in performing everyday activities.

Outcomes in the context of family caregiving have two meanings: (1) outcomes of engagement in the caregiving role and (2) the primary dependent variables in an intervention study, i.e., the major changes that are hypothesized to result from the intervention.

Overview

Extensive research over the past 40 years has explored the stress experienced by family caregivers (See ► "Caregiver Stress"). Caregiver outcomes have been characterized in two ways, as the end point of the effects of engagement in the caregiving role and as hypothesized changes expected to result from exposure to a treatment or intervention (See ► "Interventions for Caregivers of Older Adults"). Whatever the goal of the research, a particular challenge in the selection of outcomes is the heterogeneity of caregiving situations and stressors, and among caregivers themselves, their age, relationship to the care recipient, resources, and so on. Nevertheless, caregivers of persons with different illnesses or disabilities and different amounts of engagement in the role are often grouped together in studies. Even when the focus is on one group of caregivers, such as those providing help to a person with dementia, there is typically considerable heterogeneity within that group among caregivers' commitment, characteristics, and experiences.

Despite the heterogeneity among caregivers and care situations, the outcomes in caregiving research have generally been considered within a narrow focus, specifically, the caregiver's health and emotional well-being. Health has largely been measured with self-report measures of caregivers' symptoms and diagnosed illness, though recent research has used biomarkers related to the stress process (Lovell and Wetherell 2011). Well-being is usually measured by depressive symptoms, though scales measuring other emotions as well as global distress scales are sometimes included. This focus on health and emotions is derived from stress and coping models (e.g., Aneshensel et al. 1995), which have dominated the field (See ► "Stress and Coping Among Older Adults"). From this perspective, health and well-being are the temporal end-points of a process characterized by stressors and stress mediators or moderators (e.g., stress appraisals, coping, social support), which lead to changes in health and emotional well-being. Stress process models are supported by strong correlational evidence that caregiving stressors (e.g., care tasks, care recipient disability) are associated with poorer health and psychological well-being (Aneshensel et al. 1995; Watson et al. 2018). Both caregiving stressors and their effects on health and well-being outcomes have substantial implications for overall quality of life among caregivers; however, relatively few studies address quality of life or similar measures (e.g., life satisfaction) as a direct outcome of engagement in caregiving or as an explicit target of caregiver interventions.

Although stress process models have been useful in guiding research, there is a growing recognition that health and emotional well-being do not adequately represent the possible range of outcomes that might be relevant to caregivers' experiences (e.g., Fortinsky et al. 2013; Marino et al. 2017). The argument for a wider range of outcomes is based on both conceptual and empirical grounds. First, although stress models imply a temporal progression (e.g., stressors lead to outcomes), it has always been assumed that these models describe an ongoing dynamic process whereby effects of stressors accumulate and diminish over time. Moreover, "outcomes" such as depression and health problems have reciprocal effects on other elements of the stress process, for example, increasing the likelihood of encountering new stressors and leading to poorer mobilization of resources in responding to a stressor (Aneshensel et al. 1995). Additionally, consistent with cognitive theories of depression, depressive symptoms may lead to overly negative appraisals of caregiving events and caregivers' own resources, thereby decreasing their ability to manage those events. In other words, factors considered as outcomes, such as depressive and health symptoms, can precipitate new stressors and moderate caregivers' abilities for managing stressors.

A second consideration is that many caregivers do not experience depressive symptoms or worsening health (e.g., Fortinsky et al. 2013; Marino et al. 2017; Pinquart and Sörensen 2003a). Drawing on multidimensional models of well-being, Marino and colleagues propose that research on caregivers should go beyond hedonic (affective) measures that are often negative in valence and incorporate eudaimonic dimensions of well-being as outcomes, such as feelings of mastery in the care situation and deriving meaning from caregiving. Fortinsky et al. (2013) suggest that a key element in caregiving is resilience, specifically being able to maintain positive affect despite unremitting care demands and to bound back quickly from negative experiences (See ► "Resilience: Measures and Models"). This multidimensional approach has broad relevance for caregivers and addresses domains that are critical to their adaptation.

The narrow focus on affective distress and worsening health has been especially problematic in intervention research with caregivers. Most interventions have used depressive symptoms as an outcome measure. The inclusion criteria for studies, however, have mainly been based on role status (i.e., being a caregiver) and not on whether caregivers have depressive symptoms. In effect, researchers are making the implicit assumption that all caregivers will be experiencing distress and depression. Yet many participants in caregiver intervention trials have had low baseline depressive symptom scores, as well as low scores on other measures of emotional distress, caregiver burden, or health problems that may be used as outcome measures. Consequently, statistical power is decreased, since caregivers with low initial scores cannot show improvement. As a result, most studies report fairly small treatment effect sizes, even when findings are statistically significant (Zarit 2018). The exceptions tend to be studies where depressive symptom scores were relatively high at baseline or where studies have selected caregivers with higher baseline depressive symptoms and who could therefore benefit from treatment (e.g., Perlick et al. 2010).

It can be argued that this broad recruitment strategy might have a preventive effect for caregivers not experiencing depressive symptoms or other types of distress. That is a testable proposition, but some caution is needed. Some evidence suggests that giving treatment for a problem people do not have may result in adverse effects such as evoking negative emotions (Baucom et al. 2006). Furthermore, this approach may detract from resources that could be better used to support caregivers with their current issues and concerns.

A fundamental question that needs to be asked is why caregivers who are experiencing little or no depressive feelings or other distress enroll in interventions. A more precise understanding of what motivates caregivers to seek interventions and what goals they have would lead to a more varied and meaningful set of outcomes. Ultimately, this knowledge will inform targeted and person-centered interventions that address the issues that caregivers are most concerned about. Depression and health should be targets for interventions when risks in these domains are present or when prevention is an explicit goal of a study. In other circumstances, there is a need to identify outcomes that are appropriate for the sample and the intervention goals.

Next, research findings for major caregiver outcomes are discussed. Given the emphasis in the literature, this review focuses on outcomes related to the caregiving stress process, along with positive caregiving outcomes and placement of the care recipient. Other issues pertinent to the selection and application of outcomes are then considered, including sample characteristics and outcomes among both caregivers and care receivers. Finally, recommendations for future research on family caregiving outcomes are described.

Key Research Findings

Depression as an Outcome

Depression is probably the most frequently reported outcome. The term "depression" has two meanings, as an indicator of emotional well-being and as a marker of an affective disorder. Caregiver studies typically use scales that yield a score of total symptoms. Use of measures that yield diagnostic categories is less common. A widely used scale, the Center for Epidemiological Studies Depression Scale (CES-D), produces an overall sum score and also has a validated cutoff point that identifies persons with clinically significant levels of depression (Lewinsohn et al. 1997; See ► "The Center for Epidemiologic Studies Depression (CES-D) Scale"). The value of the cutoff is that it identifies people who are more likely to have or be at risk for a depressive disorder and respond to treatment for depression. Some studies use this cutoff, but other research creates categories of low and high depression based on distributions of scores on the CES-D or other measures, often without validating the cutoff.

Most views of depression implicitly assume a continuum from no symptoms to severe symptoms. The difference between a person with a high score and one with a low score on a depression scale is meaningful. The person with a high score is experiencing considerable distress and may meet criteria for a depressive disorder. If that person experiences a large decrease in symptoms during an intervention, that represents a meaningful change that is likely to be reflected in the person's overall functioning. By contrast, there is less known about the significance of differences among people who report low scores and do not meet diagnostic criteria. Furthermore, it is not known what the value might be, if any, of a person who has a low score initially on a depression scale and shows a drop of one or two points during an intervention. There is little evidence of whether or not that type of change makes a meaningful difference in the person's life, yet that is often the degree of change reported in caregiver interventions. Likewise, in nonintervention studies, where much of the sample falls in lower ranges on a depression scale, small differences in scores among participants may reflect stable individual characteristics rather than meaningful discrepancies in functioning or quality of life.

Despite these caveats, depression is important to examine as one of the possible outcomes of caregiving. Rates of depression symptoms among caregivers are higher than the noncaregivers, though differences are smaller in population-based samples compared to clinical or self-selected samples (Marino et al. 2017; Pinquart and Sörensen 2003a). Selection effects may account for these findings, as highly stressed caregivers may be more likely to volunteer for clinical studies and less likely to participate in population-based studies.

Caregiver depression scores are higher among women than men, and are most strongly associated with the care receiver's behavioral and psychological problems (Pinquart and Sörensen 2003b; Watson et al. 2018; See ► "Behavioral and Psychological Symptoms of Dementia"). Other factors associated with depressive symptoms include amount of care receivers' cognitive and physical impairment, low caregiver self-efficacy and mastery, inadequate income, and unmet caregiver needs and high activity restriction (Fortinsky et al. 2013; Pinquart and Sörensen 2003a; Watson et al. 2018).

Most studies are cross-sectional. Caregiving, however, often extends over a multiyear period, and so longitudinal research provides a different and valuable perspective on risk of depression. Studies that have followed caregivers over several years report that between 40% and 69% have consistently low levels of depression, around 20% have continually high depression, and the remaining caregivers have fluctuating periods of high and low depression (e.g., Joling et al. 2015). It will be important for future work to proactively address the needs of caregivers who are at risk for sustained high levels or increasing depression, such as those in highly stressful care situations with minimal resources.

Other Dimensions of Distress

Other dimensions of emotional distress, particularly anxiety and anger, have received some attention in the caregiving literature (Watson et al. 2018). Like depression, anxiety has a dual meaning, referring to symptoms and to disorders where anxiety is a prominent feature. Cooper et al. (2007) conducted a systematic review that identified 33 studies that used measures of anxiety. They found that anxiety affected a quarter of caregivers of persons with dementia and that scores were higher than among matched controls who were not caregivers. Using a structured diagnostic instrument that was administered to spouse caregivers every 3 months, Joling et al. (2015) reported that 54% of the sample met criteria for an anxiety disorder at one or more points during the observation period. There was, however, considerable overlap of depressive and anxiety disorders, with 32% of the sample receiving both diagnoses.

Anger is a powerful emotion that has been found to occur frequently among caregivers of persons with dementia (Coon et al. 2003). Using psychoeducational interventions that focused on either anger or depression, Coon et al. (2003) found that both interventions had positive effects on both emotions. Anger was also found to decrease among caregivers of persons with dementia with use of adult day care (Zarit et al. 1998). In a subsequent study (Zarit et al. 2014), anger and depression were found to be lower on days the person with dementia used adult day care compared to days they provided all the care. Additionally, both anger and depressive symptoms were associated with daily cortisol responses.

Subjective Stress and Burden

Measures of burden and subjective stress are role-specific ways for assessing impact on caregivers' lives. Caregiving leads to changes in the relationship of caregiver and care receiver, which may upend the pattern of exchanges of support and affection. Caregiving may also come to dominate a caregiver's time, diminishing valued activities with family and friends or at work that provide enjoyment and meaning. Feelings of subjective stress and burden result from these changes and represent a fundamental outcome of the caregiver's involvement. That's not to suggest that all caregivers experience these feelings, but rather there is the potential for all caregiving situations to generate subjective stress or burden.

Although general stress measures are sometimes used in caregiving research, role-specific stress measures tap into specific experiences in a caregiving context. Role overload (i.e., the perceived time and energy costs of caregiving) and role captivity (i.e., feeling trapped in the care role) are two widely used measures that have been responsive to the effects of interventions (Gaugler et al. 2018; Zarit et al. 1998).

Burden has been studied extensively in the caregiving literature (Pinquart and Sörensen 2003b). Although definitions of burden vary,

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most measures examine how caregivers perceive the effects of assisting a relative on their personal life and on social and family relationships and activities. Financial burden is also sometimes included. Burden shares some conceptual overlap with more global aspects of subjective well-being such as quality of life; however, it is distinct in that it centers on how different life areas are directly impacted by caregiving. Burden measures show strong associations with care stressors, particularly care receiver behavioral and psychological symptoms (Pinquart and Sörensen 2003b). They also show a moderate inverse association with social support (del-Pino-Casado et al. 2018).

Burden and other role-specific measures have been frequently used as an outcome measure in intervention research (Pinquart and Sörensen 2003b). They may be particularly useful as outcomes because they assess the specific effects of stressors that are intrinsic to the caregiving role.

Health Outcomes

Like depression, health has received considerable attention in the literature. Measures have included subjective ratings of health, objective indicators such as illness incidence and prevalence, and biomarkers of health risk such as blood pressure or cortisol. In an early, comprehensive review, Pinquart and Sörensen (2003a) reported differences between caregivers and noncaregivers in both subjective and objective measures of health, though differences were smaller than those found for depression, stress, and burden. The effects were also greater in studies that included only dementia caregivers, compared to mixed or nondementia samples

More recent work has called into question whether caregivers' health is universally at risk. In a landmark paper, Roth et al. (2015) observed that several recent population-based studies show reduced mortality and health risk among caregivers. They suggest that these findings indicate selection into the role may be associated with better health, and that there are possible health benefits of caregiving activities under some circumstances. In addition, caregivers experiencing health problems may be less likely to enroll or continue to participate in population-based studies than in convenience or clinical samples.

Although Roth et al. (2015) provide a valuable corrective to the excessive emphasis on negative effects of caregiving, it is imperative to acknowledge the extensive literature that documents a pathway from stressors to physiological markers to illness (Lovell and Wetherell 2011). A growing body of research reports associations of caregiving stressors and physiological changes. Biomarkers have included measures of the hypothalamic-pituitary-adrenal axis such as cortisol, indicators of cardiovascular risk such as C-reactive protein and high blood pressure, and measures of inflammation such as Interleukin-6. Studies have demonstrated improvement in caregivers' biomarker levels with intervention (e.g., Klein et al. 2016; Moore et al. 2013). Recent work has also found associations of care stressors and biomarkers with decline in functional health (Liu et al. 2017). Thus, while many caregivers appear to be resilient to health declines, those with greater care-related stress may be more susceptible to maladaptive biological responses that increase risk of chronic illness and disability.

Positive Caregiving Outcomes

Positive outcomes among caregivers such as psychological resources are an important direction for broadening the scope of caregiving outcomes (See ► "Benefits of Caregiving"). Using a caregiving subsample drawn from the Midlife in the United States (MIDUS) study, Litzelman et al. (2017) evaluated change in psychological resources and links to caregiver well-being over a 10-year period. Caregivers with increasing or high-stable personal mastery reported better affect, more positive social relationships, and higher levels of self-acceptance, autonomy, personal growth, and environmental mastery than those with low-stable scores. Increased persistence in goal striving (primary control) was linked to greater personal growth and environmental mastery, whereas increasing or high-stable positive reappraisals (secondary control) were associated with better affect. This study illustrates the pivotal influence of psychological resources in maintaining multiple dimensions of caregiver well-being.

With regard to care-related positive outcomes, caregiving gains (i.e., perceived rewards or uplifts from caregiving) have been found to mitigate caregiving stress. Finding meaning in the care role, for instance, partially mediates the association between caregiver burden and mental health among spouses caring for a partner with dementia (McLennon et al. 2011). Likewise, among family caregivers of older adults with Alzheimer's disease (See ► "Alzheimer's Disease"), positive aspects of caregiving mediate how care recipient depression is linked to caregiver reports of burden, anxiety, and depression (Wang et al. 2018). These findings highlight the importance of targeting caregiving gains in interventions to prevent or reduce care-related stress.

Relatively few interventions target positive aspects of caregiving, yet this may be a key strategy to promote caregiver resilience (Fortinsky et al. 2013; Marino et al. 2017). Cheng et al. (2017), for example, developed a benefit-finding intervention to restructure negative appraisals and identify caregiving gains among people caring for an individual with Alzheimer's disease. In a double-blind home-based randomized controlled trial, caregivers who received the benefit-finding intervention showed gains including significant reductions in depressive symptoms relative to caregivers receiving standard or simplified (lectures only) psychoeducation. These gains were primarily the result of increased self-efficacy in controlling upsetting thoughts. Inclusion criteria for these trials required at least mild depressive symptoms (scoring $\geq$3 on the Hamilton Depression Rating Scale; See ► "Hamilton Rating Scale for Depression") to ensure that improvements in caregiver distress were possible.

Placement of the Care Recipient as an Outcome

Placement of the care recipient is sometimes used as an outcome in caregiving studies in order to identify factors associated with placement and to examine whether interventions can delay placement. Supporting caregivers to help keep disabled older persons at home is of considerable importance. Most people prefer to live in their own home. Furthermore, the cost of nursing home care places considerable strain on families and society (See ► "Aged Care Homes"). Interventions with caregivers to delay placement have generally been ineffective (e.g., Fox et al. 2000). One reason is that many of these interventions have not presented delay of placement as a goal, and so it may be that at least some caregivers in those studies did not share that goal. Bolstering this point, there is evidence that some caregivers use services as a way of transitioning care from home to institution (Zarit et al. 1999).

One exception is the New York University Caregiver intervention (NYUCI), which reported a significant delay in institutional placement among spousal caregivers in the treatment condition by over a year compared to a control group (Mittelman et al. 2006). An adaptation of the NYUCI that served offspring of the person with dementia had similar effects (Gaugler et al. 2013). In another study of placement, wives using adult day care placed their husbands sooner than a control group not using adult day care, but daughters who used adult day care kept parents at home longer than daughters in the control group (Cho et al. 2009).

Examples of Application

Depression and Health of Caregivers

In contrast to the vast majority of caregiver interventions that assume all caregivers are vulnerable to depression or health risks, interventions could instead focus on caregivers who are experiencing or at risk for these problems. Indicated prevention approaches for caregivers with some symptoms but no disease or disorder may be especially beneficial. In a study of 725 caregivers of a person with dementia across an 18-month period, for instance, higher initial depressive symptoms and worse self-rated health were the strongest risk factors for depression (Joling et al. 2012). Pinpointing characteristics of the caregiver and care situation that confer heightened susceptibility to mental and physical health conditions will help allocate limited resources toward caregivers in greatest need.

Furthermore, studies that focus on at-risk caregivers can consider mediating and moderating processes that explain long-term changes in outcomes of interest. In a study of caregivers of older adults with Alzheimer's disease, self-efficacy for controlling upsetting thoughts was found to partially mediate the association between caregiver burden and depression over the course of a year (Grano et al. 2017). This finding suggests that training caregivers in the successful management of negative appraisals may protect them from harmful mental health consequences. Potential mediators of treatment effects elucidate the pathways through which interventions may be effective, allowing researchers to identify key components. Likewise, moderation analyses may identify individuals who respond best to a given intervention.

It is also important to consider that caregivers who are not experiencing depressive symptoms, burden, or poor health have frequently sought out interventions. Studies are needed that examine what these caregivers are seeking and to develop approaches that address their concerns. One such concern is being prepared for the problems that they will face in the future. The outcomes of this type of preventive approach could be learning skills, finding a balance of caregiving and other activities, and gaining a sense of efficacy in managing daily challenges. Over the long run, this type of approach could lead to lower occurrence of emotional distress or health problems, but the primary outcome would be gaining the skills and confidence for handling problematic situations.

Outcomes for Both Caregivers and Care Receivers

Caregiving involves a dyadic relationship in which the caregiver and care receiver shape one another's emotions and behaviors (Moon and Adams 2013). Hence, caregiving interventions should ideally evaluate outcomes among both caregivers and care recipients. Illustrating this point, Perlick et al. (2010) found that family-focused treatment for caregivers of patients with bipolar disorder benefitted both members of the care dyad. Caregivers were instructed in self-care strategies and ways to help the patient manage his or her illness. Relative to standard health education, caregiver randomization to family-focused treatment was linked to greater decreases in depressive symptoms for caregivers and patients at post-treatment. Of note, reductions in patients' depressive symptoms were mediated by concurrent reductions in caregivers' depressive symptoms. These findings underscore the interdependence within caregiving dyads and demonstrate the value of considering each care partner's outcomes.

Other interventions aim to treat caregivers and care recipients together as a unit. Dyadic interventions for medical or psychiatric conditions have generally been effective in improving the psychological well-being, coping skills, and perceived relationship quality of one or both care dyad members (e.g., Baucom et al. 2014; Moon and Adams 2013). Whitlatch et al. (2017) developed and evaluated a six-session dyadic intervention for persons with early stage dementia and their family caregivers. Caregiver-care recipient dyads were randomly assigned either to the treatment condition (called SHARE) or to a control condition. The intervention focused on discussions of future care that led to creation of a care plan that reflected the values and preferences of each care partner (See ► "Preparation for Future Care: The Role of Family Caregivers"). Dyads in the control group participated in educational sessions about dementia. Findings indicated that nearly all dyads enrolled in SHARE were able to create a care plan. Caregivers in SHARE reported implementing portions of the plan, using more services for themselves and the care recipient (e.g., respite, support groups) compared to the control group. Furthermore, caregivers in the treatment condition reported decreases in emotional disruption behaviors when interacting with the care recipient (e.g., withholding emotions to keep him or her from worrying), whereas control group reported increases in these behaviors. Caregivers in SHARE also had higher treatment satisfaction than did control group participants. This study reveals that brief dyadic interventions show strong potential for enhancing outcomes among caregivers and care recipients in the early stages of illness.

Future Directions for Research

Shaping caregiver research and outcomes toward individualized goals and away from a "one size fits all" view may have enduring advantages. Given the diversity among caregivers and care situations, it is important to determine more about what individuals need and want from care-related services and interventions. Individualized goals should be considered within the backdrop of unique stressors and resources involving caregivers, care receivers, and the wider system of relatives and nonrelatives who do or do not provide care. Identifying individual goals along with personal and situational factors that support or hinder their realization would inform personalized treatment that potentially offers a lasting positive impact on caregiving experiences.

Another critical area for future work is the design of interventions to support family caregivers who perform medical care tasks. Medical/nursing tasks such as keeping track of medications, giving injections, managing peripheral intravenous lines, and caring for wounds or bed sores are common but require specialized skills in which many caregivers lack training (Mollica et al. 2017). These tasks can be stressful, time consuming, and long term, potentially leading to caregiver distress. Notably, a national survey sponsored by the United Hospital Fund and American Association of Retired Persons (AARP) revealed that almost one-third (32%) of family caregivers engaged in medical/nursing care believe they need to constantly monitor for complications, and their worries increase with a higher number of these care tasks (Reinhard et al. 2012).

Despite the potential challenges of medical/nursing tasks, caregivers providing this care have been found to report higher caregiving gains which include enhanced closeness with the care recipient and learning new skills (Polenick et al. 2017). Training in the safe and proper delivery of medical/nursing care may help to alleviate stress and maximize positive caregiving outcomes. In a study of 641 informal cancer caregivers, those who did not receive training in the provision of medical/nursing tasks reported greater burden, and this association was partially mediated by lower confidence in caring for the care recipient's physical needs (Mollica et al. 2017). This study demonstrates the value of targeting both positive and negative outcomes to improve the well-being of caregivers who provide complex medical caregiving.

Lastly, developing strategies to promote self-care among caregivers is a promising direction for research. Caregivers often report difficulty in caring for their own health needs. Self-care encompasses a range of behaviors that sustain health, psychological well-being, and the ability to provide quality care. This includes maintaining healthy habits (e.g., physical activity), minimizing health risks (e.g., alcohol use), effectively managing one's own chronic conditions (e.g., medication adherence), and participating in noncare activities that are enjoyable and personally meaningful (e.g., spending time on hobbies).

Prior work indicates that targeting aspects of caregiver self-care may be broadly beneficial (Perlick et al. 2010). A descriptive systematic review of 14 studies evaluating caregiver physical activity interventions showed, for instance, that these strategies reduced distress and improved outcomes including physical activity levels, psychological well-being, sleep quality, and self-efficacy related to caregiving and exercise (Lambert et al. 2016). Similarly, Moore et al. (2013) evaluated a 6-week behavioral activation intervention designed to lower depressive symptoms and cardiovascular disease risk factors among dementia family caregivers by increasing engagement in enjoyable leisure activities. Compared with caregivers in an Information-Support control condition, those randomized to the intervention had greater reductions in negative affect, depressive symptoms, and interleukin-6. There were no group differences from baseline to 1-year follow-up, however, suggesting that booster sessions may be needed to maintain treatment effects. It will also be important to identify caregivers who are most likely to benefit from behavior change strategies.

Summary

Caregiving research has generally focused on a limited range of outcomes. Studies in the future should target outcomes that capture a fuller spectrum of positive and negative experiences that are central to caregivers' daily lives. Gaining knowledge of caregivers, care recipients, and situational factors to inform tailored interventions would facilitate person-centered care that accounts for individual goals, strengths, and vulnerabilities. With rapid population aging, family caregivers will play an increasingly vital part in the long-term care of older adults with chronic conditions and functional disability. A more nuanced understanding of how and under what circumstances interventions are effective in managing care-related concerns and promoting gains among caregivers is needed to preserve their optimal health, well-being, and quality of life.

Cross-References

- ▶ Adult Day Services
- ▶ Aged Care Homes
- ▶ Aging in Place: Maintaining Quality of Life for Older Persons at Home
- ▶ Alzheimer's Disease
- ▶ Behavioral and Psychological Symptoms of Dementia
- ▶ Behavioral Interventions in Dementia
- ▶ Benefits of Caregiving
- ▶ Caregiver Stress
- ▶ Dementia
- ▶ Effectiveness of Respite Care for Caregivers of Older Adults
- ▶ Hamilton Rating Scale for Depression
- ▶ Home- and Community-Based Services (HCBS)
- ▶ Interventions for Caregivers of Older Adults
- ▶ Preparation for Future Care: The Role of Family Caregivers
- ▶ Resilience: Measures and Models
- ▶ Respite Care
- ▶ Stress and Coping Among Older Adults
- ▶ The Center for Epidemiologic Studies Depression (CES-D) Scale

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Caregiving

► Benefits of Caregiving
► Self, Informal, and Formal Long-Term Care: The Interface

Caregiving Across Neurodegenerative Diseases

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Definition

Neurodegenerative disease caregivers provide and coordinate care for another person who is diagnosed with a neurodegenerative disease. Neurodegenerative diseases are chronic, debilitating, incurable, and progressive conditions that affect the neurons ("building blocks") in the brain and include Alzheimer's disease (AD), dementia, Lewy Body Dementia (LBD), Mild Cognitive Impairment (MCI), and Parkinson's disease (PD). Neurodegeneration is associated with a large amount of heterogeneity. For example, AD is the progressive deterioration of cognition and memory; dementia spans different disease groups and is associated with a large amount of heterogeneity in ADL impairments; LBD presents as 2 of: Parkinsonian symptoms, cognitive fluctuations, and/or hallucinations; MCI is cognitive decline beyond normal aging; and PD is the progressive decline in motor skills that may be accompanied by nonmotor and cognitive symptoms. Informal caregivers include partners, spouses, adult-children, family, and friends who attend to physical, mental, social and psychological needs, and/or decision-making. Specific to neurodegenerative disease, caregivers support a combination of cognitive and physical dependences with progressive, and often unpredictable, disease trajectories. Caregivers may experience burden (Zarit et al. 1980) as a result of caregiving challenges and these experiences may overlap due to shared presenting symptoms across neurodegenerative diseases.

Overview

Neurodegenerative diseases are among the top ten illnesses ending in death that cannot be cured or slowed significantly and, as such, result in the need for constant care. For example, it is estimated that Alzheimer's disease alone affects up to half of people 85 years of age, totaling 40 million worldwide (2015); the number is anticipated to grow to 135 million by 2050 (Lassonde et al. 2017). The incidence and prevalence of neurodegenerative disease increases with age, as such these caregivers tend to be older adults. Unpaid family caregivers are the cornerstone of support for someone diagnosed with a neurodegenerative disease and the burden of care often falls on caregivers at the expense of their own well-being. Caregivers of persons with neurodegenerative disease face unique challenges because of the cognitive and physical dependences specific to their care experience and adapt to continuously changing and demanding situations associated with disease progression. In addition, these caregivers tend to be older females, who may face physical and psychosocial constraints as well as the need to manage their own health concerns (Roland and Chappell 2015, 2019). Distinguishing patterns of how various care demands impact caregiver experiences across older adults with neurodegenerative disease diagnoses has implications for supporting caregiver health and well-being.

Key Research Findings

Disease-Specific Presentation

Older neurodegenerative caregivers are more burdened and depressed compared with healthy older adults. Neurodegenerative caregivers also experience higher stress than other caregiver groups. For example, providing care for a spouse with a neurodegenerative disease has a fourfold negative influence on mood compared with age-matched noncaregivers, mainly attributed to the impact of the disease on social isolation, physical health, and sleep (Roland and Chappell 2019). As such, neurodegenerative caregivers face unique disease-related challenges and pathological onset, disease severity, and associated dependence.

In studies of caring for persons living with AD, role conflict (i.e., job and family) and stressed time constrains (self and social) results in emotional strain for caregivers. Communication challenges increase caregiver distress, while mood and behavioral problems are most strongly related to negative caregiver outcomes and social isolation (Raggi et al. 2015). Caregivers report significant care hours are spent managing aggressive behavior and preventing dangerous episodes, resulting in shorter time to institutionalization and declines in caregiver health and well-being (Monteiro et al. 2018). Care recipient's mood is positively correlated with caregiver burden and depression; care recipient ADL dependence is correlated with social isolation and depression (Stella et al. 2011). However, caregivers who appraise tasks as less stressful and find meaning from caregiving have more social resources, lower depression, and higher life satisfaction. Spouses who rate their marital relationship strong and satisfying report less burden, better health, and mood than those who rate their marriage more negatively (Monteiro et al. 2018). These may act as buffers to negative health outcomes.

In studies of caring for persons living with LBD, difficult diagnostic process and delays in healthcare support contribute to isolation and burden for caregivers (Galvin et al. 2010). Motor impairments lead to increased caregiver burden and associated disability and dependence contribute to institutionalization (Leggett et al. 2011). However, the psychiatric and mood symptoms are most stressful to caregivers and correlate most strongly to negative outcomes (Zweig and Galvin 2014).

People with MCI remain relatively independent, but require some daily assistance. Those who care for persons with MCI may experience burden (Andrews et al. 2017). The uncertainty of MCI diagnosis leads to secondary role-strains on family relationships (i.e., relational deprivation, marital satisfaction) and caregivers feel overwhelmed (Dean and Wilcock 2012). Poor ADL function, behavior, and fluctuating cognitive symptoms lead to lifestyle constraints, self-loss, and caregiver depression (Springate and Tremont 2013). Growing care responsibilities increase caregiver burden, depression, and anxiety (Seeher et al. 2013).

Although characterized as a movement disorder, cognitive impairment and psychiatric disturbances are increasingly recognized as common features of PD. Caregiver burden is associated with ADL dependence and motor decline has the greatest impact in early PD stages. However, mood, psychiatric, and behavior disturbances are reported to have the greatest impact on caregiver isolation and social strain, leading to greater burden and depression (Roland et al. 2010; Hendriks et al. 2015; Mosley et al. 2017). Cognitive impairment is associated with earlier institutionalization, mortality, and increased burden. However, strong caregiver–care-recipient relationship quality directly correlates with reduced burden (Hiseman and Fackrell 2017).

Across Disease Groups

Comparing experiences and moderating factors across neurodegenerative caregiver groups may be a richer source of information to inform support services and resource allocation than examining the influence of disease-specific stressors based solely on diagnosis. Three types of caregiver experiences emerge following an examination of symptom presentation across AD, LBD, MCI, and PDD (Roland and Chappell 2015).

"*Role strain*" captures the debilitating toll that cognitive decline and changes in social and role functioning takes on the relationship between caregiver-and-care recipient. The transition to the role of "caregiver" creates significant relational deprivation, and uncertainty in disease progressive further increases uncertainty and difficulty in coping with social and role changes. These strains exacerbate communication problems, conflict, emotional distress, and social isolation.

The mounting stressors and pressure on all aspects of a caregiver's life, such as care tasks and social isolation, lead to role strain, feelings of being "*consumed by caregiving*," and result in negative health outcomes. This is typified when the care recipient's level of physical dependence increased, and cognitive impairment and neuropsychiatric complications emerge, contributing to multifactorial functional impairment often expressed in PD/PDD and LBD. As a result, caregivers express worry, hyper-vigilance, feeling consumed by managing motor symptoms, and constantly watching for falls during ADL. Neurodegenerative disease progression shrinks daily life and caregivers report constraints in their physical, social, and psychological facets of their life space. The loss of independence faced by care recipients is also felt by caregivers.

"*Care service use*," including assistive care services and medical information, is important to caregiver experiences of well-being. Especially in MCI and AD, caregivers often feel challenged with IADL and decision-making due to care recipients declining cognitive capacity. To manage, caregivers express needing help with a variety of tasks, including housekeeping, performance capacity, financial and legal advice, long-term planning, and coping strategies. Caregivers cope by using care services. For example, adult day service and respite programs assist in reducing caregiver's workload and sense of isolation. In addition, adult day program activities provide physical, cognitive, and social stimulation for care-recipients that may contribute to reduced behavioral challenges at home.

A fourfold typology is derived after examining the influence of stressors, strains, and support on caregiver outcomes; the clusters group together AD, PD, and PDD caregivers and are summarized below (Roland and Chappell 2019).

"*Succeeding*" caregivers care for mild cognitive impairments and problems behaviors and moderate ADL impairments. They use less formal support, report higher emotional support, and experience less burden and depression.

"*Coping*" caregivers care for moderate cognitive impairment, problem behaviors, and ADL impairments. They use few formal services, cite few care hours, have little emotional support, and experience little burden and depression.

"*Getting by with support*" cluster caregivers with long disease duration who care for moderate-severe cognitive impairment, problem behaviors, and ADL limitations. They are typified by moderate care hours and moderate emotional support and experience moderate burden and depression.

"*Struggling*" caregivers care for moderate-severe cognitive and behavior impairments and experience significant burden and depression. They are typified by moderate care hours, high formal service use, and low emotional support.

Policy Implications

The caregiver types presented here highlight significant unmet needs for caregivers across neurodegenerative disease groups which are greater than for general older caregivers. First, caring for persons with diminished cognition results in changing relationship dynamics and limited social opportunities. This provides insight into the fact that relationships are key to decision-making; strategies that enhance communication, considering a partner with cognitive impairment, are needed to improve care. Second, caregivers managing significant motor symptoms are hyper-vigilant, worry, and may neglect self-care. The importance of respite and social support to mitigate these growing feelings of worry and neglected self-care are also stressed. Third, caring for persons with ADL limitations, advanced cognitive decline, and psychoses report increases in care service use. This highlights the need for care services to be targeted throughout the disease trajectory, from time of diagnosis to institutionalization; this will support caregivers' understanding and expectations about the disease, coping skills, decision-making, and care planning (Roland and Chappell 2015).

Expressive support has the greatest influence on caregiving stressors, more than formal support, and provides a buffer for negative caregiver experiences (Roland and Chappell 2019). This places meaning on social relationship as a key buffer against the negative caregiving outcomes reported across all disease presentations. A focus on building social support strategies for caregivers may be beneficial to support more positive care experiences.

Future Directions of Research

Caregivers play a fundamental role in health outcomes for many older adults with neurodegenerative disease by keeping them at home instead of moving them into long-term care. This care may come at significant costs to caregivers' health and well-being, which is neither accounted for nor reimbursed by the healthcare economy. Caregiving demands and experiences are related to neurodegenerative disease presentation and may place neurodegenerative caregivers at greater risk for negative outcomes than other older caregivers. Important research initiatives are needed to understand, promote, restore, and maintain health in neurodegenerative caregivers while appreciating their contribution to healthcare. Research programs targeted at social support strategies, relationship quality, decision-making skills, coping skills, and appropriate health care for caregivers are needed. Considerations for the context in which caregiving occurs are also needed, specifically, understanding the broader healthcare system, political and social context in which neurodegenerative diseases are managed in older adults. Emerging areas of growing interest for gerontologists lie in exploring the public health opportunities, developing social support strategies, redirecting health care delivery, and developing a caregiver-friendly policy agenda. Ultimately, there is a need to critically re-examine the current caregiver situation and how we can reconceptualize health systems to better promote health and well-being, and quality of life, for caregivers and those they are caring for.

Each disease stage brings unique challenges; as such, a life course approach to studying caregiving across neurodegenerative disease trajectories is needed within the aging context. Considerations for support at each stage are needed to help caregivers understand the illness, develop skills for the present situation (communication, coping strategies, decision making), organize care responsibilities, knowledge of available services, and understand expectations to enable future care plans and decision making. In addition, lessons can be learned from further research on caregivers in midlife, distinct differences between adult child and spouse caregivers, as well as gendered differences in care role progression.

There has been enormous growth in the research at large concerning negative caregiver outcomes, such as burden; however, only limited research has focused on understanding the associated positive impacts on well-being. This is also true for research on caregiving in neurodegenerative disease. Future research needs to recognize the heterogeneity of symptom presentation, stressors, coping strategies, and resources and that, in this way, caregiving does not impact all caregivers equally. More attention to studying the heterogeneity of caregiving for neurodegenerative disease may draw out the range of experiences from at-risk and burdened to meaning and well-being.

Summary

Health researchers examine the stressors, experiences, and support strategies for caregivers of older adults across neurodegenerative disease diagnosis. The findings highlight some of the challenges and opportunities facing the healthcare system today. Community and social support for caregivers can be accomplished through improved community infrastructure and access, programs that provide comprehensive care and subsidy, and compensation; research in this area contributes to shaping caregiver-friendly policies to improve caregiving experiences. Caring for someone with motor, behavioral, mood, psychiatric, and cognitive challenges requires considerable time and effort. Behavioral, neuropsychiatric, and cognitive stressors are major contributors, over motor impairments, to caregiver outcomes. Social support and targeted resources throughout the entire unique disease trajectory are needed to support caregiver health and well-being.

Cross-References

▶ Caregiver Stress
▶ Caregivers' Outcomes
▶ Caregiving and Social Support: Similarities and Differences
▶ Cognitive Disorders in Older Patients with Cancer
▶ Dementia
▶ Family Demography

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Caregiving Among the LGBT Community

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Definition

Caregiving among the LGBT community refers to the informal unpaid care provided to or received from members of lesbian, gay, bisexual, and transgender (LGBT) communities. This may include partners, family members, friends, and neighbors.

Overview

Most caregiving models have been based on the experiences of people who are white, western, middle-class, heterosexual, and cisgender (where gender identity conforms to sex ascribed at birth) (Fredriksen-Goldsen and Hooyman 2007; Parslow and Hegarty 2013). Only recently has the experience of LGBT people been considered – mainly within western societies of North America, Europe, and Australasia. This is despite a greater likelihood that LGBT people will be caregivers compared to non-LGBT people (National Alliance for Caregiving and AARP Public Policy Institute 2015). In addition to the demands and rewards experienced by all caregivers, LGBT caregivers and care-receivers face particular challenges including invisibility, discrimination, and lack of access to services (Hash and Mankowski 2017).

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Key Research Findings

In a US national probability sample of 7600 people, 20.4% of LGBT people were reported to be caregivers of older adults compared to 16.5% of those not identifying as LGBT (National Alliance for Caregiving and AARP Public Policy Institute 2015). This confirms research reporting the comparatively high rate of caregiving among LGBT communities (Fredriksen 1999; Fredriksen-Goldsen et al. 2011).

Nonetheless, despite being more likely to be caregivers, LGBT people actually appear less likely to have access to informal caregiving when they need it. Croghan et al. (2014) reported that about 75% of the 495 LGBT older adults in their study had access to an available caregiver compared to nearly 90% of the general older population. In part this may reflect LGBT older people being more likely to live alone and to not be in a relationship (Anderson and Flatt 2018; Fredriksen-Goldsen et al. 2011).

LGBT people provide and receive care in both families of origin (e.g., parents, adult children, siblings) and families of choice (e.g., same-sex partners, friends, ex-partners, neighbors) (Metlife 2010). Compared to the general population, friends figure more prominently in the care provided by or received from LGBT people, particularly if individuals do not have a partner (Croghan et al. 2014). While some are estranged from families of origin (e.g., due to homophobia, biphobia, or transphobia), the majority of LGBT people remain engaged with members of their family of origin (Croghan et al. 2014).

As with the general population, many LGBT caregivers see caregiving as an extension of their existing relationship with the care-receiver (Brotman et al. 2007). This is the case for friends who provide care, as well as partners and biological family members. Muraco and Fredriksen-Goldsen (2011) reported that, in their study of 18 care dyads, caregiving and friendship activities occurred side-by-side and that many of these relationships continued to be characterized by mutuality. Despite the important role played by friends, there is some evidence that the quality of the dyadic caregiving relationship may be not as great when friends are providing care (Fredriksen-Goldsen et al. 2009). In an analysis of 451 older LGBT caregivers in the Caring and Ageing with Pride study, Shiu et al. (2016) found that those who provided care to friends, as opposed to partners, provided fewer types of care, fewer hours of care and for shorter durations.

LGBT caregivers face both the demands associated with caregiving and the stressors/challenges related to their minority status (e.g., Shippy 2007). There is some initial indication that these may intersect to produce lower health, social, and economic outcomes compared to both other caregivers (e.g., Anderson and Flatt 2018) and other LGBT people (e.g., Hughes 2018), although more research using large probability-based samples is needed. With respect to poverty, a nationally representative US study of caregivers identified greater financial strain experienced by LGBT caregivers compared to non-LGBT caregivers (Boehmer et al. 2018).

LGBT caregivers and care-receivers also experience challenges when accessing services, such as health care providers' questioning of partners' and friends' legitimacy in being involved in providing care (Hash and Mankowski 2017). A particular concern is estranged biological family members being involved inappropriately by service providers as substitute decision-makers for incapacitated LGBT people (Almack et al. 2010; Cartwright et al. 2012). Past experience of discrimination, fear of discrimination, or an unwelcoming environment may impact on a willingness to access services. These concerns may lead some LGBT people to not disclose to service providers their sexual orientation or transgender history, even when care is being provided in their own home (Brotman et al. 2007).

Future Directions of Research

An important critique of existing research on LGBT caregiving is its history of studying lesbian, gay, bisexual, and transgender experiences together. Because a greater proportion of LGBT research participants tend to be gay men or lesbian women, the unique experiences of bisexual and transgender people have been marginalized and subsumed within the LGBT category (Witten 2016). Future research needs to be more targeted in its examination of community experiences and prioritize bisexual and transgender people's experiences, as well as of those of intersex, asexual, queer, and gender diverse or nonbinary people (Thomeer et al. 2017). Alongside this, more intersectional research is needed, which examines the ways different identities and community affiliations intersect in different contexts to produce inequality, as well as privilege. The health equity promotion model (Fredriksen-Goldsen et al. 2014) – drawing on intersectionality, minority stress and life course approaches – appears to hold promise for investigating how caregiving among LGBT communities compares to the general population.

Substantial LGBT scholarship over the last few decades has drawn on queer theory and queer politics, although these approaches have rarely been considered in relation to caregiving and care-receiving. Queer approaches typically seek to disrupt binaries such as gay/straight, male/female, caregiver/care-receiver, as well as to explore the erotic, playful, and political dimensions of everyday life (Hughes 2006). Future research could draw upon queer approaches to better understand the transgressive dimensions of care in some relationships and settings (Kessler 2005) and the ways care, sexuality, and eroticism are enacted in nonexploitative relationships (Rainey 2018). Such investigations may relate to LGBT people's relationships and communities, as well as other nonnormative relationships, such as polyamorous and dominant/submissive relationships.

Cross-References

▶ Heterosexism and Ageism
▶ LGBT in Old Age

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C

Caregiving and Ethnicity

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Synonyms

African American caregivers; Asian American caregivers; Cultural differences in caregiving; Ethnic caregivers; Ethnic caregiving roles; Ethnic family caregivers; Ethnic family caregiving network; Hispanic American caregivers

Overview

A substantial body of literature provides evidence that caregiving families are embedded in racial, ethnic, and cultural contexts that influence their caregiving experiences. Race fosters differences in power relationships and justifies the more powerful group's authority over other groups that are considered different and generally inferior (Markus 2010). Diversity within subgroups of ethnic caregivers is seldom studied; rather group racial, ethnic, and cultural differences are compared to non-Hispanic White caregivers, investigated and explained. Researchers who support this approach view the behaviors and practices of non-Hispanic White caregivers as normative and those of other groups (i.e., African American caregivers, Hispanic American caregivers, Asian American caregivers) as nonnormative (Markus 2010). Here the focus is on cultural influences in the caregiving experiences of ethnic family caregivers living in the United States. It does not compare their experiences to non-Hispanic White caregivers.

Key Research Findings

The expectation of giving and receiving family care is an important aspect of ethnic family life deeply rooted in cultural values and traditions (Pharr et al. 2014). Most older adults therefore receive care within the family care network where family caregivers provide unpaid informal care to an older dependent or disabled loved one that generally exceeds customary support provided in social relationships (Fingerman et al. 2011). Within many African American families, caregiving is a shared responsibility among close relatives, distant relatives, and voluntary kin. Voluntary kin, who are not blood or legal relatives, accept the status, duties, and responsibilities of family membership including caring for dependent older adults and disabled loved ones (Braithwaite et al. 2010).

The ethic of caring, familism, and filial piety are cultural values that influence family dynamics and affect the family's role in providing care to dependent loved ones (Apesoa-Varano et al. 2015). Core elements of the ethic of caring, "extended family networks, respect for the elderly, the high value placed on children, and a strong religious orientation" (Hill 1997, p. 120), are held by many members of ethnic caregiving families (Black et al. 2017; Dilworth-Anderson and Moon 2019). Embracing many of the same concepts as the ethic of caring, familism (*familismo*) has been shown to influence the behaviors and practices of Puerto Rican and other Hispanic American caregivers (Apesoa-Varano et al. 2015; Knight and Sayegh 2010). Filial piety, love and respect for parents and ancestors, motivates many Vietnamese American and Chinese American families to provide in-home care for parents and older family members (Meyer et al. 2015; Sun and Coon 2019). Within families, providing care to dependent loved ones leads to changing and often conflicting roles among its family members. The multiple roles and responsibilities family caregivers take on often contribute to stress and unhappiness when caregiving leads to role conflict and poor health outcomes. Gordon and colleagues (2012) argue that multiple roles create demands on family caregivers that compete for their personal resources, time, and energy and emphasize the importance of social support in reducing role strain and role conflict.

Asian American caregivers express the belief that it is unacceptable to say "no" to family caregiving responsibilities. Saying no to caregiving threatens family harmony and dishonors the care recipient. Hispanic American and African American caregivers hold similar beliefs, that saying no to caregiving is unacceptable and violates cultural values. It is not clearly understood how maintaining harmony within the family impacts Native American caregiving practices because few studies (e.g., Dougherty et al. 2019; Goins et al. 2010) examine their cultural values, norms, and expectations for providing care. However, findings from a study of Native American caregivers from the Lakota Sioux in the Northern Plains and one community in the Southwest reveal a strong cultural value of interdependency and reciprocity among multigenerational families (Goins et al. 2010).

Ethnic caregiving roles are culturally prescribed and based on traditional gender ideology (Pharr et al. 2014). In traditional Vietnamese families, as in other Asian caregiving families, the eldest son assumes responsibility for the care of his older parents. However, as Meyer and colleagues (2015) suggest, it is usually the son's wife or another female family member who performs the day-to-day caregiving tasks (i.e. ADL assistance). Sons assume managerial or financial responsibilities. African American women's caregiving roles are rooted in a sociocultural historical tradition of providing care to their family, close friends, and neighbors (Pharr et al. 2014). Yet, many African American caregiving families display egalitarian family patterns in which decision-making, family management, and care responsibilities are shared between men and women (Willie and Reddick 2010). African American men who perform primary caregiving duties may not self-identify as caregivers. Rather, they self-identify as "just a loving husband" or a "devoted son" or "his wife's lifeline" (Black et al. 2017, pp. 11, 29).

Religious and spiritual beliefs link cultural traditions to the family caregiving experiences of many ethnic caregivers. Caregivers' whose religious beliefs enable them to manage their caregiving responsibilities report positive aspects of caregiving including low levels of perceived burden and depression (Heo and Koeske 2011). For many Mexican American caregivers, religious or spiritual practices such as attending mass, private prayer, following Bible teachings, and performing rituals help them respond positively to the demands of caring for dependent family members (Koerner et al. 2013). Chinese American caregivers, who embrace Confucianism, support the ideals of filial piety and rear children to provide for their aging parents as a sign of love, respect, and gratitude. Respect for older dependent parents and acceptance of age-related decline may contribute to Chinese Americans' positive appraisal of their caregiving experience (Sun and Coon 2019).

Heo and Koeske (2011) hypothesize that higher religious coping results in lower burden appraisal. Their hypothesis is largely supported; however, only positive religious coping strategies are considered. These strategies promote a secure relationship with God or other divine being (Abu-Raiya and Pargament 2015), foster optimism and greater connectedness to others, and improve caregivers' relationship with the care recipient (Koerner et al. 2013). Negative coping strategies reflect a pessimistic worldview expressed as the religious or spiritual struggle to maintain a secure relationship with God and find meaning in life's challenges. When highly religious caregivers believe their prayers are unanswered or view their caregiving situation as punishment, negative coping strategies are consistently associated with undesirable health outcomes. Religious coping strategies, positive or negative, may encourage caregivers to consult religious or spiritual advisors rather than healthcare professionals when seeking treatment for their dependent family members (Abu-Raiya and Pargament 2015).

Cultural beliefs embraced by caregivers from different ethnic groups and subgroups affect and are affected by their perceptions of disease and the meanings they assign to chronic illness and disability. Much of the research (see Heo and Koeske 2011; Nápoles et al. 2010; Sun and Coon 2019) on caregivers' perceptions of disease, illness, and disability focuses on Alzheimer's disease and dementia caregiving. Family caregivers who witness their loved one's memory loss and cognitive decline associated with dementia rely on their cultural beliefs to construct explanations for the disease symptoms and behaviors (Henderson 2015). Native Americans may view cognitive impairment as an imbalance in all aspects of the person's life, a punishment for misdeeds, or as "glimpses of the other side" preparing for death (Dougherty et al. 2019). Chinese American family caregivers may believe an imbalance between the *yin* and *yang*, complementary energy forms, contributes to physical and mental decline. The care recipient's decline may also be attributed to a lack of harmony or imbalance within the family (Sun and Coon 2019). Hispanic and African American caregivers often associate a lifetime of stress and worry with the symptoms of dementia-related decline (Dilworth-Anderson and Moon 2019; Dilworth-Anderson et al. 2012). When cultural perceptions of disease and normalization of illness create barriers to seeking professional and formal care, ethnic caregivers may jeopardize their own physical and emotional health and their loved one's well-being (Crowther et al. 2017).

There is little evidence that strong cultural beliefs (e.g., ethic of caring, familism, filial piety) either reduce burden or improve health outcomes. Indeed, these beliefs may increase distress or have a curvilinear relationship to distress (Dilworth-Anderson and Moon 2019). Cultural norms relating to the expression of psychological difficulty may help explain inconsistencies in psychological and physical health outcomes for ethnic family caregivers. African American caregivers report lower levels of care-related depression and psychological distress when compared to other ethnic groups while experiencing poorer physical health (Dilworth-Anderson and Moon 2019). The concept "John Henryism" (James 1994), according to Dilworth-Anderson and Anderson (1994), might explain these findings. This concept reflects a strong tendency toward high-effort coping with highly stressful psychosocial situations and is associated with positive psychological health outcomes and increased risk of negative physical health outcomes. These caregivers' reluctance to acknowledge psychological health issues that negatively affect their well-being often limit their use of professional mental health services.

Culturally Appropriate Interventions

Research discussed in this entry and a review of studies published from 1980 to 2013 (see Apesoa-Varano et al. 2015) provide evidence that cultural norms and beliefs influence caregiving experiences of ethnic caregivers. Yet, few interventions are designed to be culturally appropriate in addressing the needs of these diverse caregivers (Nápoles et al. 2010). Interventionists who would achieve long-term beneficial effects for ethnic caregivers must incorporate key aspects of the ethic of care, familism, and filial piety into their intervention strategies. Several studies offer guidelines for developing culturally appropriate interventions that support caregivers' cultural values and traditions (see Apesoa-Varano et al. 2015; Browne et al. 2017; Graham-Phillips et al. 2016; Nápoles et al. 2010) and include:

Recognize the family caregiving network. In most ethnic family caregiving situations, the caregiver-care recipient dyad in which one person provides care for a dependent relative is believed to conflict with cultural norms. The family caregiving network or system often includes multiple generations of local and distant relatives, voluntary kin, and supportive friends. The most effective interventions would be family-centered and encourage family members' involvement in the design and implementation of the intervention (Dilworth-Anderson and Moon 2019; Samson et al. 2016).

Consider cultural nuances. Cultural nuances are differences in the meaning caregivers associate with their cultural values, traditions, beliefs, and the ways in which these are expressed and practiced within a particular ethnic group or subgroup. Dilworth-Anderson and colleagues (Dilworth-Anderson and Moon 2019) advise researchers to consider four cultural nuances when designing interventions for African American family caregivers: adhere to family members' expectation to provide care to older adults needing assistance; incorporate religious beliefs and include God in the family's support network; accept physical symptoms rather than psychological symptoms of chronic stress; and recognize meanings caregivers assign to specific illnesses and symptoms of disease.

Accept language and communication differences. Designing culturally sensitive intervention materials requires researchers to consider ethnic caregivers' ability to comprehend health-related information. Gerdner (2019) suggests conceptual rather than literal translation of intervention materials. This would benefit family caregivers whose native language has no words for medical or anatomical terms used in Western medicine. Since there is no word in the Hmong language that translates to dementia, many Hmong American caregivers use the term *tem toob* to describe the memory loss and mental confusion associated with dementia (Gerdner 2019). Attention to communication style is important when working with some Native American caregivers who may offer stories about their family or tribe in response to direct health-related questions (Dougherty et al. 2019; Hendrix and Swift Cloud-LeBeau 2006). Using culturally accepted forms of address, last name and appropriate title, communicates respect for ethnic caregivers and their older adult loved ones (Sun and Coon 2019).

Use a positive approach. Female and male African American caregivers' positive appraisal of Alzheimer's disease and dementia caregiving may be explained by their high level of religiosity, acceptance of care recipient's problem behaviors, and the ability to reframe negative life experiences positively (Black et al. 2017). Intervention strategies that encourage and sustain positive appraisal of the caregiving experience without minimizing the burdens and demands associated with caregiving might lessen the negative consequences for caregivers' well-being (Carbonneau et al. 2010; Roth et al. 2015).

Directions of Future Research

Researchers often use stress and coping conceptual models (e.g., Lazarus and Folkman 1984) to explain the experiences of non-Hispanic White caregivers and adapt these models to ethnic caregivers' experiences (e.g., Knight and Sayegh 2010). Future researchers should expand stress and coping models to include cultural factors that influence ethnic caregivers' appraisal of the rewards of family caregiving and enhance their quality of life (Pristavec 2018). Adapting a conceptual model that attempts to explain positive aspects of caregiving, such as the model proposed by Carbonneau et al. (2010), will facilitate the development of interventions and services that encourage positive adaptation to caregiving roles and enhance caregiver and care recipient well-being.

When all caregivers of African ancestry are identified ethnically as African American, researchers ignore subgroups such as Caribbean Blacks (i.e., Jamaicans, Dominicans, Haitians) living in America. Future studies should explore cultural diversity within subgroups of ethnic caregivers (Thornton et al. 2017). Researchers who work with subgroups of Asian American (e.g., Chinese, Japanese, Korean, Hmong, Vietnamese, Filipino) and Hispanic American (e.g., Cuban, Mexican, Puerto Rican, Dominican) family caregivers need to investigate intragroup cultural variability. Within subgroups of ethnic caregivers are recent immigrants and descendants of immigrants who came to North America several generations ago (Ferraro et al. 2017). Native Americans are not immigrants. They "were here first and were colonized; they were invaded, not discovered" (Hendrix and Swift Cloud-LeBeau 2006, p. 147). The forced internal migration of Native Americans from ancestral lands to reservations and later movement to urban areas contributed to changes in family caregiving whereby families are seeking more community-based services (Goins et al. 2010; Hendrix and Swift Cloud-LeBeau 2006). Future research should examine immigration history (Gerdner 2019), internal migration patterns (Browne et al. 2017), and levels of acculturation (Miyawaki 2017). This research is vital to understand how immigrant caregivers' efforts to maintain their cultural traditions and beliefs while adjusting to new sociocultural environments contribute to intergenerational family interaction and influence the quality of their caregiving experiences.

There is a depth of research exploring various topics including the influence of cultural values and beliefs on caregivers' choice of coping strategies (Abu-Raiya and Pargament 2015; Knight and Sayegh 2010), psychological and physical health outcomes of caregiving (Sörensen and Pinquart 2005), and developing culturally appropriate interventions (Apesoa-Varano et al. 2015; Nápoles et al. 2010). However, none of these studies focus on the experiences of older African American male caregivers. These caregiving men are the focus of Black et al.'s (2017) work that examines the role of cultural values, beliefs, and practices in shaping the caregiving experiences of this subgroup of caregivers. Studies that investigate their effort to maintain a male identity while performing traditionally female tasks, their coping strategies to handle the stress of caregiving, and their ability to endure adverse effects of perceived social and economic discrimination are needed.

Studies of ethnic family caregiving seldom investigate families that include same-sex, bisexual or transgender family caregivers. Individuals, not the family unit, have sexual orientation. Lesbian, gay, bisexual, and transgender (LGBT) caregivers may be committed members of the family care network but are seldom recruited for family caregiving studies that do not investigate HIV/AIDS caregiving. Data suggest that LGBT family caregivers perform many of the same duties as heterosexual caregivers and experience many of the same rewards and challenges (Coon and McBride 2019). Many LGBT caregivers embrace cultural values that stress the importance of family care. Family care, however, may be provided within voluntary kin networks when biological and legal kin do not recognize the same-sex partner.

Future studies designed to increase awareness of cultural variability among subpopulations of ethnic caregivers should address barriers to their participation in research and intervention studies. Research that develops effective interventions for enhancing positive caregiving outcomes is needed. Culturally competent researchers and clinical professionals are needed to advocate for diverse groups of ethnic caregivers and their families.

Summary

The cultural context of caregiving includes cultural values, traditions, and beliefs that influence the caregiving experiences of diverse ethnic caregivers and their family caregiving networks or systems. Ethnic family caregiving practices are deeply rooted in cultural values of ethic of caring, familism, and filial piety. These values require family members to provide care for older adult and dependent relatives within the family and prescribe caregiving roles and responsibilities. To manage stress often associated with caregiving responsibilities, many ethnic caregivers develop coping strategies consistent with their cultural values and religious beliefs. Effective intervention strategies and support services must be culturally appropriate and sensitive to the cultural traditions and beliefs of ethnic caregivers and their families. Future researchers should develop new conceptual models that capture cultural nuances of ethnic caregiving experiences and practices. Studies that investigate how ageism and heterosexism negatively impact subgroups of ethnic caregivers must be conducted. With increasing numbers of older, infirmed, and dependent ethnic Americans, research on their caregivers' experience increases in importance.

Cross-References

▶ Alzheimer's Disease
▶ Behavioral and Psychological Symptoms of Dementia
▶ Benefits of Caregiving
▶ Caregiver Identity
▶ Caregiver Stress
▶ Caregiving Among the LGBT Community

▶ Employment and Caregiving
▶ Fictive Kin
▶ Gender and Caring in Later Life
▶ Intergenerational Family Dynamics and Relationships
▶ Interventions for Caregivers of Older Adults

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Caregiving and Social Support: Similarities and Differences

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Synonyms

Assistance; Care work; Caring; Informal care; Support; Unpaid care

Overview

Caregiving tends to be defined in terms of the provision of unpaid or informal assistance and support (See ► "Social Support") to family members, friends, or acquaintances who have physical, psychological, cognitive, or other health needs (Chappell 2001; Drentea 2007). Some adopt the view that caregiving is evident only when a person is dependent on another for personal care tasks or assistance with basic activities of daily living (ADLS) such as eating, dressing, bathing, or getting in and out of bed (e.g., van den Broek and Dykstra 2017). More often, however, caregiving appears to be defined as including assistance with either or both basic personal care tasks and instrumental activities of daily living (i.e., IADLs such as housekeeping or transportation – see Gaugler et al. 2002; Wolff et al. 2016). Others broaden the concept even further to include the provision of other forms of assistance, such as arranging for services, informational and emotional support, and companionship (e.g., see Drentea 2007; National Alliance for Caregiving and American Association of Retired Persons 2009). As noted by Calasanti and Bowen (2006: 261), for example: "A more inclusive definition takes into account the caregiver's mental and emotional responsibility for the care receiver, in addition to their responsibility for their physical well-being..."

Like caregiving, social support has been defined in several different ways (Cohen et al. 2000;

Gottlieb and Bergen 2010). Often, it is used to refer to the functional resources available from and/or provided by significant others such as family members, friends, neighbors, or coworkers (see Cohen et al. 2000; House 1981). These include such things as tangible or instrumental support (e.g., behavioral or material assistance with activities such as housekeeping, transportation, yard work, or finances), affective or emotional support (e.g., information leading persons to believe that they are loved, cared for, esteemed and valued – see Cobb 1976), and informational support (i.e., advice or information intended to help the individual address any difficulties they may encounter – e.g., Cohen 2004; Thoits 2010, 2011). Appraisal support (including information relevant to self-evaluations) and social companionship (such as spending time together in social or other activities) have also been included (Cohen et al. 2000; House and Kahn 1985; Sherbourne and Stewart 1991).

Insofar as caregiving and social support encompass similar forms of assistance, are they synonymous? In fact, they often appear to be used interchangeably (Chappell and Funk 2011). However, some researchers consider them to be distinct, noting that the difference lies not in the specific types of support or assistance being provided but rather in the health-related context within which they are being provided. For example, Gaugler et al. (2002) assert the need to distinguish between routine and disability-related forms of assistance, noting that only assistance that is being provided directly in response to an illness or disability should be considered a form of caregiving. Adopting a similar view, Keating et al. (2003) note that the distinction is important in that support and care networks tend to differ in size and composition, with the care network typically representing a subset of the support network.

Future Directions for Research

Focusing on the distinction between caregiving and social support draws attention to the need for research to address the relationships between social support and caregiving in the context of long-term illness and disability. For example, insofar as both may be provided concurrently, what are the most common patterns of social support and caregiving? Can some forms of assistance reflect elements of both social support and caregiving (e.g., when assistance with housework is provided as a form of support but is augmented in response to increased needs for care)? Insofar as caregiving is initiated in response to long-term illness or disability, there is also a need for research to address transitions from social support to caregiving. How do these patterns of support and care change over time as levels of illness and disability increase? What impact, if any, do increases in caregiving responsibilities have for the provision of social support?

Summary

Caregiving and social support are overlapping concepts that are often used interchangeably. Yet, researchers have noted the importance of the distinction between them. Attention to this distinction highlights the need for research to address the relationships between the two as well as the transitions that occur between social support and caregiving.

Cross-References

▶ Formal and Informal Care
▶ Intergenerational Exchange and Support
▶ Intergenerational Exchanges
▶ Personal Care
▶ Primary Caregivers
▶ Self, Informal, and Formal Long-Term Care: The Interface
▶ Social Support

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Caregiving at Terminal Life

► Caregiving at the End of Life

Caregiving at the End of Life

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Synonyms

Caregiving at terminal life; Caring for people with terminal illness

Definition

Caregiving at the end of life (EoL) refers to caregivers which could be composed of families, friends, paid personal caregivers, healthcare professionals, and/or volunteers to provide care to individuals who are diagnosed with advanced, progressive, and incurable illness and may die within 12 months to live as well as possible until they die (Hebert and Schulz 2006; Stajduhar et al. 2010; NICE 2017; Ornstein et al. 2017).

Overview

The inevitable trend in world population aging, together with the increase in longevity, leads to an increased share of deaths in the over 70s age bracket (Ritchie and Roser 2019), which makes it especially urgent to understand how to provide good palliative care to older adults at the end stage of their life. Knowledge concerning providing care to older adults with terminal illnesses is generally disease-based, with caregiving needs, challenges, and outcomes varying relatively according to the illness trajectories that they follow. Three most typical life-threatening illnesses in people aged over 70, namely, cancer, dementia, and heart failure, were selected as examples to represent the three commonly recognized illness trajectories (Murray et al. 2005; Hebert and Schulz 2006), i.e., steady progression followed by a short period of evident decline, prolonged dwindling, and long-term limitations with intermittent serious episodes, with the end-stage symptoms of the patients, challenges and needs in care, and caregiving outcomes described and discussed for each illness and its trajectory.

Key Research Findings

Cancer is the second leading cause of death worldwide according to WHO (2018). Compared to those who are in curative and life-prolonging phases, cancer patients in the advanced phase are subjected to a more serious level of fatigue, pain, appetite loss, dyspnea, multifunction decline (e.g., Beernaert et al. 2016), and, inevitably, short prognosis with a median survival of 6 months or less (Salpeter et al. 2012). However, mainly due to the extensive demanding required by patients with advanced cancer and their families, they were more likely, than non-cancer patients and families, to use a hospice/palliative care service at the end stage of life (Wachterman et al. 2016). The needs of both cancer patients and their families include pain and symptom management and emotional, psychosocial, spiritual, and informational help to reduce anxiety, to aid decision-making, to keep personal control, and to maintain quality of life (Fitch 2008). Even with the help of palliative team, taking care of a loved one with advanced cancer is also emotionally and mentally painful. Studies identified multiple problems of caregivers of people with advanced cancer, including sleeplessness, general deterioration in physical function, exhaustion, helplessness, anxiety, and distress (Duggleby et al. 2017; Salpeter et al. 2012). Focusing too much attention on the critically ill patient, cancer caregivers are usually unaware of their own heath condition and therefore at increased risk for physical and mental morbidity at palliative and bereavement phase, while their psychological burden often exceeds that of the care recipients (Williams and McCorkle 2011). Compared with caregivers of people with advanced dementia, advanced cancer caregivers reported to have similarly level of depressive symptoms, psychological distress, and caregiving burden, but the caregivers' distress explained 27.9% of the variance in the caregiving burden for cancer caregivers compared to 24.4% for dementia caregivers (Costa-Requena et al. 2015). The impact factors for the negative outcomes of end-stage cancer caregivers were primarily associated with caregivers' factors rather than patients' conditions. Caregivers who were middle-aged, adult children, employed, financially insufficient, receiving low social support, and having little psychological resources were more subject to the negative caregiving outcomes (Given et al. 2004; Lee et al. 2013).

Dementia was the fifth cause of death worldwide listed by WHO (2018). For advanced dementia patients, difficulty swallowing, weight loss, pain on movement, agitation, and apathy are most commonly reported, prior to death, aspiration and breathing difficulties will increase, and septicemia and pneumonia are the commonest acute events for dementia patients prior to death (Sampson et al. 2005, 2018). Caregivers always spend a long time on a day-to-day basis to the point that nearly 50% of them reported spending at least 46 h per week in assisting their dementia relatives in the activities of daily living (Vick et al. 2019), and more than half of them felt to be "24 h" on duty (Schulz et al. 2003). However, due to the unawareness of advanced dementia as terminal illness as well as the prognostic uncertainty, patients with advanced dementia were less like to use palliative care service before they die (Sampson et al. 2005). Meanwhile, because of the behavioral problems and psychiatric symptoms as well as their difficulties in making an EoL-care plan due to dysfunction in communication (Sachs et al. 2004), caregiving of people with advanced dementia was regarded as the most physical and psychological demanding work compared to caregiving provided to patients with non-dementia illnesses (e.g., cancer; Hebert and Schulz 2006). Caregivers of people with advanced dementia usually reported high levels of depressive symptoms and pain, great stress, little time for socialization, and feeling the need to resign or reduce employment due to heavy caregiving duties (Hebert and Schulz 2006; Schulz et al. 2003). Moreover, dementia caregivers were also found to have worse emotional and physical health than caregivers for patients with non-dementia illnesses (Clipp and George 1993). Compared with 15.4% of non-dementia, end-of-life caregivers reporting high strain, 35% of dementia caregivers reported high strain (Vick et al. 2019). And healthcare staff reported to perceive lower competence in providing care to people with advanced dementia compared to providing care to people with advanced cancer (Manu et al. 2012). Regarding factors affecting caregiving outcomes, it found that caregivers who were female, adult children, who had a bad health condition themselves, and who were spending long hours providing care were more subject to the negative outcomes of providing EoL-care service to people with advanced dementia (Vick et al. 2019).

Heart failure (HF) is the typical disease in the cardiovascular disease (CVD) group which represents the leading cause of death worldwide by WHO (2018). Patients with advanced HF (New York Heart Association Class III/IV) have unique symptoms compared to those with coronary heart disease but without HF, including more functional impairment and a higher propensity to suffer from falls and dementia. These patients, therefore, require more hours of informal and formal care (Gure et al. 2008). Meanwhile, advanced HF patients experience a high level of symptoms in dyspnea, emotional distress, fatigue, nausea, reduced appetite, drowsiness, and pain (Yu et al. 2018). Although similar symptoms were found among advanced cancer patients, advanced HF patients have been found to have more and severer physical symptoms, as well as a higher level of depressive symptoms and a lower level of spiritual well-being (Bekelman et al. 2009), which leads to their low quality of life at the end-of-life stage (Blinderman et al. 2008) compared to those with other terminal illnesses (Juenger et al. 2002). However, social support and quality of key social relationships were found to positively affect the prognosis of congestive heart failure patients (D'Alto et al. 2003). For HF caregivers, their experience is strongly associated with balancing the complex medical care of patients and self-care, disturbed sleep, and the frequent hospitalization of patients (Molloy et al. 2005). Compared with caregivers of people with other terminal illnesses, advanced HF caregivers tend to have higher levels of emotional distress, increased caregiving burden, and a reduced sense of psychological well-being (Burton et al. 2012). Even though HF caregivers showed a greater level of unmet needs for physical care, they were less likely to have access to palliative care, indicating there is a significant but overlooked burden placed on HF caregivers (Davidson et al. 2013). Similar to the findings on dementia and cancer caregivers, females are more subject to low levels of well-being and higher levels of caregiving burden, but age and kin relationship to the patients were not significant indicators (Molloy et al. 2005). Meanwhile, a low caregivers' burden is consistently associated with the low functional impairment of patients, strong social support, good quality relationship with patients, continuous care, effective coping strategies, and the high spiritual well-being of caregivers (Yeh and Bull 2012). A study also found that advanced HF caregivers tended to overestimate hours of daily care, which was significantly related with patients' functional status, caregivers' burden, age, and cohabitation (Timonet-Andreu et al. 2018).

Examples of Application

For caring people following the trajectory of a short period of evident decline (e.g., cancer), short prognosis, high access to hospice/palliative care, and abrupt, surprise deaths of the patients with unnoticeable preceding functional decline are typical experiences in EoL care. Studies indicated that timely communication with healthcare professionals, rebuilding supportive networks, cooperating with palliative care professionals, redefining caregiving situation with positive attitudes, and effective training on caregiving skills could effectively improve caregivers' confidence and self-esteem and maintain caregivers' personhood, self-efficacy, and hope (Bee et al. 2009; Duggleby et al. 2017). Meanwhile, special attention should be paid to both patients' and caregivers' need for information support where good communication with healthcare professionals and advanced care planning are consistently related to low aggressive-intervention use and high quality of care at the EoL (Brinkman-Stoppelenburg et al. 2014; Wright et al. 2016).

For caring people following the trajectory of prolonged dwindling functions (e.g., dementia), the EoL-care experience is generally associated with a high demand for long-term, round-the-clock care, high dependency in assisting the activities of daily living, unpredictable death of the patients, and easily underestimated caregiving burden as most illnesses in this trajectory are barely seen as the terminal stage. However, with global aging, not only should the attitude be changed toward illness with prolonged dwindling, but also efforts should be made to call for a collaborative cooperation to provide end-of-life care service to patients and their families living with people in a prolonged dwindling state, including healthcare professionals, informal caregivers, in-home care staff, and also volunteers in the community (Manu et al. 2012; Sampson et al. 2018). Just as suggested by Sachs et al. (2004), caregiving should not be a personal duty, but the effort should be shared by all citizens, for all of us will need to be cared for as we grow old.

While caring for people who are in intermittent serious episodes (e.g., heart failure), long-term care, frequent hospitalization, occasional acute exacerbations, and uncertain time of death of the patients are typical in EoL-care experiences. As caring people in this trajectory usually demand a high level of devoted, intensive family care due to the complicated medical care procedures, a good quality of family relationships, effective coping strategies, and high spiritual well-being are essential for reducing the caregiving burden, stress, and emotional distress. Therefore, the provision of interventions is suggested focusing particularly on improving family relationships with patients and enhancing coping strategies to caregivers with patients in this illness trajectory (Bakas et al. 2006; Dionne-Odom et al. 2017; Sullivan et al. 2016).

Future Directions of Research

Much is still unknown about caregiving at the end-of-life stage. First, more well-designed comparative or longitudinal studies need to be developed to further explore the conditions and mechanisms affecting caregiving experiences for end-of-life care. The questions to be addressed include how and to what extent caregiving experiences vary according to illness conditions and illness trajectories of people with different terminal illnesses; how and whether people who provide care to their families have different transitional experiences compared to those who do not; how cultural expectations and values affect the caregiving experience and outcomes of caregivers; and how and to what extent caregiving needs and outcomes persist over time and into bereavement. Second, in consideration of the impact factor on caregiving outcomes, more interventions should be developed that effectively decrease depressive symptoms and the caregiving burden while increasing caregivers' psychological resources. Meanwhile, as a low access rate of palliative/hospice care has been reported for patients with other terminal illnesses compared to those with advanced cancer (Sampson et al. 2005; Davidson et al. 2013), studies need to be developed to carefully examine the reasons and relevant disincentive factors for this fact. Furthermore, given the existing dearth of systematic and comprehensive approaches to quantitatively assessing the needs of patients and caregivers (Beernaert et al. 2016; Stajduhar et al. 2010), scales and inventories need to be developed with a solid theoretical basis for people living with different terminal illnesses.

Summary

Providing care to people at end stage of life could experience different caregiving burdens, challenges, and needs due to the different illness trajectories the patients follow. Caregivers of people with advanced cancer could experience high level of distress mainly due to the limited prognosis and sudden deterioration of the patients; therefore good communication and close cooperation with healthcare professionals are critical in high quality of care to people with advanced cancer. Caregivers of people with advanced dementia always report high caregiving strain due to long-term, round-the-clock care and severe behavioral and psychiatric problems of the patients. However, their burdens are most likely to be ignored, which lead to their needs in healthcare and social support being largely underestimated. Patients with advanced heart failure always report low quality of life due to their severe physical symptoms, which could also lead to the low emotional and psychological well-being of their caregivers. However, strong social support and high quality of the key relationship are vital to both patients and caregivers of people with advanced heart failure. In summary, caregiving at end stage of life is challenging but meaningful. Devotions are needed from not only the families but also the healthcare system, the communities, and the society, to try to provide a high quality of life to people at end stage of life and their families.

Cross-References

▶ Benefits of Caregiving
▶ Care Needs
▶ Caregiver Stress
▶ Caregiving and Social Support: Similarities and Differences
▶ End-of-life care
▶ Hospice and Caregiving
▶ Quality of Care
▶ Terminal Change

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Caregiving for Children

▶ Parenting and Grandparenting

Caregiving Providers

▶ Caregivers' Outcomes

Caregiving Role

▶ Caregivers' Outcomes

Carer

▶ Hospice and Caregiving

Carer Interventions

▶ Interventions for Caregivers of Older Adults

Carers

▶ Caregivers' Outcomes

Caring

▶ Benefits of Caregiving
▶ Caregiving and Social Support: Similarities and Differences
▶ Self, Informal, and Formal Long-Term Care: The Interface

Caring for Life

▶ *Yangsheng* and Longevity in Chinese Culture

Caring for People with Terminal Illness

▶ Caregiving at the End of Life

Case Management

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Synonyms

Care coordination; Care management; Care planning; Service coordination

Definition

Geriatric case management is defined by "providing client-centered assessment and care planning, facilitating access to critical resources, and coordinating health, mental health, and long-term services and supports that enhance quality of life and promote the health and functional independence of community-dwelling" older adults (Gardner and Zempsky 2015: 853). Though comprehensive, many alternative definitions exist as disciplines and settings that employ case management services for older adults vary. Lukersmith et al. (2016) identify 22 definitions which promotes role confusion and ambiguity. Similarly, Treiger and Fink-Samnick (2015) highlight definitions from six professional associations and societies, along with four from case management certification programs. Collaboration across health care and social services professions to develop a common definition, qualifications, and specified components could further the field of geriatric case management through consistency, regulation and standardization in research, practice, and policy outcomes (Treiger and Fink-Samnick 2015).

Overview

Case management is a common service for older adults to assist in continuum-of-care service coordination (Naleppa 2016). Provided by social workers, physicians, nurses, psychologists and other professionals, either independently or as a team, functions and tasks vary by setting (See ▶ "Geriatric Social Workers" and ▶ "Social Work").

Not only is case management for older adults provided by different professions, geriatric case manager tasks and activities differ by discipline and setting. In one literature review, Lukersmith et al. (2016) note 69 different case management tasks and activities. While geriatric case management competencies are determined by setting and focus (i.e., health condition), knowledge and skills common across the field include: screening, assessment/re-assessment, brokering services within/among providers, outreach, planning, implementation, monitoring, follow-up, communication, collaboration of providers, older adults, and care partners (See ▶ "Care Coordination" and ▶ "Care Management").

Using a biopsychosocial-spiritual perspective, geriatric case managers coordinate a comprehensive geriatric assessment (e.g., activities of daily living, medications, cognition, and environment), outreach, advocacy, and interagency collaborations, and legal, financial, support, and continuum-of-care planning (Gardner and Zempsky 2015) (See ▶ "Comprehensive Geriatric Assessment"). Like the variety in settings, clinicians and tasks, many models of geriatric case management are practiced including interdisciplinary models, consumer-directed programs focusing on supportive services, strengths-based case management focused on strengths over problems, programs within physician services, and task-centered case management (Naleppa 2016).

Key Research Findings

As many countries are seeking solutions to meet health and social needs of a growing aging population while balancing cost of care, research on case management for older adults has concentrated on areas such as interdisciplinary team-based case management; transitional and integrated care; chronic conditions management, disabilities, and dementia. The 2010 Affordable Care Act foregrounded case management as an important strategy for providing care, resulting in development of new models, including The Bridge model (Alvarez et al. 2016), the GRACE (Geriatric Resources for Assessment and Care of Elders) model (Counsell 2011), and Transitional Care Program (TCP) developed by Veterans Administration Medical Center (Lovelace et al. 2016). These models utilize case management and care coordination by an interdisciplinary team to address medical and social needs of older adults with chronic health conditions who are transitioning from hospital to home. Findings from initial trials demonstrate these models' effectiveness in decreasing hospital readmission rates and emergency department (ED) visits, improving quality-of-life for older adults, and reducing caregiver burden (Alvarez et al. 2016; Counsell 2011; Lovelace et al. 2016) (See ► "Aging in Place and Quality of Life").

Studies that review integrated care approaches for older adults using case management report that standards of practice and functions vary considerably which impacts service delivery (Baird and Fraser 2018; Brown and Menec 2018). Case management models are widely adapted and incorporated in a variety of approaches for dementia care. Outcomes from integrating case management approaches for dementia care include improved older adults' ability to access quality care in a timely manner, increased capacity of primary care physicians to manage dementia care, improved efficiency in using limited geriatric specialist resources (Lee et al. 2014); short-term reduced risk of long-term care placement (Tam-Tham et al. 2013); improved quality-of-life for older adults and caregiver burden (Khanassov et al. 2014; Somme et al. 2012); and decreased behavioral and depressive symptoms, hospital admission and length of hospitalization (Khanassov et al. 2014).

Examples of Application

While case management needs may be delivered in any setting that serves older adults, they are primarily integrated into community-based and acute care settings and, increasingly, in out-patient, primary care, and specialty health settings (e.g., transitional care and EDs). Goals vary across services but often emphasize: maintaining independent living (Tam-Tham et al. 2013); improved health outcomes (Counsell 2011); and decreased admission/readmission (Counsell 2011) (See ► "Aging in Place: Maintaining Quality of Life for Older Persons at Home"). In community-based environments, geriatric case management is typically provided by nurses and/or social workers, but a person-centered, collaborative, interprofessional team approach optimizes shared responsibility and accountability (Baird and Fraser 2018) (See ► "Person-Centered Care for Older Adults"). In ED settings, case managers can focus on high-risk screening, care planning, capacity-building, and post-ED follow-up (Sinha et al. 2011). With an ongoing patient relationship, geriatric case managers in primary care settings can provide more proactive and intensive services and coordinate with other providers (Khanassov et al. 2014; Lee et al. 2014).

Future Directions of Research

Along with health service utilization and costs, future research can examine older adults, family and provider satisfaction, and other health outcomes (Lovelace et al. 2016). Previous findings suggest that high intensity case management can produce positive clinical outcomes for older adults (Khanassov et al. 2014; Somme et al. 2012). Research is needed to determine cost-effectiveness of case management programs for dementia patients and their caregivers (Somme et al. 2012). Studies are emerging on interventions for depression care and suicide assessment of older adults (Alexopoulos et al. 2016; Hasche and Lavery 2015; Pope et al. 2016). Limited research suggests positive benefits of case management for end-of-life care; however, this field remains under-researched (Thomas et al. 2014). Technology use in case management practice for older adults is a novel approach (Berner et al. 2016), but warrants further research to establish feasibility, efficacy, and effectiveness.

Summary

Professionals providing care to older adults have an opportunity to enhance quality of care provided, patient and caregiver involvement, satisfaction, compliance, and health outcomes by integrating evidence-based case management strategies. Due to the growing population of older adults with increasingly complex health care needs, a shift from volume-based to value-based health care delivery and recognition of the role that social factors have in health outcomes, geriatric case managers are needed to develop, communicate, and coordinate the care plan (Case Management Monthly 2018).

Cross-References

- ▶ Aging in Place and Quality of Life
- ▶ Aging in Place: Maintaining Quality of Life for Older Persons at Home
- ▶ Care Coordination
- ▶ Care Management
- ▶ Comprehensive Geriatric Assessment
- ▶ Geriatric Social Workers
- ▶ Managed Care and Aging
- ▶ Person-Centered Care for Older Adults
- ▶ Social Work

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Case/Care Manager

▶ Care Management

Case-Mix Differences

▶ Risk Adjustment: Applications in Healthcare Markets

Casework

▶ Social Work

Cash Assets

▶ Financial Assets

Caspase-Mediated Cell Death

▶ Programmed Cell Death

Cataract

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Synonyms

Cortical cataract; Lens opacity; Nuclear cataract; Opacity; Posterior subcapsular cataract

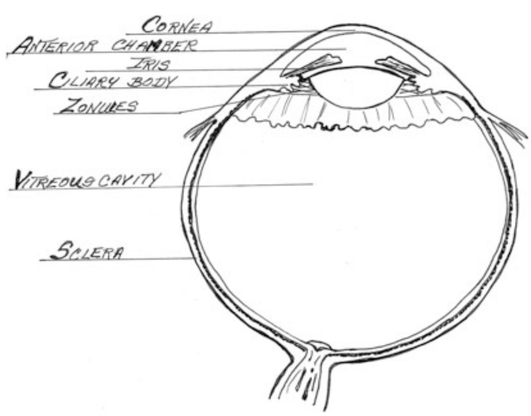
Definition

A medical condition in which the natural lens of the eye undergoes progressive opacification or clouding, resulting in blurring or loss of vision.

Overview

Eye and Lens

The eye is a delicate and complex organ, responsible for the important sense of sight. The lens is an oval-shaped (biconvex) structure, located behind the cornea (clear window in the front of the eye), iris (colored part of the eye), and pupil (the round hole or aperture through which light enters the eye). It is connected to a circular band of muscle, known as the ciliary body, via zonular fibers or zonules. Figure 1 shows a cross-sectional view of the eye, with the lens pictured behind the iris. Along with the cornea, the lens helps focus light as it enters the eye to form a clear image on the photoreceptors of the retina (nerve layer in the back of the eye). The lens is unique in that it has no nerves or blood vessels. It gets nutrients from the aqueous humor, a clear fluid that fills the space between the cornea and the lens. The lens is composed of a thin, clear outer capsule, a gelatinous layer of cortical fibers (cortex), and a central nucleus. At birth, the normal lens is optically clear and flexible enough to change shape. Contraction and relaxation of the ciliary muscle alters the shape of the lens, allowing the eye to focus on objects both near and far. The attachments of the lens to the zonules and ciliary body are depicted in Fig. 2.



Cataract, Fig. 1 Cross-sectional view of the eye: the lens is the oval-shaped structure located behind the iris. It is attached to the ciliary body via the zonules. (Illustration copyright Janet Luiz)

Cataract, Fig. 2 Cross-sectional view of the lens and surrounding structures showing relationship of the lens to the cornea, iris, and ciliary body. (Illustration copyright Janet Luiz)

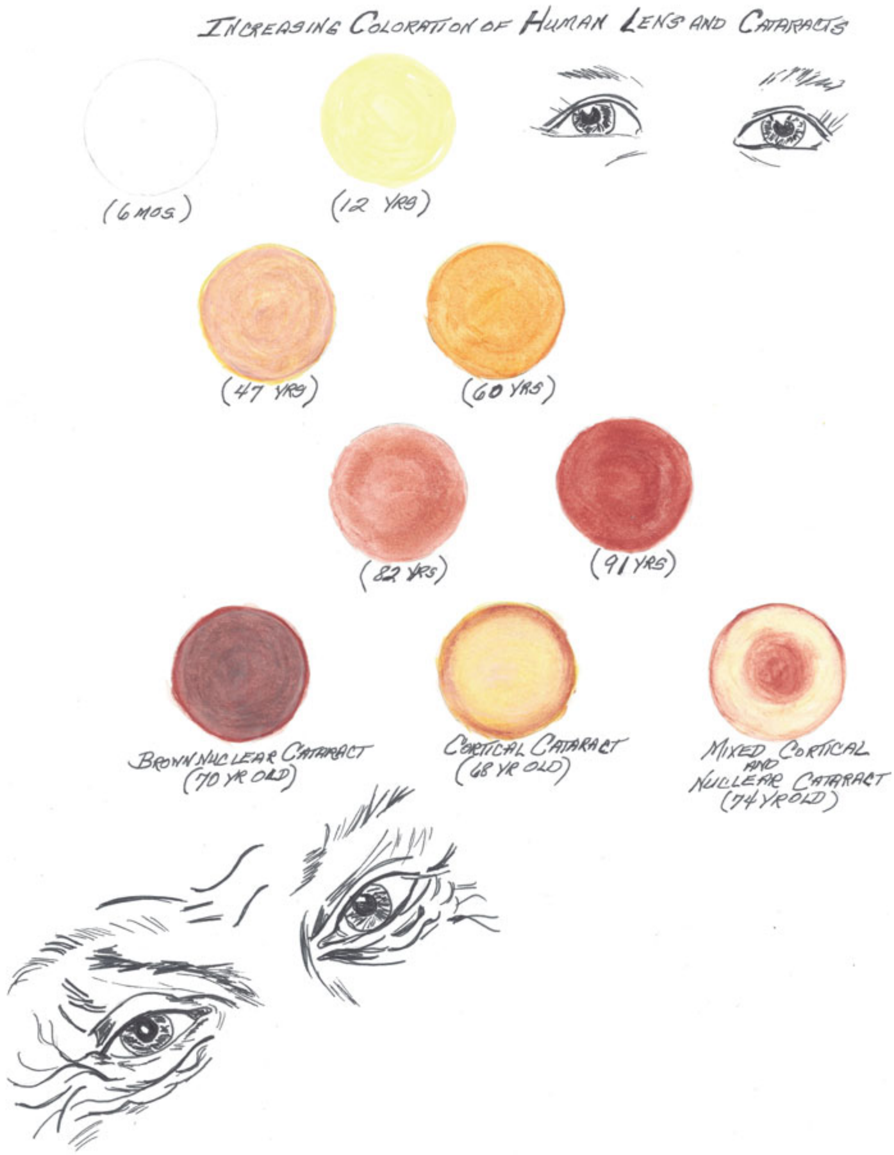
Cataract

As a person ages, changes occur in the lens. New cortical fibers are constantly generated at the periphery or equator of the lens. As these new fibers form, the central nucleus is compressed and hardens. The lens gets heavier, thicker, and less flexible. This loss of flexibility contributes to presbyopia, the loss of near vision (accommodation or the ability to focus up close) that occurs with aging. Aggregation of the proteins in the lens causes loss of transparency and scattering of light. Chemical modification of proteins results in progressive color change, from yellow to brown, and opacification of the lens (Fig. 3). Most adults over 50 years of age have some yellowing (sclerosis) of the lens nucleus. These changes are slowly progressive and result in vision loss from nuclear cataract (Fig. 4). When a person develops a nuclear cataract, his/her perception of colors, especially blue, becomes dull, and images are blurred. Over time, cortical fibers can become opacified or liquefied, resulting in a cortical cataract (Fig. 5). Glare from intense light, such as oncoming headlights, is a common symptom. Cortical cataracts can also cause double vision. A plaque-like opacity that can develop in the back portion of the lens near the capsule is called a posterior subcapsular cataract (PSC). This type of cataract can progress rapidly and cause profound vision loss. Ophthalmologists diagnose cataracts by observing these lens changes under a special microscope (slit lamp biomicroscopy). Cataracts can also develop as the result of diseases, hereditary conditions, trauma, and use of certain medications. Ultraviolet (UV) light exposure, poor nutrition, and tobacco smoking cause cataracts to develop earlier and progress faster.

Cataracts are the leading cause of vision loss, and a significant cause of blindness, worldwide (See ► “Sensory Disability”). Most blindness from cataract, which is reversible with surgery, occurs in developing nations with limited medical resources. Millions of people over age 40 in the United States (US) are affected by cataracts. The condition can result in loss of productivity and independence due to decreased vision that affects an individual’s ability to work, drive, and perform other activities of daily living (See ► “Autonomy and Aging”). This loss of independence can lead to social isolation, reduced quality of life, and depression (See ► “Social Isolation”). Visual impairment from cataract can also contribute to decreased cognitive performance as well as falls and other injuries in the elderly (See ► “Falls”).

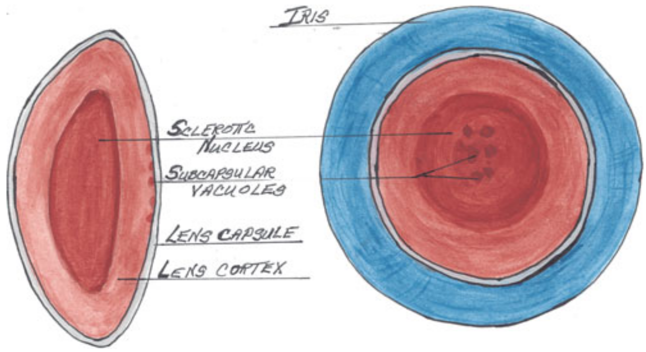
Treatment of Cataract

There is no known effective nonsurgical treatment for cataract (See ► “Nutrition and Aging: Surgical Issues”). As early as the fifth century BC, cataracts were surgically treated using a method called “couching” in which the lens is pushed into the bottom part of the eye to remove the opacity from the direct line of vision. This procedure had significant complication rates and usually only restored enough vision to see light or basic shapes and colors. In the seventeenth century, an improved technique, known as extracapsular cataract extraction (ECCE), was developed. In this

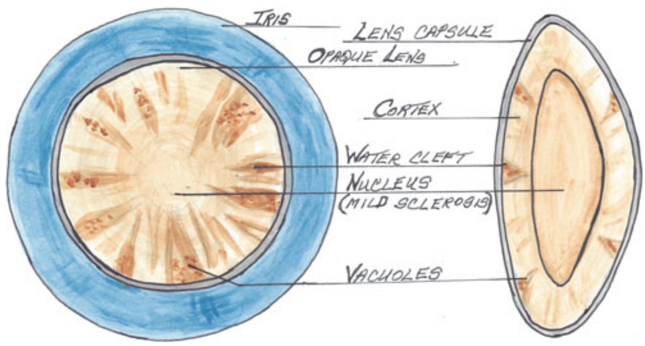


Cataract, Fig. 3 Progressive discoloration of the lens with age. (Illustration copyright Janet Luiz)

procedure, the cataractous lens was removed from the eye through an incision in the eye wall (sclera). In 1967, Dr. Charles Kelman ushered in the modern era of cataract surgery when he invented the phacoemulsification technique. In this technique, a small metal tube driven by ultrasound is used to emulsify (break into extremely small fragments) the lens nucleus and remove it from the eye. Using phacoemulsification, the cataract can be removed through a very small incision in the cornea. This allows for better wound healing, shorter operative times, and less invasive anesthesia. In most phacoemulsification cases, eyedrops are used to numb the eye, and the entire surgical procedure takes only 15–30 min. Most cataract surgeries are performed on an outpatient basis, in an ambulatory care setting (See ► "Ambulatory and Outpatient Care").



Cataract, Fig. 4 Nuclear sclerotic cataract shown in cross section (left) and en face (right). The lens nucleus becomes thickened and yellow to brown in color in this type of cataract. (Illustration copyright Janet Luiz)



Cataract, Fig. 5 Cortical cataract shown en face (left) and in cross section (right). The lens cortex becomes white and liquified with spoke-like opacities in this type of cataract. (Illustration copyright Janet Luiz)

In the early days of extracapsular cataract surgery, the patient was left without a lens in the eye (aphakic) and had to wear very thick glasses to focus the image. These aphakic spectacles were heavy and caused distortions in the vision. This changed in 1949, when Dr. Harold Ridley implanted the first artificial intraocular lens (IOL). Dr. Ridley developed the lens implant after he observed that fragments of airplane windshields, made of polymethyl methacrylate (PMMA), did not cause inflammation in the eyes of injured World War II pilots. Over the years, the design of intraocular lenses has evolved and changed. Modern IOLs can help correct presbyopia and astigmatism (abnormal curvature of the cornea), reducing patients' dependence on glasses or contacts.

Key Research Findings

Epidemiology of Cataract

Cataracts are the leading cause of blindness worldwide according to the World Health Organization (WHO), causing moderate to severe vision loss in 25% of adults 50 years and older (Flaxman et al. 2017). Cataracts cause 35% of cases of blindness worldwide, with 12.6 million people blind due to the condition, the majority of these cases in developing nations. Though the age-standardized prevalence of cataract decreased somewhat between 1990 and 2015 (36.7% vs. 35.1%), growth and aging of the population have resulted in an actual increase in the number of people affected by cataract blindness. Over this time period, the number of people affected by blindness due to cataract increased from 10.9 million to 12.6 million, and the number with vision impairment due to cataract increased from 39.6 million to 52.6 million. In the United States, the number of persons age 40 and older affected by cataracts will likely rise to 38.5 million by 2032 and to 45.6 million by 2050 (Wittenborn and Rein 2014). Rates of cataract surgery vary widely around the world. In developing countries, the rate may be as low as 50 cases per million people. Developed countries may have rates as high as 10,000 per million. Annually in the United States, about three million cataract surgeries are performed. This rate is likely to increase as the average age of the population increases. The US Veterans Health Administration performs nearly 80,000 of these surgeries annually (See ▶ "Veterans Care"). In the United States, the direct annual medical cost of outpatient, inpatient, and prescription services for cataract totals approximately $10.7 billion (Prevent Blindness 2019) and is projected to increase to $33.4 billion by 2050.

Beyond the direct financial burden of cataracts, visual impairment has been demonstrated to have significant implications for an individual's mobility, activities of daily living, social interaction, and cognitive performance to name a few. All of the aforementioned implications may have significant influence financially from an individual, family, and societal perspective (Rein et al. 2006). Cataracts may be considered to fall into the category of preventable visual impairment due to the existence of a highly effective surgical procedure to address their presence. Cataract surgery has been shown to have a dramatic effect on an individual's quality of life in the areas of daily functioning, emotional, and social life components (Lamoureux et al. 2011).

Risk Factors for the Development of Cataract

The Beaver Dam Eye Study (Klein et al. 2014) and the Blue Mountains Eye Study (Tan et al. 2008) demonstrated an increased risk for nuclear and posterior subcapsular cataracts among tobacco smokers. Other risk factors confirmed by multiple studies include ocular trauma (including previous eye surgery), extreme nearsightedness (high myopia), diabetes mellitus (See ▶ "Diabetes Management in Older Adults"), ultraviolet light exposure, and prolonged use of corticosteroid medications in the form of nasal sprays, inhalers, topical creams, or systemic pills or injections (Mukesh et al. 2006). Several studies, including the Age-Related Eye Disease Study (AREDS) 1 and 2, have examined the role of nutritional supplements including vitamins C and E, lutein, and zeaxanthin in cataract formation (AREDS research group 2001). Though these nutrients have been shown to prevent the progression of other eye disease such as macular degeneration, they appear to have a less significant role in preventing cataracts (Chew et al. 2013).

Distribution of Types of Cataract

Age, sex, and race play a role in the type and severity of cataracts. Nuclear cataracts are found in about 2.9% of persons aged 43–54 years and in about 40% of persons aged 75 or older. For these same age cohorts, the respective incidence of cortical cataract is 1.9% and 21.8% and for PSC, 1.4% and 7.3%. Women are more likely than men to have nuclear cataracts. Caucasians are more likely to have nuclear cataracts, and African Americans are more likely to have cortical cataracts, according to the Salisbury Eye Evaluation project (West et al. 1998). Incidence of PSC is similar between these two groups. Asians also have a higher rate of cortical opacification than Caucasians (Chua et al. 2015).

Examples of Application

Knowledge of the prevalence, socioeconomic variations, and quality-of-life impacts of visual impairment due to cataract worldwide has led to significant efforts to eradicate this cause of preventable/reversible blindness. For example, Dr. Sanduk Ruit and others in the Himalayan Cataract Project have pioneered new techniques of cataract surgery, intraocular lens manufacturing, and care delivery models to bring sight-restoring surgery to many persons in remote areas (Ruit et al. 1999). Their efforts to deliver care and to train other physicians in underserved countries are making a significant impact on preventable and reversible blindness from cataract (Ruit et al. 2018). In developed countries, new surgical techniques such as the use of femtosecond laser and new types of intraocular lenses designed to optimize vision without the need for glasses improve efficiency and outcomes (Li and Jie 2019).

Future Directions of Research

Research into new technology continues to advance the accuracy and efficiency of cataract surgery. Significant work is also being done to try to eliminate presbyopia, either via restoring the flexibility and elasticity of the natural lens or via advanced-design IOLs that can give patients both near and distance vision (Renna et al. 2016). It is possible that someday there may be a medical means of preventing or treating cataracts. Until then, research will focus on optimal methods and techniques for cataract surgery and IOL implantation, as well as means to ensure access to this life-altering surgery for underserved populations.

Summary

Cataracts occur when the lens of the eye undergoes progressive thickening, discoloration, and opacification. This leads to vision loss and, in some cases, blindness. Cataracts are the leading cause of vision loss worldwide. Visual impairment from cataracts leads to loss of independence, decreased productivity, falls and associated injuries, social isolation, and cognitive decline. Persons in developing countries, with less access to medical care, have higher rates of this blinding condition. Surgery is the only effective treatment for cataract. Surgical techniques have evolved dramatically over the years. Optimizing cataract surgical technique and access to care are important areas of research, particularly as population growth and aging increase the number of persons affected by this condition.

Cross-References

▶ Aging and Health Disparities
▶ Ambulatory and Outpatient Care
▶ Autonomy and Aging
▶ Falls
▶ Independent Aging
▶ Nutrition and Aging: Surgical Issues
▶ Sensory Disability
▶ Social Isolation
▶ Vetek (Seniority): The Movement for Longevity and Quality of Life
▶ Veterans Care

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Catastrophic Disability

► Consequences of Pneumonia in Older Adults

Causal Agency

► Self-Efficacy

Causes of Population Aging

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Synonyms

Demographic determinants of population aging; Demographic drivers for population aging; Sources of population aging

Overview

The process of population aging is closely linked to demographic transition which involves fertility and mortality changes. Magnitude and pace of population aging are determined primarily by trends in fertility and by mortality rates, although migration may also have some influence (Booth 2018; Kinsella and Phillips 2005). During the process, the proportion of the population that is older is rising due to a decline in fertility, and the number of older persons is higher due to a decline in mortality. By mid-century, the proportion of persons aged 60 and above is estimated to rise to nearly one third of the total population in more developed regions and to about one fifth in less developed regions (United Nations 2017). Meanwhile, the number of persons aged 60 and older around the world is expected to triple during the first half of the twenty-first century, reaching over two billion by 2050.

Fertility Decline

Fertility is the most important factor explaining population aging, especially during its initial stage (Weeks 2015). Any population with a long history of high fertility has a young age structure. A decline in the number of newborns leads to fewer younger people and thus proportionally more people at older ages. At first, a decline in fertility may not result immediately in a smaller number of births. This is because, as a consequence of high fertility in the past, the number of reproductive-age women is likely to increase sufficiently to counterbalance the fertility decline. Nevertheless, sustained low fertility would eventually reduce the size of successive birth cohorts and increase the proportion of older people.

In Europe and North America, the decline in fertility that began in the nineteenth century pushed the average number of children per woman below the replacement level of 2.1 children by the 1970s. This has led to a continual increase in proportions of older people in the total populations. In less developed regions such as Asia, fertility decline has been more recent and more rapid. Much of the less developed regions observed large reductions in fertility rates during the last half-century. The total fertility rates in a majority of these countries are now at or below replacement level. Since the degree of aging depends on the pace of fertility decline, several Asian countries including China are expected to witness the proportions of older-age population grow multiple folds between 2020 and 2050 (United Nations 2017).

Mortality Decline

The process of population aging, particularly in its later stages, is determined primarily by declining mortality through increased survival into older ages and the augmented size of the older-age population (Booth 2018). It is important to note that the early stages of mortality decline actually generate a younger population age structure. This is because the decline benefits infants and children more than other age groups as infectious and parasitic diseases can be effectively controlled by improved sanitation, advancements in medicine, and expansion of public health services and facilities (Riley 2001). Since the 1800s, the decline has contributed significantly to the gain in human longevity and increased life expectancy at birth. The early decline in mortality among the young usually takes place, while fertility is high leading to large birth cohorts and an expanding proportion of children relative to adults. Furthermore, early mortality decline is characterized by a reduction in maternal mortality, which increases the proportion of women in reproductive ages and in turn fertility rates. As the decline in mortality continues, early-life and maternal mortality reaches low levels. The decline begins to increasingly benefit older ages to a greater extent than young ages, thus contributing to population aging. The threshold for mortality decline that produces population aging is estimated to be when life expectancy reaches 65 years (Preston et al. 2000).

Research shows that mortality rates slow down at very old ages and that the age at which mortality deceleration occurs has been rising (Horiuchi and Wilmoth 1998; Lynch and Brown 2001). This might be due to a possibility that people who survive to very old ages have heathier attributes or healthier lifestyles. Another possible reason is that genes which increase mortality risks over the life course have become suppressed. As changes in mortality assume greater importance for population later in the demographic transition, the speed at which mortality at advanced ages decline will play a significant role in determining the future size of the older-age population, especially for the very old. Caselli and Vallin (1990), for instance, demonstrate the increasing importance of mortality change in the population projections for Italy. If fertility rates in Italy were to remain very low at 1.4 children per woman through 2040, over half of the increase in the proportion of the population age 60 and older would be due to mortality change and less than half due to fertility decline.

Migration

Compared to fertility and mortality decline, migration has played a less significant role in the process of population aging. Nevertheless, it can be important for the aging process of smaller populations. Emigration, which tends to involve working-age adults, affects the proportion of young adults in the origin countries as well as the future composition of young children in the sending population due to their influence on reproduction. In other words, migration may accelerate aging in the sending population while decelerating aging in the destination population. In some Caribbean countries, for example, a combination of emigration of working-age adults, immigration of retirees from other countries, and return migration of older-age former emigrants contributes to population aging (Kinsella and Phillips 2005).

Looking ahead, international migration is expected to have a more prominent role in the aging process, particularly in countries with old age structure where sustained low fertility has led to stable or even declining population size. For instance, Canada has one of the world's highest per-capita immigration rates partly to counter population aging (Mirkin and Weinberger 2000). Nevertheless, some questions the feasibility and sustainability of international migration in addressing population aging. As fertility sinks to well below replacement level, increasingly higher levels of annual net migration are required to maintain even zero population growth (McDonald and Kippen 2000).

Prospects

There have been ongoing debates regarding quantifying the contributions of demographic drivers to population aging, in particular whether fertility or mortality plays a more prominent role in driving contemporary population aging. On one hand, mortality decline is argued to replace fertility to be the main demographic source of continuing population aging. Preston and Stokes (2012), for instance, demonstrate that mortality change is primarily responsible for the continuing population aging in more developed countries from 2005 to 2010. Their argument implies that if mortality had not declined over the past century, today's population aging would have been substantially less rapid. On the other hand, Lee and Zhou (2017) argue that the principal responsibility of contemporary population aging still lies with fertility. This is particularly the case for populations that are relatively early in the demographic transition such as most of sub-Saharan Africa. Nevertheless, for the rest of the world, mortality is likely to eventually drive population aging in the future. Lee and Zhou (2017)'s comparison of the UN projection variants supports this view for continuing aging from 2095 to 2100, except in sub-Saharan Africa.

Inherent to demographic transition, the process of population aging is projected to end eventually. According to Booth (2018), if posttransitional fertility and mortality were to remain constant, assuming there is no migration, population aging would stop after human lifespan has roughly reached 100 years, but population growth (possibly negative growth) would likely continue. Furthermore, population aging is likely irreversible. An older, posttransitional age structure is both inevitable and essentially permanent (Booth 2018, p. 432).

In sum, the pace of fertility decline primarily determines the degree of population aging and the deceleration of population growth. Meanwhile, the pace of mortality decline contributes to population aging after early-life mortality has reached low levels. In other words, the pace of demographic transition directly affects the degree and speed of population aging.

Cross-References

▶ Aging Mechanisms
▶ Demographic Transition Theories
▶ Lowest-Low Fertility
▶ Population Decline
▶ Population Explosion and Implosion
▶ Population Momentum

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Cell Aging

▶ Cell Senescence

Cell Damage and Transformation in Aging

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Synonyms

Cancer; Cellular aging; Cellular senescence; DNA damage; DNA mutation; Malignant transformation

Definition

Age-dependent cell damage refers to the accumulation of DNA damage over a lifetime, which may ultimately lead cells to undergo malignant transformation, that is, transformation into cancer cells.

Overview

Aging is accompanied by an accumulation of cellular damage that ultimately leads to tissue decline and death. Over a lifetime, cells are continuously damaged by exogenous (physical, chemical, and biological agents) and endogenous sources (DNA replication errors, spontaneous hydrolytic reactions, and reactive oxygen species (ROS)), thus increasing the risk of acquiring mutations (Hoeijmakers 2009). In spite of the majority of these mutations being harmless and usually corrected by the DNA repair system, some unrepaired DNA damage may accumulate over time resulting in genomic instability (See ► "Genome Instability") and leading to cell senescence and apoptosis (Maynard et al. 2015). Genomic instability, a state with a high frequency of mutations, may initiate malignant transformation (Hanahan and Weinberg 2011).

Key Research Findings

Cells that have a great potential to give rise to malignant transformed cells tend to respond to DNA damage by inducing programmed cell death (apoptosis) (See ► "Programmed Cell Death"). Alternatively, they can prevent malignant transformed cells proliferation by inducing permanent cell cycle arrest (cellular senescence) (Campisi 2005; Kirkwood 2005). Cellular senescence was first described by showing that cultured human fibroblasts do not proliferate indefinitely but gradually decline over time due to telomeric shortening in each DNA replication in the absence of endogenous telomerase activity (Hayflick and Moorhead 1961; Muñoz-Espín and Serrano 2014). Telomeres (See ► "Telomeres") are repetitive nucleotide structures that protect chromosome ends and maintain the genome integrity and stability. Cells containing dysfunctional telomeres, which are able to escape senescence, develop chromosomal aberrations that ultimately result in malignant transformation (Maciejowski and de Lange 2017). Thus, senescence works as a protective mechanism preventing the propagation of potentially oncogenic mutations. It remains unclear how cells choose between apoptotic and senescence responses. In spite of both preventing malignant transformation, they may present cumulative deleterious effects, such as the depletion of renewable tissues of proliferation-competent progenitor or stem cells, thus contributing to aging and late-life pathologies (Campisi 2005; Rodriguez et al. 2017). p53, a tumor suppressor protein, plays an important role in the regulatory mechanisms between DNA repair, apoptosis, and senescence (Erol 2011). Upon DNA damage, p53 becomes functionally active ceasing cell proliferation and preventing the propagation of DNA mutations. p53 activation may trigger a transient cell cycle arrest, which allows cells to repair the damages and re-enter the normal cell cycle upon completion. However, in cases of severe damage, p53 activation induces apoptosis or senescence to avoid possible malignant transformation (Rodier et al. 2007; Ozaki and Nakagawara 2011). Suppression or mutations on p53 may lead to malignant transformation (Roos et al. 2016).

Aging is also associated with nonmutational changes to DNA, called epigenetic alterations which involve changes in DNA methylation patterns, posttranslational modification of histones, and chromatin remodeling (Dawson and Kouzarides 2012). Alterations occurring in DNA methylation patterns are closely related with the risk of malignant transformation. Specifically, it has been described an increased DNA methylation in a subset of genes associated with malignant transformation during both aging and early stages of tumorigenesis (Xie et al. 2018).

Future Directions for Research

Aging comes with the gradual decline of cells' ability to repair DNA damage increasing their susceptibility to malignant transformation. As the average life expectancy has been increasing, the search of methods that may delay cellular damage and transformation is paramount. Targeting key regulators such as p53, oncogenes, and telomerase may constitute promising strategies for preventing and treating malignant transformation. In recent years, several therapies have been proved to have an impact in lifespan extension. As the risk of development of cancer increases with age, the delay of the aging process using pharmacological approaches may be accompanied by an increased incidence of malignant transformation. Further studies should focus on developing aging-delaying strategies that promote a lower tumor incidence.

Summary

The accumulation of cellular damage with age can lead to malignant transformation. Although several theories have been established to reveal the relationship between aging and cancer, some fundamental questions remain to be answered. A better understanding on the underlying mechanisms of both age-dependent cellular damage and the initiation and progression of malignant transformation may aid the development of novel therapeutic strategies that could lower the risk of developing cancer and allow lifespan extension as much as possible.

Cross-References

▶ Aging and Cancer: Concepts and Prospects
▶ Cellular Aging/Senescence
▶ Cellular Repair Processes
▶ DNA Damage Theory
▶ Genome Instability
▶ Mutation Accumulation Aging Theory
▶ Oxidation Damage Accumulation Aging Theory (The Novel Role of Glutathione)
▶ Programmed Cell Death
▶ Redox Signaling
▶ Stem Cells Aging
▶ Telomeres

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Cell Morphology in Aging

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Definition

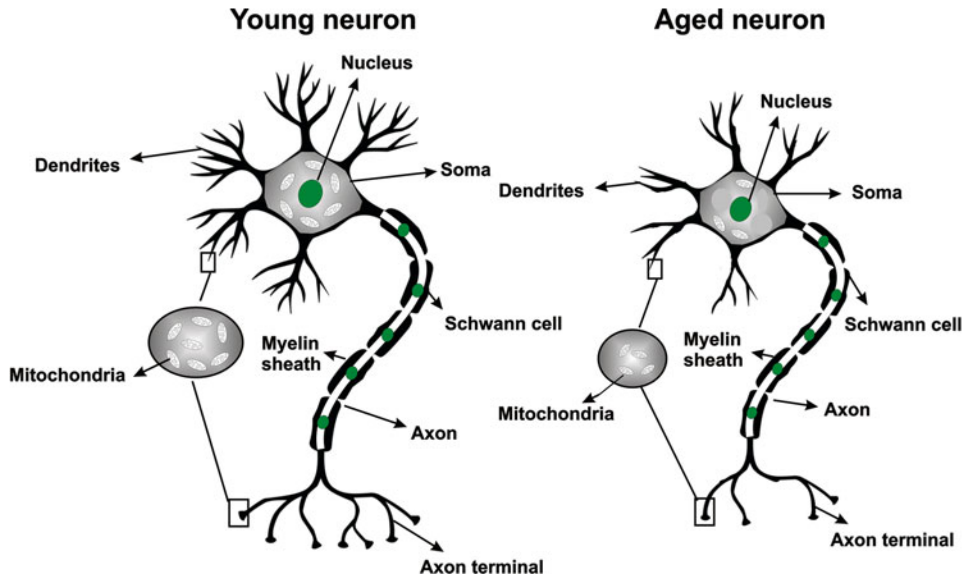
Cell morphology is the study of the size and shape of the cell.

Overview

Aging affects cells in all regions of the nervous system as indicated by the decline of sensory, motor, and cognitive functions over time (Mattson and Magnus 2006). Neurons (also called nerve cells) are the fundamental units of the brain and nervous system. These nerve cells are responsible for receiving sensory input from the external world, for sending motor commands to the muscles, and for transforming and relaying the electrical signals at every step in between. A neuron has three main parts: cell body (soma), dendrites, and an axon. The cell body contains a nucleus and organelles such as mitochondria, endoplasmic reticulum, and Golgi apparatus. Dendrites are the branching from the nerve cell body and function as small antennae which picks up signals from other cells. Exon is located at the opposite end of the nerve cell body, and is a long, thin fiber with branches at the end that sends signals. The axon is insulated by a myelin sheath made up of segments called oligodendrocytes and Schwann cells. Although it is well substantiated that no excessive loss of neurons occurs during normal aging (Pannese and Function 2011), yet other subtler morphological changes take place in individual neuronal cells. These changes include losses of dendrites and dendritic spines and shrinkage in soma size (Fig. 1). The number of the axons also decreases and their myelin sheaths may become less compact and undergo segmental demyelination followed by remyelination, alterations in neurotransmitter receptors, and changes in electrophysiological properties (Dickstein et al. 2007). These changes lead to significant losses of synapses and majorly contribute to the behavioral impairment and decline in cognitive abilities which often accompany the process of normal aging (Kritsilis et al. 2018).

Key Research Findings

Aging is associated with cognitive decline and an increased risk of neurodegeneration. During aging, it is evident that neurons undergo morphological changes such as a reduction in the



Cell Morphology in Aging, Fig. 1 Aging-induced morphological changes in neuron include reduction in the number of dendrites, dendritic spines, axon fibers, and thinning of myelin sheath. The size of the cell body (soma) also becomes smaller with significant reduction in the size, density, and number of mitochondria

complexity of dendrite arborization and dendritic length (Dickstein et al. 2007). Spine numbers are also decreased in the dendrites which eventually affect the synaptic density.

Loss of mitochondrial function is one of the major factors that is shown to be associated with cognitive decline accompanying healthy aging. Morsci et al. (2016) performed comprehensive in vivo analysis of age-associated changes in mitochondrial morphology, density, trafficking, and stress resistance in *C. elegans* neurons throughout adult life. Their study revealed three phases of increase, maintenance, and decrease in mitochondrial size and density in adult neurons. The first stage of adulthood involves increased number, size, and density of mitochondria, followed by the second stage in which the mitochondrial load, size, and density is relatively more stable. The third stage is characterized by decreased number, size, and density of mitochondria in adult neurons. In contrast, long-lived daf-2 mutants displayed a delay in age-associated changes in mitochondrial morphology, constant mitochondrial density, and maintained trafficking rates during adulthood.

Toth et al. (2012) reported two major components of morphological change in the aging *C. elegans* nervous system: first is the accumulation of novel outgrowths from specific neurons, and second is the physical decline in synaptic integrity. They suggested that morphological changes that occur during aging are neuron-specific and include new dendrite outgrowth from processes or somata, with mitochondria often situated at the branch point for the new neurite.

Neuronal dendrites play key role not only in the formation and maintenance of neural networks, but also in the regulation of synaptic plasticity and the integration of electrical inputs. Studies in humans, primates, nonhuman primates, and many other animals have shown that there was a significant reduction in the number of dendritic spines in neurons with aging (Dickstein et al. 2007).

In humans, axon fiber counts and mean axonal diameter as well as the axon fiber density decrease with age (Saliani et al. 2017). The axons are covered by myelin sheath which is formed by spiral wrapping and compaction of oligodendrocytes around the axons (Simons and Nave 2016). Myelin sheath insulates the nerve fibers and conducts electrical impulses away from the nerve cell body. In the adult central nervous system of humans and nonhuman primates, structural modifications or changes in myelin integrity/composition severely compromise neural circuit function and are associated with age-related functional decline (Seixas et al. 2018).

Many reports suggest that despite of the deposition of large amount of cellular waste which is a hall mark of aging, the cell body of a neuron retains its size (Maxwell et al. 2018; Schwarz et al. 2009). At the same time, some contradictory reports also exist where the aging neurons have been shown to undergo decrease in the size of cell body (Rizzo et al. 2015), implicating that change in the morphology of cell body might be specific to the type of neuron.

Future Directions of Research

Aging-related morphological changes in the neurons are primary cause for the cognitive decline and also lead to several neurodegenerative disorders. Reduced number, size, and density of mitochondria in axons and dendrites leads to the depletion of energy required for the normal functioning of neuron. This leads to the delay in the transmission of electric impulse through the neurons. Future research on aging-induced neuronal changes should be focused on restoring the morphology of neurons by inhibiting the factors which affect the cell morphology of neurons. For example, restoring the mitochondrial biogenesis in neurons will keep the steady energy level which is the prime requirement for proper functioning of nervous system.

Cross-References

- ► Alzheimer's Disease
- ► Brain Atrophy
- ► Central Nervous System
- ► Neuroscience of Aging

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Cell Replacement

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Synonyms

Cell therapy

Definition

Cell replacement, broadly defined, is the addition of new cells to a tissue or organ of the body for the purpose of ameliorating a disease state or repairing damage. Cell replacement falls into two non-mutually exclusive categories. First, transplanted cells can be used as vehicles for persistent delivery of factors (trophic, anti-inflammatory, angiogenic, etc.) to diseased or damaged tissues. In this case, the existing cells benefit from the released factors by increasing their survival and/or function. Second, cell therapy in a stricter sense is defined as the replacement of lost or damaged cells with new ones, whereby the new cells assume the function of the previously lost or dysfunctional resident cells. This entry is only focused on the latter category, cell therapy as functional cell replacement.

Overview

Over the past several decades, interest in cell replacement therapies has increased steadily and will likely continue to do so in the future. The interest in cell therapy is fueled by the identification, characterization, and isolation of stem cells that can be used for repairing or rebuilding tissues and organs. During development of a human individual or any other animal, tissues are generated from stem cells. As development proceeds, cells become progressively more specialized. For example, a stem cell in the early embryo at the morula or blastula stages (4–5 days after fertilization in the human, before implantation in the uterus) is pluripotent, which means that it can generate all the cells that will make up the entire body. In contrast, as fetal development proceeds, stem cells become more specialized and can only generate limited subsets of cell types – neural stem cells give rise to nervous system cells, cardiac stem cells give rise to heart cells, and so on. In the adult, specialized stem cells are present in organs that require continuous cell turnover, such as in the skin, digestive tract, and circulatory system, although stem cells with even more limited potential can also be found in some other adult tissues. Finally, using cell reprogramming technologies, differentiated adult cells, usually from skin or blood, can be induced to revert back to immature embryonic stem-like cells (induced pluripotent stem cells or iPSCs) using cell reprogramming technology. All of these stem cell types, from the early embryonic stem cells (ESC) and iPSCs to the stem and differentiated cells that reside in adult tissues, can potentially be used for tissue and organ repair. In this entry, because of the ever-growing number of examples of cell replacement therapies that are being developed in preclinical and clinical studies, only a select number of examples among an ever-growing number are provided to illustrate the overall potential of this approach to treat age-related diseases and perhaps aging itself.

Key Research Findings

Circulatory System

Traditionally, treatment of diseases involving the circulatory system – veins and arteries – has been limited to drug therapies that, for example, reduce plaque deposits, or to surgical interventions such as stents and repairing damaged vessels with grafts. There are stem cell-based improvements in development, but they are at an early stage. One of the most promising approaches was reported very recently (Colunga et al. 2019). This report described the generation from human embryonic stem cells of a stable precursor cell type, called "multipotent vascular progenitors." This progenitor cell type can also be generated from iPSCs, by guiding the differentiation of pluripotent cells along a developmental lineage called the mesothelium. Like other cell types derived from pluripotent stem cells, these "MesoT" cells were generated by experimentation designed to mimic a particular embryological process. MesoT cells are capable of self-assembling onto artificial scaffolds to form functional blood vessels with all of their components, including the inner layer (endothelium) and smooth muscle layer. The potential for these cells is enormous; they could provide a new blood supply to damaged tissue and be used surgically as an "off-the shelf" product to repair damaged vessels. There will need to be considerable research data to ready these cells for human trials, and researchers are currently testing applications in research animals.

Skin

Skin tissue comprises the first cells to be transplanted for repair in humans, primarily because of its accessibility and relatively simple two-dimensional structure. Skin transplants were initially performed in antiquity for nose reconstructions using skin from the same person as the source of the graft (Nichter et al. 1983). Since then, skin grafts to treat extensive burns, wounds, and infections have become routine. More recently, skin cells can be grown in the laboratory to form new skin that can be successfully grafted onto patients. In one case, a patient's own cells were genetically corrected by researchers and grown into new skin to treat the loss of more than 80% of his skin that had occurred due to a rare genetic disease (Hirsch et al. 2017). Despite successes in grafting the epidermal layer of skin, much progress still needs to be made in growing skin in the laboratory that is comprised of its normal full complement of cells and structures: epidermis, dermis with hair follicles and sweat glands, and hypodermis. Efforts to achieve more normal transplantable skin tissue are underway in laboratories around the world.

Heart

There has been a great deal of human experimentation using various kinds of stem cells for treatment of heart disease. Unfortunately, none of the procedures used so far has been reproducibly successful in repairing heart tissue (Curfman 2019). The most popular stem cell treatment, using mesenchymal stem cells derived from bone marrow, may actually have negative effects by increasing inflammation in the heart (Naftali-Shani et al. 2017). There is hope, however, for a restoring of heart function by transplanting cardiac muscle cells (cardiomyocytes) derived from human pluripotent stem cells. Scientists have had success engrafting hESC-derived cardiomyocytes into the hearts of nonhuman primates, although graft-associated ventricular arrhythmias emerged in some animals as in previous rodent work (Liu et al. 2018), and there are plans for clinical trials in the next few years (Chien et al. 2019).

Brain

The brain has perhaps been the most daunting target for repair and regeneration due its complex structure and composition. Nevertheless, brain repair and rejuvenation is the subject of intense research given its importance as the seat of consciousness and individuality. Repair using macromolecules (e.g., enzymes) or drugs may or may not be possible, given the complexity of the forms of damage and the need for treatments that would repair most or all forms of damage without negative side effects. On the other hand, using cell replacement for brain regeneration appears closer to being realized. Cell-based treatments for Parkinson's Disease are leading the way in brain repair. In Parkinson's Disease, a particular type of neuron in the basal ganglia, the substantia nigra dopaminergic neurons, degenerate, which leads to motor dysfunction. Dopamine neuron cell treatments in humans have been ongoing since the 1980s, in and out of formal clinical trials, with considerable success in some cases (Peschanski et al. 1994; Hallett et al. 2014; Lindvall and Bjorklund 2004; Kordower and

Olanow 2016; Boronat-Garcia et al. 2017; Barker et al. 2019). At the forefront of improved cell-based treatments for Parkinson's is an upcoming clinical trial in which a patient's own cells are used to grow stem cells in the lab that produce new dopamine neurons that are reintroduced into the basal ganglia of the same patient, thus circumventing the risk of immune rejection (Loring 2018).

In addition to transplants to the basal ganglia, cell transplant studies in model organisms have shown that embryonic-like neural precursors can – to the extents examined thus far – functionally integrate into the adult neocortex (Hébert and Vijg 2018), the part of the brain that we use for our highest cognitive processes and for long-term memory storage. Although transplants of cells for the purpose of repairing the neocortex have not yet been undertaken in humans, transplants of cells that have potential beneficial paracrine effects have been in clinical trials for age-related diseases that affect the neocortex, such as stroke and Alzheimer's Disease, establishing the safety of cell-based therapies for the aged neocortex (https://clinicaltrials.gov). Achieving brain rejuvenation by cell replacement therapies still requires much research, in particular in combining and organizing the multiple cell types that make up the brain and in being able to deliver them with minimal invasiveness.

Cartilage

Many tissues in the body are rich in cartilage. Examples include the joints between bones, the trachea (windpipe), and structures that make up the face including ears and noses. All these cartilaginous tissues are targets for current cell therapies. Several approaches are used, depending on the target tissue. For facial structures such as an outer ear, a three-dimensional scaffold made of biomaterial is printed and seeded with cartilage forming cells (chondrocytes) taken from the patients themselves to avoid immune rejection. The resulting lab-made outer ear is then transplanted into the patients where the graft and its chondrocytes survive, resulting in a new outer ear (Zhou et al. 2018). Other cartilaginous tissues such as the trachea are similarly being printed, seeded with cells, and tested by multiple groups (Fishman et al. 2014). Although various types of stem cells have been injected into arthritic or injured patients' knee joints, any positive impact on performance can to date be attributed to paracrine effects rather than repair. Nevertheless, groups around the world are developing ways of seeding cells in the knee for repair, in some cases by injecting cells in a liquid matrix that gels in place (Wolf et al. 2018). As for other tissues, future improvements will require combining than one or two cell types to better match the structure of a normal cartilaginous tissue.

Liver

Using cell replacement to treat liver disease has been the focus of intense research, both because of a shortage of liver donors and because of its innate regenerative capacity when healthy, which might facilitate regeneration of transplanted liver progenitors. Hepatocyte progenitor cell transplants in animal models have shown that transplanted cells can, at least under some circumstances, replace lost liver cells and reestablish normal liver function (Alwahsh et al. 2018). However, clinical trials involving the transplantation of liver stem cells or hematopoietic stem cells (which may have the potential to differentiate into hepatocytes, the primary liver cell) into the host organ have not shown evidence to date of liver repair, although some benefits in liver function based on circulating markers have been reported (Alwahsh et al. 2018; Kwak et al. 2018). Future efforts will likely focus on reproducing animal findings in clinical trials with human patients.

Summary

Cell replacement is in theory possible for all parts of the human body. In practice, much research is still needed before we can readily use cells to grow and replace all organs and body parts as a means of reversing age-related dysfunction.

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Cell Senescence

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Synonyms

Aging; Cell aging; Cellular senescence; Developmental senescence; Oncogene-induced senescence; Replicative senescence; Telomere-induced senescence

Definition

Cellular senescence is a stable proliferative arrest engaged by cells in response to telomere shortening, DNA damage from various sources, mitogenic imbalances, and extracellular cues including inflammatory and developmental signals. Senescent cells are characterized by a secretory phenotype which exerts pleiotropic effects in the surrounding tissue.

Overview

Cellular senescence, originally described by Hayflick and Moorhead nearly 60 years ago (Hayflick and Moorhead 1961), referred to the finite proliferative capacity of normal human fibroblasts upon extended culture in vitro. Despite their inability to proliferate, senescent cells remain metabolically active and, given regular media changes, can be maintained in culture for years. Their discovery prompted Hayflick and Moorhead to postulate that the underlying cause of this limited proliferative capacity is not due to "non-cumulative external factors" but that it "is attributable to intrinsic factors which are expressed as senescence at the cellular level" (Hayflick and Moorhead 1961). Today, we know that the observations made by Hayflick and Moorhead referred to a particular type of cellular senescence (i.e., replicative senescence) that is caused by the formation of dysfunctional telomeres, a consequence of progressive erosion of telomeres that occurs naturally following the completion of every cell division cycle (d'Adda di Fagagna et al. 2003; Herbig et al. 2004).

As no marker had been available that would allow identification of senescent cells in tissue, the biological relevance of this stable proliferative arrest remained in question for many years. Speculations emerged that replicative senescence is merely an artifact arising from cell culture conditions, as telomere erosion is slow and replicative senescence is activated only after cells had divided roughly 60 times, a number that fibroblasts in tissue likely never reach (Hornsby 2002). The discovery of novel markers of cellular senescence eventually confirmed that senescent cells indeed develop in human tissue (Dimri et al. 1995) and accumulate in an aging-associated manner in some tissues of mice (Wang et al. 2009) and long-lived mammals (Herbig et al. 2006; Liu et al. 2009). This supported the notion that cellular senescence does occur in vivo, although the underlying causes triggering senescence in tissue are not always clear. Subsequently, it was shown that senescence could be induced prematurely and independently of progressive telomere shortening, particularly by the overexpression of oncogenes in mammalian somatic cells (i.e., oncogene-induced senescence [OIS]) (Serrano et al. 1997). This also provided the first evidence that cellular senescence may act as a tumor suppressor mechanism, a hypothesis that was later confirmed using mouse models (Collado and Serrano 2010) and by the detection of senescent cells with features of OIS in early neoplastic lesions in humans (Michaloglou et al. 2005; Suram et al. 2012).

Nearly six decades after Hayflick and Moorhead's seminal discoveries, the current view of cellular senescence is that of a genetic program that normal somatic cells not only engage upon encountering a variety of stresses that can potentially disrupt cellular function but also one that cells activate as part of tissue repair and normal development (Munoz-Espin and Serrano 2014). Today, the biological relevance of cellular senescence is manifold, as it plays crucial roles in the patterning of developing structures in the embryo, modulation of tumor progression, functional decline of tissues during aging, wound healing, tissue repair, and even cellular reprogramming.

Key Research Findings

Characteristics of the Senescent Cell

The transition to senescence can be achieved by a multitude of internal and external stresses including DNA damage, telomere dysfunction, deregulation of mitogenic pathways, cytokine signaling arising from inflammatory and/or developmental processes, mitochondrial disturbances, cell fusion, epigenomic alterations, and oxidative stress (Fig.

1). Each of these inducers activates specific signaling pathways, some distinct and others converging onto a common mechanism as outlined broadly below (the reader is encouraged to visit references (Kuilman et al. 2010; Martinez-Zamudio et al. 2017) for detailed molecular mechanisms). Given the multitude of inducers and activation of cell type-specific senescence pathways, senescent cells cannot be reliably identified by a single molecular marker. Rather, the senescent phenotype is best characterized by a combination of molecular features, some of which are outlined below (Fig. 1):

Senescence-associated ß-Galactosidase (SA-ßGal) activity. The first marker that allowed detection of senescent cells in cultures and in tissues. SA-ßGal activity derives from lysosomal beta-D-galactosidase which is overexpressed in senescent cells (Dimri et al. 1995; Lee et al. 2006).

Gene expression changes. The senescence program is reflected at the gene expression level by a stark repression of positive regulators of cell cycle progression and apoptotic genes as well as by upregulation of heterochromatin-associated, inflammatory, developmental, anti-apoptotic, and extracellular matrix (ECM) genes (see below). Detection of down- and upregulated gene products is commonly used to corroborate the senescence phenotype.

Cell morphology and increased protein turnover. Senescent cells increase their metabolic rate, which is reflected by an increased size and flat morphology, as well as by the secretion of signaling molecules (see below) (Kuilman et al. 2010).

Persistent DNA damage. Most senescence inducers incur irreparable DNA damage in the form of double-stranded DNA breaks that leads to activation of a persistent DNA damage response (DDR). A primary cause of this persistent DDR is telomere dysfunction. Persistent DNA damage foci, which can be detected by immunofluorescence analysis using antibodies against DNA damage response and repair factors such as γ-H2AX or p53-binding protein-1 (53BP1), have been called telomere dysfunction-induced DNA damage foci (TIF) (Takai et al. 2003), telomere-associated DNA damage foci (TAF) (von Zglinicki et al. 2005), senescence-associated DNA-damage foci (SDF) (Reaper et al. 2004), or, more generally, DNA segments with chromatin alterations reinforcing senescence (DNA-SCARS) (Rodier et al. 2011).

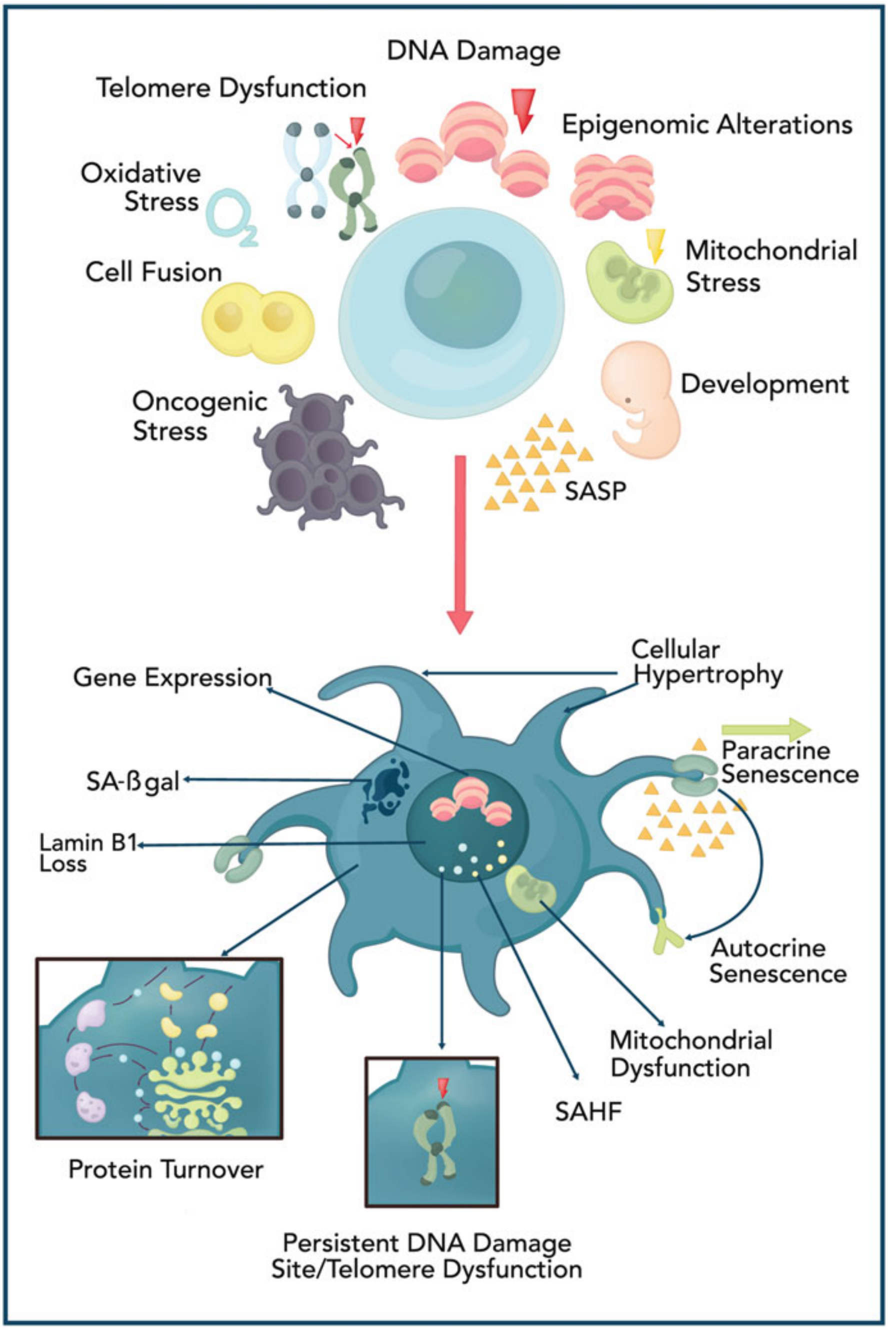
Senescence-associated secretory phenotype (SASP). Senescent cells secrete a large number of cytokines, growth factors, and ECM-modifying molecules, among others, which constitute the SASP. The composition and dynamics of secretion of the SASP changes with time and varies depending on the cell type and initial senescence inducer (Coppe et al. 2010; Hoare et al. 2016).

Senescence-associated heterochromatin foci (SAHF). Heterochromatic foci characterized by trimethylation of H3K9 and H3K27, the histone variant macroH2A and the heterochromatic protein HP1γ, develop in cells undergoing various types of cellular senescence but are most prominent in cells undergoing OIS. The formation of these structures is thought to occur by the redistribution of previously existing heterochromatic domains to silence the expression of cell cycle-associated genes (Di Micco et al. 2011; Narita et al. 2003).

Loss of Lamin B1. Lamin B1 is a structural component of the nuclear envelope, playing a critical a role in nuclear architecture. Since many types of senescence, including OIS, radiation, and replicative senescence, lead to drastic reductions in Lamin B1 levels, it is often used as a marker of this proliferative arrest (Freund et al. 2012; Shimi et al. 2011).

The Transition to Senescence: Regulation

Molecular signaling and regulation of the senescence proliferative arrest. With the exception of developmental cues, senescence-inducing signals converge in the activation of the p53/p21^{CIP1} and the p16^{INK4A}/retinoblastoma (RB1) tumor suppressor pathways. Depending on the cell type and senescence-inducing signal, as well as the strength and length of this signal, cells either activate one or both of these pathways (Fig. 2). p53 and RB1 are transcriptional regulators that play critical roles in the initiation and maintenance of the senescent phenotype. When cells proliferate, RB1 is maintained in an inactive, hyperphosphorylated form, by virtue of the catalytic activity of cyclin/CDK complexes, which precludes RB1 from

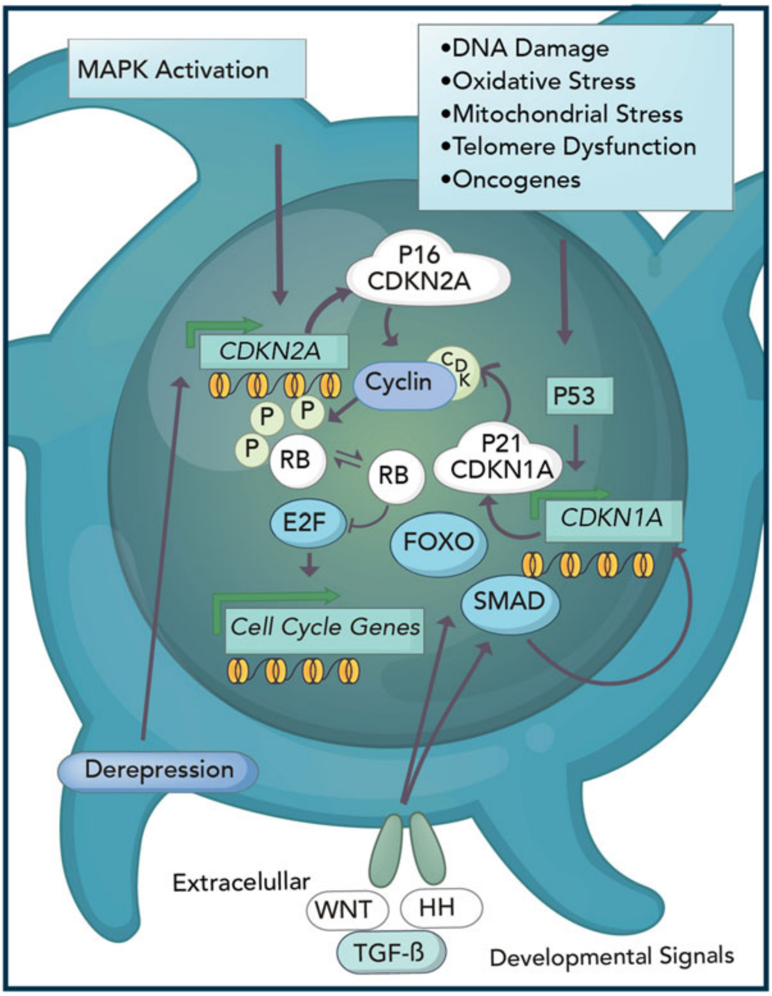


Cell Senescence, Fig. 1 Senescence inducers and characteristics of senescent cells. Normal cells can be induced to undergo senescence by exposure to a variety of intrinsic and extrinsic signals. The majority of these signals, including telomere dysfunction, increased oxidative stress, oncogene overexpression, and alteration to chromatin cause persistent DNA damage which initiates the senescence response. Nonetheless, senescence can also be induced naturally during development and in the terminal differentiation of adult cells. Although a senescence-specific marker has not yet been identified, senescent cells are characterized by the following features: an increase in metabolic activity, reflected by increased protein turnover, development of the secretory phenotype (SASP), increased lysosomal activity (SA-ßGal), and an increase in cell size. In addition, senescent cells undergo drastic changes in binding to members of the E2F family of transcriptional activators. This mechanism ensures that the E2F proteins bind to promoters and facilitate the expression of cell cycle genes, thereby stimulating cellular proliferation (Fig. 2). When the cell experiences stress, such as damage to DNA from various sources, the signals generated by these processes are integrated by the tumor suppressor protein p53. p53 directly upregulates the expression of the *CDKN1A* gene encoding the cell cycle inhibitor $p21^{CIP1}$, which restrains the activity of cyclin/CDK complexes through a physical interaction (Fig. 2) (Martinez-Zamudio et al. 2017). The expression and activation of $p16^{INK4A}$ (also known as CDKN2A) is a complex process that is not yet fully understood. What is evident, however, is that hypermitogenic signals from certain oncogenes activate the MAPK pathway, increasing the expression of the *CDKN2A* gene in a manner dependent on the combined action of transcription factors and chromatin-remodeling enzymes (Kotake et al. 2015). Similar to $p21^{CIP1}$, $p16^{INK4A}$ also represses the activity of cyclin/CDK complexes through a direct physical interaction (Fig. 2). Ultimately, the inhibition of cyclin/CDK complexes by $p21^{CIP1}$ and $p16^{INK4A}$ results in the hypophosphorylation and activation of RB1, which not only represses cell cycle-associated gene expression by sequestering E2F transcription factors but also promotes the formation of an inaccessible chromatin state at promoters of cell cycle-associated genes (Narita et al. 2003) (Fig. 2).

Developmental senescence is mechanistically distinct, as it appears to be independent of DNA damage and also independent of both p53 and $p16^{INK4A}$. Instead, the signaling molecules mediating senescence in these structures, including transforming growth factor ß (TGF-ß), Hedgehog, and WNT, are integrated and transduced by the SMAD and Forkhead box protein O (FOXO) transcription factors, which transcribe the *CDKN1A* gene, leading to a $p21^{CIP1}$-dependent arrest (Munoz-Espin et al. 2013) (Fig. 2).

Transcriptional regulation of the secretory phenotype-SASP. The SASP is perhaps the most consequential and complex feature of the senescent cell. SASP profiles generated using large-scale gene expression and antibody array studies revealed a dynamic and complex composition of cytokines, chemokines, metalloproteinases, and growth factors (Coppe et al. 2008; Zhang et al. 2003). The SASP is generated and temporally coordinated to a large extent by the transcriptional regulators nuclear factor kappa-B (NF-κB) and CCAAT/enhancer-binding protein-ß (C/EBPß), which become activated in part by the MAPK (ERK and p38 MAPK) pathway in response to persistent DDR (Fig. 3) (Acosta et al. 2013; Kuilman et al. 2008). The dynamic nature of the SASP has been best described in a cellular model of OIS. Overexpression of oncogenic $H\text{-}RAS^{V12}$ leads to a transient, initial secretion of stemness and anti-inflammatory factors, including HES1, NOTCH, and TGF-ß, during days 2 to 4 after $H\text{-}RAS^{V12}$ expression. During this period, the intracellular domain of NOTCH, N1ICD, restrains C/EBPß activity and thereby prevents production of certain inflammatory cytokines including IL6 and IL8. This inhibition is, however, transient, as from days 4 onward, the secretory profile is overtaken by an inflammatory SASP characterized by NF-κB and C/EBPß-regulated gene products (Hoare et al. 2016) (Fig. 3). In addition to persistent nuclear DNA damage, production of the SASP is also stimulated by cytosolic chromatin fragments (CCFs) that accumulate in senescent cells as a consequence of lamin B1 degradation. CCFs are sensed by cGMP-AMP synthase (cGAS) which engages the stimulator of interferon genes (STING) pathway thereby stimulating the production of type I interferons and inflammatory cytokines (Gluck et al. 2017) (Fig. 3). Although

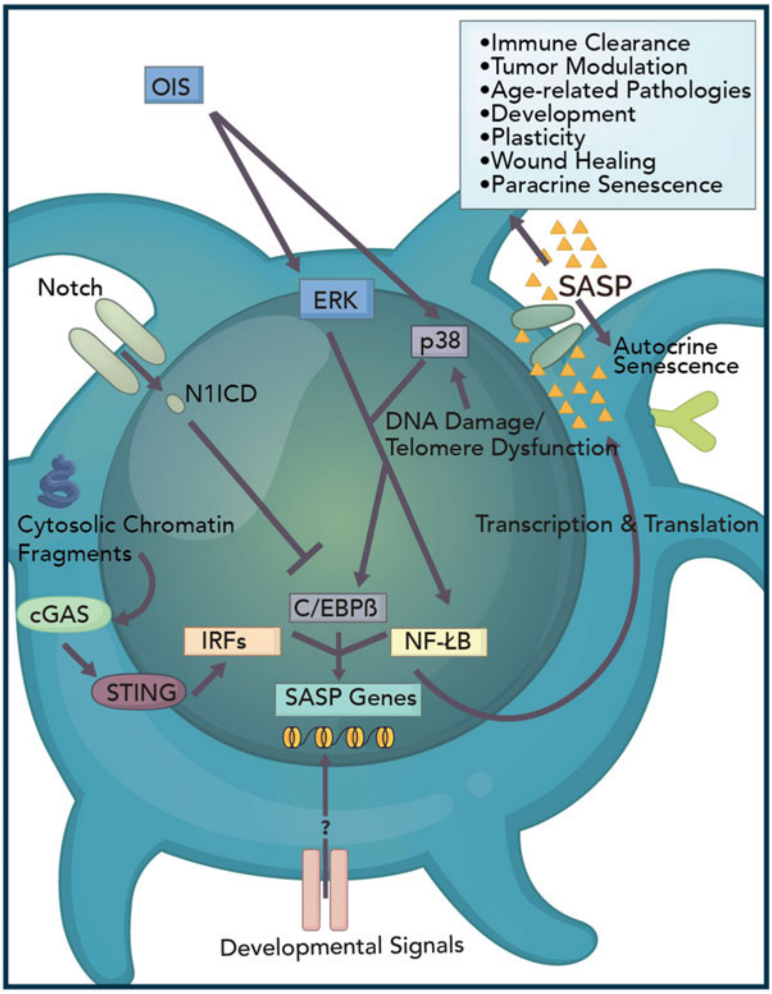
Cell Senescence, Fig. 1 (continued) chromatin organization, typified by the SAHF, develop sites of persistent DNA damage such as dysfunctional telomeres, and undergo stark gene expression changes, notably repression of cell cycle genes and lamin B1 and upregulation of SASP-associated and anti-apoptotic genes. The SASP of senescent cells causes autocrine and paracrine senescence



Cell Senescence, Fig. 2 Molecular regulation of the senescence proliferative arrest. Most senescence-inducing signals converge on the activation of the p53/p21^{CIP1} and p16^{INK4}/RB1 tumor suppressor pathways. Damage to DNA arising from various sources leads to the activation of p53, which upregulates the expression of *CDKN1A/p21*^{CIP1}. Derepression of the *CDKN2A/p16*^{INK4} locus is observed during aging, although the underlying causes are currently unclear. However, activation of the MAPK pathway by certain oncogenes has been shown to promote the expression of CDKN2A/p16^{INK4}. Developmental signals such as TGF-ß, WNT, and HH induce a p21^{CIP1}-dependent arrest that is mediated by the transcription factors FOXO and SMAD. Ultimately, p21^{CIP1} and p16^{INK4} inhibit the activity of cyclin/CDK complexes, leading to the activation of RB1, which represses expression of genes that promote cell cycle progression by binding to E2F transcription factors

developmental senescence induced by TGF-ß and WNT has been shown to induce a SASP-like secretory phenotype, the transcriptional regulators controlling the expression of these genes are currently unknown (Munoz-Espin et al. 2013).

Because of its compositional diversity and dynamics of secretion, the SASP is presently viewed as one of the key biological effectors of the senescence response in vivo. Originally described in the context of damage-induced senescence (OIS and genotoxic agents), the SASP was proposed to contribute to cancer development by modifying the tissue microenvironment through the secretion of pro-inflammatory cytokines and MMPs (Coppe et al. 2008). Since then, the SASP has also been implicated in the reinforcement of the senescent state in both autocrine and paracrine manners (Acosta et al. 2013; Hoare et al. 2016; Kuilman et al. 2008), facilitating age-related tissue degeneration (reviewed by (Campisi 2013), immune clearance of senescent cells during aging, development, tumor suppression (Munoz-Espin et al. 2013; Tasdemir et al. 2016), and cellular plasticity (Milanovic et al. 2018; Ritschka et al. 2017) (Fig. 3).



Cell Senescence, Fig. 3 Regulation and function of the SASP. The transcription factors NF-κB and C/EBPß are the key regulators of SASP expression during OIS and damage-induced senescence. OIS, DNA damage, and telomere dysfunction activate the MAPK pathway, including ERK and p38MAPK, which lead to the activation of NF-κ B and C/EBPß and thus the expression of inflammatory cytokines. During the early stages of OIS, the intracellular domain of NOTCH, N1ICD, promotes the transient production of anti-inflammatory SASP by restraining the activity of C/EBPß. Additionally, accumulation of cytosolic chromatin fragments due to lamin B1 degradation in senescent cells is sensed by the cGAS/STING complex, which activates the IRFs to facilitate the expression of type I interferons. The transcriptional regulators facilitating the SASP during development are yet to be identified. Once secreted, SASP factors have been shown to modulate a variety of processes including immune clearance, tumor modulation, age-related tissue degeneration, increase cellular plasticity, tissue repair, as well as autocrine and paracrine senescence

Senescence in Physiology and Disease

Aging. Since the original description of replicative senescence, Hayflick and Moorhead speculated that the cellular factors that were progressively lost with every cell division could be acting as a counting mechanism or "replicometer" that kept track of a cell's replicative life span, hinting at the possibility that the limited replicative capacity of our somatic cells ultimately could be a driver of aging on the organismal level (Hayflick 1997). Since then, multiple studies indeed have established a strong relationship between replicative senescence and aging. For example, the proliferative capacity of human fibroblasts, epithelial, endothelial, and adrenocortical cells (Hornsby 2002), among other cell types, decreases as a function of donor age, telomeres progressively shorten with every cell division not only in cultures but also throughout human tissue with advancing age, and senescent cells with dysfunctional telomeres increase in abundance in some tissues from mice, primates, and humans, albeit to different extents (Herbig et al. 2006; Suram et al. 2012; Wang et al. 2009). In addition, many association studies have reported a direct correlation between short average telomere lengths and various aging-associated diseases, overall supporting the notion that telomere biology is directly involved in the pathophysiology associated with natural aging in humans (Aviv and Shay 2018).

While direct evidence that telomere-induced senescence is a cause of aging is still missing, a number of studies have provided strong evidence that cellular senescence, mediated by p16^{INK4A}, promotes aging in mammals. The observations that the expression of CDKN2A/p16^{INK4A} increases as a function of age in mice and human tissues (Krishnamurthy et al. 2004; Liu et al. 2009; Melk et al. 2004) led to the idea that expression of the *CDKN2A* locus causally contributes to senescence and aging. The most convincing examples of the contribution of p16^{INK4A} to senescence and the onset of age-related pathologies have been provided by mouse models of progeria, osteoarthritis, and natural aging. Mice hypomorphic for the mitotic checkpoint protein BubR1 age prematurely develop progeroid phenotypes such as cataracts, sarcopenia, and reduced fat deposition and upregulate the expression of p16^{INK4A} and SA-ßGal activity in these tissues, suggesting that p16^{INK4A}-driven cellular senescence contributes directly to premature aging in these animals (Baker et al. 2008). This notion was subsequently corroborated in a BubR1-insufficient transgenic mouse model in which a drug-inducible caspase enzyme under the *Cdkn2a/Ink* promoter (INK-ATTAC mice) enabled the pharmacological induction of apoptosis of p16^{INK4A}-expressing senescent cells. Drug administration effectively eliminated senescent cells in aged animals and attenuated age-related phenotypes of the skeletal muscle, eye, and fat, yet it failed to fully rejuvenate these tissues. More recently, the INK-ATTAC system has also been used to study the effects of senescent cell clearance in naturally aging mice, and the results left little doubt that p16^{INK4A}-mediated cellular senescence promotes aging and aging-associated diseases, including cancer, in this organism (Baker et al. 2016). Clearance of senescent cells in otherwise normal mice increased the median life span by 24–27%, increased spontaneous activity and exploratory behavior, and reduced aging-associated pathologies including lipodystrophy, decline of renal function, bone loss, and cardiac abnormalities (Baker et al. 2016). Similar studies in an alternative mouse model in which p16^{INK4}-expressing cells can be eliminated (p16-3 M mice) have shown a contribution of senescent cells to osteoarthritis and age-related decline of hematopoietic stem cells (Chang et al. 2016; Jeon et al. 2017). In addition to cells of solid tissues that increasingly become senescent during aging, mice also develop an increasing number of senescent immune cells, including macrophages, with advancing age. Importantly, macrophages have been demonstrated to be involved in the clearance of senescent cells from tissues and thereby prevent the damaging effects of the SASP on tissue function (Hall et al. 2016). Due to a progressive and aging-associated deterioration of innate and adaptive immune responses (Ovadya and Krizhanovsky 2014), aging additionally reduces overall immunological fitness of the organism. The increasing abundance of senescent cells in tissues of aging mammals might therefore not simply be due to an accelerated generation of senescent cells with age, but it also appears to be due to an aging-associated decline of immune surveillance mechanisms that would otherwise eliminate senescent cells from aged tissues.

Cancer: The concept that senescence is a fundamental cellular mechanism to suppress cancer development was indirectly proposed by Hayflick already decades ago. He suggested that, in order for transformation to occur, cells must acquire properties that allow them to escape the "inevitability of aging" and that these properties were found only in cancer cells (Hayflick 1965). The first direct evidence that cellular senescence acts as a tumor-suppressing mechanism came from studies demonstrating that human somatic cells overexpressing an oncogenic form of H-RAS (H-RAS^{V12}) rapidly develop phenotypic changes typical of cellular senescence, including a p53- and p16^{INK4A}-dependent cell cycle arrest, SA-ßGal expression, and cellular hypertrophy (Serrano et al. 1997). This form of senescence was called oncogene-induced senescence (OIS) and was proposed to suppress cancer development in mammals by prematurely arresting cells that are at risk for malignant transformation. Since then, the tumor-suppressing properties of cellular senescence (i.e., OIS), as well as the molecular pathways activated in OIS, have been characterized in substantial detail (Collado et al. 2007). OIS occurs independently of progressive telomere shortening, but not necessarily independent of telomere dysfunction, and is engaged due to oncogene expression, deregulation of mitogenic signaling, constitutive proliferative cues, and disruption of tumor-suppressing pathways, among others.

Depending on cell type and the oncogene that is being expressed, mammalian cells activate either the p53/p21^{CIP1}, p16^{INK4A}/Rb, or both pathways to engage cellular senescence. H-RAS^{V12}, for example, causes hyperproliferation resulting in DNA replication stress and the production of reactive oxygen species (ROS) that can subsequently activate a kinase signaling cascade involving p38 and PRAK, which leads to p16^{INK4A} activation, as well as double-stranded DNA breaks (DSBs), which activate p21^{CIP1} expression (Suram and Herbig 2014). While the generation of such DSBs initially leads to growth arrest that is observed after just a few cell divisions following oncogene expression, it is the generation of telomeric DSBs (i.e., dysfunctional telomeres) that stabilizes the growth arrest and fully engages the senescence response in human cells (Suram et al. 2012). Not only has OIS been demonstrated to suppress cancer development in numerous mouse model systems, but signs of OIS, such as SAß-Gal activity, p16^{INK4A} expression, and dysfunctional telomeres, among others, are also frequently observed in premalignant human neoplasms, but not in their malignant cancer counterparts (Collado et al. 2007). Overall, numerous studies have now demonstrated that OIS is a bona fide tumor-suppressing mechanism in mammals.

While the proliferative arrest induced by OIS is a potent block against malignant cancer development, the SASP produced by senescent cells is similarly important as it activates mechanisms that promote tumor regression. For example, in conditional p53-deficient nude mice, transplantation of H-Ras^{V12}-expressing cells into the liver generates tumors that regress upon restoration of p53 function. Under these conditions, tumor regression is not a result of apoptosis, but rather it is mediated by innate immune cells which are recruited to the tumor site as a direct consequence of an inflammatory SASP secreted by senescent liver tumor cells (Kuilman et al. 2008; Xue et al. 2007). In addition to facilitating immune clearance, the SASP produced during OIS modulates the surrounding tissue through the secretion of inflammatory cytokines including the interleukins 1α and 1ß, 6 and 8, as well as the chemokine CXCR2. Significantly, some of these factors have been shown to induce autocrine senescence to reinforce the growth arrest and also cause paracrine senescence in cells of colon, skin, and liver tissues (Acosta et al. 2008, 2013; Kuilman et al. 2008). It has been suggested that this serves to amplify and stabilize the senescence arrest in premalignant tumor tissue.

In certain contexts, however, the SASP paradoxically also promotes cell growth and tumorigenesis. Senescent fibroblasts not only have been demonstrated to promote proliferation of lowly invasive epithelial cells in co-culture experiments, but they also promote tumor formation when co-injected with premalignant and malignant cancer cells into mice (Krtolica et al. 2001). The growth-stimulatory effects are mediated by SASP components that include MMPs, cytokines, and growth factors (Krtolica et al. 2001; Liu and Hornsby 2007; Tsai et al. 2005). Importantly, the SASP is unable to promote growth of normal epithelial cells, indicating that (epi)genomic alterations in tissues arising from stress or age may render some preneoplastic cells susceptible to SASP stimulation (Krtolica et al. 2001). In this context it is important to note that while somatic human cells rapidly undergo paracrine senescence in response to the SASP due to the formation of dysfunctional telomeres, cells expressing the catalytic subunit of telomerase hTERT do not arrest and are insensitive to the growth inhibitory effects of SASP factors (Razdan et al. 2018). Taken together, the effects of the SASP are dependent not only on its composition but also on the nature and integrity of cells in affected tissue.

While cellular senescence was considered to be an irreversible arrest for decades, recent reports have questioned the stability of the proliferative arrest that characterizes senescent cells, particularly those that had undergone OIS. Human fibroblasts that entered H-RAS^{V12}- or B-RAF^{E600}-induced senescence have been demonstrated to eventually escape OIS through mechanisms leading to MYC-mediated upregulation of hTERT, the catalytic subunit of telomerase. Expression of hTERT causes activation of telomerase, which can prevent a telomeric DDR due to oncogene-induced replication stress, potentially even repair dysfunctional telomeres in senescent cells, and thereby destabilize the proliferative arrest in oncogene expressing cells (Patel et al. 2016). Similarly, escape from senescence has also been reported in lymphocytic cancers. In a mouse model of Bcl2-driven lymphoma, therapy-induced senescence (TIS) of lymphoma cells induces, paradoxically, upregulation of a Wnt-dominated stem cell gene expression signature. Upon inactivation of p53 or Suv39h1, senescent lymphoma cells assume stem cell-like properties, likely through autocrine signaling of SASP-derived Wnt that can reprogram non-stem leukemia cells into leukemia-initiating cells and form aggressive tumors in mice (Milanovic et al. 2018). These studies therefore indicate that senescence is, in certain cases, a transitory cellular state which can be disrupted by cell-autonomous mechanisms including telomere stabilization and SASP-mediated self-reprogramming.

Development. Senescence plays important roles in the patterning of embryonic structures and in the maturation program of certain adult tissues. In the mouse embryo, the apical ectodermal ridge (AER), the neural tube, the endolymphatic sac of the inner ear, and the mesonephros undergo p21^{CIP1}-dependent senescence in the absence of any detectable DNA damage (Munoz-Espin et al. 2013; Storer et al. 2013). Furthermore, these structures are SA-ßGal positive and develop a SASP containing Tgf-ß, Wnt, and Hedgehog, which facilitates paracrine senescence via the Foxo1 and Smad transcriptional regulators. Senescent cells in these structures have two demonstrated fates: (i) clearance by the immune modulatory cells, which are recruited through a SASP-dependent mechanism, or (ii) a differential arrest followed by the expansion of certain cell subpopulations at later stages in development (Munoz-Espin et al. 2013; Storer et al. 2013).

Physiological senescence in adult tissues. Senescence has been detected during maturation of certain adult tissues. Megakaryocytes are large, multinucleated cells responsible for the release of platelets into the bloodstream upon maturation through exposure to the pleiotropic hormone thrombopoietin (TPO). TPO stimulation of mature megakaryocytes directly promotes the expression of the *CDKN1A* gene, leading to a p21^{CIP1}-dependent senescence arrest, increased SA-ßGal activity, and production of platelets. The senescence arrest appears necessary for terminal differentiation and proper function of megakaryocytes, as reduced expression of *CDKN1A* in patients affected by primary myelofibrosis renders these cells insensitive to TPO-induced senescence and prone to hyperproliferation (Besancenot et al. 2010). Another adult cell type, the cytotrophoblast, undergoes senescence during the cell fusion process required for the formation of the placental syncytiotrophoblast (a structure that surrounds the embryonic placental villi). Indeed, in human placenta, the syncytiotrophoblast exhibits high SA-ßGal activity and DNA damage-dependent activation of both the p53 and $p16^{INK4}$ pathways (Chuprin et al. 2013). Intriguingly, megakaryocytes and syncytiotrophoblasts are natural examples of endoreduplication, a process that leads to polyploidy. Thus, other examples of endoreduplication including osteoclasts, hepatocytes, and endometrium could represent additional examples of physiological senescence in adult tissues (Gandarillas et al. 2018).

Host immunity. Experiments performed by the Sager laboratory in the early 1990s introduced the notion that senescence evolved as a defense mechanism against oncogenic viruses (Sager 1991). The fact that a number of viruses evade senescence responses by expressing oncoproteins that block the $p53/p21^{CIP1}$ and/or $p16^{INK4}$/RB1 senescence pathways raises the possibility that cellular senescence evolved as an antiviral defense mechanism (Reddel 2010). Alternatively, infection with viruses that lack expression of such oncoproteins activates cellular senescence to prevent replication of viruses by causing double-stranded DNA break formation (Martinez et al. 2016) or by promoting cell fusion (Chuprin et al. 2013). In addition, senescent cells are resistant to infection by certain viruses, which is in line with the hypothesis that cellular senescence acts as an antiviral defense mechanism (Baz-Martinez et al. 2016).

Tissue repair and cellular plasticity. Tissue repair in response to injury is a tightly regulated process involving hemostasis, local inflammation, proliferation, and remodeling (Jun and Lau 2018). Myofibroblasts, a contractile cell type with properties of both fibroblasts and smooth muscle cells, can be induced by transdifferentiation of fibroblasts at the site of injury and play a critical role in the proliferation and remodeling stages of tissue repair through the modulation of the ECM. However, when the underlying injury is not properly resolved and the damage becomes chronic, the continued stimulation of myofibroblast differentiation and therefore the increased deposition ECM components result in fibrosis (Jun and Lau 2018). Thus, the timely regulation of myofibroblast function is critical for successful tissue repair.

Cutaneous wound healing is facilitated by senescent cells and mediated by components of the SASP. In a mouse model of cutaneous wound healing, senescent fibroblasts and endothelial cells are generated at the site of injury where they promote angiogenesis and granulation tissue formation. Secretion of platelet-derived growth factor subunit A (PDGF-AA) by senescent cells during the early stages of wound healing subsequently induces myofibroblast transdifferentiation which facilitates wound closure. Selective elimination of senescent cells delays wound healing, while topical application of recombinant PDGF-AA after ablation of senescent cells promotes it (Demaria et al. 2014). Wound healing in humans appears to also involve cellular senescence as well as components of the SASP, although the signal and mechanism that drives myofibroblast transdifferentiation in humans might be distinct from that in mice. Senescence of human fibroblasts causes early secretion of TGF-ß1, a component of the SASP and a cytokine that is critical for wound healing in humans. TGF-ß1 induces telomere dysfunction in a paracrine manner by stimulating the production of ROS in neighboring cells. The resulting persistent DNA damage response that is caused due to telomere dysfunction activates p53 which, together with SMAD3, promotes expression of $\alpha - \mathrm{SMA}$, a critical component of myofibroblasts. Significantly, expression of hTERT in fibroblasts suppresses telomere dysfunction and myofibroblast transdifferentiation, revealing that the development of dysfunctional telomeres is required for myofibroblast transdifferentiation in humans (Razdan et al. 2018).

Aside from cutaneous wound healing, cellular senescence is also important for repair of other damaged organs. In a mouse model of liver fibrosis, ablation of p53 and $p16^{Ink4}$ resulted in exacerbated fibrosis due to reduced senescence and elevated deposition of ECM components (Krizhanovsky et al. 2008). Mechanistically, the secreted protein Ccn1 causes cells to undergo senescence at sites of injury through production of ROS, ultimately activating both the p53 and $p16^{Ink4}$ pathways. In mouse deficient for *Ccn1*, topical application or injection of CCN1 ameliorates wound healing and liver fibrosis by inducing cellular senescence (Jun and Lau 2010; Kim et al. 2013).

The role of the early SASP in tissue regeneration seems to extend beyond causing myofibroblast transdifferentiation during tissue repair. Similar to fibroblasts undergoing OIS, keratinocytes expressing $H\text{-}RAS^{V12}$ express stem cell-associated genes during the early stages of senescence (Ritschka et al. 2017). When transplanted into wounds of nude mice, senescent keratinocytes exhibited regenerative properties as they promoted the formation of papilloma. The regenerative properties of senescent keratinocytes are a result of the stemness factors in the SASP, as papilloma formation was promoted by proliferating keratinocytes treated with medium conditioned from keratinocytes induced to senese by oncogene expression or irradiation (Ritschka et al. 2017). The regenerative potential of OIS- and irradiation-derived SASP, however, appears to be distinct from the SASP generated during wound healing where specific SASP factors such as PDGF-AA, CCN1, and TGF-ß are causally linked to injury resolution. Rather, damage-mediated senescence appears to induce a cellular reprogramming that attempts to rescue the cell's original function. This may not necessarily be beneficial to the organism, as a dedifferentiation toward a stem cell-like state of aggressive proliferation has been shown to occur upon OIS-mediated reprogramming of lymphoma cells (Milanovic et al. 2018).

Overall, a key message arising from the findings described in this section is that senescence is not a singular cell fate but rather a collection of cell fates that are dependent on the original senescence inducer and cell type. The function of senescent cells, therefore, is highly context-dependent and reflected by the SASP generated in each context. Furthermore, it is the composition and the dynamic secretion of the SASP that appears to play a critical role in determining the functionality of senescent cells as well as their surrounding tissue.

Example of Application/Future Directions

Senescence as a Therapeutic Target

As discussed above, senescent cells actively contribute to aging and age-related pathologies. Senescent cells thus represent attractive therapeutic targets to treat certain conditions, restore healthspan, and possibly extend life span. Indeed, the proliferative arrest, increased expression of lysosomal β-galactosidase, and resistance to apoptosis are some key features of senescent cells that are currently being exploited in the development of senotherapy. One class of senolytic drugs are rationally designed small molecules that disrupt the anti-apoptosis pathways activated in senescent cells, forcing their elimination through apoptosis (van Deursen 2014). This strategy offers an alternative to simply targeting, for example, $p16^{INK4A}$-expressing cells, as $p16^{INK4A}$ might also play important roles in other physiological processes. Some of the first senolytic drugs described, quercetin and dasatinib, induce apoptosis of senescent cells when administered in combination and thereby alleviate morbidity in normal, aging and progeroid mice (Xu et al. 2018; Zhu et al. 2015). Similarly, the small molecule ABT263, an inhibitor of anti-apoptotic molecules BCL-2 and BCL-xL, rejuvenates the hematopoietic and muscle stem cell (HSC and MuSC) compartments and reverses lung damage of sublethally irradiated mice by inducing apoptosis of irradiation-induced senescent cells (Chang et al. 2016). An alternative strategy for the elimination of senescent cells was recently described in a trichothiodystrophy (TTD) mouse model of accelerated aging. In these mice, disruption of the p53-Foxo4 interaction with a cell-penetrating peptide FOXO4-DRI induces apoptosis of senescent cells, possibly due to the mitochondrial translocation of p53 from the nucleus. Consequently, this peptide opposes the aging-associated decline of renal and liver function (Baar et al. 2017). Another approach for senotherapy takes advantage of the fact that senescent cells express high levels of lysosomal beta galactosidase. Nanoparticles coated with galactooligosaccharides are thus preferentially taken up by senescent cells, and when such nanoparticles encapsulate cytotoxic drugs, they effectively eliminate senescent cells in vitro and in vivo. This strategy to eliminate senescent cells has been demonstrated to promote tumor regression and resolve pulmonary fibrosis in animal models (Munoz-Espin et al. 2018). Together, these studies provide the proof-of-principle evidence that pharmacological elimination of senescent cells could have rejuvenating effects in humans.

Modulation of the SASP represents another avenue for the development of senotherapeutics. Indeed, specific disruption of SASP components represents an alternative chemotherapeutic strategy for cancer and other age-related disorders, as this would prevent the reprogramming of adjacent cells within the affected tissue and thus reduce disease progression. In this context, another approach to modulate the senescent phenotype uses small molecules to target critical regulators of the SASP such NF-κB, the JAK/STAT pathway, and mTOR (i.e., senomorphics). It is hypothesized that the modulation of these pathways could bring about beneficial effects such as reductions in chronic inflammation, inhibition of paracrine senescence, and restoration of tissue function (Soto-Gamez and Demaria 2017). However, due to the dynamic and compositional heterogeneity of the SASP, as well as the pleiotropic effects of its components, a road for the development of SASP-specific therapeutics is not evident. More studies on the dynamics and regulation of the SASP in response to diverse senescence inducers are required to fulfill the potential of SASP-specific therapies in the treatment of age-related pathologies.

Summary

Cellular Senescence: One or Multiple Cell Fates?

The accumulated evidence over the last 60 years has made it evident that senescence is a fundamental property of cells that fulfills specific functions throughout the entire life span of an organism. The heterogeneity of senescence inducers and types of senescence, however, naturally counters the notion of a unifying view of senescence. While the physiological functions of senescence pertain to tissue development, tissue repair, and terminal differentiation, the accumulation of senescent cells in tissues during aging of humans remains poorly understood. From a molecular regulatory perspective, developmental and damage-induced senescence are distinguishable, and this difference may underlie the ultimate fate of senescent cells throughout the life span of an organism. Furthermore, the conceptual view of damage-induced senescence remains rather generic, even though the kinetics, gene expression, and SASP profiles differ depending on the senescence-inducing signal. It is therefore possible that senescence is not a single cell fate, but rather a collection of individual cell fates that reflect the nature of the inducer; the nature of the cell type; the tissue microenvironment, which all converges in a cell cycle arrest; and the generation of a SASP. Such a view of senescence would pave the way for the identification of senescence type-specific liabilities for the development of novel senotherapies.

Cross-References

- ► Aging Mechanisms
- ► Cellular Aging/Senescence
- ► Gradual Cell Senescence
- ► Senolytic Drugs
- ► Telomerase
- ► Telomeres
- ► Telomere-Subtelomere-Telomerase System

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Cell Suicide

▶ Programmed Cell Death

Cell Therapy

▶ Cell Replacement

Cell-Mediated Immunity

▶ Influenza Vaccination in Older Adults

Cellular Aging

▶ Aging Theories
▶ Cell Damage and Transformation in Aging

Cellular Aging/Senescence

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Synonyms

Apoptosis; Biological aging; Cell senescence; Programmed cell death

Definition

Senescence signifies deterioration with age. It represents biological aging, which involves a gradual loss of function. Cellular senescence should be distinguished from senescence of the whole organism. Cellular senescence is characterized by growth arrest, the phenomenon by which normal cells cease to divide. Senescence of the whole organisms is a characteristic outcome for all multicellular organisms with germ cell-soma separation. Death is an inevitable outcome.

Overview

A hallmark of aging is the accumulation in tissues of senescent cells (Box 1). Cellular senescence is a state in which growth stops and inflammatory cytokines are released. The progressive increase in inflammatory state with aging has been termed "inflammaging" and leads to tissue accumulation of senescent cells. This results in a decline in organismal health and lifespan. Many of the molecular mechanisms responsible for cellular senescence have been discovered. Interventions have been developed to clear senescent cells from tissues of mice. This has resulted in remarkable improvements in health and longevity. Various environmental factors, by modulating conserved intracellular pathways that impact senescence, are able to affect aging and lifespan. Accompanying senescence are changes in chromatin. These include histone modifications as well as changes in DNA methylation and in the three-dimensional organization of the genome. Therapies that target the epigenome may slow senescence and aging.

Key Research Findings

Replicative senescence is a characteristic feature of somatic cells of multicellular organisms. In 1961 and Moorehead discovered that after fibroblasts undergo 50 cell divisions in culture they are no longer able to replicate (Hayflick 1965), a phenomenon known as the Hayflick limit. At each cell division, the repeated sequences of DNA at the end of chromosomes – telomeres – become shorter (Harley et al. 1990). When a critical telomere length is reached, a DNA damage response is triggered, resulting in growth arrest (Steenstrup et al. 2017). During their lifetime, most individuals do not reach a leukocyte "telomeric brink" of 5 kb signifying high risk of impending death. Telomeric brink is more common in very old individuals (aged over 95 years) (Steenstrup et al. 2017).

Other ways in which a DNA damage response can be triggered include an elevation in reactive oxygen species (ROS), the induction of oncogenes, cell-cell fusion, and mitochondrial dysfunction (Harley et al. 1990; Campisi and d'Adda di Fagagna 2007). Telomere shortening is the primary cause of replicative senescence. Loss of the shelterin complex exposes the ends of telomeres that are then recognized by the cell as DNA breaks (Bernadotte et al. 2016). Oncogene-induced senescence (OIS) involves activation of oncogenes such as RAS and BRAF. This leads to repression of transcription factors in the E2F gene family that cause proliferation, replication stress response activated by DNA damage, and senescence-associated secretory phenotype (SASP) caused by release of inflammatory cytokines by senescent cells. Mitochondria affect senescence by strongly activating both the tricarboxylic acid (TCA) cycle and SASP. Overexpression or inhibition of specific enzymes in the TCA cycle can directly influence senescence (Sun et al. 2016). Crucial to modulation of metabolism and senescence is p53-mediated repression of malic enzyme 2 leading to an increase of the TCA metabolite malate (Jiang et al. 2013). In OIS, increased pyruvate dehydrogenase, by causing pyruvate oxidation, leads to increased ROS production that activates the DNA damage response. The latter, via the ataxia telangiectasia mutated (ATM), α serine/threonine-specific kinase (ATM, also known as protein kinase B), mechanistic target of rapamycin complex (mTORC), and peroxisome proliferator-activated receptor γ coactivator 1 β (PGC1β) pathway, stimulates mitochondrial biogenesis, leading to further elevation in ROS and DNA damage. Pro-oxidative ROS and pro-inflammatory SASP are reduced by selective ablation of mitochondria (Sun et al. 2016).

The young cell is well-differentiated. Successive replication eventually leads to senescence. During this process the highly regulated chromatin marks drift between repressed and active and toward an entropic middle ground. Consequently, genes that were previously inactive tend to "leak" (commence low expression), owing to breakdown in chromatin connectivity from weakening of topologically associated domains (TADs) and insulators flanking TADs. As a result, well-defined blocks of constitutive heterochromatin are transformed into senescence-associated heterochromatin foci (SAHF). These phenomena impact the phenomenon of aging.

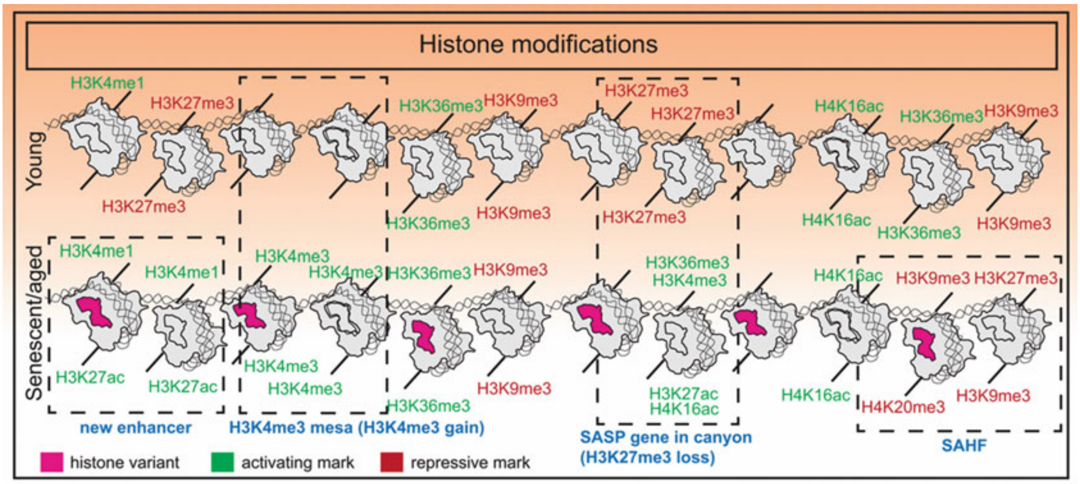
DNA damage leads p53 to bind to the p21 promoter, resulting in an increase in expression of cyclin-dependent kinase inhibitor 1A (CDKN1A; also termed $p21^{CIP1}$ and $p21^{WAF1}$). Independently, increased expression of CDKN1A/CDKN2A (also termed $p16^{INK4A}$), an inhibitor of cyclin-dependent kinases 4 and 6, along with p21, leads to dephosphorylation of retinoblastoma (Rb) protein, the end result being cell cycle arrest at the G1 phase (Adams 2009). Together, these pathways help ensure senescent cells maintain an active metabolic state in the face of a marked change in overall gene expression profile that includes a decrease in expression of cell cycle genes and an increase in SASP genes (Sidler et al. 2017). SASP gene products are associated with inflammation, proliferation, and changes in extracellular matrix. Cell proliferation and senescence are regulated by the tumor suppressors CDKN2A/B that are epigenetically regulated by antisense noncoding RNA in the "*IN*hibitors of CD*K4*" (*INK4*) locus antisense noncoding RNA in the INK4 locus (ANRIL), a long noncoding RNA at the 9q21 locus, the latter being a "hotspot" for genetic variants associated with disease (Congrains et al. 2013).

Senescence, by being antiproliferative, serves as a potent tumor suppressor mechanism. The side effect is local and systemic tissue and organ dysfunction arising from chronic DNA damage, ROS, and SASP.

Epigenetic changes, which affect gene function irrespective of DNA sequence, occur during aging (Benayoun et al. 2015). During senescence there is global hypomethylation of DNA, particularly at regions with repeat sequences (long interspersed nuclear elements [LINEs] and short interspersed nuclear elements [SINEs]) and late-replicating pericentromeric satellite DNA, as well as lamin-associated domains (LADs) that juxtapose with constitutive heterochromatin. Hypomethylated DNA at repeat regions leads to distension (senescence-associated distension of satellite heterochromatin) and derepression. There is, moreover, local hypermethylation at GpC-rich promoter sequences. This mostly correlates with gene repression. Epigenetic control is mediated here by either cytosine-5 methylation within CpG dinucleotides or adenine-6 methylation. These changes adversely affect gene expression. The DNA methylome of senescent cells may sensitize the cell to malignancy. The epigenetic drift that occurs with aging contributes to cellular dysfunction.

The methylation status of 71 CpGs is highly predictive of biological aging and has been used as an "epigenetic clock" (Horvath and Raj 2018). There is evidence for a lack of effect of DNA damage as being responsible for cellular aging, as well as the uncoupling of cellular aging and senescence (Lowe et al. 2016). Clock CpGs are not generally correlated with gene expression. It may be that the clock mirrors, as a highly sensitive readout, upstream signals such as changes in hormone levels or immune signaling that affect changes in 3D spatial configuration or phase changes in the nucleus.

Epigenetic changes during aging also involve histone proteins that bind to DNA (Fig. 1). The histone octamer is comprised of four canonical histone proteins – histone 2A (H2A), histone 2B (H2B), histone 2A (H3), and histone 2A (H4) – with two copies each of these forming a spool that DNA is wound around. Specific modifications of histones correlate with open versus closed or active versus repressed states of chromatin. Common epigenetic modifications are trimethylation of histone 3 at the lysine 4 position (H3K4me3) and at lysine 27 (H3K27me3). At promoters, H3K4me3 (which is a mark of promoter accessibility) has an activating effect on gene expression, while H3K27me3 has a repressive effect. In mice and other species in which these bivalent sites become hypomethylated with age, methylation pattern has been directly linked to regulation of lifespan. H3K9me3 and H4K20me2 histone methylation results in the formation of facultative heterochromatin (chromatin compaction), which suppresses transcription. H3K56ac and H3K14ac histone acetylation affects genome stability. The patterns and changes in modification of histones are highly specific to tissues and genes (Benayoun et al. 2015). Interventions such as caloric

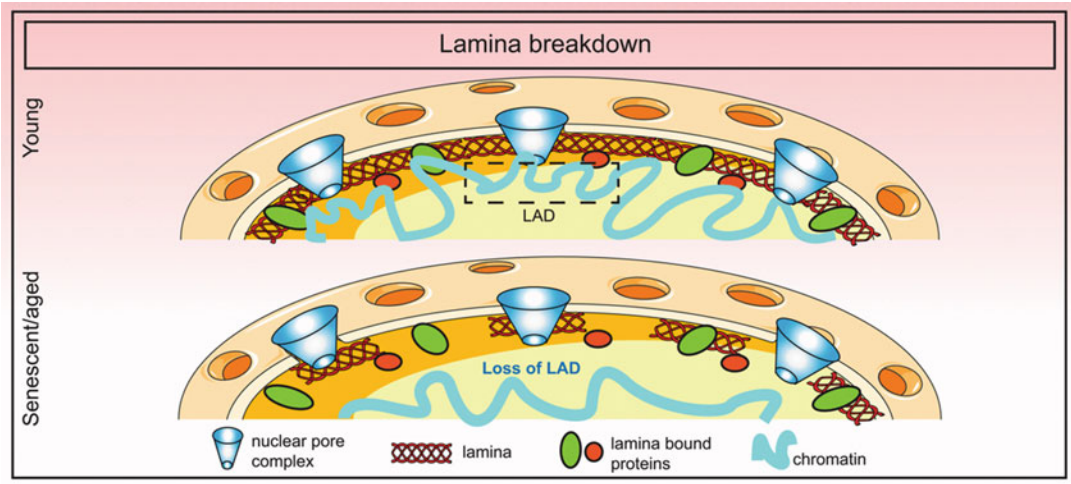


Cellular Aging/Senescence, Fig. 1 During senescence there is an imbalance of histone modifications resulting in accumulation of euchromatin marks. In addition, new super-enhancers are formed near genes involved in SASP genes in oncogene-induced senescence, H3K27me3 "canyons" where SASP genes reside, H3K4me3 "mesas" (plateaus), and formation of SAHFs. (From Yang and Sen 2018) (Source: Images for Figures were used under the Creative Commons Attribution 3.0 license that applies to articles published in Aging)

restriction and rapamycin that extend lifespan suppress hypomethylation associated with aging. In human cells, the number of core histone proteins decreases with age. During replicative senescence in cultured human fibroblast cells and in aged mice and primates, the core histone variant, macroH2A (which is a splice variant of histone H2A) increases with age (Kreiling et al. 2011). For recent extensive reviews of the senescent cell epigenome and epigenetics of aging, see Ermolaeva et al. (2018) and Yang and Sen (2018).

Senescent cells exhibit a general loss as well as a redistribution of heterochromatin, so leading to cellular dysfunction with age (Tsurumi and Li 2012). In the senescent cell, more than 30% of the chromatin is associated with senescence-associated heterochromatin foci (SAHF) (Chandra et al. 2012). These are regions of highly condensed chromatin and are associated with modifications to heterochromatic histones – H3K4me3 and H3K27me3 – as well as with heterochromatic proteins, the macroH2A histone variant, and high-mobility group A (HMGA) proteins. They are, moreover, regions in the genome that are late replicating that tend to be localized over LADs. Lamins and their associated proteins are components of the nuclear lamina. The nuclear lamina maintains the structural integrity of the nucleus. It organizes chromatin, as well as facilitating nuclear assembly/disassembly during mitosis. In addition, it serves as a scaffold for DNA repair and maintains telomere integrity. Chromatin that is located close to the nuclear lamina is mostly heterochromatic. It typically has a low gene density, as well as a repressive chromatin configuration, and is flanked by binding sites for CCCTC-binding factor (CTCF), which is an insulator protein and transcriptional repressor.

Nuclear lamina breakdown is considered to lead to a loss of organization of heterochromatin. This involves the movement of euchromatin, facultative heterochromatin, and constitutive heterochromatin away from the nuclear lamina (Fig. 2). Chromosomal high-throughput confirmation capture (Hi-C) has shown age-associated differences in local chromatin connectivity when embryonic stem cells, somatic cells, and senescent cells are compared (Chandra et al. 2015). It was suggested that senescence is an endpoint of the continuous nuclear remodeling process during cell differentiation (Chandra et al. 2015). Age-related breakdown of the nuclear lamina is accompanied by

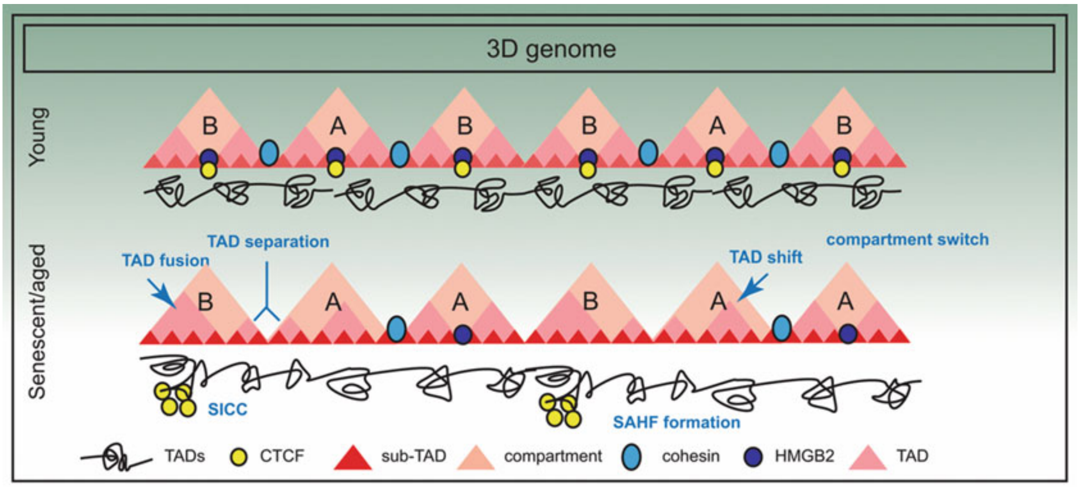


Cellular Aging/Senescence, Fig. 2 During senescence the nuclear lamina breaks down. Loss of lamin B1 triggers the detachment of constitutive heterochromatic regions (LADs). This disrupts the organization of the spatial arrangement of the genome within the nucleus. Tight control of gene regulation is lost as the inactive chromatin becomes dissociated from the nuclear envelope, TADs lose neighboring connections in exchange for long-range interaction, and the distinction between active and inactive chromatin domains becomes blurred. (From Yang and Sen 2018) (Source: Images for Figures were used under the Creative Commons Attribution 3.0 license that applies to articles published in Aging)

loss of local interactions within TADs, together with an increase in distant interactions between TADs in the senescent state. This supports the senescence-associated change in physical compaction of chromatin. A consequence is co-regulation of genes neighboring each other and that were previously isolated from one another transcriptionally. The genome regions that changed the most were those that were least accessible and that were high in AT content. These are features that characterize satellite DNA, characterized by being highly repetitive and containing high concentrations of centromeric constitutive heterochromatin. Figure 3 depicts the 3D spatial changes in the genome during senescence.

Expression of the important pro-apoptotic BCL2 (B-cell lymphoma 2) like 1 gene (*BCL2L1*) is upregulated in centenarians (Borras et al. 2016). Its transfection into mouse embryonic fibroblasts and the lymphocytes of septuagenarians caused cell cycle inhibitors to be suppressed, cell proliferation to be increased, offered protection against oxidative damage, and resulted in a delay in the accumulation of senescent cells. A constitutively active mutant of its ortholog, cell death abnormality gene 9 (*ced-9*), increased *Caenorhabditis elegans* survival (Borras et al. 2016).

LncRNAs are involved in the regulation of cellular senescence (Kour and Rath 2016). Some are antisense transcripts that suppress expression of mRNA transcripts of the same gene. Other lncRNAs are encoded by pseudogenes. In senescent cells, these negatively regulate mRNAs encoding cell adhesion molecules and components of the translation machinery. Resulting effects would include changes in the morphology, growth and division of cells, together with alterations in expression of various SASP proteins, which would contribute to cellular senescence and aging. There are also lncRNAs encoded by intergenic DNA. These affect multiple different intracellular processes, including ones that contribute to senescence and aging (Kour and Rath 2016). A class of lncRNAs containing heterogeneous 5′-UUAGGG-3′ repeats (TERRA) is associated in part with telomeric heterochromatin. TERRA, when strongly upregulated, is able to promote telomere dysfunction that includes shortening,



Cellular Aging/Senescence, Fig. 3 The 3D arrangement of the genome undergoes significant changes in senescence. This includes compartment switching, TAD fusion, TAD separation, and TAD shifting. Some of these changes are triggered by a decline in chromatin architectural proteins such as high-mobility group protein B2 (HMGB2). This leads to formation of senescence-induced CTCF clusters (SICC). However, TAD structure is generally maintained. (From Yang and Sen 2018) (Source: Images for Figures were used under the Creative Commons Attribution 3.0 license that applies to articles published in Aging)

reduced stability, and formation of heterochromatin (Kour and Rath 2016).

Besides somatic cells, tissues contain stem cells, which are rare and are located in specialized niches, exhibit suppression of metabolic activity, so reducing production of toxic metabolites, and maintenance of a state of quiescence, so reducing replication-associated DNA damage (Behrens et al. 2014). Despite these protective measures, stem cells accumulate molecular damage and lose functionality during aging. SASP may contribute to mis-differentiation of stem cells in aging tissues, resulting in defects such as muscle fibrosis and bone marrow adipogenesis (Ermolaeva et al. 2018). Chronic inflammation from accumulation of senescent cells in aging tissues may lead to stem cell exhaustion, tissue damage, and diseases such as cancer. Calorie restriction mitigates the increase in senescent cells and microglia, as well as and inflammation in the subventricular zone with aging, so preserving neural stem cells (Apple et al. 2019). Inducing mouse embryonic stem cells to differentiate into either astrocytes or to adipocytes causes many genes normally present at the nuclear periphery to relocate to the nuclear interior where they are primed to allow expression at a later differentiation state. This transition relies on histone methyltransferases and deacetylases. The maintenance of telomere function requires binding of the telomere/shelterin complex to the nuclear lamina.

Consequences

Loss of healthy cells and stem cells leads senescent cells to accumulate in tissues with age (van Deursen 2014). In age-related diseases, senescent cells accumulate at sites of pathology (Biran et al. 2017), so disrupting tissue homeostasis, decreasing capacity for regeneration, and causing low-grade inflammation, which together result in permanent structural changes and functional decline of organs and tissues (Baker et al. 2011). Immune system changes occur with aging. Increases occur in the pro-inflammatory activity of innate immune cells (which include monocytes and macrophages), along with a decrease in and immune response (Fulop et al. 2016). With increased chronological age, there is a progressive alteration in expression of 69 noncoding RNAs (comprising 56 microRNAs and 13 snoRNAs) (Munoz-Culla et al. 2017). The microRNAs regulated genes involved in pathways affecting the immune system, the cell cycle, and ones related to cancer. In aged tissues, less than 20% of cells are senescent (range approx. 1–15%, depending on tissue type), but the proportion nevertheless correlates positively with age. The paracrine release of inflammatory cytokines amplifies damage in surrounding tissue, and if spread of senescence is sufficient, deleterious consequences to health and function may result (He and Sharpless 2017).

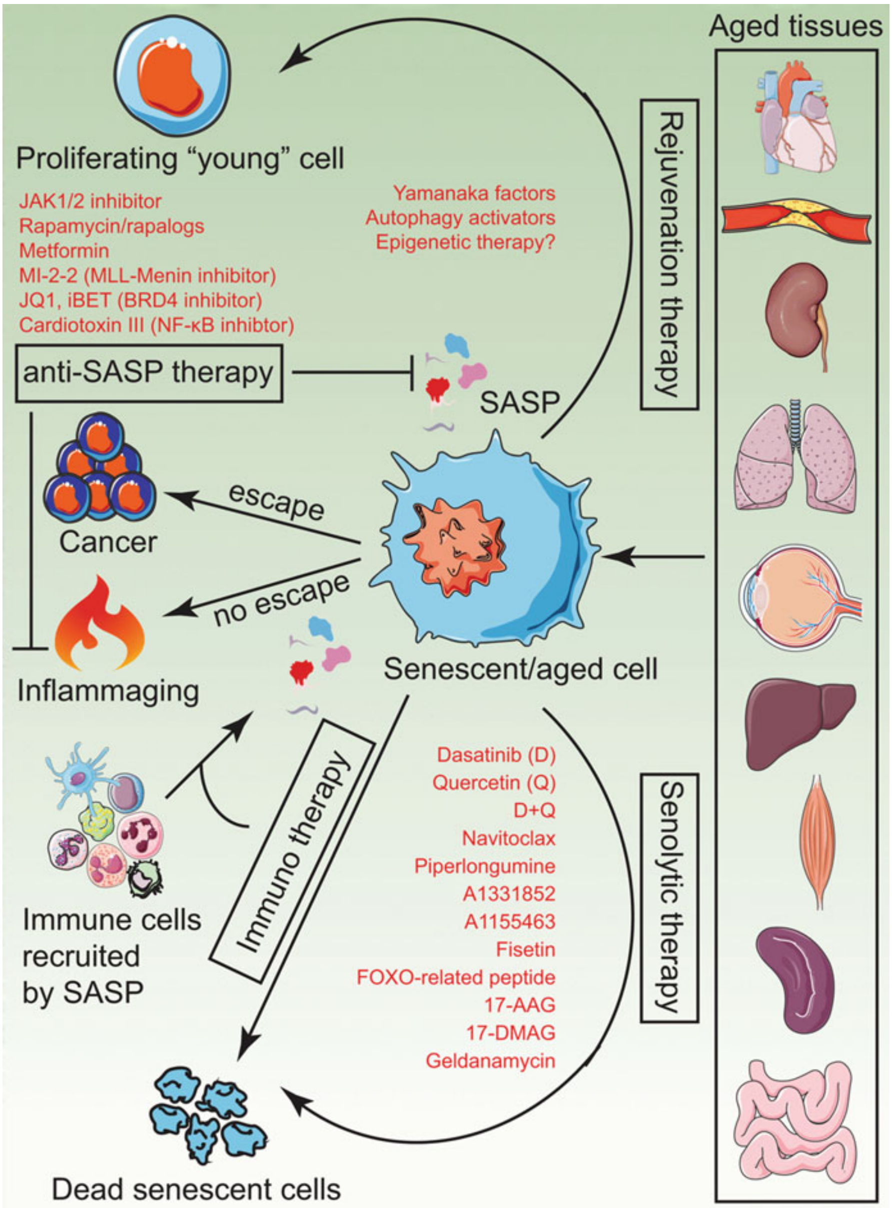
Examples of Application

By delaying the accumulation of senescent cells or reducing their burden, it is possible to delay, prevent, or alleviate multiple senescence-associated conditions (Kirkland and Tchkonia 2017). This can be achieved with senolytic (senescence-destroying) therapies involving drugs or natural compounds that primarily target an apoptotic mechanism specific to senescence (Fig. 4). As a result, senescent cells become susceptible to their own pro-apoptotic microenvironment (Kirkland and Tchkonia 2017). Several senolytic agents shown to be capable of alleviating various senescence-related phenotypes in preclinical models are poised for translation into clinical interventions capable of being transformative for age-related diseases and even aging itself. Clearance of senescent cells in progeroid (Baker et al. 2011) and naturally aged (Baker et al. 2016) mice improved health and lifespan. This also occurred in a mouse model of Alzheimer's disease (Bussian et al. 2018). A senolytic cocktail consisting of dasatinib (a multi-kinase inhibitor [brand name Sprycel®] used to treat certain cases of chronic myelogenous and acute lymphoblastic anemia) and quercetin (a plant flavanol having health benefits) had rejuvenating effects and increased the lifespan of old mice (Xu et al. 2018). Senolytics have been shown to ameliorate damage from atherosclerotic plaques and from post-traumatic osteoarthritis (Jeon et al. 2017). Sulforaphane, a cruciferous vegetable-derived metabolite, delays senescence. A screen of polyphenols found that fisetin (7,3,4′-flavon-3-ol) is a potent senolytic agent capable of increasing health span and lifespan (Yousefzadeh et al. 2018).

Drugs that target senescent cells are now in Phase II/III clinical trials. These include metformin, mitochondria-derived peptides, and small molecule senolytics. Others having potent anti-SASP effects are rapamycin and janus kinase 1 and 2 (JAK1/2) inhibitors (Laberge et al. 2015; Xu et al. 2015). Everolimus, an immunosuppressant derived from rapamycin and used clinically after organ transplantation, boosts immune function in the elderly (Mannick et al. 2018), and trials are planned for other conditions of aging.

Future Directions

More research is needed to show the relevance of cellular senescence to organismal aging, especially in humans. The extremely long-lived mole rat shows cellular senescence, but this does not affect its longevity. In mice, targeted ablation of senescent cells improved health span and lifespan (Baker et al. 2011, 2016). The development of senolytics as a therapy capable of clearing senescent cells in humans should be seen as a major research priority. Clinical trials of these potential drugs in a variety of age-related conditions should then be conducted. Further investigation of the efficacy of other interventions should be undertaken. More research is needed on SASP inhibitors (such as rapamycin and metformin) as therapies in the elderly. These can block the pro-aging arm of senescent cells while maintaining the pro-tumor arm (Yang and Sen 2018). Research on small molecules that stimulate SASP genes by inhibiting epigenetic enzymes is another aspect of future research. The importance of autophagy and mitophagy in clearing senescent cells should be further explored and exploited. The decline in immune cells with age (immunosenescence) contributes to accumulation of senescent cells. Subsets of senescent cells become resistant to immune-mediated clearance. Epigenetic interventions are needed to boost immune surveillance. Antibody-based therapies able to reverse the immune resistance of senescent cells should also



Cellular Aging/Senescence, Fig. 4 Current senolytic therapies. Aged tissues tend to accumulate senescent cells which impose detrimental changes to tissue structure, regenerative ability, and physiological function due to chronic inflammation. Current and plausible strategies to treat these adverse effects include the administration of senolytics and rejuvenation therapy. These interventions involve partial reprogramming to a "youthful" state, anti-SASP therapy to counter the generation and release of inflammatory cytokines, and immunotherapy to activate innate immune mechanisms, which can clear senescent cells. (From Yang and Sen 2018) (Source: Images for Figures were used under the Creative Commons Attribution 3.0 license that applies to articles published in Aging)

be explored. Parabiosis (injecting plasma from young mice into old mice) has shown remarkable rejuvenating effects mediated, at least in in part, by mesencephalic astrocyte-derived neurotrophic factor (MANF). The findings have led recently to clinical trials, one of which was inspired by cognitive improvements in mouse models of Alzheimer's disease after infusion of blood or plasma from human umbilical cord (see review: Castellano 2019). Despite concerns, this line of investigation shows promise. The active factor (s) responsible for the rejuvenating effect (such as MANF) could lead to novel antiaging therapies. Research is also needed to understand how the epigenetic clock can be slowed.

Future strategies might include devising ways of delaying the onset of senescence and of restoring senescent cells to a youthful state (Kirkland and Tchkonia 2017; Yang and Sen 2018). Since senescent cells have features in common with terminally differentiated cells, means of inducing dedifferentiation by overexpressing Yamanaka factors (organic cation transporter 3 [Oct3/4], SRY {sex determining region Y}-box 2 [Sox2], kruppel-like factor 4 [Klf4], and avian myeloblastosis virus oncogene cellular homolog [c-Myc] able to induce pluripotency in human somatic cells) has been accomplished both in vitro and in vivo (Ocampo et al. 2016). Reprogramming was partial, and the cells did not reenter the cell cycle. Provoking cell cycle reentry carries the risk, however, of cancer. Safer would be to develop therapies targeting enzymes having epigenetic effects on the chromatin of senescent cells (Capell et al. 2016). This could alter gene expression so as to restore a youthful state, abolish SASP, and achieve metabolic balance.

Summary

Senescence is accompanied by telomere shortening and epigenetic modifications to chromatin. The latter include histone modification and DNA methylation. Senescence is accompanied by changes in the three-dimensional organization of the genome. With aging, senescent cells accumulate in tissues, reaching 1–15% of the cell population, depending on tissue type. Release of inflammatory cytokines and inflammaging accompanies the accumulation of senescent cells in tissues with age. Cellular senescence results in a decline in organismal health and lifespan. Interventions that clear senescent cells from mouse tissues of mice have resulted in remarkable improvements in health and longevity. Healthy diet and lifestyle, by modulating conserved intracellular pathways that impact senescence, are able to affect aging and lifespan. Therapies that target the epigenome may slow senescence and aging.

Box 1

The key features of senescent cells:

- Cell-autonomous proliferative arrest
- DNA damage
- Increased β-galactosidase release from lysosomes
- Resistance to apoptosis and mitogenic signals
- A senescence-associated secretory phenotype (SASP) characterized by the release of inflammatory cytokines and chemokines
- Appearance of senescence-associated heterochromatic foci (SAHF)
- Alterations in histone modifications and DNA methylation

Cross-References

▶ Aging and Cancer
▶ Aging Mechanisms
▶ Aging Pathology
▶ Aging Theories
▶ Antiaging Strategies
▶ Biogerontology
▶ Cell Senescence
▶ Molecular and Epigenetic Clocks of Aging
▶ Nutrition and Lifestyle
▶ Oxidation Damage Accumulation Aging Theory (The Novel Role of Glutathione)
▶ Senolytic Drugs
▶ Slow-Ageing Diets
▶ Stem Cells Aging

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Cellular Degradation Due to Age-Related Diseases

► Autophagy in Aging

Cellular Maintenance Processes/Machinery

► Cellular Repair Processes

Cellular Proteostasis in Aging

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Synonyms

Protein folding; Protein homeostasis; Protein synthesis; Proteolysis; Proteostasis

Definition

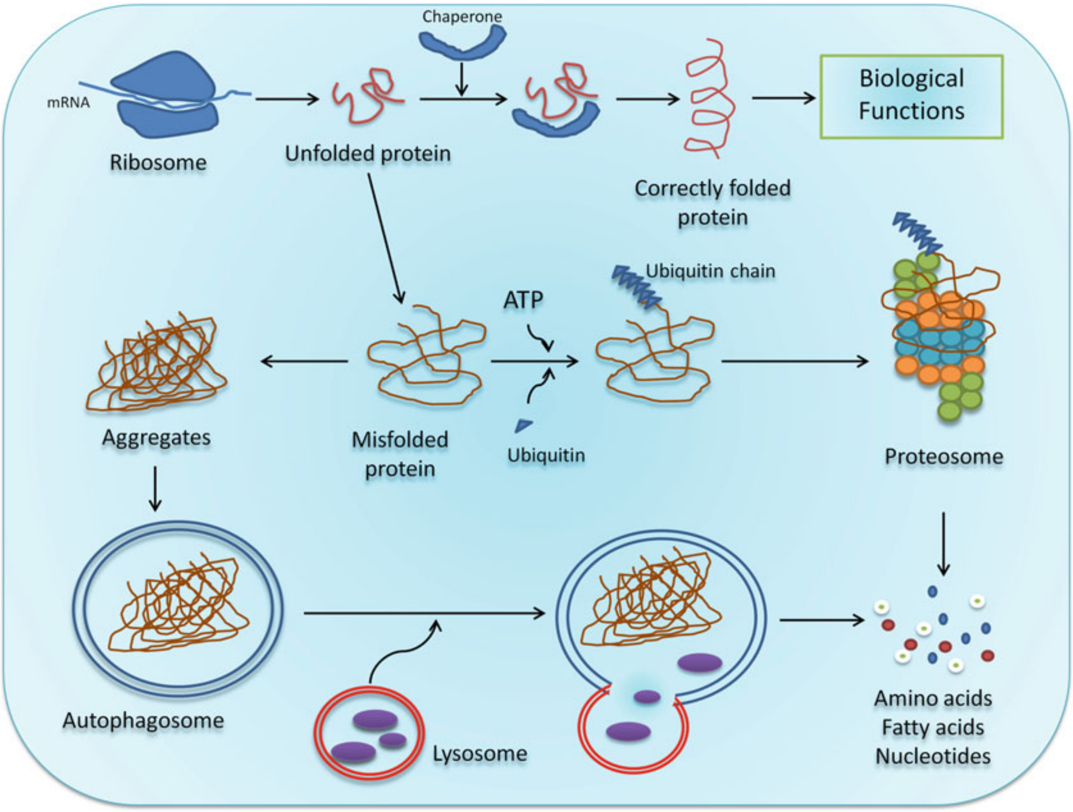
Proteostasis or "protein homeostasis" refers to the integrated biological pathways regulating the dynamic balance of functional proteins in cells. The maintenance of proteostasis balance requires proper synthesis, folding, trafficking, and catabolism of proteins.

Overview

Proteostasis constitutes the basis of proteins physiological functions within organisms and its maintenance requires the strict control of protein synthesis, folding, trafficking, and degradation (Klaips et al. 2018). Protein synthesis comprises the initial stage of protein homeostasis process. Efficient folding is necessary for newly synthesized or unfolded proteins to acquire their unique three-dimensional structures, which are essential for them to function biologically (Balchin et al. 2016). Protein degradation refers to the breakdown of proteins, impairment of which is considered closely related to the pathophysiology of age-dependent changes in organs, tissues, and cells (Nakayama et al. 2016). To adapt to their environments, cells have developed complex networks that allow them to perform diverse physiological functions and restore any stress-induced disruption of proteostasis (Klaips et al. 2018). This is an intricate network of molecular chaperones, autophagic influx, and the ubiquitin proteasome system (UPS) (Dikic 2017). Recent studies have shown that proteostasis-related pathways functions are impaired with aging, indicating that proteostasis imbalances may contribute to the aging phenotype (Kaushik and Cuervo 2015; Klaips et al. 2018) and to the development of age-associated diseases, such as neurodegenerative diseases, cancer, and type 2 diabetes (Kaushik and Cuervo 2015).

Key Research Findings

The preservation of proteostasis is mainly regulated by molecular chaperones and intracellular proteolytic systems, such as autophagy and UPS (Kaushik and Cuervo 2015). Molecular chaperones help many newly synthesized proteins to fold in the correct way. They also prevent protein aggregation inside cells. In other words, chaperones either assist cellular unfolded proteins to refold into stable conformations or promote the degradation of these proteins, depending on the different extracellular stressors present (Finka et al. 2016). Heat-shock proteins are well-known chaperones that play pivotal roles in maintaining the proteome balance (Schopf et al. 2017). They facilitate conformational changes and allow the folding of client proteins with the support of ATP and small heat-shock proteins (Kaushik and Cuervo 2015). Multiple age-associated alterations, such as the decline in mitochondrial function and decreased metabolic efficiency, limit the production of ATP (See ► "Aging Pathology" and ► "Aging Mechanisms"). Thus, the chaperone's ability to recognize unfolded proteins tends to decline with age (Hartl 2017; Soares et al. 2019), leading to an accumulation of unfolded and misfolded proteins within cells. Besides molecular chaperones, proteolytic systems are also pivotal to the preservation of proteins balance within the cells. Autophagy and proteasome activity are the two main systems that clear damaged proteins. Autophagy allows the orderly breakdown of dysfunctional proteins and aging organelles (See ► "Autophagy in Aging"). Moderate autophagy is an adaptive response to stress, and its activation is beneficial to maintaining cellular homeostasis and promoting cell survival (Carroll et al. 2018). Several lines of evidence support that autophagic influx declines during the aging process (Levine and Kroemer 2019). However, the mechanisms underlying this age-related decline are still unclear. Autophagy related genes, such as Atg5 and Atg8, are involved in the lifespan extension stimulated by autophagy (Ruckenstuhl et al. 2014). It is possible that the transcriptional activity of these genes is decreased in the human brain during aging (Kaushik and Cuervo 2015; Ruckenstuhl et al. 2014). Autophagic dysfunction causes the accumulation of abnormal proteins and toxic lysosomal hydrolases in autophagic and lysosomal vesicles, contributing to the occurrence of age-related degenerative changes in mammalian tissues (Scrivo et al. 2018). Interventions, such as caloric restriction, administration of resveratrol, and proper physical exercise are thought to play anti-aging effects through the enhancement of autophagy in organisms (Loos et al. 2017; Ruckenstuhl et al. 2014). Along with autophagy, the UPS is a major proteolytic system in mammalian cells. UPS mediates proteolysis through two successive steps: the tagging of the substrate proteins by the attachment of multiple ubiquitin molecules and the subsequent proteolytic cleavage by proteasome. The UPS is involved in signal transduction linked with protein quality control, stress, and aging. With age, the proteasome activity is gradually declined, which decreases the capacity of UPS to remove abnormal, denatured, and damaged proteins. This eventually causes the pathogenesis of several important human diseases, such as Alzheimer's and Parkinson's diseases (Vilchez et al. 2014). A summary of the proteostasis network is shown in Fig. 1.



Cellular Proteostasis in Aging, Fig. 1 The proteostasis within cells. Ribosome plays a central role in cellular protein synthesis. With the help of molecular chaperones, nascent proteins were folded into their correct three-dimension structure, where they play biological functions. Under stress conditions, nascent proteins tend to form misfolded proteins, which aggregate or are degraded by proteasome in an ubiquitin-dependent manner. Damaged and aggregated proteins can also be degraded through the activation of autophagy

Future Directions of Research

Several lines of evidence support the notion that proteostasis is one of the key processes in ensuring longevity. Nonetheless, attempts to delay the progression of aging and age-related diseases are still greatly needed (See ► "Antiaging Strategies"). In spite of being reasonable to propose that activation of intracellular proteolytic systems would have beneficial effects in the delay of aging, overactivation of the proteolytic system has deleterious consequences (Liton et al. 2009). Hence, keeping a dynamic balance of proteostasis during the treatment of age-related diseases is still a challenge. Future effort should focus on answering the question of how these systems balance their activities, especially at the onset of aging. A large number of molecules have been found to participate in the process of proteolysis, so these proteins may be promising targets to design potential compounds for the treatment of age-related diseases. However, small-molecule compounds targeting chaperones or the proteolytic systems are still limited.

Summary

Although there is still a long way to go before we truly understand the biology of proteostasis, it is clear that it is an extremely important biological process, regulating both normal aging and age-related diseases. Achieving a better understanding of the physiological and pathological changes that

occur during proteostasis and identifying the cross-talk among different proteolytic systems is critical for a systematic understanding of age progression.

Cross-References

- ▶ Aging Mechanisms
- ▶ Aging Pathology
- ▶ Antiaging Strategies
- ▶ Autophagy in Aging

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Cellular Repair Machinery

▶ Cellular Repair Processes

Cellular Repair Processes

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Synonyms

Cellular maintenance processes/machinery; Cellular repair machinery

Definition

Cellular repair processes refer to the range of machinery that maintains and restores the integrity of the functional units of the cell, constitutively or in response to insult.

Overview

The cellular environment is an extremely dynamic one, and cells are continuously subject to a range of intrinsic and extrinsic stressors that threaten the integrity of their functional units, including organelles, proteins, DNA, and membranes and functional lipids. Accordingly, systems have evolved to reduce rate of generation of endogenous damage, detoxify damaging agents, and increase the intrinsic resistance of the cell's macromolecular components to damage (Pamplona and Barja 2007).

When these preventive systems fail, however, it is essential to cell survival and function that the cell has machinery in place to repair and replace damaged functional units. The range of such machinery is vast but will be summarized briefly in this article. We will then review potential strategies toward the development of therapies to enhance or reinforce this machinery in order to intervene in the degenerative aging process and extend healthy lifespan.

Key Research Findings

Proteins

In order to fulfill their biological functions, proteins must maintain precise three-dimensional folded structures. When proteins either fail to fold during synthesis or become misfolded in the course of their cellular lifetime, they can no longer execute their biological function; in addition, the aberrant conformation may be toxic to the cell, either directly or by protein aggregation (see entry for "Intracellular Aggregates"). Such misfolding can occur as a result of errors in protein biogenesis (including mRNA transcription and maturation as well as protein translation) or in the intrinsically error-prone process of protein folding itself (Klaips et al. 2018). Acute or chronic environmental or physiological stressors (including aging) can further increase the acute or steady-state levels of such misfolded proteins (Klaips et al. 2018).

Cells are equipped with several interacting systems to assure cellular protein structural integrity (sometimes termed "proteostasis") (Klaips et al. 2018; Taylor and Dillin 2011) (see entry for "Proteostasis"). Defenses against protein misfolding exist at the levels of protein synthesis, protein folding and conformational maintenance, cytoprotective stress responses, and degradation of damaged and misfolded proteins (Klaips et al. 2018; Taylor and Dillin 2011).

At the level of protein synthesis, it is notable that several phylogenetically conserved interventions that retard aging reduce the rate of protein synthesis, which in addition to conserving energy also reduces the supply of proteins at risk of misfolding (Taylor and Dillin 2011; Tavernarakis 2008). These include calorie restriction (CR – see the entry "Diet and Caloric Restriction" in this volume), inhibition of the mechanistic target of rapamycin (mTOR) (see the entry for "Mechanistic Target of Rapamycin"), and reducing signaling through the insulin/insulin-like growth factor (IGF-1) pathway (see the entry for "Insulin/Insulin-Like Growth Factor Pathway"), although all of these interventions also affect other aspects of proteostasis. Molecular chaperones act on nascent polypeptide chains as they emerge from the ribosome, either "passively" stabilizing them into intermediates favorable to adoption of properly folded states or "actively" folding them via ATP-driven processes (Klaips et al. 2018; Taylor and Dillin 2011). Even after misfolded proteins have escaped initial conformational shaping, some chaperones can additionally protect the cell against toxic aggregates and aggregate-prone misfolded proteins by either disassembling aggregates into intermediates that can then be refolded or oppositely coordinating the aggregation of toxic aggregated or misfolded proteins into more inert assemblies (Evans et al. 2017; Taylor and Dillin 2011). Failure or insufficiency of this machinery can lead to the accumulation with age of recalcitrant aggregates that lead to cellular dysfunction.

A second layer of such protection is comprised of cellular stress responses, which upregulate components of protein quality control and/or inhibit protein synthesis when chronic or acute stressors cause the level of misfolded proteins to exceed the basal capacity of the protein maintenance machinery (Klaips et al. 2018; Taylor and Dillin 2011). Compartment-specific stress-response pathways include the heat-shock response in the cytosol and the mitochondrial and endoplasmic reticulum (ER) unfolded protein responses (UPR), all of which appear to engage in significant cross talk (Klaips et al. 2018; Kim et al. 2016). When properly functioning, these pathways act to re-establish the normal protein homeostasis of the cell, but when the chronic stress of aging and disease overwhelms the capacity of these pathways, their chronic activation can become dysfunctional and limit the dynamic range of the system to respond to new, additional stress (Klaips et al. 2018). Surprisingly, however, inhibitors of cellular stress responses can under some circumstances act to restore cellular homeostasis and function arising from the very misfolded protein stress that those pathways are engaged to relieve (Ma et al. 2013; Moreno et al. 2013; Sidrauski et al. 2013).

Finally, when other systems fail to prevent protein misfolding and aggregation, protein degradation pathways (most notably the ubiquitin-proteasomal system (UPS) and the autophagy-lysosomal system) allow the cell to degrade irretrievably damaged proteins and recycle their components (Taylor and Dillin 2011). Smaller and short-lived proteins are primarily degraded by the UPS, but larger proteins and aggregates are unable to pass through the relatively narrow proteolytic chamber of the 20S proteasome and may impede the entrance of subsequent substrates if so targeted, leading to dysfunction and protein toxicity. Such substrates are accordingly targeted to the lysosome for degradation (Liebl and Hoppe 2016; Taylor and Dillin 2011). Specific delivery of proteins to the proteasome or the lysosome is regulated by the activity of E3 ubiquitin ligases, which tag damaged proteins with ubiquitin chains that direct them to their fate (Liebl and Hoppe 2016).

Autophagy delivers damaged or no longer needed proteins (as well as organelles, parts of the ER, and intracellular pathogens) to the lysosome for degradation. It can be divided into bulk autophagy (macroautophagy) and forms of selective autophagy (Evans et al. 2017). In macroautophagy, an isolation membrane is extended over a region of cytosol, nonselectively engulfing damaged proteins and other substrates to form an autophagophore that then fuses directly with the lysosome or late endosomes/multivesicular bodies. Selective autophagy, by contrast, involves a more orchestrated process of tagging specific proteins and organelles for degradation using the ubiquitin system, followed by selective targeting to either an autophagosome or directly to the lysosome (depending on the pathway) via selective autophagy receptors.

Among the modes of selective autophagy are chaperone-mediated autophagy (CMA) and microautophagy (Evans et al. 2017; Taylor and Dillin 2011). The CMA machinery recognizes substrates bearing a KFERQ-type motif and delivers them to the lysosome, where they are trafficked across the lysosomal membrane by a protein complex featuring lysosomal-associated membrane protein 2A (LAMP2A) (Kaushik and Cuervo 2018). Microautophagy embraces several processes with distinctive membrane structures and machinery, but all feature the selective surrounding of a small region of the cytoplasm for delivery to the lysosome (Oku and Sakai 2018). (Mitophagy – the selective degradation of damaged mitochondria – and the selective autophagy of peroxisomes, inflammasomes, and certain classes of aggregated proteins (Evans et al. 2017) will not be treated here.)

Dysfunction of the cell's proteolytic machinery and associated cellular dysfunction is observed in aging and particular diseases of aging, with affected cells accumulating autophagic vacuoles that fail to fuse with the lysosome, as well as abnormal proteins and toxic lysosomal hydrolases (Friedman et al. 2015; Scrivo et al. 2018).

DNA

DNA is subject to a wide range of damaging agents of metabolic, lifestyle, environmental, and chemical origin. It is thought that the genetic code is subject to thousands of random alterations in each cell every day, yet the activity of the DNA repair machinery ensures that fewer than 0.1% of base changes continue on to be fixed as a mutation (Alberts et al. 2002). Mutations can lead to least three deleterious effects on the cell (and the organism): cell death, cellular senescence, and cancer (Hoeijmakers 2009). In addition, mutations in cells that survive in tissues without suffering these fates are widely suspected of causing cellular and (collectively) tissue dysfunction, contributing to age-related tissue decline and disease (Szilard 1959; Gorbunova and Seluanov 2016). This hypothesis has been given additional impetus by recent reports of clonal expansion of mutation-bearing cells in aging tissues in association with increased risk of diseases of aging (Risques and Kennedy 2018; Martincorena et al. 2018; Martincorena and Roshan 2015), including in some cell types that are postmitotic under normative physiologic conditions (Fischer and Stringer 2008).

The cell has a range of specialized machinery devoted to the specialized repair of specific forms of DNA damage (Ciccia and Elledge 2010; Jackson and Bartek 2009; Hoeijmakers 2009). Single-strand breaks are repaired by single-strand break repair (SSBR), with mechanisms that partially overlap with base excision repair (BER – vide infra), whereas DSBs are alternatively routed through nonhomologous end joining (NHEJ) or homologous recombination (HR).

NHEJ is the dominant mechanism for DSB repair in human cells and directly religates the broken strand of DNA. This entails the recognition, capture, and stabilization of the two broken ends of DNA to prevent nonspecific processing, the assembly of the NHEJ machinery at the site, bridging the two sections of broken DNA molecule, processing the DNA ends (if necessary) to allow them to be ligated, and finally, ligation of the broken ends and resolution of the NHEJ complex (Davis and Chen 2013). NHEJ is highly versatile, as it can religate any type of broken DNA strand and does not require a homologous stretch of DNA to act as a template for repair; this latter feature also allows it to operate in any phase of the cell cycle, as the sister chromatid is only available as a template during S and G2 (Davis and Chen 2013). The lack of a template for repair in favor of direct processing and ligation of the broken ends, however, carries the risk that genetic material may be lost.

By contrast, HR is a highly accurate if more restricted mechanism of DSB repair, using the sister chromatids as homologous templates to restore the original sequence of the broken DNA ends. Through several subpathways, the HR machinery recognizes the broken DNA ends; processes them into single-stranded DNA tails; guides them to invade the intact strand for use as a template, forming a D-loop; synthesizes the replacement sequence; and finally religates the broken DNA strands, following which the intercrossed DNA molecules are severed and restored to their normal double-stranded configuration. (Li and Heyer 2008). (As noted below, the HR machinery is also involved in interstrand crosslink (ICL) repair.)

Mismatch repair (MMR) corrects errors introduced during DNA replication or by a range of mutagenic agents, such as base mismatches and insertions or deletions.

BER is responsible for repairing minor chemical alterations of DNA bases such as spontaneous deamidation of cytosine to uracil, as well as abasic sites (which are intermediates in its repair mechanism). Distinct subpathways exist for repair of single nucleotides (single-nucleotide BER) and for the replacement of two or more nucleotides in the same damaged strand (long-patch BER). The damaged base is first recognized by a DNA glycosylase, which then removes the base through cleavage of the N-glycosidic bond. This leaves an abasic site, which is next cleaved by an AP endonuclease and then repaired via DNA polymerase and ligase proteins (Robertson et al. 2009).

Many animals and other eukaryotes can correct the more complex lesions (such as pyrimidine dimers) induced by ultraviolet (UV) light via photoreactivation of the enzyme photolyase; however, this enzyme is inactive in humans (Lucas-Lledó and Lynch 2009). Instead, these and other helix-distorting lesions are repaired via the more cumbersome nucleotide excision repair (NER) system. There are two NER pathways, which differ in the mechanism by which damage is initially recognized: global genome NER (GG-NER) scans the entire genome for bulky DNA lesions, including regions that are not transcribed, whereas transcription-coupled NER (TC-NER) exclusively detects lesions that interfere with transcription by stalling RNA polymerase II (Hoeijmakers

2009). Once detected, DNA damage is excised as part of a 22–30-base oligonucleotide; DNA polymerases are then recruited to repair the remaining single-stranded DNA, and DNA ligase seals the remaining nick (Jackson and Bartek 2009; Hoeijmakers 2009).

Interstrand crosslinks (ICLs) are adventitious covalent bonds between opposing strands of DNA. Because they prevent the unwinding of the DNA duplex by helicases, they block both transcription and DNA replication, leading to chromosome instability, breakage, or rearrangements and ultimately cell death; DNA crosslinking agents are accordingly used as cytotoxic chemotherapy. Because they involve both strands of DNA and must be repaired before cell replication, ICLs are challenging lesions for repair, necessitating an initial "unhooking" of the DNA via incisions made by nucleases on either side of the ICL, followed by the coordinated action of other canonical DNA repair pathways – a complex set of mechanisms that remain poorly understood (Hashimoto et al. 2016; Muniandy et al. 2010).

Mitochondria have a separate genome from the nucleus, which is subject to much higher levels of mutation because of its proximity to the cell's major source of reactive oxygen species (the electron transport chain) and its more error-prone replicative machinery (de Grey 1999). The most prominent lesions of mitochondrial DNA in aging – and the most closely associated with diseases of aging – are large (1.1–10-kb) deletions, for which no true repair mechanism exists; these clonally expand to occupy all mitochondrial genomes in a small fraction of (primarily postmitotic) cells in aging human tissues (de Grey 1999) (<1% in the heart, skeletal muscle, and much of the brain (de Grey 1999), but perhaps as high as 12% in the putamen (Corral-Debrinski et al. 1992)). The mitochondrial DNA repair machinery is more limited and less well-understood than that of the nucleus but includes forms of BER and MMR and possibly HR as well (Ma and O'Farrell 2015; Chen 2013).

The DNA Damage Response

While the DNA repair machinery is specifically recruited to repair individual lesions as they arise, a threshold level of cellular DNA damage activates the DNA damage response (DDR) – a coordinated network of signaling pathways that regulate DNA repair, cell cycle progression, and ultimately cell fate (return to normal cell cycling, apoptosis, or senescence) (Mirzayans et al. 2017; Maréchal and Zou 2013; Jackson and Bartek 2009). The kinases ataxia-telangiectasia mutated (ATM) and ATM- and Rad3-related (ATR) (and some would add DNA-dependent protein kinase (DNA-PKcs) Maréchal and Zou 2013) are, respectively, recruited primarily by DSBs and by replication stress or other broad types of DNA damage. They orchestrate the phosphorylation of hundreds of protein targets directly, as well as additional secondary targets through phosphorylation of CHK1, CHK2, and p38 MAPK (Maréchal and Zou 2013; Jackson and Bartek 2009).

A key nexus of the DDR machinery is the transcription factor p53, whose specific phosphorylation mediates its stabilization and cellular localization, and thereby its activity (Mirzayans et al. 2017). Upon activation, p53 activates cell cycle checkpoints to allow an opportunity for DNA repair and determines cell fate based on the level and type of genotoxic stress signaling it receives from ATM and ATR, as well as cell type and additional intrinsic and extrinsic properties of the cell (Mirzayans et al. 2017). Signaling from ATR to withdraw from the cell cycle is responsive to the ongoing progress versus stalling of DNA repair during G2 (Feringa et al. 2018). Once activated, p53 activates both pro-growth-arrest and pro-apoptotic mediators in response to genotoxic stress, but the threshold for execution of apoptosis is higher due to the restraining influence of anti-apoptotic proteins, such that the level of DNA damage dictates which fate will prevail (Kracikova et al. 2013). Otherwise, the cell can proceed into a permanent state of growth arrest (senescence) or return to status quo ante after DNA repair is complete – the latter function carried out by the serine/threonine phosphatase WIP1 (wild-type p53-induced phosphatase 1) (Mirzayans et al. 2017).

Membranes

The integrity of the cell membrane is essential to cell survival and function, maintaining an intracellular environment favorable to cell function and selectively controlling the entry and exit of needed substrates and wastes, as well as helping anchor the cell in its anatomical position externally and the cytoskeleton internally. Under normal physiologic conditions, different cells are exposed to cyclic, periodic, or constant mechanical sheer and stretch, in addition to membrane trafficking and remodeling processes, depending on the cell and tissue type, which may puncture or otherwise damage it. Additionally, membranes can be damaged by extrinsic or metabolic insults and acute attack by pathogens or lymphocytes. Mechanisms for membrane repair are therefore essential to cellular integrity.

The simplest mechanism of membrane repair is a thought to be a spontaneous self-sealing action of membrane tension, which can repair small (<1 μm) breaches via physical forces that oppose the "line tension" created by the phospholipids surrounding the membrane breach (McNeil and Terasaki 2001; Tang and Marshall 2017). In nucleated cells, it has been proposed that larger breaches of the membrane elicit a Ca^{2+}-regulated exocytotic response, forming a "patch vesicle" that fuses with the edges of the membrane breach and seals it (McNeil and Terasaki 2001; Tang and Marshall 2017). Alternatively, membrane-patching materials can be derived from the fusion of membrane materials derived from organelles and existing intracellular vesicles that "explode" outward to the breach, in an "explodosis" mechanism (Tang and Marshall 2017).

Muscle sarcolemma exhibits what may be either one variant of this broad conceptual model, a distinct repair mechanism, or an alternative explanation for the observations underlying the patch model in other systems. Dysferlin, the protein whose mutation is responsible for Miyoshi muscular dystrophy 1, regulates vesicle trafficking and fusion, and mutant muscle cells fail to properly repair after injury, including notably deficits in the repair of cell membranes (Han 2011). Injured muscle cells were shown to be repaired by individually exocytosed lysosomes that were tethered to the cell membrane by a mechanism requiring dysferlin (Defour et al. 2014).

An additional Ca^{2+}-regulated mechanism involves the "purse-string" contraction of actomyosin around the breach, drawing the remaining membrane and associated cortical actin cytoskeleton together to close the gap (Tang and Marshall 2017).

The initial repair of cell membranes is followed by a more protracted period of repair and reorganization that ultimately restores full membrane function (McNeil and Terasaki 2001).

Examples of Application

Biomedical gerontology has long been focused on modulating the repair machinery of the cell in hopes of better maintaining the molecular fidelity, function, and survival of cells (and therefore organisms) with age. To some extent, this has been evident in successful antiaging interventions in model organisms. Genetic or pharmacological inhibition of the mTOR pathway, for instance, extends total and healthy lifespan in numerous species, and attenuates many gross anatomical aging phenotypes at necropsy, presumably in large part by decreasing the accumulation of a variety of damaged cellular components, though evidence for the latter is mostly confined to transgenic models bearing disease-associated mutations (Johnson et al. 2013; Wilkinson et al. 2012) (see entry for "Mechanistic Target of Rapamycin").

In another notable study, the age-related decline in the abundance of the lysosomal receptor for CMA (LAMP-2A) was opposed via a repressible LAMP-2A transgene whose expression was restricted to the liver, in which organ its age-related decline is best characterized (Zhang and Cuervo 2008). In young (6-month-old) animals, withdrawal of the suppressing agent prevented the age-related decline of degradation of a typical CMA substrate (GADPH), while the age-related decline in UPS, overall proteolytic activity, and possibly macroautophagy were ameliorated. In parallel, the ultrastructural and gross morphological features of the aging liver were better preserved, along with liver function and mitochondrial morphology and function. Similar benefits were obtained in late-onset (22-month-old) animals, albeit at substantially reduced efficacy (Zhang and Cuervo 2008). However, CMA continued to decline with age despite the additional LAMP-2A protein, in part due to a rise in its instability at the lysosomal membrane; moreover, accumulation of lipofuscin (a persistent, recalcitrant intracellular aggregate (see entry for "Intracellular Aggregates")) was attenuated but not arrested or reversed (Zhang and Cuervo 2008).

Calorie restriction (CR) – the most well-characterized of antiaging interventions – clearly attenuates many of the cellular aberrations of aging, but in many cases in ways that seem to involve reduced *generation* of aging lesions rather than upregulation of repair, and it cannot undo forms of aging for which there is no intrinsic repair mechanism. For instance, while CR reduces the rate of accumulation of nuclear DNA mutations in several tissues with age (Garcia et al. 2008), it does not appear in most cases to proactively upregulate most elements of the nuclear DNA repair machinery, though it does retard their age-related decline (e.g., Wikinson et al. 2012; Rao 2003; Licastro et al. 1988 – but contrast Cabelof et al. 2003 and others for BER). Meanwhile, CR lowers BER activity in muscle and brain mitochondria while elevating it in the liver (Stuart et al. 2004). Again, CR appears to retard the rate of generation of focal electron transport chain abnormalities in skeletal muscle associated with large deletions in mitochondrial DNA (most likely by reducing the rate of stochastic ROS generation at Complex I and by increasing the resistance of mitochondrial membranes to oxidation (Pamplona and Barja 2007)), yet does not retard their spread once initiated (Bua et al. 2004).

Metabolic pathways are inherently fraught targets for intervention, inasmuch as they are the very processes that maintain the life of the organism, and are poised to balance competing risks by millennia of natural selection. For instance, pathways involved in cell proliferation, apoptosis, and senescence balance the risk of tissue denudation versus cancer; the regulation of the autophagy machinery and protein synthesis via mTOR and other regulators must balance the benefits of rapid growth against loss of protein and organellar fidelity; and robustly engaging the antimutagenic activity of DNA-PK during aging comes at the cost of metabolic disease (Park et al. 2017).

"Strategies for Engineered Negligible Senescence" (SENS) (see entry of this title) is proposed as an alternative and potentially more powerful approach to the repair and maintenance of molecular, cellular, and organismal integrity with age, and thereby health and survival with age, in part because it conceptually offers the potential to bypass these metabolic dilemmas (de Grey et al. 2001; de Grey and Rae 2007). In this "damage-repair" heuristic, the cellular and molecular lesions that accumulate in aging tissues are targeted directly, rather than targeting the metabolic determinants of damage generation or repair. Depending on the nature of the lesion, these "rejuvenation biotechnologies" remove, repair, replace, or render harmless particular forms of aging damage through their own action, with minimal perturbation of metabolism (de Grey et al. 2001; de Grey and Rae 2007). Examples include the delivery to the lysosome of engineered hydrolases to degrade intracellular aggregates implicated in age-related disease (de Grey 2002; de Grey et al. 2005) (vs. modulating autophagy and other proteostatic machinery) (see entry for "Intracellular Aggregates"), senolytic agents to remove senescent cells (vs. "senomorphic" agents, which modulate the senescence-associated secretory phenotype or inhibit or reverse the conversion to senescence) (Kim and Kim 2019) (see entries for "Cell Senescence" and "Senolytic Drugs"), and allotopic expression of mitochondrially encoded proteins, in order to obviate the effects on cell function of acquiring a homoplasmic mitochondrial population bearing large, irreparable deletions in the mitochondrial DNA, as occurs in a minority of cells with age (Boominathan et al. 2016; de Grey 1999; de Grey and Rae 2007). An additional argument in favor of this approach is

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that it allows for the targeting of recalcitrant forms of damage that the organism may not have the intrinsic capacity to remove or repair, such as large mitochondrial DNA deletions or advanced lipofuscin (de Grey et al. 2001; de Grey and Rae 2007; contrast Zhang and Cuervo 2008).

Future Directions for Research

Although there are many putative "accelerated aging" models (Miller 2004) based on mutations in elements of the DNA repair machinery, there is no unconfounded evidence that upregulation of DNA repair retards "normative" aging (Gorbunova and Seluanov 2016). A convincing test of this general hypothesis would be a valuable contribution to the field.

Additionally, as noted, the nature and extent of mitochondrial DNA repair mechanisms remain poorly understood and should be further explored. Moreover, the dysfunction of the autophagic/lysosomal pathway observed in affected cells in aging and specific diseases of aging presents several potentially attractive targets for therapies to reverse these age-related defects, though with the potential for perverse effects of imbalancing the integrated system as a result of selectively inducing steps in the pathway (Friedman et al. 2015). A proposed alternative following the direct "damage-repair" approach of SENS is the introduction of novel engineered lysosomal hydrolases to target specific damaged proteins that accumulate in aging cells (de Grey 2002; de Grey et al. 2005). Preliminary evidence supports this approach (Mathieu et al. 2012; Schloendorn et al. 2009), including the recent demonstration that recombinant manganese peroxidase reduces the burden of the main toxic bisretinoid implicated in age-related macular degeneration in model Stargardt's macular degeneration mice (Moody et al. 2018), and two candidate enzymes that have emerged from this work have been licensed to biotechnology startups for therapeutic development. More challenging are targets that accumulate as cytosolic inclusion bodies, with uncertain capacity for lysosomal targeting or degradation. Further work in both areas is needed.

Brain neuron and other cell membranes exhibit a number of changes with age, including disordering of lipid rafts, a shift to more unsaturated fatty acyl groups in phospholipids, and alterations in cholesterol and sphingomyelin content and distribution (Colin et al. 2016; Fülop et al. 2012). In rodents, CR is known to oppose several of these changes (Babenko and Storozhenko 2016; Hernández-Corbacho et al. 2011; Tacconi et al. 1991). Discovery of whether these changes are adaptive changes in response to primary aging damage or are themselves a form of primary age change, and means to oppose these changes, would be useful contributions.

Summary

Cells resist the accumulation of damage through intrinsic molecular stability, detoxification of damaging agents, tuning the metabolic generators of such damage, and also by mechanisms of repair for proteins, DNA, and membranes. Nonetheless, a significant amount of damage eludes these mechanisms; degenerative aging is driven by the accumulation of unrepaired damage in the tissues, leading to loss of functional capacity and ensuing specific diseases of aging along with nonspecific loss of homeostasis and resilience. Augmenting these repair mechanisms – either by modulating the endogenous damage-repair machinery or through direct removal, repair, and replacement through exogenous biotechnology – is a promising strategy for extending life- and healthspan.

Cross-References

▶ Cellular Senescence
▶ Diet and Calorie Restriction
▶ Proteostasis
▶ Senolytic Drugs
▶ Strategies for Engineered Negligible Senescence

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Cellular Senescence

▶ Aging Theories
▶ Cell Damage and Transformation in Aging
▶ Cell Senescence

Cellular Theories of Aging

▶ Stem Cells Aging

Centenarian Rate, Life Expectancy, and Autoimmune Diseases

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Overview

The autoimmune diseases are among the ten leading causes of death for women and are the number two cause of chronic illness in America (Gameiro et al. 2010; Walsh and Rau 2000). With underlying mechanisms of an immune response against own cells and tissues, autoimmunity is partially responsible and a predisposing factor for the development of other diseases, like cardiovascular diseases, cancer, and respiratory diseases, including asthma, which are the three leading causes for noncommunicable diseases' deaths (Lim et al. 2014; García-Gómez et al. 2014; Sun et al. 2014; Rose 2002). Diabetes is the fourth leading cause of death in Europe (World Health Organization 2014), with a growing incidence of autoimmune type 1 diabetes (Katz and Laffel 2015; Chiang et al. 2014). Autoimmunity is the underlying cause of more than 100 serious, chronic diseases (Rose 2002). Their influence on the longevity could be determined by use of longevity parameters (Lens-Pechakova 2016). The number of living centenarians or the centenarian rate (Kim 2013) as well as the life expectancy data (Livingstone et al. 2015) can be used as a measure of longevity. Clarifying the connection between different parameters of longevity and autoimmune diseases could promote healthy aging and longer lifespan.

Key Research Findings

The autoimmune diseases being almost hundred different diseases attacking all different organs are rarely being studied as a group and are conventionally treated by separate medical specialties according to the type of organ involved (Rose 2002). Their connection with the patients' lifespan has been noted by some scientists: A significant correlation has been found between childhood type 1 diabetes incidence rates and infant mortality and wealth (Patterson et al. 2001). Data on rheumatoid arthritis and multiple sclerosis (Thewissen et al. 2005) and on autoimmune type 1 diabetes (Katz and Laffel 2015) have shown that the patients who showed premature senescence have a higher mortality or shorter lifespans (Livingstone et al. 2015).

Studies on different autoimmune diseases have shown that they are multifactorial results from interactions between genetic (Corradin et al. 2013; Okada et al. 2013), epigenetic (De Santis and Selmi 2012), environmental (Tobón et al. 2010), economic, and other factors, factors potentially affecting longevity and other immune system disorders (See ▶ "Immune Aging, Autoimmunity, and Autoinflammation"). Mutations in human sirtuins, best known for their role in aging, were also found causing a familial form of autoimmune diabetes (Hughes and Herold 2013). Studies have suggested that the role of gender in autoimmune diseases (Wilhelmson et al. 2018; Zhen and Christopher 2012) and in the regulation of longevity may be linked to gender-specific differences and the factors that affect the development of autoimmune diseases and the regulation of longevity may share common mechanistic pathways.

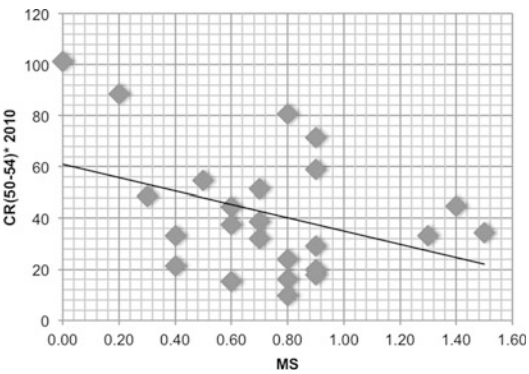
Patients with some autoimmune diseases could be used as a model of accelerated immunosenescence (Thewissen et al. 2005; Bulati et al. 2011).

Centenarians, from the other side, are used as a model of successful aging (See ▶ "Centenarians"), having better preserved several immune parameters (Bulati et al. 2011; Caruso et al. 2012). Centenarians are known to show very low levels of organ-specific autoantibodies (Condo 2019; Lisa et al. 2009; Mariotti et al. 1992). Centenarians have a higher inflammatory response than any other group of old individuals, but the counter-regulatory anti-inflammatory response is also stronger than in the others (Arai et al. 2015). Even with heavily dysregulated immune response, a person may live until 100 years if the network of regulation is compensating for the changes. Centenarians are the living example of the role of the well- balanced immune system in the aging process (Fulop et al. 2019).

Preserving the integrity of the immune system over the lifespan is central for the survival of the organism (See ▶ "Human Immune System in Aging"). Despite the large numbers of mostly cross-sectional studies comparing various parameters between young and old immunity, biomarkers of immunosenescence that have been shown to really correlate with clinical outcomes are rare in the extreme (Pawelec 2018). Use of centenarian rate instead of number of centenarians enabled the control of migration and infant mortality on the population numbers (Kim 2013). Centenarian rate (CR) can be calculated by dividing the number of centenarians in a given year by the number of people aged 50–54 living 50 years before that year, multiplied by 10,000 (Kim 2013; Lens-Pechakova 2016), which can be used as parameter of longevity.

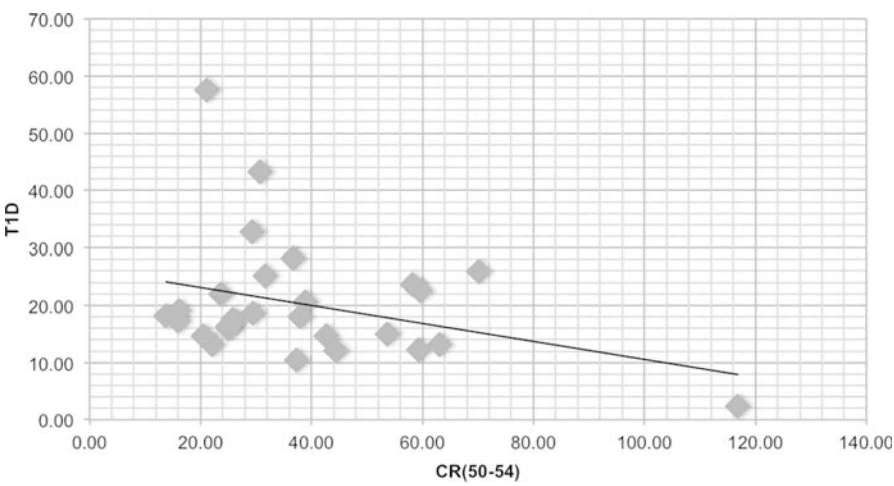
Multidisciplinary analyses of data on the accelerated or delayed aging could show a distinct relation pattern, help to identify common factors, and determine new important ones that contribute to longevity and healthy aging. One recent study examined the relationships between the levels of mortality rates of multiple sclerosis, rheumatoid arthritis, asthma, and the incidence of type 1 diabetes from one side and the longevity measured by centenarian rate and life expectancy from the other side (Lens-Pechakova 2016). The results show a clear tendency of diminishing the centenarian rate (CR) and the life expectancy in countries where the incidence of type 1 diabetes (T1D) in children of age 0–14 years and the death rates of multiple sclerosis (MS), rheumatoid arthritis (RA), and asthma are higher. The associations with the two sets correlated centenarian rates correspond to an inverse correlation with different degrees of linearity. The Pearson correlation coefficients r and r∗ corresponding to the two sets centenarian rates CR and CR∗ are as follows: for (r∗) MS ($r = -0.37$ and $r* = -0.38$), for T1D ($r = -0.33$ and $r* = -0.16$), for asthma (r = −0.34 and r∗ = −0.30), and for RA (r = −0.24). The fewer incidence of T1D and the lower the mortality rates of MS, asthma, and RA, the higher the centenarian rate, representing the numbers of the living centenarians in the country (Figs. 1 and 2).

An inverse linear correlation between the life expectancy and the death rates was also observed with a strong linearity and Pearson coefficients r° between life expectancy and Asthma r° = −0.63, and RA r° = −0.33, and MS with a lower degree of linearity (r° = −0.15) and a practically inexistent linear relation with the incidence of T1D (Lens-Pechakova 2016). The observed negative correlations indicate that the higher the death rates of asthma, RA, and MS in a country, the lower the country's life expectancy (Figs. 3 and 4). The differences in the longevity parameters in neighboring countries (Table 1), which supposedly have similar genetic profiles and environment, as well as the lower degree of linear relation observed in some cases, could point to the importance of other factors (lifestyle, social, economic, etc.) and to complex interactions of several factors, influencing the processes of the autoimmune diseases and longevity in different degrees and in the opposite direction.

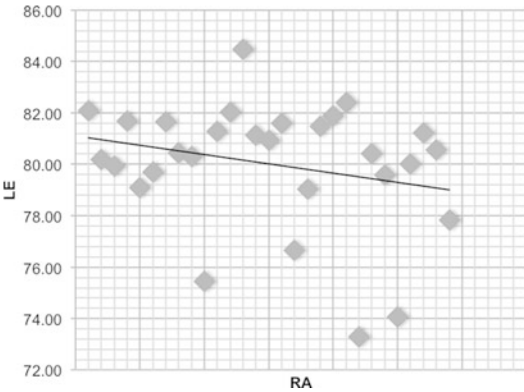


Centenarian Rate, Life Expectancy, and Autoimmune Diseases, Fig. 1 The scatterplots of the death rates of multiple sclerosis MS for the centenarians rate CR. (X = Estimated death rates of multiple sclerosis per 100,000 population, Y = Centenarian rate CR∗)

The observed negative correlation between the longevity parameters from one side and the autoimmune diseases from the other side (Lens-Pechakova 2016) could suggest common mechanisms and factors affecting the development of the autoimmune diseases that are previously rarely studied in a group. The same mechanisms and factors most probably play a role in the processes of aging, longevity, and preserving the centenarians' optimal immunity. The expanding of the autoimmune diseases cannot possibly be, opposite to what often has been



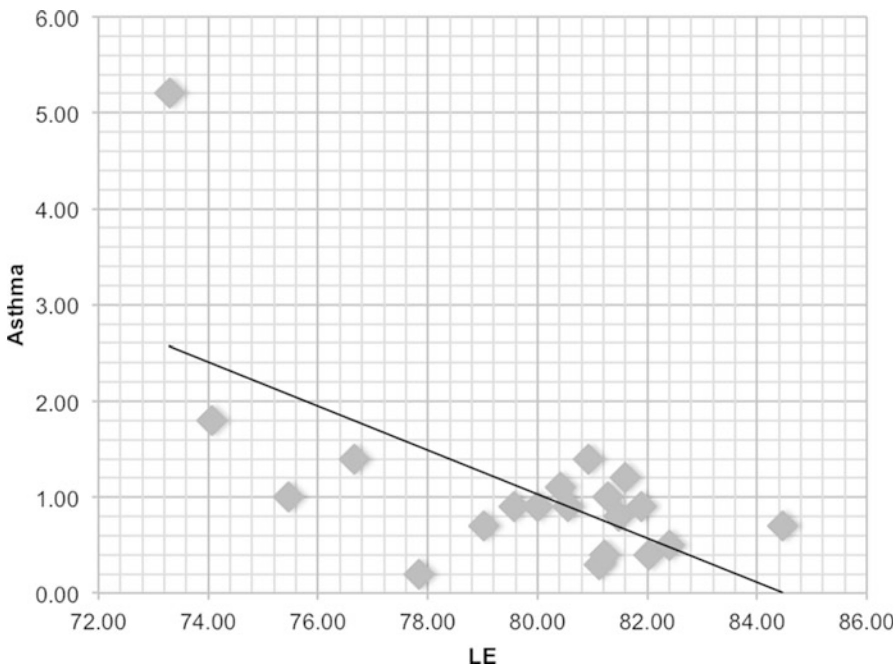
Centenarian Rate, Life Expectancy, and Autoimmune Diseases, Fig. 2 The scatterplots of the incidence of Type 1 diabetes T1D for the centenarian rate. (X = Centenarian rates CR, Y = Incidence Type 1 diabetes mellitus (0–14 years old) per 100,000 population) suggested, a necessary consequence of the growing numbers of the aging population as it clearly diminishes the lifespan, i.e., it has a negative influence on the longevity, on the numbers of the centenarians, as well as on the numbers of the aging population.



Centenarian Rate, Life Expectancy, and Autoimmune Diseases, Fig. 3 The scatterplots of the death rates of rheumatoid arthritis for the life expectancy. (X = Estimated death rates of rheumatoid arthritis per 100,000 population, Y = Life expectancy)

Summary

Due to underlying mechanisms of an immune response against own cells and tissues, autoimmunity is partially responsible and a predisposing factor for the development of other diseases, like cardiovascular diseases, cancer, and respiratory diseases, which are the three leading causes for noncommunicable diseases' deaths. Some recent studies showed that countries with higher incidence and mortality of some autoimmune diseases showed lower life expectancy and lower number of centenarians. Possible common mechanisms, genetics, and other factors affecting the development of the autoimmune diseases play a role but in the opposite direction in the processes of aging, longevity, and preserving the centenarians' optimal immunity. Further integrated multidisciplinary studies incorporating



Centenarian Rate, Life Expectancy, and Autoimmune Diseases, Fig. 4 The scatterplots of the death rates of asthma for the life expectancy. (X = Life expectancy, Y = Estimated death rates of asthma per 100,000 population)

Centenarian Rate, Life Expectancy, and Autoimmune Diseases, Table 1 Data on centenarian rates, life expectancy and death rates of MS, RA, asthma and incidence of T1D

Country	Centenarian rates CR*2010 (Lens-Pechakova 2016)	Living centenarians in 2010, thousands	Aged 50–54 in 1960, thousands	Centenarian rates CR2011 (Kim 2013)	Life expectancy LE	Type 1 diabetes incidence T1D	Multiple sclerosis death rates MS	Rheumatoid arthritis death rates RA	Asthma death rates
Australia	**54.74**	**3**	548	**59.56**	**82.07**	**22.50**	**0.50**	**0.40**	**1.20**
Austria	**19.76**	**1**	506	**25.89**	**80.17**	**17.50**	**0.90**	**0.20**	**0.90**
Belgium	**16.1**	**1**	621	**24.98**	**79.92**	**15.90**	**0.80**	**0.40**	**1.60**
Canada	**71.51**	**6**	839	**70.04**	**81.67**	**25.90**	**0.90**	**0.50**	**0.50**
Denmark	**34.25**	**1**	292	**31.61**	**79.09**	**25.10**	**1.50**	**0.80**	**1.80**
Finland	**37.45**	**1**	267	**21.06**	**79.69**	**57.60**	**0.60**	**1.00**	**0.80**
France	**51.28**	**15**	2925	**59.26**	**81.66**	**12.20**	**0.70**	**0.30**	**0.80**
Germany	**23.79**	**13**	5464	**23.64**	**80.44**	**21.90**	**0.80**	**0.20**	**1.00**
Greece	**44.34**	**2**	451	**37.25**	**80.30**	**10.40**	**0.60**	**0.30**	/
Hungary	**15.31**	**1**	653	**13.81**	**75.46**	**18.20**	**0.60**	**0.40**	**1.00**
Israel	**88.49**	**1**	113	**53.56**	**81.28**	**14.90**	**0.20**	**0.30**	**1.00**
Italy	**33.23**	**12**	3611	**44.43**	**82.03**	**12.10**	**0.40**	**0.30**	**0.40**
Japan	**101.2**	**42**	4150	**116.78**	**84.46**	**2.40**	**0.00**	**0.50**	**0.70**
Netherlands	**32.10**	**2**	623	**29.43**	**81.12**	**18.60**	**0.70**	**0.30**	**0.30**
New Zealand	**80.65**	**1**	124	**37.89**	**80.93**	**18.00**	**0.80**	**0.50**	**1.40**
Norway	**44.64**	**1**	224	**29.29**	**81.60**	**32.80**	**1.40**	**0.60**	**1.20**
Poland	**17.9**	**3**	1676	**15.99**	**76.65**	**17.30**	**0.90**	**0.60**	**1.40**
Portugal	**21.23**	**1**	471	**22.07**	**79.01**	**13.20**	**0.40**	**0.50**	**0.70**
Spain	**48.57**	**8**	1647	**38.80**	**81.47**	**20.60**	**0.30**	**0.20**	**0.80**
Sweden	**38.61**	**2**	518	**30.73**	**81.89**	**43.20**	**0.70**	**0.60**	**0.90**
Switzerland	**29.07**	**1**	344	**63.12**	**82.39**	**13.10**	**0.90**	**0.30**	**0.50**
Turkey	**9.84**	**1**	1016	**1.59**	**73.29**	/	**0.80**	/	**5.20**
UK	**33.21**	**12**	3613	**36.61**	**80.42**	**28.20**	**1.30**	**0.70**	**1.10**
USA	**59.03**	**61**	10,334	**58.15**	**79.56**	**23.70**	**0.90**	**0.50**	**0.90**
Estonia		**0**		**26.01**	**74.07**	**17.10**	**0.50**	**0.70**	**1.80**
Luxembourg		**0**		**16.16**	**80.01**	**19.00**	**0.90**	/	**0.90**
Iceland		**0**		**42.69**	**81.22**	**14.70**	**0.90**	**0.30**	**0.40**
Ireland		**0**		**24.95**	**80.56**	**16.30**	**0.70**	**0.90**	**0.90**
Slovenia		**0**		**20.46**	**77.83**	**14.60**	**0.90**	**0.80**	**0.20**

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and comparing genetic data, mechanistic pathways, and environmental, economic, and other factors connected to autoimmune diseases with those of longevity could clarify the processes involved, in order to promote the healthy longevity and healthy aging.

Cross-References

- ► Centenarians
- ► Human Immune System in Aging
- ► Immune Aging, Autoimmunity, and Autoinflammation

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Centenarian's Diet

► Healthy Diet

Centenarians

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Synonyms

Long-lived individuals

Definition

Centenarians are individuals who are aged 100 years or older. Researchers tend to use the term "centenarian" to generally indicate long-lived humans, and its definition slightly differs across studies. Some studies have employed the term "near centenarian" (i.e., at least 95 years old) (Brodaty et al. 2016), some targeted people older than 100 years, and some studies focused on individuals who had just reached 100 years old and identified them as "centenarians" (Herr et al. 2018). Current research on centenarians set in developed and aging societies, such as Japan, the United States, and some European countries, is shifting focus to age ranges of 100 or older (centenarian), 105 or older (semi--supercentenarian), and 110 or older (supercentenarian).

Overview

Research on centenarians is conducted worldwide in response to their rapidly increasing numbers. The World Population Prospects 2019 Data Booklet published by the United Nations (2019) reported that the global number of centenarians in 1990 was 92,000, which increased to 294,000 in 2010 and 417,000 in 2015. In other words, the global population was 3.2 times larger in 2010 than in 1990 and it increased 4.5 times in 25 years. The number of centenarians is estimated to increase to 1,173,000 by 2030, to 3,195,000 by 2050, and to 19,093,000 by 2100.

The United States had the largest centenarian population in the world in 2015, which was estimated at about 65,000. Japan was a close second, with an estimated 57,000 centenarians; however, Japan had the most centenarians per 10,000 persons (about 4.5). France had about 3.3 centenarians per 10,000 individuals (United Nations 2019).

Because female life expectancy at birth is longer than that of males, the estimated and projected numbers of female centenarians are higher than those of males. Among the centenarians in 2015, the sex ratio was 3.7 females to 1 male. However, the projected centenarian sex ratio at the global level is expected to decrease to 1.9 females per male during the twenty-first century based on the theory that the female lifespan might reach its biological limit and males catch up to them because of health advancements (Robine and Cubaynes 2017).

In Japan, the Ministry of Health, Labour and Welfare (1963–2009) has reported the actual number of centenarians every September since 1963 when there were 153 of them. By 1984, the number had increased tenfold, and the 2001 number was 100 times the 1963 count. Japan's most recent count of centenarians was 69,785 in 2018, and the female-to-male sex ratio was about

9:1 (Ministry of Health, Labour, and Welfare 2018). Between 1963 and 2017, life expectancies at birth increased from 67.2 years to 81.1 years for males and from 72.3 years to 87.3 years for females.

Key Research Findings

Limits to the Human Lifespan

A main reason for studying centenarians is to learn their secrets of longevity and apply that knowledge to increasing healthy longevity at the individual and societal levels. Clarifying lifespan limits is one of researchers' fundamental tasks because the life and health trajectories before and after age 100 are believed to vary greatly depending on whether there is a biological limit. For example, if we determined that the human lifespan is about 120 years, we might be able to set clear goals for maintaining functional independent living with dignity until the end of life. If it became clear that there is no lifespan limit, the gap between the chronological lifespan (the length of life) and the healthy lifespan (the length of life without morbidity or disability) never could be zero.

Two opposing views prevail regarding a limit to the human lifespan, one supporting the biblical assertion of a limit of about 120 years (Dong et al. 2016; Gavrilov and Gavrilova 2019) and the other arguing that a limit has not been confirmed (Medford and Vaupel 2019; Oeppen and Vaupel 2002). A wide variety of data sources have been used to estimate the human lifespan, but, to resolve the debate, accurate data on the world's oldest individuals are essential because an error regarding age at death of just one case might significantly influence mortality estimates for ages beyond 100.

Humans do not have biological age signatures, such as tree rings. We are limited to the detailed age identification method to document people's lives, construct their ancestries, and examine the extent of consistency between their ages and the ages of their biological relatives, although we also use the testimonies of the people involved in their lives (Poulain 2010). Questions were raised about the actual age of the world's longest-lived human (a Frenchwoman named Mrs. Calment), who died at 122 years and 164 days old (Zak 2019). A large amount of documentation and statistical estimation allowed scholars to answer the question (Robine et al. 2019). Answering questions like this one is important to accumulating precise scientific evidence on the limits of the human lifespan. Incidentally, to the best of our knowledge, the oldest male in the world was a Japanese, Mr. Jiroemon Kimura, who died at age 116 years and 54 days (Gondo et al. 2017).

Biomedical Characteristics of Centenarians

Most studies on centenarians examine biomedical factors, and there have been interesting findings. One common characteristic of centenarians is their lower prevalence of diabetes. For example, in Japan, the prevalence of type 2 diabetes progressively increased from 2.6% in the individuals in their 30s to 6.3%, 11.6%, and 15.3%, and in the 70s, it was about 14.7%. However, its prevalence was 8.2% for those aged 100 or older, 6.3% for those aged 105 or older, and 3.5% among those aged 110 or older, suggesting that type 2 diabetes is important to longevity in Japan (Arai et al. 2014).

Regarding overall health, the New England Centenarian Study, which included 424 centenarians (aged 97–119 years) or their proxies, classified centenarians by their morbidity history. In this classification, the males (24% of the male subjects) and females (43% of the female subjects) with at least one age-related disease before age 80 were identified as "survivors." The males and females (44% of the male and 42% of the female subjects) with later onset of those diseases (at age 80 years or older) were named "delayers." Last, the males and females (32% of the male subjects and 15% of the female subjects) with none of these diseases until at least 100 years old were named "escapers" (Evert et al. 2003). These results imply that it is not unusual for those who live long lives to be free of disease near the end of life. Moreover, the ages of onset of age-related diseases were older among centenarians than younger people. The New England Centenarian Study reported that later onset of major diseases and shorter disease-free periods were more prevalent among the semi-supercentenarian than supercentenarians in their study (Andersen et al. 2012). Thus, centenarians' disease experiences tend to be compressed toward the end of life, and they seem to experience age-related problems less than younger people.

Identifying a longevity gene has been a major focus of biomedical research on centenarians. However, success has been elusive, and, to date, no single gene with a strong influence on longevity has been identified. The early studies identified several candidate genes, but there is no consensus about them, and few genes have been commonly identified across the studies. In other words, studies that observed unique genotypes in centenarians compared to a younger control group were rarely replicated. The Apolipoprotein E (APOE) (Schächter et al. 1994), a known risk factor of Alzheimer's disease, and Forkhead box 03 (FOXO3) (Willcox et al. 2008; Zeng et al. 2010), which relates to many metabolic pathways, are two genes frequently observed to have different genotype distributions in centenarians compared to younger people. Recently, researchers have used new approaches, such as genome-wide association studies and focused analysis of supercentenarian samples, to identify genes related to longevity. However, these efforts have not yet met the overall objectives.

Centenarians' Functional Status

Studies have consistently reported relatively low functional status among centenarians (Andersen-Ranberg et al. 2001; Gondo et al. 2006; Zeng and Vaupel 2002). Zeng and Vaupel (2002) reported lower functional capacity of the centenarians than the persons aged 80–89 and 90–99 years old in China. Approximately 54.3% for males and 66.2% for females of the centenarians were in mild disability or severe disability statuses. Gondo et al. (2006) developed a three-dimensional standard to comprehensively evaluate centenarians' overall functional status: sensory functions (vision and hearing), cognitive functions, and physical functions. Using this standard, the researchers classified centenarians into functional groups and found that just 2% of the centenarians were classified as exceptionally functional (no problems in any functional dimension) and an additional 18% were classified as healthy (declines in sensory functions but not in cognitive or bodily functions). More than one-half (55%) of their subjects were classified as frail based on declines in either cognitive or bodily functions, and one-quarter (25%) were identified as fragile because they had declines in cognitive and bodily functions. In addition, a large gender difference was found regarding the healthy and exceptional subjects (39% of the males and 14% of the females). Many centenarian studies have found similar gender differences in functional status, but this finding points to be ironic because the sex ratio of centenarians overwhelmingly favors females. As reported above, it was 9:1 in 2018 in Japan.

High levels of dependency are common among centenarians in developed countries. The Five Country Oldest Old Project was designed to compare centenarians across Denmark, Sweden, Switzerland, France, and Japan. Among other things, it found that, overall, about 72% of the centenarians were classified as frail, but there was significant variation among the countries, with the lowest prevalence in Denmark (52%) and the highest prevalence in Sweden (78%) (Herr et al. 2018).

Cohort differences in functionality across countries provide helpful information. A Danish centenarian study compared the levels of ability regarding activities of daily living among centenarians exactly 100 years old in 1995 and 2015 and found that the disability rates were smaller for the more recent cohorts (Rasmussen et al. 2018). The same trend was observed in a centenarian study conducted in Georgia in the United States (Cho et al. 2012). However, because of the healthcare and social welfare systems and the strong cultural emphases on caring for older people (e.g., filial piety) in some societies, cultural backgrounds and the quality, quantity, and availability of healthcare might explain these country-level differences.

Dementia

Another important research concern is whether dementia is inevitable. Although dementia rates differ across studies, a marked increase in dementia prevalence at the oldest ages is commonly observed. Dementia prevalence is estimated at about 1.5% for people in their 60s, it increases with age, and estimates for the oldest old people are as high as 25–48% (Evans et al. 1989). A recent multicenter study in Japan reported a 77% dementia prevalence at ages 95 to 99 (Ikejima et al. 2012). Because centenarians likely represent the final stage of the human development and aging, studying centenarians is likely to provide important evidence for answering the question, “Is dementia inevitable?”

If the marked increase in dementia prevalence were close to 100% in the centenarian population, then it would be reasonable to conclude that dementia is inevitable. This conclusion implies that individual differences in the pathogenesis of dementia might contribute to the observed individual differences in the brain as it ages. Therefore, we would assume that dementia is part of the so-called “normal” aging process, even though dementia’s causes are not just age-related and unitary, particularly among the oldest old people (Pierce and Kawas 2017). On the other hand, if large numbers of centenarians were free of dementia, rejecting the assumption that dementia is natural seems more likely and the conclusion that dementia is a pathological age-related disease would be more logical (Pierce and Kawas 2017).

Some studies have found the prevalence and incidence of Alzheimer’s disease were relatively low in nonagenarians (persons aged 90 to 99 years) (Kawas and Corrada 2006; Ritchie and Kildea 1995). For example, a Cache County study found a higher incidence of Alzheimer’s disease up to age 90, followed by lower incidences during the early 90s among males and until the late 90s among females (Miech et al. 2002). Individuals who have survived without dementia until their late 90s might have a particular protective factor. Considering the average lifespan of 8 years after the onset of dementia and the lower incidence of dementia among nonagenarians, it seems reasonable that many people who live to 100 years might not experience dementia. However, studies have reported a wide range in dementia prevalence among centenarians (from 33% to 100%) and an average prevalence of 62% (males, 48.5%; females, 66.1%) (Ishioka and Gondo 2016). One reason for this wide range might be methodological differences across centenarian studies. Recently, researchers involved in the International Centenarian Consortium conducted an integrated study to estimate dementia prevalence in near centenarians and centenarians (Brodaty et al. 2016). Their final report is expected to be available in the near future.

In this context, dementia prevalence in a group of centenarians who participated in the Tokyo Centenarians Study and the National Centenarians Study (on people older than 105 years) was estimated. Dementia prevalence among the males was 46% and 55% among those aged 100 to 104 years and those aged 105 to 108 years, respectively. Among the females, prevalence was 74% and 92% for the same age ranges, respectively (Gondo et al. 2013a). The results suggest that males are less likely than females to experience dementia late in life and that dementia might be part of females’, but not males’, biological aging process. However, these results were inconsistent with some case studies on women supercentenarians without dementia (den Dunnen et al. 2008). The longest-lived woman, Mrs. Calment, underwent extensive cognitive testing at age 118, and dementia was not found (Ritchie 1995). Finally, in-person interviews revealed that many people older than 110 years expressed no evidence of dementia (Robine and Jagger 2003). In sum, a dementia-free life might be possible, even for people as old as 110 years, and the likelihood of dementia seems to be higher among females than males.

Psychosocial Characteristics

Personality relates to health outcomes and longevity (Roberts et al. 2007), but, as the term “wise old man” suggests, it is possible that people’s personalities continually develop throughout their lives. Do centenarians have particular personality characteristics that help them to live long lives or have they developed mature personalities through their long years of learning and experience? Regarding the first part of this question, the Big Five Personality Traits (neuroticism, extraversion, openness, agreeableness, and conscientiousness) are commonly used in surveys. Although results on the individual dimensions are mixed, low levels of neuroticism with high levels of extraversion, openness, and conscientiousness often are associated with relatively good health or longevity in samples of young and older people, including centenarians.

There are some problems with these studies, however. To date, few of them directly examined the question because of methodological challenges. For example, even if a score on one personality trait differed between centenarians and younger people, distinguishing cause (personality leading to longevity) from effect (longevity influencing personality development) is difficult. The Tokyo Centenarian Study (TCS) has a unique approach for minimizing this problem. The researchers compared centenarians' test scores to an estimated average test score for people aged 100 years old that they calculated using a younger control sample (Masui et al. 2006). Because average personality test scores correlate with age, they were able to predict future scores. They found that males and females scored high on openness and females scored high on extroversion and conscientious.

The Australian Centenarian Study asked centenarians about their current and past personalities and found high neuroticism, extraversion, and conscientious and low openness as past personality traits (Law et al. 2014). This profile result slightly differed from the TCS and some other centenarian studies that found low neuroticism (or anxiety). The TCS and the Australian Centenarian Study found high conscientiousness scores strongly predicted health outcomes (Law et al. 2014; Masui et al. 2006). Other studies have directly compared centenarians' personality test scores to population means or to control data and found relatively low neuroticism among centenarians. However, the results have been mixed, which might reflect that some of the explanation for longevity relates to personality. All these results were consistent with previous studies about the relationship between personality and mortality.

Regarding the aging-related development of personality, Shimonaka et al. (1996) reported that Japanese centenarian males scored relatively high on femininity in the Bem Sex-Role Inventory. Because femininity in men is low at younger ages, high femininity is speculated to be caused by age-related changes rather than factor for survival. The TCS found relatively high openness (Masui et al. 2006). Because centenarians experience obvious loss of their bodily functionality over time, their personalities might develop in response to these experiences to help them to accept their aging minds and bodies (Jopp et al. 2016a). High femininity and openness scores might be helpful for reducing stress, receiving social support, and a general attitude of acceptance. Aging-related change in some personality dimensions would say reasonable.

On the other hand, cultural differences, such as the emphasis on individualism in the United States, might mean that adaptive changes to personality might differ in different cultures. The Georgia Centenarian Study in the United States found high levels of suspiciousness in centenarians (Martin et al. 2002). Developing suspiciousness might be an adaptation among the oldest old people who live in a culture that rewards personal independence. However, it is too soon to conclude that personality characteristic of centenarians. Further research, such as pooled analyses of longitudinal centenarian data, might provide evidence to support both personality hypotheses.

Centenarians' Well-Being

Jopp et al. (2016) argued that centenarians face crucial limits of psychological resilience or self-regulatory adaptation, and it might seem surprising that previous studies have reported that centenarians have fairly well-maintained emotional well-being regardless of these limits (Dello et al. 1998; Gondo et al. 2013b ; Hutnik et al. 2012; Jopp et al. 2016b; Jopp and Rott 2006; Margrett et al. 2010; Wong et al. 2014; Zeng and Shen 2010). An Italian study surveyed 38 centenarians and found relatively low levels of anxiety and depression despite their relatively low functional levels (Dello et al. 1998). A very large Chinese survey of 8,000 people, named the Chinese Longitudinal Healthy Longevity Study (CLHLS), found that, among the respondents aged 80 to 100 years, the psychological resources that support positive emotions were present regardless of functional level (Smith et al. 2008). Moreover, using data from the CLHLS, Gu and Feng (2018) indicated the positive relations between resilience and subsequent survival and health in centenarians and higher resilience could maintain their self-rated health and life satisfaction. The TCS evaluated the subjective well-being of 62 subjects without dementia using the revised PGC Morale Scale, and the centenarians' scores were higher than expected for their age (Gondo et al. 2013b). The results of these studies suggest that an "aging paradox" regarding well-being (Mroczek and Kolarz 1998) is observable in centenarians and that a psychological or social adaptive system in the background might explain this phenomenon (Gondo et al. 2013b).

Implications and Application

The results of centenarian studies are useful for understanding the future of humanity and to help us find ways to live in aging societies. Demographic research paints an unexpected picture for the life course that includes a long life. Without precise data, it is impossible to plan one's life course, particularly regarding finances, when long life is anticipated. Although humans are increasingly likely to live to 100 years or older, functionality tends toward frailty and dementia, which implies a late-life period of decline in physiological functional capacity for the longest-lived people. Although solutions to this situation are not easy to find, strong evidence helps us to plan and be prepared at the personal, social, and societal levels.

Research findings about centenarians' psychosocial characteristics are highly applicable for developing health promotion programs and frameworks for happy aging. Daily behaviors assumed to derive from high conscientiousness might increase individuals' extraversion and openness, and those personality traits might be effective targets for behavior modifications.

Recent biological studies have suggested that reaching centenarian age is no longer a privilege of biologically superior elite humans. Progress in precise diagnostics and treatment methods combined with medication might have influenced that change. Recent research indicates that positive images of aging triggered good health outcomes. If we use successful centenarians as models to introduce people to their ways of achieving healthy and happy long lives, it will encourage people to engage in healthy behaviors. Although centenarians face problems, such as high likelihoods of dementia and frailty, they tend to maintain a strong sense of psychological well-being regardless of their health conditions. Focusing our attention on the positive factors and educating the public would be a population-level approach to health promotion.

Future Directions of Research

Most existing centenarian studies have reported various important characteristics of centenarians and potential factors for longevity. However, these findings should be interpreted carefully and understood as having some limitations because centenarian studies have methodological problems (Sachdev et al. 2012). The first problem is the lack of control groups for comparison. A perfect control group would comprise people of the same birth cohort as the study subjects, but who would not survive to be 100 years old. Although some studies used younger old people as control groups, there is no reason to assume that some of them would not become centenarians, in which case they no longer would qualify as "control" cases.

To overcome this problem, some studies such as the Danish 1905 Cohort Survey (Engberg et al. 2008) followed 93 people born in 1905 for 7 years and compared survivors to non-survivors regarding factors relevant to survival. A similar method was used in a supercentenarian study

(Arai et al. 2014) to reveal important characteristics. The SONIC study (Gondo et al. 2016) also followed a panel to identify factors relevant to becoming a centenarian. Thus, large-scale longitudinal studies are recommended for research focused on explaining longevity.

Another way to address methodological problems is to compare siblings or offspring of centenarians and their same cohort counterparts. Several studies have reported survival advantages among them (e.g., Perls et al. 2002; Willcox et al. 2006), and biologically related individuals are believed to share the familial component of longevity comprised of genetic and environmental factors. The New England Centenarian Study used this method and found that centenarians' offspring were healthier and had healthier personality traits, such as low neuroticism and high extraversion (Givens et al. 2009).

An important methodological problem concerns measurement. There are no standard measures for centenarians' physical, cognitive, or emotional states. Consensus has not been reached among researchers on which tests to use or which circumstances are appropriate to specific tests. One study found that older people perform better in the morning than in the afternoon (May et al. 1993), so centenarians' test results might reflect a bias created by a timing effect. In addition, inconsistencies from 1 day to the next should be considered because of frailty problems. Last, standardized procedures to correct data are needed. Considering their functional limitations, evaluation methods that use long-term observations might be helpful, such as using questionnaires for cognitive evaluation by proxy rating (Gondo et al. 2013a).

When centenarians in multiple countries or cultures are studied, differences in their characteristics must be carefully addressed. It can be challenging to conduct centenarian studies maintaining constant conditions across countries with different contexts because of variation in registration systems, criteria for accessing residential information, and differences in ethical standards. For example, some countries prohibit interviews with dementia patients. Thus, although the number of oldest old people and centenarians is increasing on a global scale, our knowledge about these people is not keeping pace with our need to know. Further research collaboration across countries with standardized methodology is strongly advised.

Summary

Research on centenarians has been conducted over the past four decades, starting with the first national survey of Japanese centenarians in 1972. Centenarian studies have revealed many important things about the conditions of long-lived humans and the factors that might contribute to their long lives. Regarding biology, centenarians might age relatively slowly and be able to avoid age-related diseases compared to people who die at younger ages. Some exceptional individuals have lived longer than 110 years with intact cognitive functions. However, dementia and frailty are common among centenarians. Although they might not experience these conditions, most centenarians have aging-related declines in physical and cognitive functions similar to younger old people.

Centenarians' personalities might reflect two characteristics that contribute to longevity and wisdom. Further studies with longitudinal designs are needed to distinguish between them. It is important that centenarians have a relatively strong sense of psychological well-being regardless of their functional limitations, which gives us hope for the future of societies with aging populations.

Recent centenarian studies are focusing on social factors, and more studies are needed to understand centenarians' social situations. Many centenarian studies have been multidisciplinary because a wide range of scientific disciplines are involved in longevity and centenarians' current conditions. Considering the contextual influences of the aging process, more integrated research, including cultural considerations, is needed for a sophisticated understanding of centenarians.

Cross-References

- ▶ Chinese Longitudinal Healthy Longevity Survey (CLHLS)
- ▶ Cohort Study of Centenarians in Hainan, China (CHCCS)
- ▶ Danish Centenarians Studies
- ▶ Genomics of Aging and Longevity
- ▶ Iowa Centenarian Study
- ▶ Italian Centenarians and Semi-supercentenarians Surveys
- ▶ Maximum Lifespan
- ▶ Supercentenarians
- ▶ The Georgia Centenarian Study
- ▶ The Tokyo Centenarian Study
- ▶ (World) Supercentenarian Database

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Central Nervous System

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Definition

The central nervous system (CNS) is comprised of two major structures: the brain and spinal cord. Together, these structures integrate information from the peripheral nervous system and sensory organs and send output signals to the skeletal muscles (for the purpose of voluntary and involuntary movement) (see also ► "Neuromuscular System") and to the autonomic nervous system (see also ► "Autonomic Nervous System"), which regulates the body's internal organs (Waxman 2017). Thus, as the "command center" of the entire body, the effects of aging on the CNS are therefore ubiquitous and have significant implications for essentially all bodily functions (and, therefore, daily functioning).

Overview

Within the CNS, the spinal cord and brain have specialized subfunctions. The spinal cord carries information from the peripheral nervous system to the brain, and it also sends motor information from the brain to the somatic and autonomic motor systems. The brain, in turn, controls essentially all bodily functions (speech (see ► "Speech Capability"), cognition, bodily movements, organ function) (Banich and Compton 2018).

The spinal cord and the brain are partly made up of nerve cells called neurons. A neuron functions to communicate. The axon of one neuron's cell body and another neuron's dendrite, or neuron branch that extends from the cell body to receive incoming synaptic information, communicate at the synaptic cleft, or gap between neurons. In the brain, the myelin-coated axons are on the inside, while the axon-dendrite network is on the outside. In contrast, in the spinal cord, this arrangement is reversed (Jacobson et al. 2011).

Spinal and brain regions are said to be broadly comprised of white and gray matter. White matter primarily describes myelinated regions. Myelin (the insulating covering around nerve fibers) is white because it is made of proteins and phospholipids that make it white. White matter in the spinal cord surrounds the gray matter and carries info up the spinal cord to the brain, via sensory tracts, and from the brain down the spinal cord, via motor tracts. Gray matter refers to the neuron cell bodies and glial cells (they play many important roles, and without them, neuronal communication would be less effective). Gray matter in the spinal cord is where many neurons synapse (i.e., where a neuron passes an electrical or chemical signal to another neuron) (Patestas and Gartner 2016).

The other major group of cells in the CNS are the neuroglia, also known as glia. There are several types of neuroglial cells. Oligodendrocytes produce the myelin covering of nerve fibers in the CNS, and astrocytes provide support for the CNS by providing an ionic homeostatic environment for neuronal signaling, developing synapses, storing glycogen, and maintaining the blood-brain barrier (Bear et al. 2015).

Key Research Findings

Broadly defined, the effects of aging on the central nervous system, from peripheral neurons through the brain, can be linked to at least three major, ubiquitous changes with age: (1) aging astrocytes fueling pro-inflammatory aging processes (Matias et al. 2019) (see ► "Neuroinflammation"), (2) slower reflexes and fewer motor neurons in spinal neural circuitries (Deschenes 2011; Hunter et al. 2016), and (3) neuronal loss (Rutten et al. 2007).

Aging astrocytes fueling pro-inflammatory aging processes. Due to the multifaceted roles of astrocytes, mentioned earlier, it should not surprise that astrocytes are an important aspect of the aging CNS. While the effects of astrocytes on aging are numerous and quite complex, in short, most changes in aged astrocytes may fuel pro-inflammatory aging processes, leading to a heightened inflammatory state that impacts the functioning of other CNS cells, with aging (Palmer and Ousman 2018). Drawing from animal models, for example, aging astrocytes, can inhibit the synaptic function of neurons by increasing expression of *Sparc*, an astrocyte-secreted protein that inhibits the function of another protein that induces synapse formation (Boisvert et al. 2018; Kucukdereli et al. 2011). Understanding the many roles of astrocytes has the potential to contribute to the development of treatment strategies to reduce the loss of cells in the CNS and the functional and cognitive impairments associated with age-related diseases (Liddelow et al. 2017). Additionally, astrocytes are known to support the myelinating function of oligodendrocytes, but since oligodendrocytes rely on cholesterol synthesis from astrocytes to produce myelin, and aging astrocytes have impaired cholesterol synthesis, the oligodendrocytes may not receive the proper amount of cholesterol, which results in a reduction in myelin production in the aging brain. Overall, the interactions of aged astrocytes with other CNS cells can lead to dysfunction of multiple cell types and, more importantly, functional impairment in diseases associated with aging (Palmer and Ousman 2018).

Slower reflexes and fewer motor neurons in spinal neural circuitries. Spinal neural circuitries provide a simple translation of sensory information into movement, via stereotyped reflexes, yet these reflexes have been found to be slower in advancing age. Additionally, there is a reduction in the number of motor neurons (neurons that originate in the spinal cord and synapse on muscle fibers to enable muscle contraction) with aging. Prior studies have also found impaired modulation and reduced efficiency of spinal reflex pathways in the aging process. Future studies are required in order to fully understand the functional consequences of spinal reflex pathway changes that occur with age (Geertsen et al. 2017); however, gaining an understanding of spinal neural circuitries can better allow for interventions targeted at retaining motor skills with age.

Neuronal loss. Brain atrophy (see also ► "Brain Atrophy"), or the loss of brain volume, is one candidate for the neuroanatomical bases of cognitive aging, as measures of total brain volume have been shown to consistently positively correlate with cognitive ability throughout adulthood (Ritchie et al. 2015). To better understand how brain volumes are impacted by the aging process and to address pathological, age-related neural changes in neural disorders associated with aging, the effect of aging on brain volume was examined, and it was found that gray matter loss occurs linearly with advancing age, yet white matter first increases with rising ages, peaking in adulthood, and then declining thereafter. Additionally, cerebrospinal fluid increases exponentially with advancing age, which may be a result of gray matter and white matter converting into cerebrospinal fluid, a process known to occur in advanced adulthood (Beheshti et al. 2019). The loss of gray and white matter is important for the aging adult, as global gray matter loss and levels of white matter hyperintensity load (See also ► "White Matter Hyper-Intensities") (acquired lesions that disrupt neural connectivity and are the consequence of cerebral small vessel disease) have been shown to contribute to cognitive decline (Fletcher et al. 2018), which can lead to functional impairment in aging. It is important to note that these changes may not all be due to intrinsic aging processes, but to cumulative exposure with longer life to major risk factors. These include (a) genetics (e.g., ApoE4) (Reiter et al. 2017) (see also ► "Genetic Control of Aging"), (b) cerebrovascular factors and associated lifestyle risks (HBP, obesity) (Miller et al. 2012; Stanek et al. 2009, 2011) (see also ► "Hypertension", ► "Hypertensive Cardiovascular Diseases", and ► "Vascular Diseases of Ageing"), (c) cumulative injury (e.g., concussions, mild TBI) (Rushby et al. 2016), and (d) toxins and environmental exposure (Yu et al. 2016) (see also ► "Genetics: Gene Expression").

Future Directions

The advancement of methods and techniques used to study the brain and spinal cord, and how this relates to behavior and diseases of aging, will be crucial in furthering our understanding of pathologies of aging. Future research should seek to elucidate the processes by which the brain ages via imaging technology (see also ► "Neuroimaging"). With these advancements, future studies will also better understand the best path for developing suitable rehabilitation strategies (Anderson and Grady 2001). For example, higher levels of education, a healthy diet (see also ► "Healthy Diet"), and regular exercise (see also ► "Aerobic Exercise Training and Healthy Aging", and ► "Exercise and Healthy Cardiovascular Aging") are all protective factors that can lead to slowed biological aging and lower risk of age-related diseases, like dementia (Phillips 2017) (see also ► "Dementia", ► "Vascular dementia"). These modifiable, lifestyle factors can help mitigate age-related decline by protecting cognitive functioning and brain health.

While major advances have been made in our understanding of the fundamental biological processes that govern brain aging and its pathologies (see also ► "Neuroscience of Aging"), the relationship between brain changes across multiple levels (cellular, structural, and across networks) remains an area of emerging science. Tracking both structural and functional changes over time, in addition to examining age-related differences in structure and function, is another important next step.

Summary

The global impact of aging on the CNS has substantial consequences for cognitive and bodily functioning and, in turn, one's ability to function in daily life. Understanding age-related changes in the CNS is important when one considers our growing older adult population and the importance of cognitive and bodily functioning for preserving functional independence in old age. Additionally, it is important to understand what types of changes in cognition and bodily functioning should be expected as part of healthy aging and what changes could suggest brain disease. Emerging evidence suggests that healthy lifestyle choices may decrease the rate of age-related cognitive decline, which may help prolong the onset of cognitive and functional decline (see also ► "Prevention of Age-Related Cognitive Impairment, Alzheimer's Disease, and Dementia") associated with age-related diseases (Murman 2015).

Cross-References

- ► Aerobic Exercise Training and Healthy Aging
- ► Autonomic Nervous System
- ► Brain Atrophy
- ► Dementia
- ► Exercise and Healthy Cardiovascular Aging

- ▶ Genetic Control of Aging
- ▶ Genetics: Gene Expression
- ▶ Healthy Diet
- ▶ Hypertension
- ▶ Hypertensive Cardiovascular Diseases
- ▶ Neuroinflammation
- ▶ Neuroimaging
- ▶ Neuromuscular System
- ▶ Neuroscience of Aging
- ▶ Prevention of Age-Related Cognitive Impairment, Alzheimer's Disease, and Dementia
- ▶ Speech Capability
- ▶ Tumors: Brain
- ▶ Vascular Dementia
- ▶ Vascular Diseases of Ageing
- ▶ White Matter Hyper-Intensities

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Cerebral Hemorrhage

► Middle Cerebral Artery Strokes

Cerebral Infarction

► Middle Cerebral Artery Strokes
► Stroke

Cerebral Metabolism

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Synonyms

Brain metabolism; Energy metabolism

Definition

Cerebral metabolism encompasses a set of biochemical reactions that is linked to the consumption of energy resources that facilitate brain function and is associated with cerebral blood flow, cerebral oxygen consumption, and cerebral glucose utilization.

Overview

The human brain is one of the most metabolically active parts of the body. It comprises only 2% body mass yet accounts for over 20% of total energy consumption at rest (Attwell et al. 2010). Approximately 55% of overall energy expenditure by the brain is related to neuronal activity and 45% facilitates basal metabolic processes such as molecule synthesis and maintaining intracellular ion balance related to neuronal excitation and conduction. With high metabolic needs and low capacity for glycogen storage in the brain, stable supply of energy metabolites is absolutely critical to sustain normal cerebral functions. During the normal aging process, an estimated 28–50% reduction in cerebral blood flow between the ages 30–70 significantly reduces delivery of glucose, oxygen, and other energy metabolites (Ainslie and Bailey 2013). However, there is evidence for variability in cerebral metabolism in older adults depending on health-related factors and outcomes (Bastin et al. 2012; Tarumi et al. 2014). The following serves as an overview of structural and functional mechanisms that regulate cerebral metabolism, age-associated changes that increase the risk for neurovascular disease, and potential interventions to promote optimal brain health.

Key Research Findings

Oxygen in the brain is primarily dedicated toward the oxidation of glucose into cellular energy. This is primarily achieved through production of high energy phosphates such as adenosine triphosphate (ATP) (Dienel 2019). This cerebral oxygen consumption continues unabated throughout the day, even at rest and during sleep. Complete oxidation of glucose takes place in three sequential reactions: (1) glycolysis occurring in the cytoplasm, (2) the tricarboxylic acid (TCA) cycle within the mitochondrial matrix, and (3) the electron transport chain (ETC) and oxidative phosphorylation occurring in the inner mitochondrial membrane. Upon completion of this process, each molecule of glucose is completely reduced to carbon dioxide, water, and approximately 36 molecules of ATP (Camandola and Mattson 2017). Alternate mechanisms of energy delivery are also available, such that in hypoglycemic conditions, cerebral tissue can use ketone bodies (beta-hydroxy butyrate, acetone) for energy metabolism. Glycogen stored in brain astrocytes can also maintain cerebral metabolism, though for a very short time period (Mergenthaler et al. 2013).

Overall, the brain's functional capacity is limited by the availability of intracellular energy substrates (e.g., glucose, oxygen), which in turn is critically dependent on cerebral blood flow (CBF) rate. This well-known linear association between cerebral metabolism and CBF is known as *flow metabolism coupling,* which essentially allows the brain to vary blood flow to match metabolic activity (Peterson et al. 2011). This "neurovascular coupling" is also facilitated by numerous, "upstream" cardiovascular factors (Tarumi and Zhang 2018). For example, arterial blood pressure, a determinant of cerebral perfusion pressure, helps to maintain blood flow at an appropriate level. Partial pressure of carbon dioxide modulates cerebral vasomotor tone, increasing or decreasing CBF through vasodilation and vasoconstriction, respectively. Overall cardiac output and autonomic neural activity are also critically involved in cerebral autoregulation. Alterations in these cardiovascular determinants can significantly impact brain physiology and function, with strong potential to impair cerebral metabolism and result in cognitive dysfunction.

Regulation of cerebral metabolic rate primarily depends on continuous cerebral circulation in order to provide sufficient oxygen delivery. At baseline, the brain consumes approximately 50% of available oxygen and 10% of glucose from arterial blood from overall cerebral blood supply (Zauner and Muizelaar 1997). Inadequate cerebral blood flow (CBF) or disruption of energy production can result in brain dysfunction. Thus, CBF is tightly regulated to prevent dramatic reductions in glucose and oxygen stores. Normal CBF is 50 mL/100 g per minute, while 15–20 mL/100 g per minute results in reversible ischemia and <10–15 mL/100 g per minute is irreversible (Fields and Bhardwaj 2010).

Additionally, regulation of CBF is primarily controlled by cerebral vasoreactivity, or the ability of the cerebral arterioles to respond to changes in arterial CO_2 partial pressure, in order to meet changes in energy demands. In normal circumstances, increased arterial CO_2 partial pressure causes vasodilation of the cerebral arteries, thus reducing vascular resistance and increasing cerebral blood flow (CBF). In contrast, decrease in arterial CO_2 partial pressure causes vasoconstriction, thereby increasing vascular resistance and reducing CBF. Changes in this dynamic cerebrovascular autoregulation pattern affect the vessels' ability to adapt to changes in the brain's metabolic needs.

Aging and changes in cerebral energy metabolism. Cerebral blood flow is determined by variety of health-related indices oxygen extraction ratio (OER), oxygen utilization ($CMRO_2$), and cerebral blood volume. Aging effects in these various indices are well documented, though exact pathophysiological mechanisms are somewhat unclear. For example, Leenders et al. (1990) reported a concurrent ~5% decline of in CBF, $CMRO_2$, and blood volume, with no change in OER. Others reported a larger decrement in CBF relative to $CMRO_2$, with a coincident increase in OER (Aanerud et al. 2012). Peng et al. (2014) suggest that the brain of older adults adjust to these age-related changes by expending more energy via a compensatory increase in cerebral metabolic rate of oxygen relative to younger individuals. This may explain why older adults generally function well into advanced age despite a decline in brain structure and overall decline in CBF. Nonetheless, reductions in CBF appear to be as great as 6%, and divergence in findings reflects differences in methodology across studies or presence of health comorbidities (e.g., hypertension, diabetes). Others estimate a more conservative annual decline of 0.38%, or an approximate 4% decline per decade of life, after accounting for age-associated brain atrophy within a relatively healthy sample (Chen et al. 2011).

In addition to these various molecular and chemical shifts, the brain also undergoes multiple structural and functional changes in normal aging that ultimately affect various aspects of cerebral hemodynamics including cerebral vasoreactivity, CBF pulsatility, and neurovascular coupling (Purkayastha and Sorond 2014). These changes are the consequence of long-term cardiovascular disease. Decreased vascular elasticity along with collagen and calcium deposition leads to thickening and stiffening of the large arteries. Microvascular damage occurs due to changes in various cellular substrates, which impedes cell cycle proliferation, reduces vascular response, or irreversibly damages vascular cell-repair systems (Purkayastha and Sorond 2014). This alteration of vascular tone and function manifests in several downstream changes including increased arterial pulse-wave velocity and elevated pulse pressure vis-à-vis concomitant increase in systolic hypertension and decreased diastolic blood pressure (Benetos et al. 2000). Overall, the heart compensates for increased workload, resulting in left ventricle hypertrophy and changes in left atrial size. In the long term, this leads to higher risk of cardiovascular disease, atherosclerosis, and cerebrovascular disease (Fleg and Strait 2012).

Aging is also known to result in higher pulsatility index values, a measure of CBF pulsatility that is defined as the difference between maximum and minimum blood flow velocity. This increased pulsatile stress results from central artery stiffness associated with advancing age that decreases dampening of pulsatile forces on the cerebral arteries. This, in turn, leaves highly perfused organs, such as the brain, highly susceptible to microvascular damage and subsequent pathologic conditions affecting the brain including leukoaraiosis, lacunar infarcts, normal pressure hydrocephalus, and dementia syndromes (Zarrinkoob et al. 2016). Neurovascular coupling (NVC) also appears to be altered with aging, in which brain hypoperfusion results, secondary to suboptimal blood flow. Consequently, oxygen and glucose delivery are inefficient to accommodate increased neural activity, and poor NVC contributes to poor cerebral white matter integrity (Sorond et al. 2013).

Examples of Application

Decline in cerebral metabolism with age is likely multifactorial in etiology. Although initial efforts focused on age-associated brain atrophy as a pathological mechanism for cerebral hypoperfusion over time, more recent investigations show that disrupted or impaired cerebrovascular hemodynamics may provide a better understanding of the aging process (Chen et al. 2011). Notably, reduced CBF and cerebral vasoreactivity in normal aging appears to be observed more often in the higher cortical structures, which could explain higher vulnerability to neurological disorders in older adults (Girouard and Iadecola 2006; Leoni et al. 2017). Thus, there is a focus on potential interventions that might slow down brain aging. In particular, physical exercise, caloric dietary restriction, and social and intellectual engagement all have the potential to both improve brain functioning by promoting brain plasticity and neurogenesis and protect against brain injury and disease by activating cellular defense mechanisms against neural inflammation and oxidative stress (Mattson 2015). Better management of various health risk factors in the geriatric population (i.e., diabetes, hypertension) is also important given the impact of each on energy metabolism and cerebral vasculature (Glodzik et al. 2014; Seaquist 2015). Additionally, cognitive reserve appears to moderate individual resting-state cerebral metabolism in normal aging (Bastin et al. 2012).

Future Directions of Research

To date, most studies on cerebral metabolism across the life span are cross-sectional designs, where longitudinal analysis is critical for future research efforts. It will also be important to disentangle the influence of vascular and metabolic disease processes from normal aging, as these are well-known accelerants of brain aging (Mattson and Arumugam 2018) and potential confounds. Moreover, while regulation of cerebral metabolic rate is a primary determinant of blood supply, many of the underlying cellular and local chemical factors that control cerebral blood flow are yet to be discovered. In the same vein, various genetic and environmental factors that affect cerebral metabolism in normal aging will also be an important focus for future studies (Camandola and Mattson 2017). Other outstanding questions include the viability or interchangeability of alternate metabolic substrates in sustaining different brain functions, as well as ways to take advantage of current knowledge on cerebral metabolism and designing treatments of neurodegenerative disease and brain injury in aging adults (Mergenthaler et al. 2013).

Summary

Cerebral metabolism and regional blood flow are the primary physiological processes that support brain function through oxidation of glucose and alternate energy-generating mechanisms that promote intracellular ion maintenance and neurotransmitter generation. With constant energy demands, the brain requires a stable supply of energy metabolites that is achieved only through the tight neurovascular coupling that allows the brain to modulate blood flow and match cerebral metabolic activity. Perturbations in this process have wide-ranging implications for normal aging and the numerous diseases known to affect the brain. Despite the large body of empirical studies on cerebral metabolism, certain aspects are still unclear, particularly with respect to the aging effects on cerebral blood flow and its contributing cellular and subcellular substrates. Further insight and clarification into these exact pathophysiological mechanisms not only provide a better understanding into the determinants of cerebral metabolism but may also help to clarify ways to promote optimum brain health and function.

Cross-References

▶ Aging Theories
▶ Atherosclerosis
▶ Hypertension
▶ Prevention of Age-Related Cognitive Impairment, Alzheimer's Disease, and Dementia
▶ Vascular Diseases of Ageing

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Cerebral Palsy

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Synonyms

Cerebral palsy spectrum disorder

Definition

Cerebral palsy (CP) describes a group of permanent disorders of movement and posture, causing activity limitation, which is attributed to nonprogressive disturbances that occurred in the developing fetal or immature brain. The terminology "cerebral palsy" was first mentioned by Sir William Osler in his classic 1889 monograph "The Cerebral Palsies of Children" (Osler 1889). Rosenbaum and Bax proposed a definition for cerebral palsy a decade ago. This definition is rooted in the WHO's International Classification of Functioning, Health, and Disability framework (World Health Organization 2001). Afterwards, this definition has been widely and consistently used in research, clinical, rehabilitation, and health services.

Although CP affects children early in fetal or neonatal periods, most of the affected children are now expected to live to adulthood (Brooks et al. 2014a). Compared with those without CP, adults with CP are also more likely to acquire impairments and illnesses associated with later life.

Overview

Epidemiology

Data from developed countries demonstrate that the prevalence of cerebral palsy is 2–2.5/1000 live births, and has remained stable for the past 40 years (Odding et al. 2006). Due to the increased survival of more preterm and severely affected children, the overall morbidity of cerebral palsy has not significantly changed with time (Johnson 2002). There are no epidemiological data on adults with CP, but we know the majority of affected children are now expected to live to adulthood (Brooks et al. 2014a).

Although the mortality rates among adolescents and adults with CP have not decreased in recent decades, the ratio of the mortality rate for adults with CP to that in the general population has increased by 1.7% yearly since the 1980s (Brooks et al. 2014b).

Causes and Risk Factors

Cerebral palsy is caused by an abnormality in brain development. In many cases, the exact reason is not known. Factors that may lead to problems include: mutations in a fetus's genes that lead to abnormal brain development; maternal infections affecting the fetus, such as rubella; fetal stroke, a disruption of blood supply to the developing brain; lack of oxygen to the brain associated with difficult labor or delivery, which is much less commonly a cause than the previous view; infant infections that cause inflammation in or around the brain; a traumatic head injury to an infant from a fall or an accident.

Ten risk factors were reported by McIntyre that were significantly related with cerebral palsy in children born at term in 2013: low birth weight, meconium aspiration, placental abnormalities, major and minor birth defects, emergency caesarean section, birth asphyxia, neonatal seizures, respiratory distress syndrome, hypoglycemia, and neonatal infections (McIntyre et al. 2013).

Prevention

Most cases of cerebral palsy cannot be prevented, but risks can be lessened. If you are planning to have a baby or you are already pregnant, you can take these measures to be healthy and minimize pregnancy complications as below:

Keep healthy. The healthier you are going into a pregnancy, the less chance you will develop an infection that may lead to cerebral palsy.

Be vaccinated. Vaccination against diseases such as rubella may prevent an infection that could result in fetal brain damage.

Take early and continuous prenatal medical care. Consulting a doctor early and regularly can help prevent infections, low birth weight, and premature birth. Regular visits to a doctor during pregnancy are helpful to reduce health risks to you and your baby to be born.

Provide a child's safety. Avoid head injuries by providing your child with a bicycle helmet, a car seat, safety rails on beds, and appropriate examinations.

Symptoms

Symptoms and signs of cerebral palsy always occur in infancy or preschool years. In general, cerebral palsy causes impaired movement associated with abnormal reflexes, unsteady walking, weakness or spasticity of the extremities and trunk, abnormal posture, involuntary movements, or a combination of these.

People with cerebral palsy may also have problems with swallowing and eye muscle coordination, and in the circumstance of the latter, the patient's eyes cannot focus on the same object. Patients with cerebral palsy also may suffer a reduced range of motion at various joints of their bodies because of muscle stiffness.

Chronic pain was previously under-recognized in children with cerebral palsy (Kingsnorth et al. 2015). A study demonstrated that three out of four children with cerebral palsy experience pain (Novak et al. 2012). Pain is common and may result from the inherent deficits associated with the condition, or along with the numerous procedures that children typically face (Mckinnon et al. 2019).

The functional abilities of people with cerebral palsy vary greatly. Some affected people can walk while others cannot. Some people show close-to-normal or even normal intelligence, but others may have intellectual disabilities. Epilepsy, deafness or blindness, malnutrition, sleep disorders, and mental health disorders, such as depression and anxiety, are also common in these patients (Jones et al. 2015). Obesity or a more severe Gross Motor Function Classification System assessment, in particular, is considered a risk factor for multimorbidity (Cremer et al. 2017).

Although CP is the result of a static destruction to the developing brain, the following signs and symptoms may alter as the person matures and ages. A growing body of literature has documented that age-related physiological changes occur earlier in adults with CP, and that the prevalence of secondary conditions such as pain, fatigue, osteoporosis, musculoskeletal, and joint problems is higher in adults with CP compared with age-matched adults without CP (Horsman et al. 2010; Ando and Ueda 2000). Adults with cerebral palsy may have a higher likelihood of cerebrovascular disease, ischemic heart disease, trauma, and cancer (Krigger 2006).

Treatment

Cerebral palsy has no cure and few disease-modifying interventions; symptom management is the mainstay of treatment. Various forms of therapy are available to people living with cerebral palsy as well as caregivers and parents. Treatments may include one or more of the following: physical therapy; occupational therapy; speech therapy; water therapy; drugs to control seizures, alleviate pain, or relax muscle spasms (e.g., benzodiazepines); surgery to correct anatomical abnormalities or release tight muscles; braces and other orthotic devices; rolling walkers; and communication aids such as computers with attached voice synthesizers.

A 2013 systematic review found that many of the present therapies used to treat CP lack a good evidence base; therapies (fitness training, casting, goal-directed training, bimanual training, constraint-induced movement therapy, context-focused therapy, hip surveillance, home programs, occupational therapy after botulinum toxin, pressure care), medications (anticonvulsants, botulinum toxin, bisphosphonates, diazepam), and surgery are the treatments with the most supporting evidence. Surgical intervention in CP children is mainly divided into orthopedic surgery and neurosurgery (selective dorsal rhizotomy) (Novak et al. 2013).

Because the severity and complexity of cerebral palsy vary across the lifespan of the patient (Trabacca et al. 2016), CP can be considered as a combination of conditions in circumstances of management purposes. A multidisciplinary team for cerebral palsy management is recommended (Trabacca et al. 2016), focusing on "maximizing individual function, choice and independence" in accordance with the International Classification of Functioning, Disability and Health's goals (National Guideline Alliance. 2017). A pediatrician, a social worker, a physiotherapist, a health visitor, an occupational therapist, an orthotist, a speech and language therapist, a teacher helping children with visual impairment, an educational psychologist, an orthopedic surgeon, a neurosurgeon, and a neurologist are recommended in the team.

As they get older, the wear and tear of living with CP can begin to cause other physical difficulties. Some long-term effects of aging and CP can include: enhanced levels of pain and discomfort, pain and stiffness in the joints, increase in spasms or contractures, tight muscles, digestion problems, new or increased back pain, and incontinence. All the above make the treatment problems more complicated (NHS Choices 2017).

Key Research Findings

The accuracy of the term "cerebral palsy" has been doubted recently. One 2018 article put forward the error in continuing to use the term "cerebral palsy," implying a unitary disease phenomenon when the heterogeneous nature of this term is self-evident. A transition in nomenclature to "cerebral palsy spectrum disorder" has recently been put forward for the scientific community's consideration (Shevell 2018). Stem cell trials are carried out for the management of cerebral palsy, focusing on both acute injury and chronic symptoms later. Although many institutes around the world are offering this treatment, the evidence is only anecdotal at present (Ruff et al. 2013).

In 2014, NHS England commissioned five centers to provide selective dorsal rhizotomy in a 2-year evaluation project. Prospective data on spasticity, function, and quality of life, before and after the procedure, were collected. International data demonstrated that selective dorsal rhizotomy successfully reduces spasticity in the long term and improves gross motor function in children (GMFCS level 2 and level 3) in both the short and longer term (Dudley et al. 2013). It also reduces the orthopedic needs of children with cerebral palsy.

Virtual reality (VR) has emerged as a therapeutic tool facilitating motor learning for balance and gait rehabilitation. The evidence, however, has not yet resulted in standardized guidelines. Most studies presented poor methodologic quality, lacked a clear rationale for intervention programs, and did not utilize motor learning principles meticulously. RCTs with more robust methodologic designs were widely recommended (Cano Porras et al. 2018).

Robot-assisted activity can improve upper-arm function in adults with impaired mobility after stroke (Lo et al. 2010). Preliminary data suggest that this type of therapy also improves motor function in the upper and lower limbs that are caused by CP or other acquired brain injuries. These data suggest that use of such interventions in children with CP can improve movement and function as they do in adults with stroke.

Future Directions of Research

Diagnosis and treatment for children with cerebral palsy should be improved by the publication of new guidelines from the National Institute for Health and Care Excellence (NICE) on January 25, 2017. The new guidelines focus on the causes, early diagnosis, and how to treat common comorbidities such as saliva control, pain, mental health, and communication issues. Virtual reality has been incorporated into physical interventions to increase motivation and perhaps could take advantage of neuroplasticity. Functional MRI, monitoring motor cortex function and transcranial magnetic stimulation, can potentially provide insights into typical neuromotor maturation and guide potential therapeutic endpoints (Garvey and Mall 2008). These and many other advances at the interface of technology and rehabilitation can shed light on future therapeutic programs. Theoretically, it is thought that the damage to the central nervous system causes a change in collagen structure, adults with CP have a higher level of deposition of collagen around the muscles, increasing throughout life (Bartels et al. 2020). The research on treatments to delay or prevent this collagen accumulation may give CP patients a better prognosis in the future. Finally, it is worth considering whether the term “cerebral palsy” will remain appropriate. The root meaning of “palsy” is paralysis which clearly does not describe the impairment in the vast majority of people with cerebral palsy. Some also question whether the name “cerebral palsy” has a similar characteristic to previously used terms such as “a spastic.” The shift in nomenclature to “cerebral palsy spectrum disorder” is put forward for the community’s consideration (Shevell 2018).

Summary

Cerebral palsy has varying severity and complexity across the lifespan, and it should be considered as a collection of conditions for management purposes. For older adults with CP, a coordinated effort of a general practitioner, specialist, and therapists is necessary to provide optimal care.

Cross-References

▶ Atherosclerosis
▶ Cardiovascular System
▶ Cerebral Metabolism
▶ Circulatory System
▶ Middle Cerebral Artery Strokes
▶ Peripheral Arterial Disease
▶ Stroke

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Cerebral Palsy Spectrum Disorder

▶ Cerebral Palsy

Cerebrovascular Accident

▶ Ischemic Attack

Cerebrovascular Insult

▶ Ischemic Attack

Cervical Cancer

▶ Tumors: Gynecology

Cessation of Somatic Growth Aging Theory

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Synonyms

Aging begins when linear growth ends; "Bidder's hypothesis"; Determinate growth and holistic aging; Efficient performance vs extended longevity; Fixed body size limits lifespan; Structural/physical constraints on somatic longevity; Theories of aging

Definition

"Bidder's hypothesis" states that aging due to cessation of growth upon reaching young adulthood is the "price" for acquiring a body size that is most capable of efficient performance.

Overview

In 1932, George Parker Bidder published a hypothesis that he felt identified the cause of natural aging and determinate life span in terrestrial animals. It was based upon empirical evidence that aging begins when linear growth ends. The purpose of this review is to assess the validity of Bidder's hypothesis. It will also argue that while specific details may be incorrect, the general concept that senescence is initiated and accelerated by a process involving the total organism, not by expression of unique "gerontogenes" nor as the result of a specific, maladaptive, and cellular/metabolic event(s), is valid. This unique holistic view of aging will be interpreted from a contemporary perspective using empirical data to better explain how aging and determinate life span occurs in iteroparous mammals and perhaps all other sexually reproducing animals when they are protected from predators and other causes of death.

Historical Perspective: *Introduction to the Theory*

George Parker Bidder (b. 1863–d. 1954) was something of a Renaissance man having had various interests and occupations ranging from hotel and yacht owner to inventor, entrepreneur, activist, and diplomat. However, they all related in some way to his lifelong love and study of marine biology. His interest and expertise in sponges in addition to his invention of a device to study bottom water movements made him an authority in his chosen field (Bidder 1955). Paradoxically, he is most remembered today for what may be considered a relatively minor focus of his work, a theory of aging. Unlike Weismann's (1889) earlier theory that defined aging as a genetically programmed "*death* mechanism," Bidder (1932) proposed that aging was the "unimportant after-result" of a "*survival* mechanism" that evolved in "swiftly moving land animals." His theory linking specific size to determinate life span focused on mammals and especially humans in which growth ceases and aging begins upon completion of the developmental program. However, because it was testable, most interest in Bidder's theory focused upon the reciprocal possibility that *aging does not occur* in certain aquatic species such as long-lived teleosts and invertebrates that may display persistent growth and indeterminate body size. Although certain aspects of Bidder's hypothesis are disproven, it continues to be scrutinized even today, as does a recent modification of Weismann's programmed aging theory (Skulachev 1997). The reasons for continued interest in Bidder's concept are that it not only provides empirical data for testing but also because it brings a unique view of aging as resulting from a process involving the whole animal rather than one or more of its parts.

Key Research Findings

Why Cessation of Growth Causes Aging: *Influence of Body Size on Survival*

The theory was influenced by derivation of Galilean concepts of force and motion from which Bidder proposed that swiftly moving land animals cannot increase their body sizes indefinitely and maintain similarly proportional increases in their parts. If disproportionate growth continues unabated, then at some point agility must be lost. Calculations of this relationship showed that as body size of a land animal increases, its weight increases as the cube of its length. In contrast, cross-sectional areas of the bone and muscle corresponding to the same gain in body weight increase only as the square of its length. Thus, if an animal doubles its length without altering the proportions of total size to that of its parts, then its ability to overcome forces quadruples, while the forces it has to overcome increase by a factor of eight (see Bidder 1932; Singer 2013). In contrast, animals living totally immersed in an aquatic environment do not have to overcome the same physical barrier to indeterminate growth since their weight gain is "counterpoised to the extent of an equivalent volume of water." To accommodate the constraints of indeterminate growth on agility, a mechanism evolved to limit growth of land animals to a specific size "within an error not impairing adequate efficiency" (see Singer 2013). The detrimental effect of disproportionate growth of the body and its parts on agility is clinically demonstrable in acromegaly, a pathology of growth hormone hypersecretion causing gigantism (Dantas et al. 2013).

Regarding this size limitation in humans, Bidder assumed the common height of an adult male to be within 20 percent of 5½ feet no matter his race or epoch in time. He reasoned that due to the erect human posture, proportions of length to weight are accurately maintained for efficiency in running, thereby explaining why a mechanism evolved to stop natural growth upon reaching a specific size.

Conservation of Energy and Aging

In addition to performance efficiency, Bidder felt that conservation and allocation of resources for preservation of species were another factor limiting growth, a concept similar to that of Kirkwood (1977). He reasoned that species accumulate as much "capital" as possible from food consumption for their own survival. However, that "capital" is not totally utilized exclusively by the consumer, since some of it is distributed in reproduction and/or as food for offspring. Exceptions to this rule were animals with indeterminate growth. Bidder referenced by example female plaice (*Pleuronectes platessa*), a commercially important flatfish, that seemingly does not age, remains fertile indefinitely, and grows up to 12 times in weight and twice in length when compared with its size upon first reaching maturity. He reported finding no evidence of senescence, nor cause of death other than violence in these animals. Similarly, indeterminate growth in sponges, tunicates, and water voles seemed to be linked with negligible senescence. To better contrast the fates of terrestrial and aquatic predators, Bidder compared survival of wolves and primitive humans with cods and squids, respectively. In doing so, he stressed that the terrestrial animals have determinate growth, ubiquitous senescence, and an ever-increasing risk of cannibalism by their young. On the other hand, the aquatic species rarely acquire specific size, display negligible senescence, and enjoy diminishing danger of being eaten by older adults as their size increases. From such observations he asked, "are not these differences correlated?" and went on to describe his concept of why cessation of growth is the primary cause of aging.

How Cessation of Growth Causes Aging: *Actions of the "Regulator"*

Bidder proposed that since indeterminate growth is fatal to swiftly moving land animals, their ancestors evolved a mechanism for maintaining specific size within an error not to impair adequate efficiency.

He called that mechanism the "regulator" and distinguished his choice of its name from the word "inhibitor" wanting to avoid a "physiological assumption." It would seem that his intent by distinguishing "regulator" from "inhibitor" is that of the difference between perception and detection (Pennebaker and Hoover 1984) in which the former implies the use of both internal physiological and external environmental information for understanding visceral state, while the latter connotes the subject's use of only physiological information, to the exclusion of all other factors. In any event, while acknowledging his ignorance of its nature, Bidder felt that actions of the "regulator" could be traced in anthropometric statistics. For humans these were presumably demonstrated as a steady decline in growth rate from maximum at puberty to cessation in the early twenties. The relevant statistics were that:

- Between the ages of 18 and 60 years, man is within 2 cm of the same final height at the end of growth.
- On average there is a 1 cm increase in height from age 20 to 27.

- Of the prior increase, approximately 1 cm is lost by the early 40s.

Thus, if at age 18, a primitive man were to beget a son, then by age 37 when the son could hunt for himself and for the grandchildren, the species would have no further need of the father. As a matter of fact, by that time he approached 50 years of age, the father would have lost considerable vitality and endurance due to physical consequences of aging such as dwindling of cartilage, muscle, and nerves resulting from "negative growth." Nonetheless, so long as his growth remained stabilized and he maintained his parental competence between the ages of 20 and 40, further negative growth (resulting from continued expression of the "regulator") and ultimate death commonly before the age of 60 were of no consequence to survival of his race. This rule held true until the development of language which thereafter allowed elders to share their long experience and thus regain some societal value, despite no longer being able to fight or hunt.

Determinate Growth Is "Unnatural"

Bidder reasoned that the "regulator's" deteriorative action on the body was inevitable because "giant trees, cultures of chick cells and of paramecium, measurements of plaice and of sponges," all indicate that indeterminate growth is "natural." Thus, adequate efficiency of land animals could only be achieved by the evolution of some mechanism to stop growth, a maladaptive effect on the body, as soon as specific size is reached.

Although growth cessation degrades the soma and is detrimental to individual survival, Bidder argued that "negative growth" resulting from persistent expression of the "regulator" has population benefit and is necessary for welfare of the species. Furthermore, despite having population benefit, he claimed that the deteriorative action and subsequent death of the soma were not a product of natural selection but rather an "unimportant by-product" of a beneficial mechanism that evolved to ensure proper jointing of mammalian limbs within a specific size for *survival* of the organism and its race. Thus, the implication of his theory is that in mammals, aging is the "price" for achieving and maintaining an optimal body size for efficient performance.

The linking of growth cessation with the onset of aging was also drawn for nonmammalian species. Lansing (1947, 1948) reported that at any time during active growth of the rotifer (*Philodina citrina*), it is at least potentially immortal and only begins aging when growth ceases. If correct, then the reciprocal assumption is that some or all continuously growing poikilotherms are non-aging, i.e., that they theoretically enjoy indeterminate life spans. However, evidence from marking and growth measurement in wild fish populations indicates that natural mortality does in fact increase over time in unfished populations. Even though there is some supporting evidence for continued growth, vigor, and non-senescence in halibut and sturgeon, the maximum life span (if any) of these animals in captivity has not been determined. The results of several experimental studies that do not comport with the concept that aging and indeterminate growth are mutually exclusive have been reported for the guppy fish (*Lebistes reticulatus Peters/Poecilia reticulata*) and the sea hare (*Aplysia californica*). Comfort (1961) demonstrated that guppies age while growing, and Reznick et al. (2001) reported that *sexual maturation* was a key factor in determining their life expectancy not cessation of growth. Similarly, Hirsch and Peretz (1984) provided actuarial evidence that *Aplysia* grow linearly without approaching a limiting size while at the same time demonstrating characteristics of aging. The authors concluded that aging is not a by-product of growth cessation.

Contemporary Analysis of Bidder's Hypothesis: *Relationship of Development and Aging*

The reports of Reznick et al. (2001) and others (Blagosklonny 2006; De Magalhaes 2012; Walker 2011) provide stronger support for Bidder's idea that aging is initiated at cessation of growth rather than being prevented by its continuance.

However, the relationship of growth cessation to aging is coincidental with other life events such as sexual maturation and acquisition of young adulthood that may be more evolutionarily relevant (Reznick et al. 2001). As a matter of fact, the time scale provided by Bidder to support his theory is more reflective of developmental progression unto aging than of growth termination, in and of itself. In other words, it is not growth cessation that is operable but rather completion of development which in Bidder's own time scale sets the "regulators" onset at young adulthood, with its effects continuing thereafter into old age.

Holistic Aging

Since the time of Bidder, significant strides have been made in our understanding of the origins of aging. Many hypotheses have been published, but basically they fall into two broad categories, i.e., non-programmed and programmed (Libertini 2015; Gavrilov and Gavrilova 2002). While there is little agreement among researchers as to which category, much less which theory is correct, they all tend to agree that some specific metabolic/genetic trait(s) is responsible for initiating and sustaining aging unto death. However, Bidder's hypothesis and one other (Samis 1968; Walker 2011, 2017, 2019) differ from the rest in that they identify the cause and progression of aging (at least in man and other iteroparous animals) as a property of the whole organism, not of one or more of its individual parts/genes. From its very onset, the process of aging negatively affects complete genome stability rather than being the product of specific metabolic events or gene(s) expressions (Belancio et al. 2015). This concept is consistent with an opinion of Williams (1957) that "Senescence should always be a generalized deterioration, and never due largely to changes in a single system." It also comports with the view of Gould and Lewontin (1979) that under the "adaptationist program," evolutionists tend to "atomize" organisms into traits that are then assumed to have been designed by natural selection for specific functions. The authors further argued that organisms are integrated entities, not collections of discrete units. When part-by-part optimization fails critical analysis, then interaction is acknowledged but with the caveat that organisms cannot optimize each of their parts without imposing expenses on others. Thus, "the notion of 'trade-off' is introduced, and organisms are interpreted as best compromises among competing demands." The resulting sub-optimality of the unit is then accepted as its contribution to the best possible design for the whole. The possibility that it might represent another function or an artifact of organismal change is not usually considered. This paradigm is ultimately used to identify certain "genetic trait(s)" underpinning the process of organismal senescence and is directly applicable to all theories of aging, except for those of Bidder and of Samis/Walker. The search for "gerontogenes," whether causal of or caused by aging, e.g., phenoptosis vs antagonistic pleiotropy, respectively, is irresolvable since they do not exist per se (Rattan 1995). Instead, changes in the organism itself alter the timing of gene expressions (Kim 2008; Pincus and Slack 2008; Lezzerini et al. 2013) and the impact of maladaptive epigenetic factors upon them (Issa 2014), thereby explaining antagonistic pleiotropy.

Future Research Directions

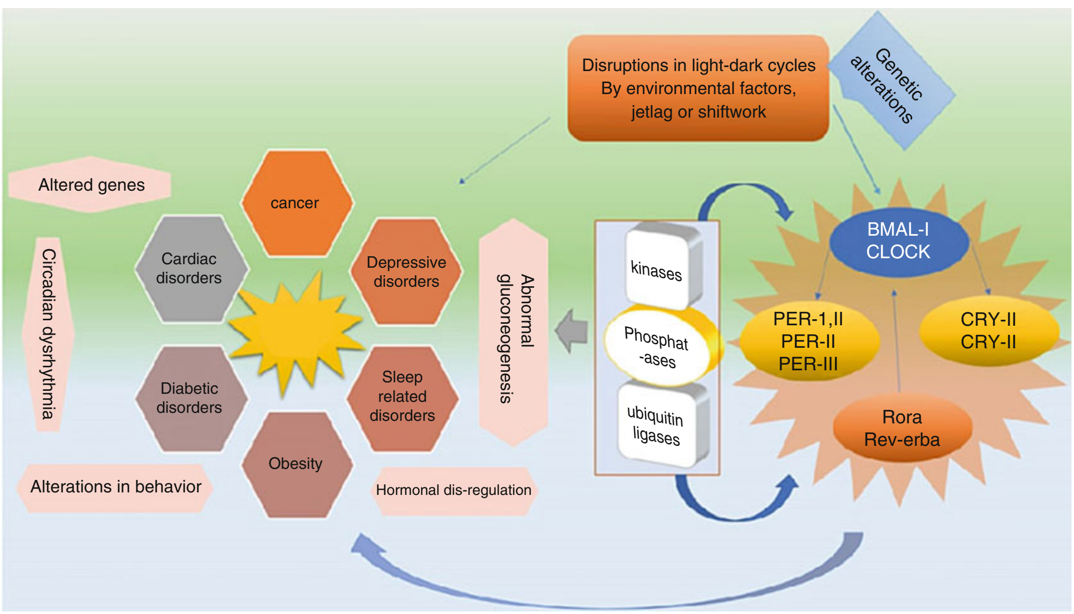
Circadian Rhythms and the Process of Organismal Aging

The global effect that initiates and accelerates aging of the total organism is "*a progressive decline in the stability, continuity, and synchronization of multi-frequency oscillations in biological processes to a temporally disorganized state*" (Belancio et al. 2015). Consistent with Bidder's hypothesis (1932), Samis (1968) and later Cooper et al. (1980) and Walker (2011, 2017, 2019) provided empirical evidence for a testable theory that aging is a simultaneous function of the organism and is not initiated by theoretical, maladaptive actions of specific genes/parts.

Nearly all processes in the brain and body are controlled by circadian rhythms that provide an adaptive mechanism for organisms to coordinate cellular processes, physiological functions, and behaviors with the predictable 24-hour cycle of light and dark on earth (Arendt 2012). These circadian rhythms are entities in their own right existing as parameters of every organism's total time structure that was acquired during their evolution on earth (Halberg 1963).

Circadian rhythms are synchronized by the hypothalamic suprachiasmatic nucleus (SCN) within which resides the master circadian pacemaker for the brain and body. However, the genes that control circadian rhythms are expressed in nearly every cell and are important in regulating the sleep/wake cycle, metabolism, alertness, cognition, and other processes of the normally functioning soma (Albrecht 2012, Patel et al. 2014). This control effect can be demonstrated when environmental or genetic disruptions of circadian rhythms are imposed on the body, resulting in chronic sleep problems, lowered immune function, metabolic and psychiatric abnormalities, as well as increased rates of cancer, gastrointestinal disease, and reproductive disorders (Baron and Reid 2014, Foster and Kreitzman 2014, Khan et al. 2018; Fig. 1).

Long-term, externally induced disruption of circadian rhythms in younger animals is associated with development of perhaps all maladaptive and pathophysiologic effects of advancing age (Khan et al. 2018). As a practical example, epidemiologic studies show that women who experience circadian disruption due to shift work cycles are at an increased risk of breast cancer and possibly colorectal cancer (Davis and Mirick 2006). Additional support for the view that the primary process of senescence is loss of body time structure derives from the fact that temporal disorganization occurs spontaneously in the aging female reproductive system, which requires strict coordination of humoral signaling between the brain, pituitary, and ovary to successfully achieve ovulation. We and others reported that menopausal/estropausal, ovulatory irregularity, and failure are



Cessation of Somatic Growth Aging Theory, Fig. 1 Genetic and pathophysiologic effects of externally induced temporal disorder. Temporal perturbations resulting from shiftwork or jetlag disrupt circadian gene expression. The genetic disruptions cause age-related intrinsic diseases such as cardiovascular, diabetic, sleep and depressive disorders, obesity, abnormal gluconeogenesis, and hormonal dysregulation. (∗Reproduced with permission; Ivyspring International Publisher, from, Khan et al. (2018). ∗*Blanket permission of Publisher: Request to reproduce figures or tables in other publications or journals: There is no need to obtain permission if copyrights of the figures or tables belong to Ivyspring International Publisher. Please acknowledge the original source of publication in our journal with full citation. If the copyrights of the figures or tables belong to other publishers or authors, please contact the original publishers or authors for permissions*) associated with progressive shifting and attenuation of the preovulatory luteinizing hormone "surge" (LH surge), putting it out of phase with the ripening Graafian follicle (Cooper et al. 1980, Eskin et al. 1988; Wise et al. 1999).

Spontaneous loss of coordinated rhythms in the 24-hour cycle has been reported for waking activity, core body temperature, release of hormones, fasting plasma glucose levels, and neuronal firing, especially in the hypothalamic suprachiasmatic nucleus, the central "clock" of the body. The SCN's function is relevant to aging and loss of temporal order because SIRT1, a protein deacetylase that activates BMAL-1 and CLOCK transcription factors thereby governing circadian rhythms, decreases in the SCN during aging (Chang and Guarente 2013). These changes are associated with disrupted activity patterns that are also reported for cases of premature aging and age-related pathologies (Kondratov et al. 2006). Changes in the rhythms are characterized by dampening, shortening, or advancing and delays relative to their dependent functions (Hood and Amir 2017). Thus, the *process* of aging is a function of whole animal physiology within which temporal organization is progressively eroded upon completion of development.

Homeodynamics and the Mechanism of Organismal Aging

Evidence that progressive disorganization of time structure within the whole organism initiates and sustains intrinsic diseases and aging throughout the body comes from observation of its detrimental effects in experimental models and adverse life experience paradigms (Maury et al. 2010). Similar circadian rhythm changes occur spontaneously in aging individuals (Hood and Amir 2017). However, disruption of circadian rhythms may not be the "*primary mechanism*" subserving the aging phenomenon. Instead, age-related loss of time structure may result from decay of strict regulatory oversight and optimal control of physical/functional dynamics that is gradually lost after somatic assembly is complete and/or transformation of the body persists beyond its optimal conformation. This maladaptive "overgrowth" of the optimal termination of physical/functional development is called developmental inertia (Walker 2011) which negatively complements decay of homeodynamics.

Homeodynamics is a perspective on biology that places the organism not the gene at the center of life, thereby transcending the preference for genetic reductionism which has been long favored by gerontologists (Rose 1999). Despite decades of effort, this approach has failed to define a genetic cause, process, or mechanism for aging. While genes that affect *rates* of organismal aging have been identified (Kenyon 2002), they generally impact an individual metabolic event that slows or quickens the general pace of development and/or aging. For example, mutation of daf-2, a specific gene that encodes a protein resembling the insulin/IGF-1 receptor, slows progression of aging in *Caenorhabditis elegans*. This has also been demonstrated in mutant mice lacking IGF-1 (Bartke et al. 2001). However, the growth hormone neuroendocrine axis is necessary for development as well as aging to proceed at its "natural rate." Modulation of the gene expression does not demonstrate the actions of a virtual gerontogene since its hypo- or hyper- expression has parallel consequences on the rates of aging. Thus, no matter how its rate of expression is modified, aging proceeds. If a genuine aging gene could be identified, its silencing would actually terminate further aging not simply alter its rate of progression. Assuming such a hypothetical condition could be created, then animals would remain fixed physically and functionally at the chronological age when intervention occurred. Rates of aging would completely stop, not be slowed nor accelerated.

During development, activity cycles among cells and systems are attuned to environmental and nutritional signals that are strictly regulated by homeodynamic control mechanism(s) that is/are the product of natural selection and is/are essential for maintaining sequential and temporal "order" within the *internal milieu*. Bidder (1932) first recognized that after maturation, selection pressures to evolve or sustain mechanisms that ensure continued functional somatic integrity decline with increasing age (see Williams 1957). This principle is consistent with earlier work of Haldane, Medawar, and Comfort and is generally accepted today (Kirkwood 1977, 2002). However, the reason for declining pressure of natural selection during aging may actually be different from those typically assumed, and that difference will be briefly discussed upon conclusion.

Upon reaching sexual and physical maturation, phase relationships and dissociation of linked interdependent functions are an empirical, maladaptive process that is characteristic of the onset of senescence and progression of its sequelae (Hofman 2000; see Walker 2011, 2017, 2019). Such loss of synchronized timing among interactive systems/functions results from post-maturational decay of homeodynamic control mechanisms. These were selected and essential for integrated assembly of the soma from conception to maturation (Rattan 2007). Thereafter, strict regulatory constraints on homeodynamic maintenance and repair progressively fail because it is thought that life history strategies favor reproduction over repair and maintenance of the post-maturational organism (Kirkwood and Melov 2011). Alternatively, natural selection may decline during aging because determinate life span increases evolvability, provides population benefit, and thereby is adaptive (Mittledorf 2017). Furthermore, immortality is an evolutionary dead end, thus indicating that the universal presence of aging in sexually reproducing animals is a product of natural selection. If so, then post-maturational neglect of the soma could be due to second-order selection (Woods et al. 2011) of an adaptive trait that evolved with the Developmental Program by the process of Coincidental Evolution (CE; see Walker, 2019). CE has been previously reported to occur when an adaptive trait (aging) that was not the direct product of selection (development) emerges as a coincidence or accidental by-product of selection for the "primary" trait (Adiba et al. 2010, Levin and Svanborg Eden 1990). If this is true, then natural selection doesn't become inoperable with advancing age. Instead, adaptive aging was selected thereby negating further selection of any other trait emerging after its onset. Perhaps this is another reasonable explanation for why the effects of natural selection seem to decline with advancing age.

Summary

Bidder's hypothesis states that a mechanism to limit somatic size of land animals evolved so as to accommodate the constraints of indeterminate growth on agility. Although "negative growth" resulting from persistent expression of the "regulator" also causes the soma to age and die, he argued that the process has population benefit and thereby is necessary for the welfare of species. He also felt that aging was not "selected" but rather was an "unimportant by-product" of a beneficial mechanism that evolved to ensure proper jointing of mammalian limbs within a specific size for *survival*. While the central assumption of Bidder's hypothesis (that growth cessation due to actions of the "regulator" initiates aging) is incorrect, the general concept he introduced is valid. Simply stated, aging of the entire organism begins simultaneously upon completion of development, a time in life that correlates with the onset of temporal disorganization, erosion of strict homeodynamic control, and coincidentally with cessation of linear growth. As with Bidder's hypothetical "regulator," the mechanism(s) controlling homeodynamics during somatic assembly is/are still undefined but may involve, at least in part, progressive failure of "clock" genes that control time structure (Buhr and Takahashi 2013; Khan et al. 2018). This suggestion is supported by the undisputed decay of homeodynamics that occurs coincident with unremitting dissociation of circadian temporal organization with advancing age (Hood and Amir 2017). Such change undoubtedly disrupts the *internal milieu*, thereby contributing to age-related genetic and epigenetic drifts (Issa 2014, Lezzerini, et al. 2013). These could reasonably provide a supportive environment for expression of antagonistically pleiotropic genes (Williams 1957). In conclusion, erosion of whole body time structure, not cessation of growth, is the *process* that initiates and accelerates aging. However, it is decay of homeodynamics, the moment-to-moment control over regulatory maintenance of the soma, that allows it to happen. Thus, post-maturational failure of regulatory systems that maintain temporal order by coordinating functional dynamics throughout the soma is the actual *mechanism* that causes the body to lose vitality, deteriorate, become vulnerable to intrinsic diseases, and ultimately die. So, in addition to loss of temporal organization, the question "why do we age?" will be fully answered if and when the operational construct of homeodynamics is ultimately defined.

Cross-References

- ▶ Aging Definition
- ▶ Aging Mechanisms
- ▶ Aging Theories
- ▶ Antagonistic Pleiotropy Aging Theory
- ▶ Disposable Soma Aging Theory
- ▶ Ethics of Lifespan Extension
- ▶ Evolvability Theory of Aging
- ▶ Life-span Development
- ▶ Life-span Theory of Control
- ▶ Longevity Activism
- ▶ Maximum Lifespan
- ▶ Non-evolutionary and Evolutionary Aging Theories

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Challenging Behaviors

► Disruptive Behaviors

Change of life

▶ Menopause

Changes in the Governance Structure of the Aging Policy

▶ Aging Policy Transfer, Adoption, and Change

Chemotherapy Side Effects

▶ Chemotherapy Toxicity

Chemotherapy Toxicity

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Synonyms

Chemotherapy side effects

Definition

Undesirable impact of chemotherapy on symptoms or organ function.

Overview

Aging is associated with a decrease in functional reserve and the ability to withstand stresses such as, for example, chemotherapy. However, such a decrease varies widely by organ and by individual. In order to maximize the risk/benefit ratio of chemotherapy, a proper estimate of biological and functional fitness needs to be conducted. A key tool is a comprehensive geriatric assessment (CGA) (see "Comprehensive Geriatric Assessment"). Risk assessment tools to predict toxicity from chemotherapy have been validated.

Key Research Findings

As we age, our functional reserve and our ability to withstand physiological stress decrease. One such stress is side effects from cancer chemotherapy. Whereas chemotherapy offers increased chances of cure, prolonged survival, or symptom control, both older patients and their oncologists are concerned about the risk and impact of side effects. This has led to a tendency to undertreat older cancer patients (OCPs). Yet, as half of the cancers occur beyond the age of 70, proper access to treatment is key for this patient population. Research over the last decades has led to a better understanding and management of those side effects.

A common way to grade and report chemotherapy side effects is the US National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE). The CTCAE rate the severity of those events from 1 to 5: 1 = mild, 2 = moderate, 3 = severe, 4 = life threatening, and 5 = death (NCI 2019). About half of older patients will experience a grade 3 or 4 adverse event during their treatment (Hurria et al. 2011, Extermann et al. 2012). Yet, many of these adverse events are of short duration, easily controlled, with limited functional impact, or asymptomatic(Chen et al. 2003, Extermann et al. 2015). As a result, many OCPs continue treatment at full or reduced dose with good functional tolerance (Chen et al. 2003, Extermann et al. 2015). There is still a subgroup of patients who experience severe complications, as would happen in younger patients. A key to this good tolerance is good planning and proactive supportive care. A geriatric screening allows recognition and management of potential risk factors.

Aspects Specific to the Older Patient

Hematologic toxicity: As bone marrow reserve decreases with age, older patients have a higher incidence of hematologic toxicity. As a result, guidelines recommend considering age > 65 as a risk factor for febrile neutropenia (see, for example, National Comprehensive Cancer Network (NCCN) guidelines for hematopoietic growth factors: www.nccn.org).

Digestive toxicity: Older patients are less likely to experience acute nausea (defined as nausea <24 h after chemotherapy) than younger patients. On the other hand, they are more sensitive to delayed nausea (2–5 days after chemotherapy). Therefore, attention should be paid to providing nausea coverage for the days after chemotherapy, at least PRN. Long-acting antiemetics such as palonosetron are useful in this setting. As the thirst reflex decreases with age, as well as the body's water content, OCPs are at risk of dehydration from diarrhea.

Neurologic toxicity: Many older patients have preexisting neuropathy or hearing deficits. A good baseline assessment will provide reference for management down the line. One of the first signs of peripheral neuropathy can be autonomous signs, such as orthostatic hypotension, and should be watched for. Other multifactorial elements may affect blood pressure as well (steroids, endothelial growth factor pathway inhibitors may increase it, diet changes, antiemetics, pain medications, weight loss, neuropathy may decrease it). Diabetic patients are particularly at risk of neurotoxicity from taxanes (Hershman et al. 2016).

Cognitive side effects: Ageing and age-associated disorders do affect baseline cognition in cancer patients. However, cancer itself can also affect it, and the prevalence of cognitive problems is higher in OCPs than in the general population (Edwards et al. 2018). As this baseline impairment can easily be missed clinically, it is essential to systematically screen for it, with simple tools such as, for example, the Mini-COG. Chemotherapy itself may cause cognitive side effects, popularly known as "chemobrain." Several studies have assessed the impact in older patients. Eberhardt et al. found that while initially memory was more affected than in younger patients, 6 months outcomes were similar in both groups (Eberhardt et al. 2006a, b). Hurria et al. found that 25% of patients had a decline of >1SD in cognitive tests whereas the others were unchanged or improved (Hurria et al. 2006). Chemotherapy is a risk factor for delirium in vulnerable individuals, especially if they experience infections or dehydration. Delirium is frequent and often underrecognized, so procedures for systematic screening should be put in place(Boyle 2006).

Falls: Chemotherapy does increase the risk of falls in older patients. Confusion, dehydration, general muscle weakness, and peripheral neuropathy are key risk factors (Boler et al. 2007; Tofthagen et al. 2012). In patients at risk for falls, efforts should be made to avoid using taxanes.

Polypharmacy: OCPs take on average half a dozen medications, which carries a significant risk of drug interactions with chemotherapy and targeted therapies. A study showed that the presence of drug interactions doubled the risk of severe toxicity from chemotherapy, and if one of the interactions was involving a chemotherapy drug, the risk of toxicity was tripled (Popa et al. 2014).

Examples of Application

Approaches to Reduce Side Effects

Recognizing the potential side effects should lead to proactive supportive care and strategies to reduce their impact. Such strategies include:

– Doing a geriatric assessment. There is solid evidence that a geriatric assessment leads to cancer treatment plan modifications in about one in four cancer patients (Hamaker et al. 2014, Puts et al. 2014).
– Calculate a chemotherapy risk score. Several ways of estimating risk of toxicity have been proposed, and two scores have been formally validated in the older patient: the Chemotherapy Risk Assessment Scale for High-Age patients (CRASH score) (Extermann et al. 2012) and the Cancer and Aging Research Group (CARG) score (Hurria et al. 2011, Hurria et al. 2016). These two scores integrate

Chemotherapy Toxicity, Table 1 CRASH (Chemotherapy Risk Assessment Scale for High-Age Patients) scoring analysis

CRASH (Chemotherapy Risk Age Scale for High Risk Patients) Scoring Analysis

Chemotherapy risk (see table)		
Hematologic risk factors		
Diastolic blood pressure (greater than 72 = 1)		
IADL (less than 26 = 1)		
LDH (greater than 168 = 2)*		
Non-hematologic risk factors		
ECOG PS (1-2 = 1; 3-4 = 2)		
MMS (less than 30 = 2)		
MNA (less than 28 = 2)		
Heme score (incl. chemo risk)		
Non-heme score (incl. chemo risk)		
Combined score (count chemo risk only once)		

Individual risk

	CRASH score (points / % with severe toxicity)			
Sample	**Heme subscore**	**Non-Heme subscore**	**Combined score**	**Risk Category**
Derivation (n=347)	0-1: 7% 2-3: 23% 4-5: 54% Greater than 5: 100%	0-2: 33% 3-4: 46% 5-6: 67% Greater than 6: 93%	0-3: 50% 4-6: 58% 7-9: 77% Greater than 9: 79%	Low Int-Low Int-High High
Validation	0-1: 12% 2-3: 35% 4-5: 45% Greater than 5: 50%	0-2: 42% 3-4: 59% 5-6: 66% Greater than 6: 100%	0-3: 61% 4-6: 72% 7-9: 77% Greater than 9: 100%	

Reference: (Extermann, Boler et al. 2012)

Warning: This score is for use by oncologists familiar with chemotherapy administration. It is aimed at supporting clinical decision making and should in no way supersede it. It is to be used in addition to drug-specific dose adaptations. Further individual or treatment plan characteristics might lead the oncologist to depart from these risk estimates.

* Moffitt ULN = 225 (points for value ≥ 0.75 ULN)

A scoring tool with the chemotherapy regimens (scores 0–2) can be found at https://moffitt.org/for-healthcare-providers/clinical-programs-and-services/senior-adult-oncology-program/senior-adult-oncology-program-tools/ (or google "SAOP tools" or "CRASH score")

elements from a geriatric assessment and classic oncology predictors (Tables 1 and 2). They allow classifying patients into 3 (CARG score) or 4 risk groups (CRASH sore) for side effects from chemotherapy. In clinical practice, they are particularly helpful as dilemma breakers, when contradictory clinical impressions make it difficult to estimate treatment risk (Mohile et al. 2018).

– Be aware of which chemotherapy agents have modifications of their pharmacokinetics and pharmacodynamics with age and sex.

Chemotherapy Toxicity, Table 2 CARG score

• Age > 73	2 pts
• GI/GU cancer	3 pts
• standard dose chemo	3 pts
• Polychemo	2 pts
• Hb <11 in males, <10 in females	3 pts
• creatinine clearance <34	3 pts
• falls in last 6 months	3 pts
• hearing impairment (fair or worse)	2 pts
• limited in walking 1 block (MOS)	2 pts
• needs help with meds (IADL)	1 pt
• decreased social activity (MOS)	1 pt

Scoring:

Score	G3–5 toxicity (derivation)	G3–5 toxicity (validation)
Low risk (0–5)	27%	37%
Mid risk (6–11)	53%	62%
High risk (> = 12)	83%	70%

Available online at http://www.mycarg.org/Chemo_Toxicity_Calculator or google "CARG score"

– Systematically calculate creatinine clearance. Even if older patients have a normal creatinine, the majority have a creatinine clearance under 60 ml/min(Giannelli et al. 2007).
– Review and trim medication list applying tools such as the Beers or START/STOPP criteria.
– Administer prophylactic growth factors starting with the first cycle of chemotherapy in patients at risk.
– Educate the patient on hydration issues if they develop diarrhea, and to seek prompt intervention.
– Ensure proper home support to allow early recognition and management of side effects. In the Moffitt Senior Adult Oncology Program (SAOP), we generally recommend that patients have a family member at home, at least at the beginning of chemotherapy.
– Be ready to modify antihypertensive regimens, as OCPs often have changes in blood pressure during chemotherapy (up or down).

Future Directions of Research

Although it is now well demonstrated that geriatric assessment modifies the management of OCPs in about a quarter of cases, research is still ongoing to assess how geriatric assessment and co-management impacts the long-term outcomes of these patients. Some early results are available on the impact on the geriatric issues themselves (Extermann et al. 2004, Puts et al. 2014), and on the outcomes of cancer surgery (McCorkle et al. 2000). In patients receiving chemotherapy, early studies show a decrease in toxicity with geriatric interventions (Kalsi et al. 2015) or stratification (Corre et al. 2016), but an impact on function and survival still remains to be demonstrated.

Summary

The evidence shows that OCPs in good condition can tolerate chemotherapy as well as younger patients, provided appropriate management is conducted. Therefore, standard approaches and dosing should be considered for such patients. On the other, it is important to conduct a formal geriatric assessment to (a) identify vulnerabilities and frailty features that should lead to adapted treatment and/or preventive measures; (b) identify patients who despite initial impression may be resilient; and (c) initiate proactive supportive care for optimal outcomes.

Cross-References

▶ Aging and Cancer: Concepts and Prospects
▶ Cancer Screening
▶ Cancer
▶ Chemotherapy Toxicity
▶ COVID-19 Pandemic and Geriatric Oncology
▶ Immunotherapy
▶ Prehabilitation in Older Adults with Cancer
▶ Radiation Therapy
▶ Targeted Therapies
▶ Telerehabilitation (Remote Therapy)

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Chewing Ability

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Synonyms

Masticatory ability

Definition

Chewing ability is a general term referring to the ability to put food in the mouth, bite it, crush and grind it, form a bolus mingled with saliva, and then swallow the bolus. This term encompasses the whole ability from after catching the food with one's mouth to the swallowing threshold. As chewing ability relies on oral functions involving occlusion and the temporomandibular joint, tongue, and muscles of mastication, it is reduced by senile changes of these functions.

Overview

Chewing ability is composed of the ability to perform multiple steps ranging from holding the food with one's mouth to swallowing it. Babies obtain masticatory function after 18 months of age. Numbers of teeth and functional tooth units are correlated with chewing ability. Chewing ability declines with age, leading to worsening of health status and nutritional status, lowering of quality of life (QOL), development of sarcopenia, and an increase of risk for mortality. The method of chewing ability evaluation is classified into two types, i.e., direct and indirect method. Rehabilitation of chewing ability may improve nutritional status, general health, quality of life (QOL), and cognitive function in older adults.

Key Research Findings

Chewing ability is related to the oral phase, the first stage of three stages of swallowing (the other two stages are the pharyngeal and esophageal stage). Regarding chewing ability, during development, babies can hold food with their lips by 5–6 months of age (primary weaning period), squash the food with the dorsum of their tongue by 7–8 months of age, and mash the food by 9–11 months of age (middle weaning period). Babies aged 12–18 months (last weaning period) can chew rhythmically using their tooth or tongue. The chewing force of a 3-year-old infant, possessing complete deciduous dentition, is usually 1/5 of the chewing force of an adult, average range 130–150 N[†] (Maki et al. 1992). [One Newton (1 N) is the force needed to accelerate one kilogram (1 kg) of mass at the rate of 1 meter per second squared (1 m/s^2) in the direction of the applied force.] In infants, various factors affect the development of chewing ability, such as decayed and/or missing tooth, malalignment, malocclusion, and unilateral mastication. Importantly, empirical evidence suggests an association between chewing and functional development of the brain (Ono et al. 2010). Results from experimental studies showed that juvenile mice fed with a powder diet to reduce masticatory stimulation during growth period had a smaller number of neurons compared to controls, as well as less neurogenesis and neuronal activity in the hippocampus (Fukushima-Nakayama et al. 2017).

Chewing ability declines with age (Hsu et al. 2011; Kimura et al. 2013; Locker 2002; Morley 2001). Poor chewing ability is closely associated with a less varied diet and lower food intake, leading to malnutrition, worsening of health status, lower QOL, sarcopenia, and, in elders aged 70 or older, increased risk of mortality (Kimura et al. 2009, 2013; Lee et al. 2014; Lo et al. 2016; Murakami et al. 2015). Chewing ability is closely related with metabolic syndrome. Results from an epidemiological study showed that deterioration of chewing ability increased the prevalence rate of metabolic syndrome by 1.67–1.90 times (Kikui et al. 2017). A recent study suggests that self-perceived chewing ability is significantly associated with early-onset physical impairment, often followed by older adults requiring long-term care (Moriya et al. 2012). Recent findings from epidemiological studies also indicate that chewing ability is closely correlated with cognitive function in the older adults (Kimura et al. 2013; Miura et al. 2003; Mummolo et al. 2014; Takata et al. 2009; Weijenberg et al. 2011). Lower chewing ability, as assessed via a color-changeable gum, is significantly associated with frailty in community-dwelling older adults (Iwasaki et al. 2018). An 8-year follow-up study revealed that older adults with unsatisfactory chewing ability tend to need more emergency services and have longer hospital stays (Lo et al. 2016). These evidences strongly suggest that maintenance of chewing ability is critical for good health in older adults.

Multiple lines of evidence have shown that chewing ability is associated with the number of teeth present (Ekelund 1989; Ow et al. 1997; Slade et al. 1996; Tatematsu et al. 2004; Zeng et al. 2008). The number of functional tooth units is also associated with chewing ability (Ueno et al. 2008, 2010). A majority of edentulous older adults reported their chewing ability as very or fairly good (Unell et al. 2015). Chewing efficiency after wearing full dentures is one-sixth of that of natural dentition. Degree of alveolar ridge resorption is not associated with chewing ability after restoration with a full denture; however, denture adhesive use increases chewing performance (Goncalves et al. 2014). Canine-guided occlusion of full dentures is associated with chewing satisfaction in edentulous patients (Zhao et al. 2013). Wearing removable partial dentures partially improves the chewing ability, although it may not be able to fully restore the chewing function (Bessadet et al. 2013). Chewing performance after wearing a partial denture is better than that after wearing a full denture (Schimmel et al. 2017). Taken together, wearing a removable dental prosthesis is not an ideal treatment option for restoring chewing ability. While wearing dentures has limited effect on chewing ability, chewing after wearing a denture activates the prefrontal area, suggesting that it may improve cognitive function (Kamiya et al. 2016).

Because chewing ability includes many abilities regarding oral function, it can be assessed through various methods. Such methods can be classified into two categories: direct and indirect methods. The direct methods use chewable material, such as peanut, chewing gum, gummy jelly, or polyethylene film. The sieving method is used to assess the ability to crush the food. The crushed particles of the masticatory sample, such as peanuts or raw rice, are gathered from the mouth, and the size of the particles is measured with a sieve. Other methods for assessing the state of crunched particles are the precipitation method and light cutoff method. The eluted substance from the crunched chewing sample, for example, glucose from chewing or gummy jelly, is also used. Color-changeable chewing gum is used to assess the ability to mix bolus. As a subjective assessment, some questionnaires on chewable foods were developed. As for the indirect methods, they assess factors related to mastication, such as jaw movement, masticatory muscular activity, or occlusal contact. Indirect methods can take advantage of the fact that the movement pathway and the rhythm of the mandible are closely correlated with chewing ability (Shiga and Kobayashi 1990). An example of indirect method is the analysis of regularity of waveform in the electromyogram, which is used to assess the stability of the chewing rhythm.

Examples of Interventions

Improvement of chewing ability leads to the amelioration of nutritional status, activity of daily living, cognitive function, and QOL in older adults. As rehabilitation for chewing ability, regular gum-chewing exercises are contrived. The protocol of the exercises was as follows: a gum-chewing exercise with a soft gum was carried out for 2 weeks, followed by a 2-week rest period, and then a gum-chewing exercise with a hard gum for 2 weeks. This method contributes to the improvement of occlusal force, amount of saliva secretion, and mucosal moisture in older adults with natural bilateral posterior occlusion (Nakagawa et al. 2017). Increasing food consistency for older adults with dementia not accompanied by dysphagia is also effective in improving chewing ability and QOL (Weijenberg et al. 2013). The speech therapist diagnoses swallowing disorder to evaluate the need for pureed food. Participants who are given pureed food without a medical need will be reintroduced to more solid foods. All participants able to masticate normally are offered food of tougher consistency, such as apples, bread, crunchy cookies, and raw vegetables. The intervention will increase masticatory activity. In addition, an interesting trial that involved a mirror neuron system revealed that watching videos of other people chewing has a beneficial effect on the chewing ability of older adults with dementia (Douma et al. 2016). The protocol of the exercises was as follows: the videos of other people chewing are without sound and are shown on tablet-PCs placed behind the plate of each participant during lunchtime. There are ten different videos having a duration of approximately 40 min. The focus of each video is on the face of the person being displayed. Intervention period is 3 months.

Future Directions of Research

Considering the continuous aging of the population and importance of chewing, the next decades will require a great effort to support chewing ability, particularly in older adults. Currently, there are various chew-swallow managing (CSM) foods being developed for dysphagia patients. In the swallowing process, processing food (i.e., making a bolus by chewing food and mixing it with saliva) and stage II transport (transporting the bolus to the pharynx during chewing through the squeeze back action of the tongue) operate concurrently (process model). Considering the process model, CSM foods need to possess a chewable hardness at the oral stage and a pasty texture at the pharyngeal stage. With the increasing median age of the population, the need for rehabilitation using CSM foods is expected to continuously grow in the future. Finally, supporting chewing ability in this aging population will require not only morphologic restoration, such as denture, but also functional recovery via training and rehabilitation.

Summary

Chewing ability is critical for older adults to maintain their general health, nutrition status, and QOL. Dentists and dental hygienists maintain and improve the chewing ability of older adults via functional support based on the evaluation of the chewing ability in not only the clinic but also in the nursing home or at the patients' home.

Cross-References

- ▶ Artificial Nutrition at Old Age
- ▶ Cognition and Frailty
- ▶ Malnutrition
- ▶ Nutrition and Frailty
- ▶ Prevention of Age-Related Cognitive Impairment, Alzheimer's Disease, and Dementia
- ▶ Sarcopenia

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Child Service(s)

► Social Work

Childless Older Adults

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Definition

Childless people are persons who do not have children. In the following, "older childless" are people in the second half of their life (50 and over) without children. Childlessness can be a voluntarily decision or an involuntary fact, and few older people also outlived their children.

Overview

Fertility and specifically childlessness are important topics in nowadays discussions about population aging across Western societies. Having fewer or even no children does not only affect lives on the individual and family level, but it also puts modern welfare states under pressure. Especially countries with pay-as-you-go pension schemes face challenges to ensure pensions with less contributors (smaller workforce) and more receivers (more pensioners) (Lee 2003). Apart from guaranteeing social security in an aging society, the adequate provision of care for frail older people is also at risk (Colombo et al. 2011). Many welfare states rely on the family to ensure old age care (Saraceno 2016). The literature on care and hands-on help consistently states the importance of children, especially daughters, as main support resource in old age (e.g., Schmid et al. 2012). Declining fertility, including childlessness, therefore adds a critical component to the future sustainability of the modern welfare state.

Given this importance, surprisingly little is known about childlessness and childless older people. Rowland (2007: 1333) even characterized them as an "invisible" group. In recent years, however, more and more research about childlessness in general and about childlessness in older age has gathered reliable information, mainly on Europe and the USA. Our entry gives a short overview about the main findings of such research on childless older people. The main topics are prevalence of and reasons for childlessness, characteristics of childless people, and social support for childless people in older age.

Key Research Findings

How Many Are Childless?

The question how many people have no children is surprisingly hard to answer. While most countries and data collectors like OECD or Eurostat do report on fertility, information on childlessness is scarce. This is especially a problem for information on older cohorts (see Dykstra 2009 for a short description of this problem) but partly also for younger cohorts and specific country contexts. Often census data offers information on living children or children within the current relationship only, and does not account for all children a women had. In some countries information is not available from official data sources (see also Sobotka 2017 or Rowland 2007 on data sources for childlessness).

The percentage of childless older people in Europe (50 years and over) was around 10% based on the Survey of Health, Ageing and Retirement in Europe (Deindl and Brandt 2017). The largest proportion of childlessness was found in Switzerland with 15%, followed by Austria, France, and Germany. The lowest prevalence of childlessness in older age was found in the Czech Republic, Sweden, and Denmark with 6–7%. Most other countries were close to the European mean. While this was calculated based on a sample of older women and men, most research on the prevalence of childlessness, similar to fertility research, is based on women only. Sobotka (2017) based his analysis of childlessness in Europe on women born between 1900 and 1972, finding a U-shaped pattern of childlessness with higher levels of childlessness in cohorts born earlier and declining childlessness in younger cohorts. At the beginning of the century, childlessness in Western European women (France 1900, Belgium 1910, Ireland 1925) was at 25%. This declined to 10–14% in the middle of the century and rose afterward to 14% in France and 16–19% in Belgium, Ireland, the Netherlands, England, and Wales (Sobotka 2017: 28). Nordic countries showed similar results with 25% as starting point followed by a decline in childlessness with a rise to 12–14%, therefore similar to the current levels in France. Sobotka found a third cluster of countries encompassing Southern Europe, Germany, Austria, and Switzerland with higher levels of childlessness than Western and Northern Europe. In Germany and Switzerland, childlessness was around 20%. In Germany, however, differences between East and West were immense, with low rates of childless people in Eastern Germany and higher levels of women without children in West Germany. Italy and Spain shared similar patterns with childlessness going from 25% to 11–12% and rising again to 20% of the younger cohorts of women (born 1960 to 1970). Portugal, however, has a lower prevalence of childlessness in the younger cohorts with 12%. In Eastern Europe, childlessness remained low in the 1940 to 1950 cohorts and did not rise for younger cohorts.

The U-shaped development with a high at the beginning of the century with a decline for cohorts born in the first half of the century and rise of younger cohorts was also reported by Rowland (2007) for Europe, Australia, America, and Japan and birth cohorts between 1890 and 1854. He found that childlessness was more common among older women in the USA and Australia (countries with data on older cohorts). After this peak childlessness declined for women born around the middle of the century and went down to 10%. Younger cohorts again showed higher numbers of childless people, with little differences between these countries and continents. Dykstra (2009) expanded the work of Rowland by including younger cohorts and more countries, especially from Eastern Europe. This comparison again offers interesting insights into country differences. Especially Eastern Europe (including East Germany) is unique in fertility history with a high fertility before the fall of the wall and a large drop in fertility afterward (see Adler 1997 or Goldstein et al. 2009 for more details on Eastern Europe).

Reasons for Childlessness and Characteristics of Childless People

Why do some people remain childless and how can differences over time and across countries be explained? One important distinction is whether people are voluntarily or involuntarily childless. Involuntary childlessness is most often caused by infecundity. Reasons for this are often not influenced by social developments, but, as fecundity declines with age, prolonged fertility has the potential to foster fecundity problems. However, Dykstra (2009: 677, citing Bonneux et al. 2009) reports that in the Netherlands, only 1% of women are childless due to infertility caused by postponement. Keizer and colleagues

(2008) argue that not having children is not necessarily a decision and couples or individuals who have no children might have simply “remained childless” (see also DeOllos and Kapinus 2002). Abma and Martinez (2006) found that in the USA voluntary childlessness was more prevalent than involuntary childlessness. Moreover, “pathways of the childless were more often characterized by late starts in independent living, education, and marriage” (Hagestad and Call 2007: 1358), and in some cases, childlessness also resulted from a priority given to working life (DeOllos and Kapinus 2002). Accordingly, Gemmill (2019) found that the decision to remain childless was not stable and changes over time (the individual life course) based on US data. Looking at fertility decisions of childless women, she found that while some women had the stable wish to remain childless (24%), some changed their plans over time. Based on sequence analyses, she found these changes to happen early (before the age of 30, 32%), some later (20%), some gradual (11%), and some from “high to none” (13%) (Gemmill 2019: 139). Switches in early years are likely an indication of partnership or the start of the working careers. Changes later in life might be caused by biological problems or a missing partner or simply the “adaptation to childless lifestyles” (Gemmill 2019: 144). Black women had higher odds to belong to the “high to none” group. Women from rural areas were more likely to switch early in their life to childlessness, and women from “fundamentalist Christian traditions” were more likely to have the consistent wish to remain childless – contradicting findings from Abma and Martinez (2006) who stated that for more religious women, childlessness was less of a voluntary decision. Women who were never married were more likely to belong to the “high to none” cluster opposed to women who married before the age of 30. Women who experienced “marital disruption” were more likely to belong to gradual switching to childlessness. Women who were not in the labor force for two surveys were more likely to not want children and lower odds for a late switch.

Taking a life course perspective, Hagestad and Call (2007) found that the lives of childless people were characterized by late starts concerning starting an independent life, education, and marriage. Childless people lived longer in the parental home, which affected the proportion of married negatively. Also, people who left the parental home earlier reached higher education, and the transitions from work to leaving the parental home and marriage were faster among people who became parents. This is consistent with Rowland (2007) who found that changes in marriage patterns were one major factor in explaining the historic development of childlessness (even though causal mechanisms cannot be implied here). Childless people married later and a higher proportion never married (Rowland 2007: 1324).

The connection between work and childlessness is less clear (Mynarska et al. 2015), and the multiple links between education, employment, and fertility are not easily determined. The low number of childless women in postwar generations in Eastern Europe (Sobotka 2017) went hand in hand with high female labor force participation. Abma and Martinez (2006) found that childless women had more work experience and that higher educated women delayed childbearing.

Over and above, societal context obviously matters – directly and indirectly by influencing and providing the different micro- and meso-level conditions mentioned. Historic events like the great depression in the 1930s and World War I and II had a profound impact on childlessness by delaying on childbearing (Rowland 2007). Looking at the low rate of childlessness in Eastern Europe and in Eastern Germany (see Kreyenfeld 2004 for West and East Germany), for example, one can also assume that contextual features were at play here. The exceptionally low rates of childlessness in Eastern Europe before the fall of the wall were likely linked to a low age of marriage, universal childcare, a favorable labor market situation, negative attitudes toward childless women, and similar factors (Sobotka 2017).

Still, findings are not at all clear and there is still a lot to be found out. Research has provided mixed results regarding differences in individual characteristics of parents and childless people, partly depending on the cultural background and the specific samples (cohort, age, gender). Differences in social and personal resources were often very small (e.g., Keith 1983a) and partly due to other factors related to childlessness such as partnership histories (e.g., Keizer et al. 2010). According to data from the Netherlands, fathers between age 40 and 59 had higher incomes than childless men, but their higher well-being was based on their partnerships (Dykstra and Keizer 2009). We generally see relatively little differences between parents and childless people in regard to their economic, psychological, or social well-being – at least in some contexts. However, this might differ according to the specific groups studied: People who were voluntarily and involuntarily childless, for example, differed in later life well-being (McQuillan et al. 2012), and in collectivistic societies, childlessness might be more detrimental to well-being due to the higher value of and dependence on family networks (e.g., Quashie and Pothisiri 2018). Accordingly, there is an entire body of research looking into the effects of parenthood on well-being and the "parental happiness gap," trying to disentangle different causal mechanisms – and up to now producing inconclusive results (for an overview, see Hansen 2012).

Taken together, remaining childless is a complex process involving partnership, employment history and education, as well as contextual conditions (Hagestad and Call 2007; Keizer et al. 2008; Mynarska et al. 2015). It is important to account for different kinds of childlessness when assessing the differences between older people with and without children, who have likely been different from the start, but might also experience different trajectories in terms of their socioeconomic position and well-being. It is important to take a life course perspective and account for the selection into different kinds of childlessness and parenthood within different contexts when assessing differences between childless and parents in later life.

Social Networks and Social Support

Across different contexts, children and partners are the mainstays of informal support in old age. As established above, childlessness is closely linked to partnership history. Therefore, childless older people often lack two crucial support components: children and a partner. With regard to social support networks, there are two major research topics: differences in (a) the composition of social networks and (b) the availability and exchange of social support. The links between social networks, support, and childlessness are not easily predicted: Childless people could well be more socially integrated than parents because they had more time and resources to invest in their social networks – however, they miss an important network building mechanism in terms of meeting other parents via their children. In line with that, research yields competing findings, depending on the sample and method used: According to Gray (2009) parents are less likely to be lonely. Dykstra (2006) supports this by finding that childless people are more likely to be socially isolated and have smaller networks. Still, childless women and men in the Midwestern USA were not disadvantaged in terms of the availability of social support in very old age (Keith 1983b). Deindl and Brandt (2017) found that the support networks of childless older people differed substantially from those of parents. More than half of support relations in the case of parents who received support within the last year were children. Childless older people compensated this lack by more support from neighbors and acquaintances, the extended family, friends, and siblings. Thus, surprisingly, there was no difference in the likelihood to receive (any) informal support between childless older people and parents. This is in line with Albertini and Mencarini (2014) who also found that that likelihood of receiving support was similar between parents and childless people. While childless people received more emotional support, they, however, lacked support networks that provided hands-on help and care. Moreover, according to Deindl and Brandt (2017), the intensity of informal support (hours) was lower for childless, and they took up formal support and a mix of formal and informal support more likely. Again, there also exist contradicting findings concerning formal support uptake: Childless in the USA seemed to subjectively lack support in times of illness more than parents; however, they were not more likely to use social services than their counterparts when controlling for other important predictors such as availability of information about informal support (Choi 1994). Support deficits were not even compensated by formal public services in a developed welfare state like Sweden (Larsson and Silverstein 2004). Taken together, most studies agree that childless face at least some support deficit (Gray 2009; Larsson and Silverstein 2004; but also Keith 1983b) due to lower and faster declining availability of informal support and differences in network composition (Grundy and Read 2012; Johnson and Catalano 1981).

There are only a few studies looking at support provision of childless older people. Parents are heavily involved with financial transfers toward their children (e.g., Brandt and Deindl 2013). For childless older people, studies suggest that they give less financial transfers within the family and are more likely to support friends, relatives, and charity organizations than parents, but taken together give less (Albertini and Kohli 2009; Hurd 2009).

Summary

The prevalence of childlessness changes over time. Over the last century and in most Western contexts, it followed a U-shaped curve with the percentage of childless people lowest in the middle of the century and highest at the beginning of the century and at the end. There are, however, important differences between countries. Women in Eastern European countries showed rather low levels of childlessness during the communist era. Remaining childless is not necessarily a voluntary decision. The main contributors to remaining without children (besides biological issues) are education, work, and partnership histories. Childless and parents thus differ in individual characteristics; they experience different life course trajectories and face different well-being outcomes in older age, partly depending on the context. Availability of (any) social support is similar for parents and childless older people; however, there is evidence that the network composition and the intensity and types of (in)formal support received differ from parents in older age, at least in some groups and societies.

Cross-References

▶ Intergenerational Exchange and Support
▶ Intergenerational Family Caregiving in Welfare Policy Context
▶ Intergenerational Family Structures
▶ Intergenerational Relationships
▶ Kinship Networks

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Childless Older Adults Without Any Income Sources

▶ "Three-No" and "Five-Guarantee" Older Adults

Child-Rearing by Grandparent

▶ Grandparenting

Children's Attitudes Toward Aging and Older Adulthood

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Synonyms

Ageism in children

Overview

Ageism, or negative attitudes and stereotypes toward older adults, is conceptualized as the tendency to hold and/or display stereotypical attitudes and discrimination against people due to their old age (Butler 1995). According to Butler (2001), ageism enables younger generations to see older people as different from themselves, in order to reduce their own fears regarding aging and dying. The manner by which children formulate and internalize their perception of older adults can be viewed through the prism of several theoretical accounts, which take into consideration different aspects of the developmental pattern of internalizing and displaying stereotypes and negative attitudes (see Levy and Hughes 2009; Mendonça et al. 2018). One of the most influential theories in this regard is social learning theory (Allport 1954), which suggests that children acquire prejudicial attitudes through observing and imitating important role models, such as parents. According to this theory, as children are often subjected to their parents' and teachers' negative attitudes/stereotypes toward older adults, their own attitudes will be on par with those whose views and opinions they value.

An additional source of ageism in children is the relative lack of knowledge regarding the aging process and older adults. Moreover, as direct contact with older adults is usually limited to family members (as opposed to contact with other children and younger adults), children may not be able to acquire correct knowledge and information about older adults and the aging process, and this may promote stereotypical perceptions. Moreover, the growing availability of electronic media and child-oriented materials, which often depict older adults in a negative manner, may also contribute, in the absence of concrete and accurate information, to the formulation of biased views of older adults (see Bergman 2017; Mendonça et al. 2018).

A different approach is offered by the cognitive-developmental theory (Piaget and Weil 1951; see also Aboud 1988). According to this theory, the development of negative attitudes is the consequence of the child's limited cognitive skills, which restrict his/her ability to perceive people and individuals, thereby causing him/her to overgeneralize certain salient characteristics. In this regard, it is also important to take into account that as children mature, the salience of different social groups and the importance of defining oneself as a member of these groups, which are often characterized by age (e.g., "children" vs. "adults"; "kindergarten students" vs. "first-graders") become more pronounced. Since group identity is an important aspect of the construction of one's personal identity and self-esteem, as suggested by social identity theory (e.g., Tajfel et al. 1979) and its developmental derivation (Nesdale 1999), it is feasible that older adults may be perceived by children as members of a specific out-group, which is rarely approached and little understood. When this idea is paired with the relative lack of contact with older adults, which is an important factor for reducing negative attitudes (i.e., intergroup contact theory; Allport 1954; Pettigrew 1998), these factors may play an important role in the formulation and internalization of a negative perception of aging and older adults in children.

Negative attitudes toward older adults may also be viewed from an evolutionary perspective. According to this approach, children's comprehension of social groups is guided by inherent theories which assist them to focus on important group information, while disregarding irrelevant information (Hirschfeld 1995). This, for example, may provide a partial understanding for the fact that young children often link death with illness and old age (Slaughter and Griffiths 2007). In this respect, research has demonstrated that children acquire the ability to differentiate between pictures of faces that differ in age from early infancy (Lasky et al. 1974), and can systematically use age labels by the age of three (Montepare and McArthur 1986). However, as stated by Levy and Hughes (2009), this approach may be suited for understanding the underlying mechanisms of negative attitudes, whereas social learning theory or cognitive-developmental models are more relevant for the specific aspects of negative attitudes.

Key Research Findings

In order to evaluate the current knowledge regarding children's attitudes toward older adults, two main issues need to be addressed: First, ageism is a multidimensional phenomenon, and it is therefore essential to examine different aspects of ageist attitudes. Second, ageism can be examined both directly (i.e., explicitly) or indirectly (i.e., implicitly), and consequently, it is important to take into account the manner by which attitudes are assessed (see Bergman 2017; Mendonça et al. 2018).

While initial evidence demonstrates that views of older adults and aging become more positive as children grow older, the results are often inconsistent. One of the main sources of this discrepancy stems from the fact that children's appraisal of older adults can be assessed through cognitive features (i.e., how they conceive older adults and old age), affective features (i.e., how they feel about them), and behavioral features (i.e., how they respond to them; see also Eagly and Chaiken 2007). The cognitive dimension was mostly examined through direct questionnaires and measures, and findings indicate that younger children show increased negative bias in comparison with older children (Haught et al. 1999). Moreover, this negative bias increases from younger ages until school age, where it remains stable (Isaacs and Bearison 1986). The affective dimension is usually explored through semantic differential scales, and the results demonstrate that younger children tend to see their own aging process adversely and ascribe negative feelings to being old (Jantz et al. 1977; Newman et al. 1997). This trend was also found when implicit measures, such as children's drawings of older adults, were employed, as younger children associated being old with loneliness and physical deterioration (Falchikov 1990). It should be noted, however, that some studies report a more balanced view of older adults (Villar and Fabà 2012), and when children were asked to draw a picture of a familiar older adult, their depictions were mostly positive (Robinson et al. 2014). The few available behavioral assessments indicate that young children react more negatively to older adults in experimental settings when compared with younger adults, and judge them as less competent (Isaacs and Bearison 1986; Kwong See et al. 2012).

Examples of Application

When examining possible applications for reducing negative attitudes, the importance of intergenerational contact cannot be underestimated. Frequent contact with older adults enables children to see aging and older adults in a more realistic manner, thereby assisting them in reducing the stereotypical perception of older adults as "warm and incompetent," as suggested by the stereotype content model (Cuddy and Fiske 2004; Cuddy et al. 2005). In the last decade, many intergenerational programs in the United States, aimed at reducing stereotypes through contact, have been established. While these programs vary greatly in duration, content, and aims (see Bishop and Moxley 2012), most include direct contact between children and older adults, and focus on what the two groups may offer each other (e.g., sharing life stories; see Gaggioli et al. 2014). Others, however, focus on indirect learning and concentrate on information regarding older adults and the aging process. While findings concerning the outcome of direct intergenerational contact are inconclusive among younger children, the majority of studies report that such contact reduces negative attitudes among schoolchildren (see review by Bergman 2017), provided that the contact is in line with the tenets of intergroup contact theory (see Pettigrew 1998). It should be noted that such encounters may be generalized to a much wider range of cognitive abilities (Fair and Delaplane 2015), and may influence not only the child's attitudes, but his/her family as well (Garcia Biggs and Knox 2014).

With regard to indirect contact and learning, school curricula aimed at providing accurate information about older adults and aging were associated with an improvement in middle schoolers' perception of both (Lichtenstein et al. 2001). Interestingly, it seems that among younger children, prior negative information and knowledge (even if incorrect) may hinder the positive effects of the contact, whereas this effect did not occur in older children (Kang and Inzlicht 2012). In this regard, it may be useful to review constructs from school programs designed for promoting multiculturalism (see Banks 2016), and examine their applicability for reducing ageism by providing accurate information regarding older adults and the aging process. It should be noted that an intervention program which takes into account the two aspects of contact and learning was recently proposed by Levy (2016), who suggested that education with regard to the aging process, combined with contact with a positive older role model, could be beneficial in reducing age-related stereotypes, and it is important to examine the applicability of this interactive model among children.

Future Directions of Research

While research on children's perceptions of older adults and aging has gained momentum in the recent years, there are several issues which remain unclear. First, many of the scales used to examine such attitudes are problematic (see Mendonça et al. 2018), and there is a need for a valid and reliable instrument which assesses the various aspects of ageism in a clear and age-appropriate manner. Second, there seems to be a strong connection between ageism and sexism in children, to the point that laboratory studies on ageism prefer to use a female target (i.e., an older woman) in order to maximize the effect of the experimental manipulation (e.g., Kwong See et al. 2012). As the preference for older men versus older women has been observed in very early ages (Seefeldt et al. 1977), it is important to examine further how and why children tend to foster a view of the "wise old man" versus the "wicked old witch" (Bergman 2017). Third, there is little doubt that the processes of acquiring negative age attitudes on the one hand and altering them upon exposure to various stimuli on the other hand require cognitive, social, and psychological abilities, which gradually develop throughout childhood and adolescence. Accordingly, it is important that future research will focus not only on the child's age and attitudes, but on his/her psychological skills and capabilities in reference to his/her age. Fourth, research has mainly focused on younger children, and more information is needed with regard to the depth and constancy of ageist attitudes among adolescents. Fifth, as noted by Levy and MacDonald (2016) in their review, research has mostly focused on the negative aspects of ageist stereotypes. However, there seems to be a fine line between the negative aspects of ageism, described here, and more positive aspects of these attitudes (e.g., offering one's seat on the bus to an older person), and it is important to examine the manner by which both paths are internalized and manifested among children. Finally, while intergenerational contact programs have mostly demonstrated a positive change in attitudes, it is still unclear whether this change is short-lived or long-lasting, and there is an urgent need for longitudinal designs which will examine this issue, as well as the other issues raised in this section.

Summary

The formulation of negative perceptions of aging and older adults is, without a doubt, a complex phenomenon, which gains strength from a myriad of biological, social, and cultural factors. This process can be seen through the prism of various theoretical accounts, but regardless of one's theoretical stance, it seems that the child's experiences play an important role in determining how he/she will perceive old age and older adults. While research points to a certain trajectory in the development of negative attitudes in this regard, there are several ways in which individuals, professionals, and society can intervene in order to provide children with accurate information which will allow them to develop a more positive view of their own aging process and of older adults.

Cross-References

▶ Age Stereotypes
▶ Ageism in the Family
▶ Aging in Children's Literature
▶ Intergenerational Programs on Anti-ageism
▶ Prosocial Behavior
▶ Racism and Ageism
▶ Reducing Ageism
▶ Sexism and Ageism

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China Health and Nutrition Survey, 1989–2019

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Overview

The China Health and Nutrition Survey (CHNS) is an ongoing, open-cohort, international collaborative project between the Carolina Population Center at the University of North Carolina at Chapel Hill (UNC-CH) and the National Institute for Nutrition and Health (NINH) at the Chinese Center for Disease Control and Prevention (CCDC). In 1979, China opened up its economic and social systems and implemented major land, social, and economic reforms. The country's economy and agricultural productivity changed greatly after this time, with remarkable shifts in diet, activity, and body composition; however, no studies documented these changes or examined the ways economic and social change affected a range of health behaviors in this large country. To fill this gap, Dr. Barry M. Popkin initiated this study with two colleagues – Dr. Gail Henderson and Dr. John S. Akin, who no longer work with the CHNS – and chose to collaborate with the CCDC (formerly the Chinese Academy of Preventive Medicine), under the leadership of Dr. Chunming Chen (who passed away in 2018), Dr. Keyou Ge, and Dr. Fengying Zhai (Popkin et al. 2010). Currently, Dr. Barry M. Popkin and Dr. Penny Gordon-Larsen lead the UNC-CH team, and Dr. Bing Zhang, Dr. Gangqiang Ding, and Dr. Huijun Wang lead the CCDC team.

The CHNS was approved by institutional review boards from UNC-CH, NINH, and CCDC. Each CHNS participant provided oral consent before 2006 and written, informed consent thereafter. Further information on survey procedures and the rationale of the CHNS can be found in the cohort profile (Popkin et al. 2010; Zhang et al. 2014) or at http://www.cpc.unc.edu/projects/china.

Project Goals

The CHNS was designed to document the changes in health, nutrition, and family planning policies and programs implemented by national and local governments in China and to examine how the social and economic transformation of Chinese society is affecting the health and nutritional status of its population across the life cycle. This in-depth survey collects detailed data on (a) cognitive and physical function (e.g., memory, counting, orientation, activities of daily living [ADL], and instrumental activities of daily living [IADL]); (b) in-depth health-related behaviors (e.g., dietary intake, physical activity, time use, and tobacco and alcohol use); (c) mental health and well-being (e.g., stress, sleep, quality of life, and self-rated health); (d) physical health (e.g., anthropometry and blood pressure); and (e) detailed individual, community environment, and sociodemographic data (e.g., urbanization, household size and composition, intergenerational transfers, and assets). The 2009 and 2015 surveys included biomarkers from fasting blood, toenails, and genome-wide association data, and the 2015 and 2019 surveys included microbiome and metabolome data. The lengthy time span of coverage and geographic scope provides substantial temporal and spatial variability, capturing extraordinarily rapid modernization- and environment-related changes in individual, household, and community environments across the past 30 years.

China is unique globally. It is aging more rapidly than any country has in world history. In 30 years, it has transitioned from a society dominated by poverty, undernutrition, and infectious diseases to one where geriatric conditions and noncommunicable diseases are prevalent. The CHNS captures major events from 1989 to 2019, including numerous changes in family planning and welfare schemes (Short et al. 2001; Short and Foster 2003); aging and shifts in population age distribution, health, and health care (Blumenthal and Hsiao 2005; Caprio 2012); the introduction of the free market for food, entry into the World Trade Organization, and concomitant structural changes in tariffs; the increased modernization of the Chinese food system; continued dissemination of modern technology in manufacturing, transportation, and leisure; housing, health system, and educational system changes; new pressures on labor, environment, and social systems; and recent trade wars (Bhattasali et al. 2004). Social, economic, and health consequences of these events continue to emerge and have also been documented with the CHNS from 1989 through 2019.

One of the most important and unique features of the CHNS is that from its inception it was created as a publicly available data set that scholars from across the globe could obtain for free. The CHNS was the first large-scale survey data created in such a fashion with individual-, household-, and community-level data in China.

Study Design and Features

The CHNS was designed to capture a range of economic and demographic circumstances and to provide data from randomly selected households in eight provinces that vary substantially in geography, economic development, public resources, and health indicators, including Liaoning, Shandong, Henan, Jiangsu, Hubei, Hunan, Guizhou, and Guangxi (from north to south). It was not designed to be representative of the country because data to create a national representative sample were not available when the study was initiated in 1988. The original survey in 1989 used a multistage, random cluster design to draw a representative sample in each of the eight provinces. Using this sampling strategy, two cities (one large – usually the provincial capital, and one smaller – lower income city) and four counties (stratified by income: one high-, one low-, and two middle-income counties) were randomly selected. Within cities, two urban and two suburban communities were randomly selected; within counties, one community in the capital city and three rural villages were randomly chosen. Twenty households per community were then randomly selected for participation. In 1989, only children younger than 5 years and young adults aged 20–45 years were invited to participate, but since 1991 all household members have been invited.

From 1993 onward, all new household members and new households derived from the original households were also added. In 1997, Heilongjiang province was added because Liaoning was unable to participate (Liaoning was added back in 2000). New households and communities were added to replace those lost due to urban reconstruction and natural disasters (flood and earthquake) thereafter. In 2011, the three largest municipal cities (Beijing, Shanghai, and Chongqing) were added. In 2015, three new provinces (Shaanxi, Yunnan, and Zhejiang) were fully funded by the Chinese government to participate. By the time of the most recently completed survey in 2015, the CHNS included 15 primary sampling units (province/autonomous city) and 360 secondary sampling units (community), incorporating 60 urban neighborhoods, 60 suburban neighborhoods, 60 county capitals, and 180 villages, with 42,829 individuals from 11,130 households participating. The CHNS cohort initially mirrored national age, gender, and education profiles, and by 2018, the provinces included in the CHNS sample constituted about 60% of China's population (according to the 2010 census).

China Health and Nutrition Survey, 1989–2019, Table 1 Response rates (%) in the China Health and Nutrition Survey, 1989–2015

	1989	1991	1993	1997	2000	2004	2006	2009	2011	2015
Community										
N	180	189	181	191	215	216	218	217	289	360
Response rate		99.4	95.8	82.3	96.9	98.1	99.1	98.6	99.1	97.9
Household										
N	3,795	3,619	3,456	3,875	4,396	4,387	4,467	4,517	5,923	7,319
Response rate		95.3	93.6	78.5	89.2	85.7	89.7	83.7	89.6	77.2
Individual										
N	15,907	14,797	13,895	14,441	15,831	12,308	11,860	12,178	15,725	20,914
Response rate		88.1	88.2	71.5	84.0	63.7	75.7	72.4	75.8	68.7

The CHNS has collected data in 1989, 1991, 1993, 1997, 2000, 2004, 2006, 2009, 2011, 2015, and 2018–2019 (underway). Given that new provinces and autonomous cities and households have been added and participants who left may have returned in later years, determining response rates or attrition is complex. If response rate is defined as those who participated in previous surveys remaining in the current survey, the response rates were 97.9% at community level, 77.2% at household level, and 68.7% at individual level in 2015. Details are presented in Table 1.

There have been several major causes of loss to follow-up. The first was urban reconstruction and natural disasters. The Chinese government pledged more than 10 trillion yuan (approximately $1.4 trillion) to tackle the Asian financial crisis in late 1998 and the international financial crisis in 2008. One of this major spending was redevelopment of housing and relocation in all large urban areas. Historical flooding in 1997 affected more than 25% of our rural sample and destroyed many villages. The second cause of loss to follow-up was schoolchildren attending boarding schools or entering universities and colleges. The third cause was young and middle-aged adults seeking employment out of their provinces. Because of funding limitations, CHNS was unable to follow participants who moved out of their original communities. Last, a few people rejected or failed to participate because of travel or hours of work (Zhang et al. 2014).

Major Findings

The CHNS has been used for an array of research across dozens of disciplines and journals. Below are a few examples of recent research related to chronic disease.

Dietary and lifestyle change in China. Since 2004, there has been a marked change in the dietary behavior of Chinese children and young adults. Snacking tripled from 2004 to 2006 and again from 2006 to 2009. There has been a concomitant increase in the proportion of foods consumed from traditional to modern, highly processed foods. CHNS data showed 20-year increases in key indicators of the Western diet, animal-source foods, and edible oils; declines in coarse grains and vegetables; shifts from steaming to frying; and more away-from-home eating. The majority of these dietary changes resulted in declines in the intake of antioxidants and anti-inflammatory nutrients and increases in pro-inflammatory nutrients, all of which are associated with severe dementias. Similar shifts have occurred in all aspects of activity: transportation movement, occupational activity, leisure activity, and home production. Given the intergenerational households, grandparents may serve as caregivers, which may be protective against cognitive decline. Yet the demographic shifts that have led the younger generation to out-migrate in search of work have, in many cases, left older adults behind, which have detrimental cognitive and physical health effects (Wang et al. 2012; Xie et al. 2014).

Urbanization and health outcomes. There is considerable geographic and temporal variation in timing of urbanization and development in China. Classification of places as either urban or rural is typically based on an absolute threshold of population and/or population density. However, conceptual definitions of urbanization and urban city encompass dimensions beyond just population size and population density. The crude classification of places as urban or rural coupled with infrequent updates to this information create a measure that is prone to misclassification error. Therefore, 12 components were identified and used to develop a validated multidimensional measure of urbanization that would capture a number of critical domains that represent modernization and urbanization. Because the scale was constructed and tested using established scaling procedures and a wide array of variables, it represents an improvement over previous attempts at such a scale and will provide a reliable and valid measurement tool for researchers in this arena (Jones-Smith and Popkin 2011).

Cardiometabolic risk in China. Prevalence of diabetes and inflammation in China exceeds that of the United States. Of adolescents 12–18 years of age, 1.9% have diabetes, compared to 0.5% in the United States. Similarly, Chinese males have higher inflammatory risk than US males (12.1% vs. 8.5%). Among adults, the CHNS 2009 data suggest that 82.1 million Chinese adults have diabetes and 334 million are prediabetic as measured by HbA1c. Approximately 42% of children have at least one of the following: prediabetes or diabetes, hypertension, dyslipidemia, and inflammation; 70% of males and 60% of females aged 18–40 years and more than 86% of males and females above 40 years have at least one of these conditions. For the vast majority, these cases represent untreated diabetes, hypertension, and dyslipidemia (Yan et al. 2012; Gordon-Larsen et al. 2014). CHNS diet measures strongly predict cardiometabolic risk in China. While there is strong evidence tying cardiometabolic risk factors to severe dementias, hypertension (particularly systolic blood pressure) is of critical relevance (Dong et al. 2017).

Sodium intake and hypertension. CHNS data show a more than tripling of hypertension prevalence, from 10.3% in 1991 to 33.6% in 2015. The major addition to knowledge is the large array of different patterns and trends across urban and rural China by education–income class and between the north, south, and central provinces. In the past, all focus has been on interventions in northern China; however, these results will redirect provincial pilot studies and interventions to central China where this study has demonstrated high intakes of sodium and a high sodium-to-potassium ratio. This study revealed that strategies to decrease sodium intake and increase potassium intake in China should be different from those used in the Western world. Furthermore, CHNS data show the need for different strategies to reduce sodium intake in urban and rural areas. Based on the results from this study, the US Centers for Disease Control and Prevention and the Chinese government jointly funded a large-scale sodium reduction intervention study in China, covering more than 200 million people (Du et al. 2014).

Cognitive decline in China. Although the prevalence of disability in basic ADLs among Chinese older adults is decreasing and stroke and multiple cardiometabolic diseases appear to become less disabling over time (Liang et al. 2015), cognitive impairment and decline is considerably increasing with age. CHNS data show blood pressure variability associated with faster cognitive decline (Qin et al. 2016), and fish intake (Qin et al. 2014) and the adapted Mediterranean diet (Qin et al. 2015) with a slower rate of cognitive decline.

Future Plans

CHNS team will continue to seek funding to add new rounds of CHNS data, including dissemination of all raw data and associated metadata. New executive function, sensory, and biomarker measures are proposed in the next survey. It is anticipated that the multipurpose resource will enable innumerable future studies, including additional social and demographic studies to address any range of outcomes. The stored blood and toenails will allow other studies on any variety of multiomics topics. The findings will shed light on understanding the intersection of genetics, cardiometabolic risk, demographic trends, obesity, lifestyle behaviors, mental health, and cognitive decline, which is critically needed to reduce the major burden of mild cognitive impairment, Alzheimer's disease, and other dimensions.

Summary

The CHNS study design allows for multilevel investigations on a wide variety of topics.

The CHNS is the largest and most complete study with extensive, detailed, quality individual, household, and community environmental data along with biomarker, gut microbiome, and metabolome data. Rapid environmental changes, demographic shifts, and the burden of cardiometabolic diseases have increased exponentially in China, providing a unique model for examining the development of risk. The biomarker, microbiome, metabolomics, genetic, and environmental data open new areas of study for this major longitudinal study in the world's most populated country and in this unique model of environmental change. The wide age range, geographic diversity, and different patterns and pace of change across CHNS communities allow the exploitation of individual, age, and gender differences in patterns of clustering of risk factors, which vary greatly in China and thus may offer important clues about etiology.

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China Health and Retirement Longitudinal Study (CHARLS)

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Overview

The importance of research on aging is recognized worldwide, where numerous high-quality surveys modeled after the US Health and Retirement Survey (HRS) are ongoing. With the largest aging population in the world, China is experiencing one of the highest aging rates in the world today. It is projected that the proportion of those aged 65 or over will increase from 7% of the population in 2010 to 26% in 2050, whereas the old-age support ratio (the number of prime-age adults aged 15–64 divided by the number of adults aged 65 or above) will drop from about 9.9:1 in 2010 to 2.3:1 in 2050 (United Nations 2017).

Related to the aging process, China has been undergoing a rapid health transition in which the nature of health problems changes from infectious diseases which affect mainly the young to chronic diseases which affect the older people (Yang et al. 2013). Moreover, China is undergoing the aging process at much lower income levels than was the experience in industrial countries. Compared to most other countries with Health and Retirement Studies, China is much more rural, with lower levels of schooling among the older people, lower levels of public services available, and an enhanced importance of the family for social security. Given these major challenges facing China to meet the needs of a rapidly aging population, there is significant value in collecting a high-quality panel data set on aging available to researchers.

Prior to CHARLS's baseline survey implemented in 2011–2012, scientific studies of China's aging-related issues were at an early stage, the greatest obstacle being a lack of sufficient micro-longitudinal data. The existing data tended to be small scale in parts of China, not collecting the breadth of data necessary for good social scientific analysis of health and retirement of the older population. CHARLS is the first nationally representative longitudinal survey of the older population that enables the study of health, retirement, and intergenerational support of the older population in China patterned after US Health and Retirement Study (HRS) and related aging surveys around the world (e.g., the English Longitudinal Survey of Aging (ELSA) and the Survey of Health, Aging, and Retirement in Europe (SHARE), Japanese Study of Aging and Retirement (JSTAR), the Longitudinal Aging Survey of India (LASI), the Indonesia Family Life Survey (IFLS), the Korean Longitudinal Survey of Aging (KLoSA), etc.).

Study Design

CHARLS is a longitudinal survey that aims to be representative of the residents in mainland China aged 45 and older, with no upper age limit. The national baseline survey was conducted in 2011–2012, with wave 2 in 2013, wave 3 in 2015, and wave 4 in 2018.

Baseline Sampling

CHARLS's baseline survey includes one person per household aged 45 years of age or older and their spouse, totaling 17,708 individuals, living in 10,257 households in 450 villages/urban communities (see Table 1, Zhao et al. 2013a). A stratified (by per capita GDP of urban districts and rural counties) multistage (county/district-village/community-household) PPS random sampling strategy was adopted.

At the first stage, all county-level units were sorted (stratified) by region, within region by urban district or rural county, and by GDP per capita (Tibet was the only province not included). Region was a categorical variable based on the NBS division of province area. After this sorting (stratification), 150 counties or urban districts were chosen with probability proportional to population size (Zhao et al. 2013a). For each county-level unit, three PSUs (villages and urban neighborhoods) are randomly chosen with probability proportional to population (see Zhao et al. 2013a). Hence CHARLS is nationally representative of both rural and urban areas within China. Counties and districts in 28 provinces are included in the CHARLS sample.

In light of the outdated household listings at the village/community level due to population migration, CHARLS designed a mapping/listing software (Charls-GIS) that makes use of Google Earth map images to list all dwelling units in all residential buildings to create sampling frames.

In each sampled household, a short screening form was used to identify whether the household had a member meeting the age eligibility requirements. If a household had persons older than 41 and meeting the residence criterion, one of them will be randomly selected. If the chosen person is 45 or older, then he/she became a main respondent, and his or her spouse was interviewed. If the chosen person was between ages 41 and 44, he/she was reserved for refresher samples for future waves. In wave 2, respondents who were aged 43–44 in wave 1 (plus their spouses) were added from the refresher sample, the same for waves 3 in 2015, out of those aged 41–42 in wave 1.

After applying sampling weights created using the sampling procedure, the CHARLS baseline sample demographics mimics very closely that of population census in 2010 (Zhao et al. 2014).

Interviewing and Tracking Protocol

In the baseline survey, 2 interviewers were sent to each county to interview about 72 households located in 3 communities. In waves 2, 3, and 4, one team consisting of six to eight interviewers was sent to six villages/communities in two counties. The interviewers were trained at Peking University by CHARLS staff members, and the interviews took place in respondents' homes with the use of CAPI technology. CHARLS respondents were followed through a face-to-face CAPI interview in 2013, 2015, and 2018.

Main respondents and their spouses in the baseline survey are tracked if they exit the original household. They are followed throughout the life of CHARLS or until they die. If a main respondent or spouse remarries, the new spouse is interviewed so long as they are still married to the baseline respondent at the time of the specific wave. Exit interviews were conducted on respondents who died between waves, including verbal autopsies using the 2012 version from the World Health Organization.

For respondents in the baseline, more than 90% of them were recontacted in each of the follow-up waves. In addition, we did not give up the households or individuals that we could not find in the baseline and contacted them in follow-up waves, so are respondents who failed to respond in any one or more waves.

Households or individuals who move away from original sample villages/communities are tracked. Counting refresher samples and age-eligible respondents who failed to be found in the baseline but successfully contacted in the follow-up waves, the total number of individuals (main respondents plus spouses) has increased from 17,708 in wave 1 to 19,817 in wave 4 (Table 1).

Table 1 describes the age/sex composition of the CHARLS sample. We have data on 17,708 individuals in the national baseline sample, of which 52.1% are female. While most of the sample are the younger old, 40% are aged 60 years and older.

Response Rates

The response rate for the baseline survey was 80.5% (94% in rural areas and 69% in urban

China Health and Retirement Longitudinal Study (CHARLS), Table 1 Number and age/sex structure of individuals: 2011–2018

	Baseline, 2011			Wave 2, 2013			Wave 3, 2015			Wave 4, 2018		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
–44	483	74	409	435	76	359	718	137	581	255	31	224
45–49	3,575	1,643	1,932	3,153	1,398	1,755	3,175	1,503	1,672	1,960	820	1,140
50–54	2,707	1,310	1,397	2,827	1,348	1,479	3,551	1,694	1,857	3,500	1,664	1,836
55–59	3,520	1,721	1,799	3,406	1,655	1,751	3,095	1,532	1,563	3,045	1,429	1,616
60–64	2,823	1,432	1,391	3,152	1,581	1,571	3,594	1,723	1,871	3,375	1,665	1,710
65–69	1,836	928	908	2,084	1,051	1,033	2,537	1,297	1,240	3,162	1,512	1,650
70–74	1,291	681	610	1,466	756	710	1,679	823	856	1,997	1,003	994
75–79	850	427	423	981	511	470	1,083	577	506	1,330	656	674
80+	612	260	352	750	331	419	841	368	473	1,192	560	632
Obs.	17,697	8,476	9,221	18,254	8,707	9,547	20,273	9,654	10,619	19,816	9,340	10,476

Note: There are 11 individuals in 2011, 10 individuals in 2013, and 11 individuals in 2015 lacking age information areas, lower in urban areas as is common in most surveys undertaken in developing countries; Zhao et al. 2013a). A description of the sample and response rates in waves 2, 3, and 4 are provided in Table 2.

The response rate of the tracked sample (panel sample) remains at higher than 86% in any of the follow-up waves. Specifically, among those respondents which were interviewed in the baseline survey, about 88% of them completed at least one module in wave 2 in 2013 (92% in rural areas and 83% in urban areas). In waves 3 and 4, about 87% and 86% of the tracked respondents completed at least one module (Table 2).

Content

Core Interview Topics of the Household Survey

The core survey of CHARLS consists of the following sections: (1) demographics; (2) family structure/transfer; (3) health; (4) health insurance and healthcare utilization; (5) work, retirement, and pension; (6) relative income; (7) family income, wealth, and expenditures; (8) personal income and assets; and (9) housing characteristics.

In addition to the wealth of individual social, economic, and behavioral data, CHARLS is characterized with the rich information in the respondent's health. The section of health begins with the self-reports, including the respondent's self-assessment of general health, questions asking about diagnoses by doctors of a set of chronic diseases; questions about eyesight, hearing, and dental health; questions on hedonic well-being; and questions on activities of daily living (ADLs), instrumental activities of daily living (IADLs), and physical functioning. Sections on depressive symptoms and cognition follow. Furthermore, information is collected on several health behaviors. These include detailed information on smoking, drinking, and physical activities.

Biomarkers

Following ELSA and HRS, detailed biomarkers, both blood and non-blood, were collected. Non-blood biomarkers such as anthropometrics and blood pressure were collected in waves 1, 2, and 3. Venous blood biomarkers were collected in waves 1 and 3.

In CHARLS data are collected on height, lower leg and upper arm lengths (useful to get measures related to height not contaminated by shrinkage), waist circumference, blood pressure (measured three times), grip strength (measured by a dynamometer twice for each hand), lung capacity measured by a peak flow meter, and a timed sit to stand (five times starting from a full sit position on a common, plastic stool). We also conduct balance tests and a timed walk at normal speed for 2.5 meters.

In addition, we have collected venous blood samples and assayed them for high-sensitivity C-reactive protein (hsCRP), glycated hemoglobin (HbA1c), total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, glucose, blood urea nitrogen (BUN), creatinine, uric acid, and cystatin C. A complete blood count (CBC) analysis was done at local county health centers, including hemoglobin, hematocrit, white blood cell count, platelet counts, and mean corpuscular volume. The first blood collection of CHARLS was conducted in the baseline survey from 2011 to 2012, and we collected blood samples for 11,847 individuals. The second follow-up wave of blood collection was done in wave 3 (2015), and we collected blood samples for 13,013 individuals.

Auxiliary Data

Life Histories

A special wave to collect life histories was fielded in 2014. Life histories can greatly add to aging surveys because they help to fill in very important details regarding earlier periods in the respondent's life that are germane to understanding outcomes when older. Ways to minimize recall error have been greatly improved primarily through the use of calendars that are anchored to key lifetime or calendar events (both national events, like the Cultural Revolution, and local, like a

China Health and Retirement Longitudinal Study (CHARLS), Table 2 Response rates: 2011–2018

		Baseline, 2011–2012[a]	Wave 2, 2013		Wave 3, 2015		Wave 4, 2018	
			Cross section[b]	Panel[c]	Cross section[a]	Panel[b]	Cross section[a]	Panel[b]
Response rate (%)	Total	80.51	82.63	88.30	82.13	87.15	83.84	86.46
	Rural	94.15	91.74	92.18	91.32	93.13	91.40	92.79
	Urban	68.63	72.20	82.61	71.64	78.45	74.55	77.24
No. of households	Total	10,257	10,629	9,022	11,797	8,715	12,012	8,288
	Rural	6,033	6,340	5,547	6,993	5,483	7,169	5,226
	Urban	4,224	4,289	3,475	4,804	3,232	4,843	3,062
No. of respondents	Total	17,708	18,264	15,196	20,284	14,522	19,816	13,567
	Rural	10,537	10,950	9,439	12,075	9,200	11,811	8,622
	Urban	7,171	7,314	5,757	8,209	5,322	8,005	4,945

[a]The response rate in the baseline is computed as the number of households which completed at least one main module divided by the number of implied age eligible households
[b]The cross-sectional response rate in the follow-up waves (2013, 2015, and 2018) is computed in the same way as that in the baseline
[c]The panel response rate in the follow-up waves (2013, 2015, and 2018) is computed as the percentage of baseline wave respondents who completed at least one main module in the current wave or died

major flood) that are salient to respondents' memory. Such calendars have been developed.

The CHARLS life histories are developed using the ELSA and SHARE life histories as a base. The CHARLS life history includes retrospectives on domains that cover family background when the respondent was a child, child health and health care, work and retirement, marriage, childbirths, and migration. Some retrospective information on income, wealth, and poverty status when young, and schooling is collected. Some special history issues germane to China are also included, such as experiences during the Cultural Revolution, the Great Famine, and local events such as a major local flood.

In 2014, 20,547 respondents (including both the age eligible samples and refresher samples in the baseline) in 12,250 households were interviewed.

CHARLS HCAP

CHARLS HCAP was implemented in wave 4 (2018) in order to assess dementia and mild cognitive impairment among the CHARLS respondents aged 60 and older. As a first step, a validation study was done in 2017 when a formal sample was collected from which all of the HRS HCAP tests and doctor diagnosis were conducted. From these data a statistical model was built to use interview tests to predict dementia and CIND. As a result of this study, in wave 4 the following tests were selected for the respondents: they are the Mini-Mental State Examination (MMSE), the HRS TICS questions not in MMSE, the CERAD version of immediate word recall and delayed word recall, animal naming, word list recognition, and the brief CSI-D. An informant interview to a person who knew the respondent well was also administered, in which we used the Jorm IQCODE, the Blessed Part 2, and the CSI-D informant interview.

In wave 4 (2018), 11,021 CHARLS respondents and spouses both of whom aged 60 and older were contacted. Out of these, 10,133 completed the tests and had informant interviews completed; another 965 had informant interviews but could not do any tests.

Key Findings

With more and more publications using CHARLS data, CHARLS has greatly enriched the international landscape of aging studies. With the national representative longitudinal data, the prevalence rates are of interest, and the change of these rates could also be tracked.

With rapid aging process, China has been undergoing a rapid health transition from infectious to chronic diseases. The CHARLS wave 3 (2015) data show that the hypertension prevalence rate for the 60+ people in China was 54% in 2015. Some 33% have high levels of depressive symptoms, defined by a score of 10 or more on the 10 question version of the CES-D index. In general, older women have worse non-blood health outcomes than men, as found in most other countries (Zhao et al. 2019).

Prevalence of chronic conditions remains at high levels: the CHARLS wave 3 data show that 38% of Chinese people 60 and older suffer from disabilities, defined as having a problem with at least one ADL or IADL, and 23% in 2015 need help with at least one ADL or IADL. In 2015 some 31% of these people report suffering at least some bodily pain (Zhao et al. 2019).

The CHARLS data show that socioeconomic conditions (education, rural-urban registration, per capita expenditure) are positively associated with many dimensions of health outcomes, including cognition. CHARLS reveals large sex-related differences in cognition to the disadvantage of women (Lei et al. 2014a, b; Huang et al. 2013), with the large sex-related gap in education being the primary reason for this. These sex-related disparities are eliminated in younger cohorts. There is strong transmission of childhood health status into adulthood (Smith et al. 2012).

CHARLS measures the height as well as limb lengths (lower leg and upper arm). This enables the study of height shrinkage among older people. Huang et al. (2013) use younger cohort (aged 45–49) to establish the relationship between measured height and limb lengths and estimate height shrinkage for respondents 60 and over. They find a mean shrinkage of 3.3 cm for men and 3.8 cm for women. They also find a strong negative association between height shrinkage and socioeconomic factors such as education, rural residence, and current household per capita expenditure.

Biomarkers along with reports of doctor diagnoses can also help to document and analyze patterns of undiagnosed disease, a very important issue in the Chinese context. As one example, the CHARLS national baseline data show that among hypertensive respondents, those measured as hypertensive or who have been diagnosed by a doctor, 44% of those with rural hukou and 30% of those with urban hukou are not diagnosed (Zhao et al. 2013b).

Public support of the older people through social security has been traditionally very low in China, particularly among those with rural hukou. Mainly due to expansion of the new rural pension program (NRPP), the CHARLS data shows that China's pension coverage has expanded greatly from 48% in 2011 to nearly universal in 2015. Despite the high coverage rate, there exists great disparity in benefits across different pension programs. The new rural pension system (NRPS) benefit is less than 1/30 of government and institutions' pension (Zhao et al. 2019). Furthermore, the gender pension gap and its underlying causes are investigated by Zhao and Zhao (2018). Their results show that women's pensions are substantially lower than men's and much of the gender pension gap can be explained by gender differences in employment and earnings, which suggest that the large gender gap observed in the labor market has translated into an even larger income gap at older ages under the current pension program.

Future Plans

Waves 5 and 6 are scheduled to be implemented in 2021 and 2024.

Innovations

CHARLS has been innovative in several dimensions. Sampling selection methodology is one of the examples.

CHARLS is unique in using mapping operation to construct household sampling frames at the primary sampling unit (PSU) stage (Zhao et al. 2013a). In each PSU, we selected a sample of dwellings from our frame, which was constructed based on maps prepared by mappers/listers with the support of local informants. In order to get an accurate sample frame of households in each village or community, a mapping/listing software named CHARLS-GIS was developed.

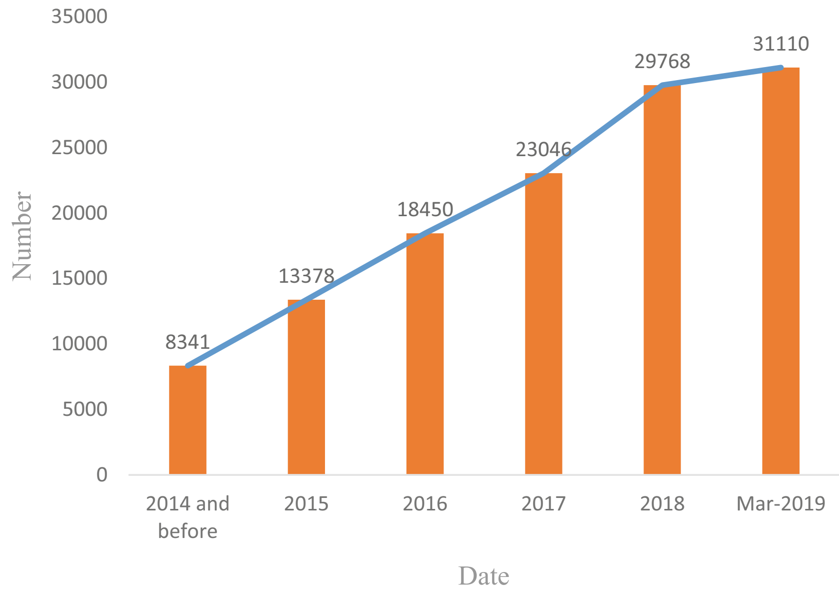
For each PSU, a mapper was first sent to the community with a GPS unit to collect the boundary, and then the CHARLS office used the boundary information to capture Google Earth map images, which were used as the basis for the mapping and listing. Then, all buildings in each PSU were enumerated with photos and GPS readings, and dwellings within each building were listed, which provided detailed information for the interviewers to find the exact dwelling after it was randomly selected.

By using mapping instead of roster listing which was more commonly used in other surveys in China, CHARLS has well reduced the sampling error in coverage in areas where there was lots of frequent migration.

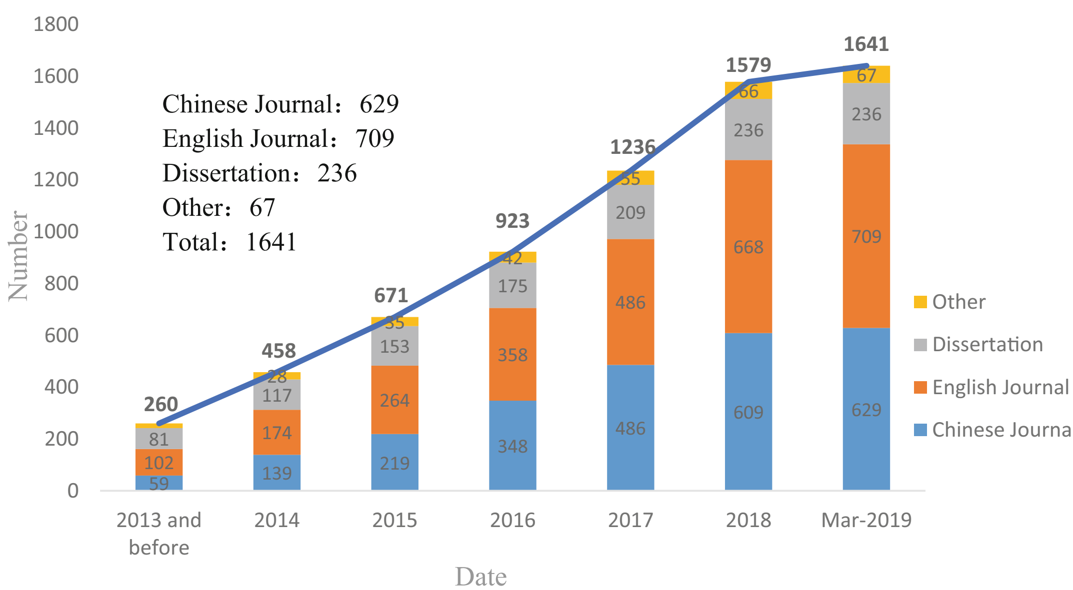
Data Access

All data collected in CHARLS are maintained at the Institute of Social Science Survey of Peking University, Beijing, China. Following the completion of data cleaning, construction of weights, and creation of a user's guide and codebook for the study data, all of the data will be accessible to researchers around the world at the CHARLS project website (http://charls.pku.edu.cn/en). Currently, the 2008 pilot survey data, national baseline data, wave 2, wave 3, and life history data are all available on the project website.

To date, more than 31,000 users, including about 11% from outside of China, have downloaded the released data, and the number of users has been increasing at an increasing rate (Fig. 1).



China Health and Retirement Longitudinal Study (CHARLS), Fig. 1 Cumulative number of CHARLS users



China Health and Retirement Longitudinal Study (CHARLS), Fig. 2 Cumulative number of CHARLS publications

Accordingly, due to the high quality of the data, more than 1600 papers using CHARLS data have been published; more than 40% of them are published in international journals (Fig. 2). And a higher scientific payoff is expected when CHARLS continues to be an ongoing, longitudinal survey to give researchers the advantages of longer panels.

Cross-References

▶ Indonesia Family Life Survey
▶ Longitudinal Aging Study in India

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China's Birth Control Policy

▶ One-Child Policy and Population Aging in China

China's Family-Planning Policy

▶ One-Child Policy and Population Aging in China

Chinese Healthy Longevity Survey

▶ Chinese Longitudinal Healthy Longevity Survey (CLHLS)

C

Chinese Longitudinal Healthy Longevity Survey (CLHLS)

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Synonyms

Chinese healthy longevity survey; Chinese survey of determinants of healthy longevity; Health and longevity survey of Chinese older adults

Overview

The Chinese Longitudinal Healthy Longevity Survey (CLHLS) is a nationwide ongoing survey focusing on older adults in mainland China (hereafter China). It aims to: (1) investigate the social, behavioral, environmental, and genetic factors and their interactions that may influence healthy longevity; (2) fill in the data gap for academic research and gain a better understanding of demographic and socioeconomic conditions, as well as of health status and care needs of the older populations in mainland China; and (3) provide a scientific basis for sound policymaking and implementation so as to improve the quality of life of Chinese older adults. The principal investigator is Professor Yi Zeng, and the CLHLS has been supported by the National Institute on Aging (NIA), the National Natural Science and Social Sciences Foundations of China, United Nations Population Fund (UNFPA), and several other domestic and international resources. This survey has got ethnical approval from Duke University and Peking University.

By 2020, the CLHLS has accomplished a total of eight waves of surveys in 1998, 2000, 2002, 2005, 2008/2009 (briefly as 2008), 2011/2012 (briefly as 2011), 2014, and 2017/2019 (briefly as 2018), respectively. The ninth wave is planned to start in 2021/2022. Throughout the two decades, the survey conducted nearly 113,000 interviews from more than 56,700 participants; the majority of these interviews are from adults aged 80 years or older. All interviews were face-to-face with informed consent. With this sample size, the CLHLS becomes one of the largest nationally representative longitudinal samples of oldest-old adults in the contemporary world. All follow-up waves of the CLHLS collected data before dying for the deceased persons between two adjacent waves from the next-of-kins or the primary caregivers of the deceased. In total, the CLHLS collected data for about 29,000 deceased persons. The CLHLS also collected data from adult children of the participants in 2002, 2005, and 2008/2009. Table 1 lists the sample distribution by age and sex for each wave, including those deceased persons between two adjacent waves. Since the year of 2008, the survey further collected data from seven areas of mainland China, which have the exceptionally high density of centenarians, and thus are defined as the longevity areas by the Chinese National Research Center on Aging. Finally, from 1998 to 2018, the CLHLS collected blood and saliva samples from 41,000 Chinese older adults. The response rate in each wave ranged 85-90%, with an average 88%.

Survey Design

The CLHLS was conducted in 22 of the 31 provinces in China, and within each of the

Chinese Longitudinal Healthy Longevity Survey (CLHLS), Table 1 Sample distributions of the 1998, 2000, 2002, 2005, 2008/2009, 2011/2012, 2014, and 2018/2019 waves of the CLHLS

Sex and age	Surviving interviewees at each wave									Deceased interviewees in each survey interval							
	1998	2000	2002	2005	2008/2009	2011/2012	2014	2017/2019	Total	1998–2000	2000–2002	2002–2005	2005–2009	2008–2012	2011–2014	2014–2019	Total
Men																	
35–64	–	–	2,945	1,834	1,908	271	65	52	7,075	–	–	–	–	4	–	0	4
65–79	–	–	2,560	2,787	2,257	1,712	1,294	2,699	13,309	–	–	272	218	210	128	137	965
80–89	1,787	2,467	2,128	1,932	2,148	1,316	1,082	1,900	14,760	339	481	721	539	549	325	307	3,261
90–99	1,299	1,645	1,584	1,659	1,897	1,017	705	1,571	11,377	574	543	855	880	988	543	395	4,778
100+	481	518	676	581	688	287	170	709	4,110	348	292	450	429	437	203	144	2,303
Total	3,567	4,630	9,893	8,793	8,898	4,603	3,316	6,931	50,631	1,261	1,316	2,298	2,066	2,188	1,199	983	11,311
Women																	
35–64	–	–	1,301	732	1,892	238	20	43	4,226	—	–	–	–	2	–	1	3
65–79	–	–	2,447	2,538	2,028	1,437	1,075	2,657	12,182	–	–	229	172	127	82	66	676
80–89	1,741	2,451	2,111	1,977	2,124	1,324	1,125	2,117	14,970	262	367	627	419	399	251	220	2,545
90–99	1,714	2,167	2,163	2,293	2,699	1,416	949	1,970	15,371	612	677	1,085	1,050	1,204	655	452	5,735
100+	1,937	1,913	2,513	2,216	2,725	1,170	707	2,170	15,351	1,213	930	1,635	1,502	1,722	692	504	8,198
Total	5,392	6,531	10,535	9,756	11,468	5,585	3,876	8,957	62,100	2,087	1,974	3,576	3,143	3,454	1,680	1,243	17,157
Both sex																	
35–64	–	–	4,246	2,566	3,800	509	85	95	11,301	–	–	–	–	6	–	1	7
65–79	–	–	5,007	5,325	4,285	3,149	2,369	5,356	25,491	–	–	501	390	337	210	203	1641
80–89	3,528	4,918	4,239	3,909	4,272	2,640	2,207	4,017	29,730	601	848	1,348	958	948	576	527	5,806
90–99	3,013	3,812	3,747	3,952	4,596	2,433	1,654	3,541	26,748	1,186	1,220	1,940	1,930	2,192	1,198	847	10,513
100+	2,418	2,431	3,189	2,797	3,413	1,457	877	2,879	19,461	1,561	1,222	2,085	1,931	2,159	895	648	10,501
Total	8,959	11,161	20,428	18,549	20,366	10,188	7,192	15,888	112,731	3,348	3,290	5,874	5,209	5,642	2,879	2,226	28,468

22 provinces, a half of the counties and cities were randomly selected for investigation, with a few exceptions for the 2008, 2011, and 2014 waves when some cities/counties were oversampled. Totally, about 850–950 counties/cities were included in different waves of the CLHLS. There are nine provinces excluded from the CLHLS, all in the West and North-West parts of China where the proportions of ethnic minorities are relatively high and the age-reporting tend to be less accurate amongst older adults (Zeng et al. 2001). Since 2008, however, Chenmai County with Han as the dominating ethnic group in Hainan Province, one of the nine excluded provinces, was included.

The CLHLS aims to interview all centenarians in the sampled counties and cities, thus it adopted a targeted random-sample research design. Specifically, for every three interviewed centenarian, four nearby octogenarian and four nearby nonagenarian, and five adults aged 65–79 were interviewed with predesignated age and sex. "Nearby" is defined loosely – it could be in the same village or street, or in the same sampled county or city, or another sampled neighboring county or city. This sampling design yielded comparable sample sizes for each single year of age and sex, thus oversampling oldest-old adults as well as older men. It avoids obtaining very small sample sizes of these subgroups if the random sampling was implemented.

As a panel study, since 1998, the CLHLS has kept tracing the same participants in subsequent waves. For those who died between the waves, as mentioned, the CLHLS interviewed their next-of-kin or the primary caregiver to collect information near the end-of-life. For each of follow-up waves, the CLHLS recruited new participants to compensate for the sample attrition due to deaths, refusals, and losses to follow up. The newly recruited participants usually have the same sex and the similar age within 2–3 years difference. Due to the budget constraint, nationwide new recruits were suspended in the waves of 2011 and 2014, but soon resumed in the 2018 waves. For the unique sampling design of the CLHLS, appropriate weights are required in the estimation of prevalence of the population. A basic sampling weight is constructed in each wave to reflect the age-sex-urban/rural distribution of the total population in the sampled provinces. The CLHLS project also collects county/city-level aggregated indicators for sample areas to better examine the linkages between contextual or macro level factors with health and longevity of older adults. More details of the CLHLS can be found elsewhere (Zeng et al. 2001, 2008; Zeng 2012).

Main Modules of Data Collected

The CLHLS has collected a comprehensive constellation of information of Chinese older adults with multiple modules in regard to health and longevity and their associates/determinants, including, but not limited to, physical and psychological health, cognitive function, behavior, diet and nutrition, lifestyles, social engagement, care needs and costs, social support, social services, socioeconomic status, family structure, living arrangement, intergenerational relationships, social relations, and end-of-life issues. The CLHLS also collected biological data in terms of biomarkers and genetic data for both the older proband as well as his/her offspring and other sampled comparative persons. The major modules of the CLHLS data are summarized below.

Sociodemographics

The CLHLS collected data on age, sex, ethnicity, place of birth (city, town, or rural) and province of birth, current address of residence (city, town, or rural), years of schooling, lifetime primary occupation, the primary and secondary financial resources, housing ownership (since 2005), decision power within family (since 2008), social security, self-reported financial sufficiency, per capita income, socioeconomic conditions at childhood, parents' primary occupation and education (since 2008), and education of the coresident persons (since 2008), and so forth.

The CLHLS collected data on histories of marriage and childbearing of each respondent, including ages at each marriage formation and dissolution, marriage quality, age at each birth of a child, sex, and survival status of these children, as well as their coresidence and frequency of contacts with the respondent. For the ever-married respondents, data on socioeconomic status and health of their spouses were collected in the 2005 wave and beyond. The survey also collected data on the dates of birth and death of father and mother of a respondent, and sociodemographic data of a respondent's siblings such as age, survival status, education, occupation, and current residence. These parental and biological sibling's data of could be used for genealogical studies.

The CLHLS further asked about the living arrangement of a sampled older adult, including whether the respondents was living alone, with spouse only, with children and/or grandchildren, or in an institution. For each coresiding family member(s), the survey further asked about his/her age, sex, education (since 2008), smoking status (since 2011), and relationship with the sampled older adults. Expectation on living arrangement was also asked since 2005. For institutionalized samples, the date of admission and the monthly cost were collected as well.

Health Outcomes

Disability and Functional Limitation

The CLHLS collected data on activities of daily living (ADL) and instrumental ADL (IADL) to measure disability at the time of survey. The six items of ADL examine if a respondent has difficulty in bathing, dressing, indoor transferring, toileting, eating, and continence. The ADL items are adopted from the Katz ADL scale (Katz et al. 1963). Data on the number of days needing assistance in each ADL item (since 2005) and the corresponding primary caregiver (since 2002) were collected if a respondent reported to need help. Attention is needed for comparative studies before and after 2008, because the CLHLS oversampled respondents in some cities/counties in 2008 onward.

The eight items of IADL ask respondents if they have difficulties in using of public transportation, doing laundry, shopping, cooking meal, visiting neighborhood, continuously crouching for three times, lifting a 5 kg object, and walking for 1 km without a stop. These IADL questions are mainly adopted from the Nagi scale (Nagi 1965), and reflect the states at the time of survey. Besides these self-reported measures of disability, the CLHLS also collected data on the performance of functional limitations, which include tests of lifting hands, putting hands at low back, putting hands behind neck, standing up from sitting in a chair, picking a book from floor, and turning around for 360°.

Psychological Characteristic and Life Satisfaction

The CLHLS designed seven variables relevant to psychological characteristic: (1) Do you look on the bright side of things? (2) Do you keep things neat and clean? (3) Can you make your own decisions concerning your personal affairs? (4) Do you feel as happy as when you were young? (5) Do you feel fearful or anxious? (6) Do you feel lonely and isolated? (7) Do you feel useless? The first four questions reflect positive affect of psychological traits, while the latter three questions refer to the negative affect. These questions are mainly derived from the Positive Affect and Negative Affect schedule (PANAS) scale, and could also be considered a short version of the recently developed Scale of Positive and Negative Experience (SPANE) (Diener and Biswas-Diener 2009; Gu 2017b). Furthermore, the CLHLS adopted a single question with a five Likert scale on the overall life satisfaction since 1998. Questions related to psychological well-being were added since 2014, and 10 questions related to the CES-D-10 scale for depression symptom was included in 2018.

Cognitive Function

To meet the cultural and socioeconomic conditions in China, the CLHLS developed and validated a Chinese version of the Mini-Mental Status Examination (MMSE), in which the questions are easily understandable and practically answerable among normally functioning oldest-old Chinese (Zeng et al. 2001). This index consists of 24 questions based on six major domains of the cognitive function: orientation, registration, calculation, drawing, recall, and language. The total possible score of MMSE is 30, with lower scores indicating poorer cognitive ability. All MMSE questions are answered by the respondent, not by a proxy. Due to poor health condition, quite a few participants were not able to answer these questions in the survey. Thus, in analyzing these self-reported variables on cognition as well as psychological well-being, cautions are needed to clarify reasons of nonresponses, or alternatively, to impute the missing responses if applicable.

Physiological Biomarkers and Comorbidity

The physiological set of indicators of the CLHLS includes the blood pressure (diastolic and systolic), heart rate, heart rhythm, and hearing and vision conditions. Basic anthropometric traits such as weight, length of waist circumference (since 2011), calf circumference (since 2011), arm length, leg length, and height (since 2008) are also included. These indicators were measured on site with trained interviewers, and mostly with a local medical professional together.

The CLHLS also asked about comorbidity with a list of over 20 main chronic diseases and conditions, including hypertension, diabetes, heart disease, stroke or cerebrovascular disease, bronchitis/emphysema/asthma/pneumonia, pulmonary tuberculosis, cataracts, glaucoma, cancer, prostate tumor, gastric or duodenal ulcer, Parkinson's disease, bedsore, arthritis, and so forth. These conditions were self-reported, but mostly with doctors' diagnoses (90%+). Numbers of hospitalization (up to three times) and the corresponding lengths of stay in last 3 years (or since the last interview) were also collected. In addition, the CLHLS collected data on the number of natural teeth, left-handedness, and oral health (since 2014).

Overall Health Rating

The self-reported global health (or simply self-rated health, SRH) was asked in the CLHLS through a single question with a five Likert scale categories: very good, good, so so, poor, and very poor. A response of "unable to answer" is included for those who could not provide an answer, mainly due to the poor health. This global health rating is accompanied by a comparative question, which asks the respondent to provide his/her current condition in comparison with the status a year ago. The CLHLS also asked the interviewer to rate the overall health condition (or simply interviewer-rated health, IRH) of the respondent at the end of the interview, with four categories: surprisingly healthy (almost no obvious ailments), relatively healthy (only minor ailments), moderately ill (moderate degrees of major ailments or illnesses), and very ill (major ailments or diseases, bedridden, etc.). The mortality-predictive power of SRH and IRH has been investigated by Feng et al. (2016). The finding revealed that IRH could be a good supplementary measurement for well-adopted SRH (Feng et al. 2016).

Nutrition and Lifestyles

The CLHLS collected data on the type of staple food of the respondent, as well as the frequency of intakes of fresh vegetable, fresh fruit, red meat, fish, egg, bean products, salted vegetable, sugar/candy, tea, garlic, milk and milk products, nuts (since 2008), algae (since 2008), multivitamins (since 2008), and so forth. The survey also collected the timing information of activities such as smoking, alcoholic consumption, and heavy physical labor work. The data on regular exercise, tourism, and social participation, and leisure activities were collected in the CLHLS. The leisure activities include homemaking, outdoor activity, planting flowers or keeping birds, raising pets, reading books and newspaper/Internet surfing, playing cards or Mahjong, and watching TV or listening to radio. In the 2002, the CLHLS collected data on religious involvement. Since 2011, the data on passive smoke exposure, tobacco/nicotine dependence, alcohol abuse and dependence have been further collected, as well as smoking status of coresidence persons.

Social Relation and Intergenerational Support

Since 2002, the CLHLS has started to collected data on intergenerational relations, including emotional relation and intergenerational exchange. Three questions were designed to measure the emotional relation: who is the first person when the respondent wishes to tell something private, who is the person the respondent mostly talks to in daily life, and who is the first person for the respondent to ask for help when needed. The intergenerational exchange is measured by several questions on monetary and instrumental exchanges, downward and upward. Furthermore, in the 2002, 2005, and 2008 waves of the CLHLS, one adult child of the participants was interviewed, bringing in more detailed information on intergenerational exchanges between the sampled children and their older parents (including the proband older adults), the family dynamics, and the career development of the sampled adult child.

Healthcare Services and Social Services

The CLHLS collected data on availability of medical insurance and access and barrier to health care. Data related to family care resources were also collected. From the 2005 wave onward, the CLHLS started to collect information on care costs and caring hours for ADL disabled respondents. The CLHLS further collected information on needs and uses for home- and community-based services as well as the availability of social services in neighborhood.

Data on End-of-Life Issues

From the very first follow-up wave in 2000, the CLHLS collected data related to end-of-life issues from the next-of-kin or the primary caregiver of the individuals who deceased between two adjacent waves of survey. In addition to basic demographics and socioeconomic conditions, the data of the deceased include the date of death, primary cause of death, diseases suffered before death, medical cost in the last year of life, severity of ADL disability, and length of such disability prior to death. Date and cause of death were confirmed with the death certificate, and another confirmation was usually needed from the local neighborhood committee if the death certificate was not available. From the 2005 wave onward, questions on quality of death were included in the questionnaire.

Community-Level Dataset

The CLHLS collected various aggregated data for each of the sampled counties/cities in every wave. These county/city-level data were filled by local officials in the sampled areas. The data hold information on geographical coordinates and elevation (centroid or the seat of county/city government), temperature and climate, topographic types, population demographics, socioeconomic development, environmental quality, major disasters in the past 100 years, and local old-age care policy and related eldercare allowance. This dataset can be merged with individual level data.

DNA Samples and Home-Based Health Examinations

Along with the rich information collected in the interviews, the CLHLS has also collected blood and saliva samples from the participants, which is fully on a voluntary basis with informed consent. Biological material was collected either by venepuncture (1895- and 1915-West birth cohort; subsamples of the 1905 birth cohort) or by dried blood spots on filter cards (1905-, 1910-, and 1915-birth cohorts at baseline). Cheek swaps were used to collect DNA as an alternative to finger pricking for dried blood spots since 2008 onward. The DNA samples were collected from 41,000 Chinese older adults, including 8,431centenarians, 8,773 nonagenarians, 8,860 octogenarians, 10,139 individuals aged 65–79, and 4,609 individuals aged 40–64 years.

In the 2008/09, 2011/12 and 2014 waves of the CLHLS, health examinations were performed for 2.035, 2.862, and 2.651 participants in some sampled longevity areas, respectively, by local certified doctors and nurses who were affiliated with the China Center for Disease Control & Prevention (CDC). The medical personnel used standard instruments to check heart, lungs, breast, waist, lymph, limbs, and thyroid of the participants. They also wrote down impressions and symptoms of disorder of the respondents if any, and furthermore enquired about their family disease history and current medications.

Data Quality

The data quality of the CLHLS has been evaluated to be good, in terms of the assessments on mortality rate, proxy use, nonresponse rate, sample attrition, reliability and validity of major health measures, and the rates of logically inconsistent answers (Chen 2018, 2021; Gu 2008; Shen 2010).

The rates of logically inconsistent answers and incomplete data in the first four waves were as low as 1–3%. The data quality of morbidity is slightly better than that of the National Health Service Survey in the first three waves (Gu 2008). The consistency of the cognitive function, physical health, and function limitations is high in the CLHLS data (Chen 2018, 2021; Gu 2008; Shen 2010; Zeng et al. 2001). For consistency between relevant questions, both cross-sectionally and longitudinally, the CLHLS is comparable to the data quality of other similar surveys in the world (Gu 2008).

Accurate age reporting is crucial for studies on aged people. Age exaggeration is common in many developing countries (Coale and Kisker 1986), yet the accuracy of age reporting of Han Ethnicity in China is likely acceptable because of the practice of the traditional Chinese zodiac. Zeng and colleagues (2001) showed a relatively accuracy of age reporting among centenarians recruited in the CLHLS, which was similar to that of Canada under the same mortality level. Although some studies have shown mortality underestimation at oldest-old ages in the China's 2000 and 2010 censuses (Gu et al. 2016a), fortunately, such mortality underestimation was not observed in the CLHLS because of its relatively restricted age validity process implemented in the survey. Gu and Dupre (2008) showed that the mortality data quality in the CLHLS 1998 and 2000 waves was better than that in the 2000 census, especially after age 95. Figure 1 compared the sex-age-specific death rates in selected years from waves of 2002 to 2018 of the CLHLS and the census. The two red lines indicate the 2000 and 2010 censuses obtained from the tabulations of censuses (National Bureau of Statistics of China 2002, 2012). The results indicate that with few exceptions for ages after age 100 in more recent waves and for ages 95–100 in the 2011–2014 waves, the death rates observed in the CLHLS do not have many dips after age 95 and the rates for years before 2010 (gray lines) are all above the two red lines, which indicates that the quality of mortality data is higher than that of the census for both men and women.

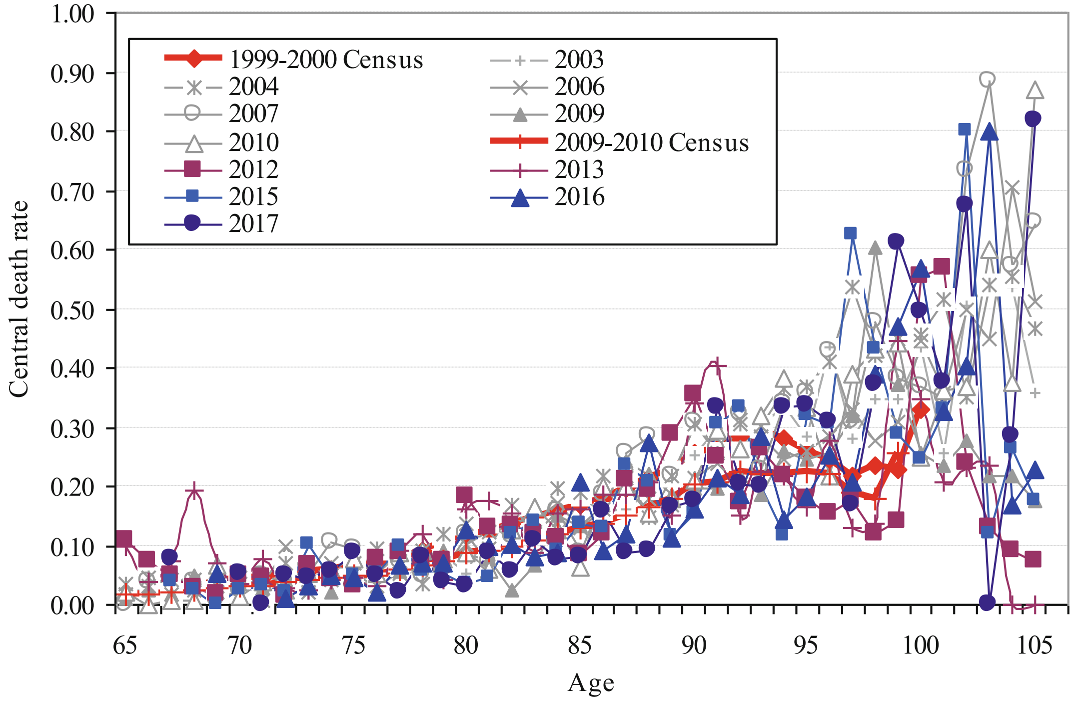
Major Findings

According to incomplete records, there had been more than 9,000 registered CLHLS users worldwide by mid-June 2020, excluding many students and/or research assistants who may not register but can also access the CLHLS data via their supervisors. More than 350 SCI/SSCI journal articles, more than 450 Chinese journal articles, and 17 books were published by mid-June 2020 with 35 Ph.D. dissertations, 104 master theses, nearly 60 policy reports. Below is a brief summary of selected findings on factors associated with health and longevity from these publications.

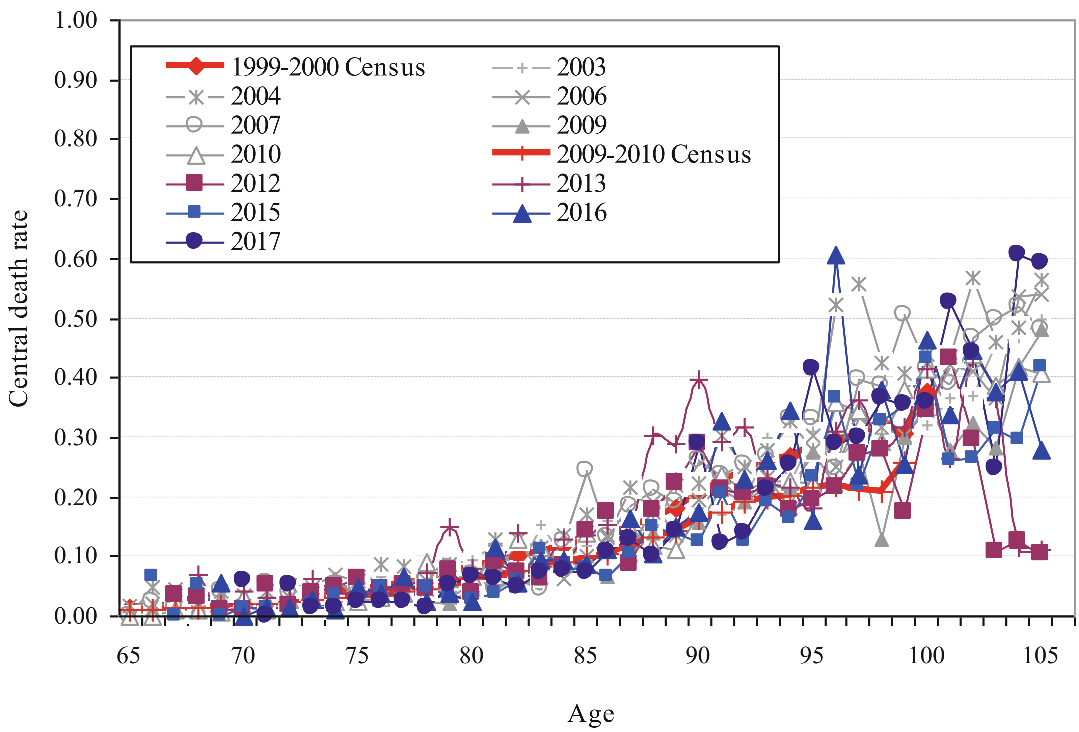
Findings from Sociogerontology

A plenty of studies have analyzed the associations between individual level of socioeconomic status (SES) and disability, cognitive impairment, and mortality (e.g., Zeng et al. 2007; Wen and Gu 2011; Zhang et al. 2010). The major conclusions of these studies include: (1) SES at older ages or at oldest-old ages is still associated with various health outcomes (Wang et al. 2019; Zhu and Xie 2007); (2) childhood SES have long-arm effects on various health outcomes at older ages and even oldest-old ages (Zeng et al. 2007; Wen and Gu 2011); (3) the childhood adversity can be substituted by an upward mobility in SES in adulthood; however, a downward mobility in SES at adulthood could worsen health outcomes at later ages (Wen and Gu 2011); (4) higher community-levels of socioeconomic developments and educational attainment are associated with better health outcomes (Zeng et al. 2010a); (5) rural-to-urban migration (i.e., from born in a rural area to living in an urban area at present) is associated with better cognitive function and lower mortality (Gu et al. 2017a; Xu et al. 2017); (6) self-perceived SES is more predictive than objectively measured SES (Wang et al. 2019). These findings mainly support that the theories of persistent disparity at older ages (see ▶ "Socioeconomic Differentials in Health: Divergence, Convergence, and Persistent Inequality Theories").

a) Men



b) Women



Chinese Longitudinal Healthy Longevity Survey (CLHLS), Fig. 1 (continued)

Findings from Behavioral and Nutritional Gerontology

The studies in this field have confirmed the role of health lifestyles in later life. Li et al. (2020) examined leisure activities and mortality among the oldest-old and found that frequently involvement in leisure activities was associated with 10–20% lower mortality, which is consistent with some earlier findings (Sun and Liu 2006). Yu et al. (2020) found that frequent involvement in exercise could postpone the decline of cognitive impairment. Gu et al. (2016b) examined that older adults who were involved in tourism is associated with better self-rated health. Zhang (2008) found older adults who were involved in religious activities were associated with lower mortality (see ▶ "Religious Involvement, Health, and Longevity"). Zeng et al. (2011) found the religious beneficial effect was stronger in young-old men than in oldest-old men.

Social participation was also found to be associated with improved better cognitive function and such association was stronger in rural older adults than in urban older adults (Sun and Lyu 2020) and reduced risk of incidence of disability (Gao et al. 2018).

There are other findings that healthy lifestyles are associated with better health outcomes. For example, Qiu (2011) found that older adults who sleep either 9+ hours or less than 6 hours tended to have a higher risk of mortality. Shi et al. (2015) found that daily intake of vegetables and fruits was associated with 15–25% lower mortality risk compared to seldom or never intake. Tea drinking is found to promote health. For example, it could reduce risk of depression symptom (Shen et al. 2019), regardless of types of tea, independent of other risk factors (Yao et al. 2021). Tea drinking is also associated with lower mortality risk among men (Qiu et al. 2012), and lower risks of disability, cognitive impairment, prevalence of cardiovascular diseases, and self-reported poor health (Feng et al. 2012; Qiu et al. 2012).

Findings from Financial Gerontology

Research using CLHLS on financial gerontology is mostly in combination with social factors socio-gerontology. A few recent studies found that greater financial resources were associated with lower negative self-ageism and lower mortality risk (e.g. Xiang et al. 2018). And the factors of subjective rated financial condition were found to have a stronger predictive power in mortality (Wang et al. 2019).

Findings from Psychogerontology

Most studies in this field took psychological factors as outcome variable in their analyses with few exceptions, which studied the associations between psychological resilience or Positive Affect and Negative Affect scale (PANAS) and several health outcomes. For example, using the cohort data, Zeng and Shen (2010) found that those more resilient older adults had a greater survival probability to become nonagenarians and centenarians. The findings using PANAS approach confirmed that higher resilience could lead to greater longevity (Gu et al. 2017b).

Using the Grade of Membership method (a fuzzy set analysis), Gu and Feng (2018) further confirmed that resilience was associated with lower mortality, normal cognitive function, free of disability and comorbidity, better self-rated health, and life satisfaction. Such association was valid regardless of gender and age from age group 65–74 to centenarians. In addition, resilience was associated with lower incidence of disability, cognitive impairment, and comorbidity and poor self-rated health and poor life satisfaction, and such associations were also valid regardless gender and age exception among centenarians.

Chinese Longitudinal Healthy Longevity Survey (CLHLS), Fig. 1 Age-sex-specific death rate in the CLHLS in a given year (Jan 1 to Dec 31). (Note: Central death rate at age x = (deaths at age x)/(person-year lived in age x). Census data were from National Bureau of Statistics of China (2012). For years of 1999 and 2001, see Gu and Dupre (2008))

Findings on Access to Healthcare

There are a number of studies in this field, revealing the importance of health care for older adults. Hao et al. (2020) found that self-rated adequate access to health care could increase life expectancy at by 2.0–2.5 years age 65 and 1.0–1.2 years at age 85, although such added life expectancies were reduced to 1–1.5 years at age 65 and 0.6–0.8 at age 85 when adjusting for a wide set of covariates. Gu et al. (2009) found that self-rated adequate access to health care could also improve healthy survival by combining frailty at follow-up and mortality risk together. They found that adequate access to health care at baseline could was associated with 22–68% higher odds of being in a healthy status in a sequent wave, and access to health care at childhood was also associated with 18% higher odds of being healthy survival. These patterns were more or less similar for both men and women, for urban and rural areas, across ages, as well as across socioeconomic statuses. Zhang et al. (2017, 2018) found that inadequate access to health care was associated with higher odds of disability, cognitive impairment, and higher mortality, and that the association was stronger in young-old aged (65–79) and slightly stronger in women than in men in rural areas.

Findings from Environmental Gerontology

There are good studies using the CLHLS to investigate how the environment affects later life. Zeng et al. (2010a) found that county-level per capita GDP was associated with better cognitive function, but higher ADL disability, that labor force participation was associated with lower risks of ADL disability, cognitive impairment, frailty, and mortality, that higher educational level was associated with lower risk of ADL disability and higher cognitive function, that air pollution was associated with higher risks of ADL disability, cognitive impairment, frailty, and mortality, that too lower temperature was associated with higher risk of ADL disability and mortality, that too higher temperature was associated with higher risk of disability and frailty, and that older adults living in greater rainfall and hilly areas were associated with lower risk of ADL disability.

Wen and Gu (2012) found that exposure to outdoor air pollution was associated with subsequent reductions in life expectancy, active life expectancies, disability-free life expectancy, disease-free life expectancy, cognitive-unimpaired life expectancy, good-self-rated health life expectancy among Chinese older adults. The gap in life expectancy between areas with good air quality and moderately heavily polluted areas was 3.78 years for women of age 65 and 0.93 years for men. The differences in Health Expectancy (HE) at age 65 were also large, ranging from 1.47 years for HE for good self-rated health in men to 5.20 years for activity of daily living disability-free HE in women. Sun and Gu (2008) explored the interaction between air pollution and per capita GDP and found that older adults who live in more developed urban areas are more susceptible to the effect of outdoor air pollution than their counterparts living in less developed areas.

Findings About Frailty and Mortality

The Frailty Index (FI) is defined as a proportion of deficits present out of the total number of age-related conditions considered for an older adult (see ► "Measurement of Frailty"). The validity of FI in the CLHLS has been established (Gu 2009). Gu et al. (2009) showed that the age trajectory of FI follows a logistic function. The individual variation in FI tended to be increase with age. A higher FI score is associated with greater risk of mortality. Gu and Feng (2015) further showed that the FI differential in mortality risk among centenarians is still significant.

Disability Trends and Trajectories

There are a few studies using the CLHLS data to examine the trend of disability and mortality of Chinese older adults. Gu et al. (2015) showed that both ADL and IADL disabilities witnessed a decline from 1998 to 2008. Zimmer et al. (2012) used a group-based modeling approach to jointly estimate disability and mortality trajectories over time based on data from the population aged 80 and older in China. They identified three hierarchical groups of disability trajectory for each sex: starting low and rising gradually, starting low and rising quickly, and starting moderate and remaining stable. They found the trajectory is linked with individual socioeconomic characteristics and varies by sex. Zeng et al. (2017) used for the CLHLS data in the 1998 and 2008 year to compare the survival and health situation of (1) the elderly of the 80 years age group in 1998 and 2008, (2) the elderly of the 90 years age group in 1998 and 2008, and (3) the elderly of the 100 years age group in 1998 and 2008. They found that the annual mortality rate and disability rate in 2008 had a significant drop compared with that in 1998, regardless of age groups; at the same time, the objectively measured physical function and cognitive ability displayed a significant fall in 2008 in contrast to 1998. They use "benefits of success" and "costs of success" to explain the twisted relation as illustrated above. This finding was confirmed by Liu et al. (2019).

Findings from Genetic and Interactions of Gene-Environment Research

One advantage for genetic studies in Chinese population is that the Han Chinese are relatively genetically homogeneous due to low international migration (Xu and Jin 2008). This is different from most Western countries that are relatively heterogeneous genetic compositions due to a long history of international migration that has mixed with populations from parts of the world. Below are summaries from selected papers using the genetic data collected in the CLHLS.

Some genes associated health and longevity. Based on genotypic/phenotypic data from 1,817 centenarians and younger individuals, Zeng et al. (2010b) and Li et al. (2009) found that three SNPs on the FOXO1A gene and three SNPs on the FOXO3A gene were associated with longevity trait in Han Chinese populations. They identified eight independent SNPs overlapped across Han Chinese, European, and US populations, and APOE and 5q33.3, were confirmed as longevity loci. Integrated analysis indicates four pathways (starch, sucrose, and xenobiotic metabolism; immune response and inflammation; MAPK; calcium signaling) highly associated with longevity in Han Chinese (Zeng et al. 2016a). Zhao et al. (2018) identified 11 copy number variations (CNVs) that are strongly associated with longevity; four of them located in the chromosome bands, 7p11.2, 20q13.33, 19p12, and 8p23.3, and overlap partially with the CNVs identified in long-lived Danish or US populations. The genome-wide association study (GWAS) identified 28 significant SNPs and 4 genes, ESR1, PHB, RYR3, and GRIK2, that are associated with the cognitive impairment though immunological systems, brain function, metabolic pathways, inflammation, and diet in Chinese populations (Han et al. 2020).

Gene-environmental interaction effects on health and longevity. Zeng et al. (2016b) found that the gene-environmental interaction between FOXO genotypes and tea drinking was significantly associated with health of older adults. Specifically, the associations between tea drinking and reduced mortality are much stronger among carriers of the FOXO1A-209 genotype compared to noncarriers, which indicates that tea drinking may inhibit FOXO1A-209 gene expression and its biological functions, which reduces the negative impacts of FOXO1A-209 gene on longevity. It also found that associations between tea drinking and reduced cognitive disability were much stronger among carriers of the genotypes of FOXO1A-266 or FOXO3-310 or FOXO3-292 compared with noncarriers, which implies that the health benefits of particular nutritional interventions, including tea drinking, may, in part, depend upon individual genetic profiles (Zeng et al. 2015). Interactions between social/behavioral factors (i.e., regular exercise, social-leisure activities, etc.) and certain SNPs on the ADRB2 gene are also significantly associated with cognitive function, self-reported good health, and negative emotion of older adults (Zeng et al. 2013).

Sex differences in genetic associations with longevity. Zeng et al. (2018) examined sex differences in genetic associations with longevity based on CLHLS genotypic/phenotypic data using polygenic risk score (PRS) analyses. They found that 11 male-specific and 11 female-specific longevity loci ($P < 10^{-5}$) and 35 male-specific and 25 female-specific longevity loci ($10^{-5} < P < 10^{-4}$) were associated with longevity among Chinese older adults.

Future Plans

Look forward, the field work of the 2021/2022 wave was launched in the summer of 2021. In this round, the scope of data coverage will continue to enlarge to include more aggregated data from the sampled counties/cities. The sampling coverage is also expected to expand to all provinces in mainland China. The expected new samples in the nine provinces that were previously not included in the CLHLS will be mainly young older adults. Furthermore, with the release of community-level data, more research using multilevel analyses by incorporating county-level data with individual data should be expected. Particularly, spatial analyses using the CLHLS data may expect a good increase. Finally, with the availability of biomarker and genetic data from the CLHLS, more studies examining the impacts of gene and environmental interaction on health and longevity would also be expected.

Cross-References

▶ China Health and Retirement Longitudinal Study (CHARLS)
▶ Cohort Study of Centenarians in Hainan, China (CHCCS)

Disclaimer The views expressed in this chapter are solely those of the authors and do not reflect those of the United Nations, the National University of Singapore, Xiangtang University, Duke University, or Peking University.

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Chinese Medicine

► Traditional Chinese Medicine

Chinese Survey of Determinants of Healthy Longevity

► Chinese Longitudinal Healthy Longevity Survey (CLHLS)

Cholesterol Levels

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Synonyms

Aging and Cholesterol Metabolism; Cholesterol metabolism; High-density lipoprotein cholesterol; Low-density lipoprotein cholesterol

Definition

Cholesterol is indispensable for tissues and cells of human beings. It is not only an important substance participating in the formation of cell membranes but also a kind of material for the synthesis of bile acids, vitamin D, and steroid hormones. A human being can get cholesterol from routine diet. But the main source of cholesterol is synthesized by the liver. Cholesterol is transported through the blood by the apolipoprotein to vessels, adrenal gland, ovary, and other oranges or tissues. However, excessive cholesterol can be deposited in the vascular wall, leading to a variety of cardiovascular diseases. LDL-cholesterol (LDL-C) and HDL-cholesterol (HDL-C) are two main components of plasma cholesterol. High total cholesterol and high LDL-C levels are widely regarded as casual predicted factors for cardiovascular events. However, the relevance of HDL-C level to cardiovascular disease is not certain (Holmes et al. 2018). Cardiovascular disease is a leading cause of death worldwide, and it has now surpassed tumor diseases as the main killer of human beings. Monitoring and maintaining cholesterol homeostasis is an important means of preventing cardiovascular disease.

Overview

Aging is a natural process of human life. The functions of multiple organs and systems decline gradually, and the metabolism changes correspondingly, including cholesterol metabolism. The changes in plasma cholesterol levels cause various physiological and pathological effects, which in turn affect various organs of the body and interfere with normal physiological functions. As a result, it causes multiple diseases further, especially cardiovascular diseases. Very low-density lipoprotein cholesterol (VLDL-C) is formed from the liver cholesterol pool. Lipoprotein lipase (LPL) partially hydrolyzes VLDL-C to form medium-density lipoprotein cholesterol (IDL-C), a kind of low-density lipoprotein cholesterol (LDL-C) precursor. IDL-C is further hydrolyzed by liver lipase to form LDL-C. VLDL, IDL, and LDL transport triacylglycerol and cholesterol to tissues. High-density lipoprotein (HDL) can remove cholesterol from tissues and transport it back to the liver for metabolism. Elevated plasma level of LDL-C is a good predictive factor for cardiovascular disease risk (Ference et al. 2017), while the plasma level of high-density lipoprotein cholesterol (HDL-C) is negatively correlated with cardiovascular risk. There have been many simple and effective methods to reduce the level of LDL-C, and they can effectively decrease the risk of cardiovascular disease. However, elevating HDL-C level in the prevention and treatment of cardiovascular diseases is not necessarily effective as that we expected. Cardiovascular risk is not reduced by solely elevating plasma HDL-C level (Soria-Florido et al. 2020). It is necessary to improve the function of HDL while raising HDL-C level. Cholesterol level management is a simple and effective strategy to maintain the health of older people.

Key Research Findings

Changes in Cholesterol Metabolism During Aging

An abnormal feature of aging is the dysregulation of cholesterol metabolism of the whole body (Mc Auley and Mooney 2014; also see “Aging and Cholesterol Metabolism” in this volume). The clinical manifestation of this process is an age-related rise in the plasma levels of VLDL-C, IDL-C, and LDL-C (Abbott et al. 1983; Dayimu et al. 2019). VLDL-C, IDL-C, and LDL-C in the circulation can be absorbed into the hepatic cells by the LDL receptor (LDLr) (Veniant et al. 1998; Spolitu et al. 2019). However, the hepatic LDLr decreases with age, which results in the accumulation of LDL-C in the circulation (Millar et al. 1995; Mc Auley et al. 2012). On the contrary, the level of HDL-C decreases with age (Wilson et al. 1994; Cho et al. 2020). It has been reported that estrogen deficiency can cause female dyslipidemia (van Beresteijn et al. 1993; Taylor et al. 2017). In addition, the level of follicle-stimulating hormone (FSH) in peripheral blood circulation increases during menopause. Blocking the effect of FSH can inhibit hepatic cholesterol synthesis and reduces plasma cholesterol (Guo et al. 2019). Metabolism of cholesterol can be affected by the decline of organ function in the aging process of human body, and it is an important index to judge whether the aging process is normal.

Changes in Cholesterol Levels Affect Aging

Cardiovascular and cerebrovascular diseases are common diseases in older people. They are the leading cause of mortality internationally (Lozano et al. 2012). VLDL transports cholesterol in the circulation, where it is hydrolyzed to form IDL, a precursor of LDL. Then, IDL is further hydrolyzed to form LDL. Plasma VLDL-C is closely related to cardiovascular disease and it can be a predictor of coronary events (Sacks et al. 2000). Similarly, decreasing plasma IDL-C can effectively improve cardiovascular health (Zambon et al. 2014). Hirowatari introduced the anion-exchange chromatographic method to obtain IDL-C, which may serve as useful markers for risk of cardiovascular disease in chronic kidney disease patients with hemodialysis treatment (Hirowatari et al. 2012). Apolipoprotein (Apo)C-II, ApoC-III, and ApoE are three VLDL-associated apolipoproteins in de novo lipogenesis, glucose metabolism, complement activation, blood coagulation, and inflammation. In addition, ApoC-II/ApoC-III/ApoE correlated with a pattern of lipid species previously linked to coronary vascular disease (CVD) risk (Pechlaner et al. 2017). ApoC-III is a vital apolipoprotein for ApoB lipoproteins, which may contribute directly to atherogenesis by activating endothelial cells and recruiting monocytes to them (Kawakami et al. 2006a, b). Drug targeting ApoC-III succeeds in lowering plasma levels of ApoC-II, ApoC-III, triacylglycerols, and diacylglycerols, but increasing ApoA-I, ApoA-II, and ApoM without affecting ApoB-100 (Pechlaner et al. 2017). This supports the concept of targeting triacylglycerol-rich lipoproteins to reduce the risk of CVD.

Elevated plasma total cholesterol or LDL-C level is an important risk factor for cardiovascular events (Wadhera et al. 2016). LDL-C level is positively correlated with the risk of cardiovascular diseases. Atherosclerosis is the basic vasculopathy of multiple cardiovascular diseases, characterized by cholesterol deposition in macrophages in large and medium-sized arteries. Elevated plasma LDL-C level leads to increased adhesion of circulating monocytes to arterial endothelial cells. In addition, under various pathological stresses, LDL can undergo chemical modifications, turn to modified LDL or caused oxidized LDL. Modified LDL is cytotoxic, which makes LDL particles more proatherogenic, contributing to the damage of endothelial cells. Decreasing LDL-C level has been proved to be effective in reducing the incidence of cardiovascular diseases (Cannon et al. 2015).

High-density lipoprotein (HDL) can reversely transport cholesterol back to the liver for metabolism and excrete them from bile or stool to prevent lipid oxidation and deposition in the peripheral blood vessel wall (van Vlijmen and Herz 1999). In addition, HDL has been proved to be of anti-oxidative, anti-inflammatory, and protective for vascular endothelium (Nofer et al. 2002; Norata et al. 2005). The level of plasma HDL-C is negatively correlated with the risk of cardiovascular disease (Castelli et al. 1986). However, solely elevating plasma HDL-C level cannot effectively reduce the occurrence of cardiovascular events. Cholesteryl ester transfer protein (CETP) can promote the transport of cholesterol esters from HDL to LDL and VLDL (Ohashi et al. 2005). CETP inhibitors significantly increase the plasma HDL-C levels, but the risk of cardiovascular disease does not decrease accordingly (Schwartz et al. 2012). On the contrary, statins and exercise effectively reduce the cardiovascular risk while elevating plasma HDL-C level. But statin has limited effect on the increase of HDL-C level (Grundy et al. 2001). It is now believed that statins may play a protective role in improving the function of HDL. Similarly, exercise can not only increase the level of plasma HDL-C (Igarashi and Nogami 2019) but also improve the function of HDL (Blazek et al. 2013). Compared with HDL-C level, the function of HDL may be more critical. While suffering from pathological stress, HDL may lose its normal physiological function. At present, there is a lack of easy and effective methods to evaluate the function of HDL.

Examples of Application

Cholesterol level is of great importance for health. There are many clinical treatments for cholesterol dysregulation.

Application of Reducing LDL-C Level

A number of approaches for LDL-C lowering have been well studied, such as lifestyle interventions, pharmacologic treatment, and surgical therapy. When the baseline level of plasma LDL-C is high, lowering LDL-C can reduce cardiovascular mortality more effectively (Navarese et al. 2018).

Statin Therapy

Statin is an inhibitor of rate-limiting enzyme for cholesterol synthesis, hydroxy methylglutaryl coenzyme A reductase. It can reduce the production of endogenous cholesterol by inhibiting the synthesis of cholesterol, thus reducing LDL-C. A 1 mmol/L of LDL-C reduction was associated with 38% and 31% decreases in the relative risk of major vascular events (nonfatal myocardial infarction, coronary death, coronary revascularization, or stroke) in subgroups of 5-year predicted risk $<5\%$ and $\geq 5\%$ to $<10\%$, respectively (Mihaylova et al. 2012).

Nonstatin Pharmacologic Therapies

Many drugs have been used clinically to reduce LDL-C levels such as bile sequestrant resins, fibrates, nicotinic acid drugs, ezetimibe, and ω-3 fatty acid drugs. Cholestyramine, a bile acid sequestrant, 24 g/d lowers LDL-C levels by 53.4 mg/dL and TC levels by 50.7 mg/dL compared with matching placebo, with a trend toward reduced risk of CAD (odds ratio 0.81) (Ross et al. 2015). Fibrates can reduce triglycerides by 20–50%, LDL-C levels by up to 20% (Wierzbicki 2009). Fibrates alone can reduce cardiovascular events by 10–15% (Jun et al. 2010). The study of heart and renal protection (SHRP) trial shows that simvastatin, combined with ezetimibe, is able to significantly reduce the mortality of primary endpoint events such as nonfatal heart failure or coronary events and nonhemorrhagic stroke, and that the combined group did not show any adverse reactions like increased cancers, myolysis, or liver damage (Baigent et al. 2011).

Surgical Therapy

The partial ileal bypass has been shown to reduce LDL-C levels before statins appear. Liver transplantation has become the most effective method to implant LDLr in homozygous family hypercholesterolemia patients with gene mutations affecting the LDLr (Ishigaki et al. 2019). However, surgical therapy will inevitably cause great damage and many complications.

Application of Improving HDL Function

Several clinical studies have reported that elevating plasma HDL-C levels by CETP inhibitors fail to reduce cardiovascular risk. Currently, more attention has been paid to improve HDL function.

Apolipoprotein A-I (ApoA-I) Mimetic Peptide

ApoA-I, a major component protein of HDL, is an important carrier of ABCA1-mediated reverse cholesterol transport (Wang and Tall 2003). Rubin reported that the overexpression of ApoA-I increased the plasma levels of ApoA-I and HDL. As a result, the progress of arterial lipid plaque was impeded (Rubin et al. 1991). Studies have shown that ApoA-I mimetic peptide can improve HDL function, which not only inhibits the formation of atherosclerosis but also prevents the development of pulmonary hypertension (Sharma et al. 2014; Ou et al. 2005; Navab et al. 2002).

Statins

Otocka-Kmiecik and colleagues suggested that statins may play a role in improving HDL function and delaying the progression of atherosclerosis (Otocka-Kmiecik et al. 2012). Patients accepting simvastatin therapy, who were with noncoronary heart disease and scheduled to undergo heart operation, had a significant improvement in cardiac function, oxidative stress, and inflammatory reaction after cardiac surgery compared with the control group. Subgroup analysis showed that simvastatin significantly decreased HDL proinflammatory index in patients with valvular heart disease (Almansob et al. 2012). HDL of patients treated with simvastatin was improved significantly, suggesting that simvastatin promotes recovery of patients after cardiac surgery at least partially by improving HDL function (Chang et al. 2014).

Future Directions of Research

Many studies have achieved great success in reducing the level of LDL-C. New drugs for lowering LDL-C have been put on the market gradually, while HDL research is still in its infancy. More attention should be paid to the changes in HDL function and its subcomponents while suffering from diseases, and we should think about how to prevent new HDL from becoming pro-inflammatory HDL and improve the functions of pro-inflammatory HDL. There have been some methods to detect the function of HDL, such as its ability to reverse cholesterol transport, anti-apoptotic activity, the number of HDL particles in circulation, and so on. However, these methods have their own disadvantages, such as lack of standardization and unstable clinical correlation, which makes it impossible to integrate these indicators into risk prediction model or to evaluate the clinical efficacy of new lipid-lowering drugs. It is an urgent need to develop an easy and reliable method to accurately evaluate the function of HDL in clinical practice.

Summary

Cholesterol is an important nutrient. It not only participates in the composition and renewal of cell structure but also plays an important part in the signal transmission between human cells through the synthesis of steroid hormones. Cholesterol that ingested from food or synthesized by the liver is then transported to peripheral tissues by combining with apolipoproteins to form VLDL, IDL, and LDL. The excessive cholesterol from peripheral tissues is transported back to the liver to be discharged from the body through HDL, thus maintaining the delicate balance of cholesterol metabolism in the human body. If excessive cholesterol synthesis is ingested or peripheral cholesterol cannot be removed in time, excessive cholesterol will be deposited in peripheral tissues and organs, resulting in organ dysfunction and even disease. Aging is accompanied by the functional decline of organs, which affects the normal metabolism of cholesterol. Therefore, older people are prone to suffer from various lipid metabolic dysregulation, as well as cardiovascular and cerebrovascular diseases, which seriously threaten the health in older people. Various interventions have been applied to regulate the metabolism balance of cholesterol in clinical practice, and plasma cholesterol level has been used as a diagnosis reference of cardiovascular diseases. It is of great benefit to judge and utilize cholesterol levels in the prevention and treatment of various cardiovascular and cerebrovascular diseases in older people.

Cross-References

▶ Aging and Cholesterol Metabolism
▶ Atherosclerosis
▶ Biogerontology
▶ Cardiovascular Response
▶ Circadian Amplitude
▶ Circulatory System
▶ Congestive Heart Failure
▶ Exercise and Healthy Cardiovascular Aging
▶ Heart Failure
▶ Hypertension
▶ Hypertensive Cardiovascular Diseases
▶ Ischemic Attack
▶ Middle Cerebral Artery Strokes
▶ Myocardial Infarction
▶ Peripheral Artery Disease
▶ Stroke

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Cholesterol Metabolism

► Cholesterol Levels

Christian Scriptures

► Biblical Perspectives on Aging

Chromatid

► Chromosome

Chromatin

► Chromosome

Chromosomal Mutation

► Mutation

Chromosome

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Synonyms

Chromatid; Chromatin; DNA; Gene; Genetic code; Heredity; Nucleic acid; RNA

Definition

Chromosome consists of nucleoprotein that appears as a microscopic threadlike structure inside cell. By arranging into genes, chromosome is responsible for transmitting the hereditary characteristics of the living organism.

Overview

Chromosomes are threadlike microscopic complexes of tightly coiled DNA (deoxyribonucleic acid), which can be circular or linear in shape. Arranged on the chromosomes are genes which contain genetic information vital for proper cell functions.

The genome is the full set of chromosomes within a cell. Humans have 22 pairs of autosomes, and 2 allosomes (sex chromosomes), making a total of 23 pairs. Paired chromosomes are called homologous chromosomes, with each of the homologous pair inherited from each parent. Homologous chromosomes are similar but not identical, because they carry the same genes at a particular gene location, or locus, but each of the allele may code for a different phenotypic trait. Autosomes are labeled as 1–22, and allosomes are labeled as XX and XY. Females have two copies of X chromosomes; males have one copy of the X chromosome inherited from the mother and one copy of the Y chromosome inherited from the father (Alberts et al. 2015).

Normal members of a particular species usually have the same number of nuclear chromosomes. Among sexually reproducing organisms such as humans, the number of chromosomes in the body (somatic) cells is diploid (2n, a pair of each chromosome), twice the number of chromosomes as in gametes, which are haploid (1n). Haploid gametes are produced by a process called meiosis from diploid germline cells. During fertilization, gametes from the sperm fuse with gametes from the egg to form a diploid zygote. As all of the mother's eggs possess X chromosomes, and half of the father's sperms contain X chromosomes and half contain Y chromosomes, sperm is the viable factor in determining the sex of the offspring. Some organisms are polyploid. For example, bread wheat is hexaploid and has 42 chromosomes in total. In contrast, in species that reproduce asexually, the chromosome number is the same in all the cells of the organism, which can be haploid or diploid (Alberts et al. 2015).

Location of Chromosome

In eukaryotes such as plants, fungi, and animals, chromosomes are contained in a membrane-bound nucleus with a few exceptions such as the red blood cells. Eukaryotic cells also contain small circular mitochondrial genome (mtDNA) that are inherited maternally and can be variable in numbers. Mitochondria, which contains mitochondrial genome, is an organelle that is necessary to fuel the cell's energy source through supplies of ATP (adenosine triphosphate), as well as other essential roles in cell metabolic homeostasis, signaling, differentiation, and senescence (Zhu et al. 2019). ATP is produced via a process called the oxidative phosphorylation, which produce reactive oxygen species (ROS) as a natural byproduct which could damage DNA. During ageing, this process of oxidative phosphorylation becomes even less effective. As a result, higher level of ROS is produced, and mutation in mtDNA accumulates. This feed-forward cycle of DNA-damaging ROS production and accumulation of mtDNA mutation causes further functional changes in the oxidative phosphorylation system, mitochondrial dysfunction, cell senescence, and apoptosis (Zole and Ranka 2018; Sahin and DePinho 2012). We are only about to understand the relationship of how mtDNA influences the ageing pathologies and more researches are indeed needed.

Prokaryotes such as bacteria and blue-green algae (archaea) have their DNA exist as a single chromosome called the genophore. In addition to the main chromosome, bacteria possess small circular cytoplasmic DNA called the plasmids, which play a major role in horizontal gene transfer. The copy number of plasmids is highly variable as this is determined by the rate of cellular division. Prokaryotes lack a discrete nucleus and nuclear membrane as eukaryotes, and prokaryotic chromosomes are organized in a defined region called the nucleoid. Prokaryotic chromosomes and plasmids are supercoiled and are only uncoiled during cell division and transcription (Alberts et al. 2015).

Chromosome Structure

Chromosomes have a very complex structure. DNA, which makes the base of the structure, is made up of a two strands of nucleic acid base pairs. The bases in the DNA are cytosine, adenine, thymine, and guanine. The double helix structure formed by the two strands of DNA is due to complementary base pairing on the opposite strands where adenine pairs with thymine and guanine pairs with cytosine. The phosphate-deoxyribose backbone keeps the DNA strand intact (Alberts et al. 2015).

The long DNA strand is then tightly coiled around histone proteins like a loop. A strand of 150–200 nucleotides long is wrapped twice around a core of histone octamer, which is made up of two units each of histones H2A, H2B, H3, and H4. This bead-like structure is called the nucleosome, and a series of nucleosomes are interconnected by DNA strand resembling bead on a string. Histone proteins provide structural support and play an important role in regulating gene expression. Gene expression is determined by how densely packed the gene is, which is in turn regulated by the activation or deactivation of the relevant histone proteins, thereby contract or expand the chromosome respectively, and can suppress or activate the corresponding genes. Active genes that are constantly expressed are packed less tightly than inactive genes. Chains of nucleosomes are further coiled into an even denser structure, known as the solenoid, which is stabilized by the histone H1. The solenoid structure further coils around scaffold proteins to form a long thin tube called the chromatin. Each of our cell contains approximately 1.8 m of DNA, but each DNA strand is less than 1×10^{-8} m thick. This allows the very long DNA to fit inside the cell nucleus (Alberts et al. 2015). During ageing, it has been shown that chromatin structure at specific loci changes with age. For example, in humans, there is a reduction of heterochromatin during normal ageing which is associated with lower levels of HP1 and H3K9me3 and a loss of nucleosome occupancy at these loci. The premature ageing diseases Hutchinson-Gilford progeria syndrome (HGPS) and Werner syndrome in humans are also characterized by a reduction in heterochromatin and lower levels of H3K9me3, H3K27me3, and HP1. Yet, ameliorating the loss of nucleosome occupancy in yeast was shown to increase lifespan (Booth and Brunet 2016).

Chromatin is the uncoiled, long, and thin structure inside the nucleus. During cellular division, more scaffold proteins are activated, and chromatin fibers are further condensed into a ribbonlike structure called the chromosome. Chromosomes help to ensure that the replicated DNA is distributed properly in daughter cells. Chromosome is only visible during the metaphase and anaphase of cellular division under a light microscope. Locating at the constriction point of each chromosome is the centromere, which divides the chromosome into the p (short) arm and the q (long) arm (Alberts et al. 2015).

At both ends of the chromosome is called the telomere, which is a specialized chromosomal DNA-protein structure that protects the chromosome ends from being recognized as linearized double-strand DNA breaks by the DNA damage repair machinery. The telomere also inhibits chromosomal fusion and recombination, maintains chromosomal integrity, and preserves the genomic sequence (Alberts et al. 2015). This protection mechanism is based on the maintenance of telomere length and its protective structure: in human, telomere consists of TTAGGG repeats that ends in single-stranded 3′ G-overhang, which forms a protective secondary structure called the t-loop and associates with shelterin. Telomeres progressively shorten with age and with each cell division due to the end-replication problem, and when a critical length is reached, telomere loses its protective structure as t-loops and its associated binding with shelterin (Zole and Ranka 2018). As a result, the DNA damage response (DDR) is triggered, a signaling cascade that ultimately upregulates p53 (Zhu et al. 2019) to induce downstream signaling cascade to result in replicative senescence and mitochondrial dysfunction (Sahin and DePinho 2012).

In fact, individuals with loss of function mutations in telomerase, an enzyme that normally functions to extend the telomeres, are predisposed to premature ageing. For example, those with mutations in the TERC (the RNA component of telomerase) and TERT (the catalytic subunits of telomerase) demonstrate premature ageing syndrome dyskeratosis congenita (Sahin and DePinho 2012). Experiments that extend the telomere lengths in mice reverse the premature ageing phenotypes (Zhu et al. 2019).

Bacterial genes are expressed in groups known as the operons, and bacterial genes lack introns. Eukaryotic genes are more complex in sequence-based structure and are organized into exon, intron, and regulatory sequences instead. Exon is the coding region that specifies a sequence of amino acids; intron is the noncoding region, and regulatory sequences determine when and how much protein synthesis should be (Alberts et al. 2015).

Cell Division Through Mitosis and Meiosis

To ensure that DNA in chromosomes are passed from parent to daughter cells, cells divide through two processes: mitosis and meiosis. Mitosis occurs in somatic cells, while meiosis occurs in germ cells. In mitosis, diploid parent cell divides and produces two genetically identical diploid daughter cells, each with the same number of chromosomes as in the parent cell. In meiosis, DNA replication is followed by two rounds of cell divisions (meiosis I and meiosis II), where parent cell produces four haploid daughter cells; the unique recombination process involved in meiosis produces genetically distinct gamete that can enhance genetic variation. At fertilization, haploid ovum and haploid sperm fuse to form a diploid zygote. The phases of cell division are similar for both mitosis and meiosis (prophase, metaphase, anaphase, and telophase), where both are preceded by interphase (DNA replication) and followed by cytokinesis, the cytoplasmic division of the daughter cells (Alberts et al. 2015).

All phases of cell cycle follow one another in strict order and are regulated by a range of cell cycle proteins such as the cyclins and cyclin-dependent kinases. As a result, the cell has to fulfill every checkpoint before proceeding to the next phase of the cell cycle. In cases where the environment became overcrowded or the cell became specialized, the cell may leave the cell division and enter G0 phase to stop dividing.

Meiosis does not occur in archaea or bacteria as these organisms reproduce asexually via binary fission. This occurs when DNA are horizontally transferred from one species to another and are subsequently recombined into the chromosome (Alberts et al. 2015).

Chromosomal Aberrations

Abnormal segregation of chromosomes or sister chromatids during meiosis I or meiosis II, or non-disjunction, can result in the production of gametes with abnormal numbers of chromosome sets, or aneuploidy (Alberts et al. 2015). In humans, most aneuploidies are lethal because of the ensuing imbalance in gene expression. Aneuploidies on sex chromosome are mostly tolerated because X inactivation maintains near-normal expression levels for X-linked genes. Aneuploidies on some small chromosomes can sometimes be tolerated, but they usually result in severe developmental genetic disorders. Common aneuploidies include the Down syndrome (trisomy 21), Patau syndrome (trisomy 13), Edwards syndrome (trisomy 18), Klinefelter syndrome (extra X chromosome (s) in males), Turner syndrome (the presence of only one X chromosome in females), Triple X syndrome (trisomy X in females), XYY syndrome (an extra Y chromosome in males). Genetic counseling is offered for families affected before planning to conceive. During normal ageing, which is characterized by a progressive decline in functions, is also associated with an overall genomic instability in both nuclear and mitochondrial DNA (Zole and Ranka 2018).

Karyotyping is a technique for determining the karyotype of the chromosomes. Cells are first arrested in mitotic metaphase in vitro by applying colchicine, chromosomes are then stained to generate distinctive banding patterns, photographed, and chromosome pairs are then arranged in order of length, with allosomes at the end. Karyotyping can easily detect aneuploidies and subtle chromosomal structural changes. Normal banding pattern of a chromosome can be graphically represented in a chromosome map in the form of an idiogram, showing the coordinates, relative sizes, and morphological characteristics of each banding (Mosby's Medical Dictionary, eighth edition. (2009). Retrieved November 292,018 from https://medical-dictionary.thefreedictionary.com/idiogram). Idiogram allows cytogeneticists to identify any structural abnormalities, including deletions, duplications, and translocations, down to a few megabases of DNA accuracy (Alberts et al. 2015).

In order to detect mutation at a molecular level, fluorescence in situ hybridization (FISH) can be used to detect and localize the presence of specific DNA sequences on chromosomes. This molecular cytogenetic technique uses labeled fluorescent DNA or RNA probes that hybridize to the complementary DNA sequences on the chromosomes. Multiple probes, each labeled with different fluorescent dyes, can be used simultaneously, generating colorful image upon fluorescent microscopy. FISH techniques are routinely employed in clinical cytogenetics to identify commonly mutated genes. For example, FISH is used to detect the Philadelphia chromosome (Ph), which is a reciprocal translocation of the *ABL1* gene of chromosome 9 onto the *BCR* gene of chromosome 22, creating a fusion gene *BCR-ABL*1. Individuals with *BCR-ABL*1 have a particularly high risk in developing chronic myeloid leukemia (CML) (Alberts et al. 2015).

There are two ways to describe a gene's location on the chromosome. The standardized way is made up of three components, (1) chromosome number or letter, (2) p arm of q arm of the chromosome, and (3) the position of the gene, represented by a two-digit number, and is sometimes followed by a decimal point with one or more digits representing the region and the cytogenetic bands of the gene. An example is the tumor necrosis factor-alpha (TNF-α) gene in human with chromosomal location 6p21.33. The second way to describe a gene's location is to determine its molecular location based on sequencing of the base pairs. Although this method is more precise, varying sequencing methods can result in variations in the coordinates. Taking the above TNF-α gene as an example, its molecular location is NC_000006.12 (31,575,567 to 31,578,336).

Summary

In this book chapter, the function, structure, location of chromosomes, chromosomes under the process of cellular division through mitosis and meiosis, and chromosomal aberrations including under the effects of normal ageing are described. Finally, modern techniques to study chromosomes and ways to describe different chromosomal locations are also examined.

Cross-References

- ▶ Alleles
- ▶ DNA Chip
- ▶ DNA Damage Theory
- ▶ Genetics: Ethnicity
- ▶ Genetics: Gender
- ▶ Genetics: Gene Expression
- ▶ Genotype
- ▶ Mitochondrial DNA Mutations
- ▶ Nucleotides
- ▶ Whole Genome Sequencing

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Chromosome Ends

▶ Telomeres

Chronic Disease Self-Management

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Definition

Self-management is one's personal contribution to the direction of his or her health and health care in consideration of his or her context.

Overview

In the 40 years since the concept of self-management emerged from the asthma research by Creer and colleagues (Creer and Burns 1979), and later from Lorig and colleagues' endeavors in arthritis (Lorig et al. 1984), interest in self-management has grown considerably. Prior to this seminal work, individuals living with chronic conditions were observed to be inactive participants in their care. Today, self-management, one's "ability to manage the symptoms, treatment, physical, and psychosocial consequences and lifestyle changes inherent in living with a chronic condition" (Barlow et al. 2002, p. 178), shifts this view to patients as collaborative members of healthcare treatment teams. Self-managers are confident problem-solvers and thoughtful decision-makers who possess the ability to promote their own health and seek to maintain active, independent lives despite the onset of chronic conditions.

Background

Interest in self-management is influenced by the change in aging demographics and the increased prevalence of multiple chronic conditions (MCC) due to the population shift in the U.S. The first group of baby boomers, Americans born between 1946 and 1964, turned 65 in 2011. This segment of the population will rise to just over 82 million people in 2040 and bring with them an increased burden of chronic conditions (Administration for Community Living 2018). In the early 1900s, top causes of death were pneumonia, influenza, and other infectious diseases (Centers for Disease Control and Prevention n.d.). Over the last century, advances in health care and improvements in public sanitation and housing conditions have reduced deaths due to infectious diseases. Now, chronic conditions that persist for longer periods are among the top leading causes of death and disability. Chronic conditions are common, affecting three in four older adults. Further, chronic conditions are expensive to treat costing the US healthcare system \$0.71 of every dollar (Agency for Healthcare Research and Quality 2014). Poorly managed chronic conditions may cause serious health complications or death. For example, older adults undergoing hemodialysis due to irreversible kidney disease have to carefully monitor their diets. Because the kidneys balance the body's electrolytes, and diminished kidney functioning disrupts this balance, diets high in potassium and phosphorus can have dangerous consequences. Thus, one may learn to prepare "kidney-friendly" foods to avoid undesirable symptoms and maintain healthier lives.

Self-Management

Self-management involves the daily undertaking of tasks that promote health such as maintaining a healthy diet, participating in regular physical activities, and engaging in relaxation and stress-reducing techniques. Some tasks are common across conditions and others are disease-specific. Creer (2000) stated, "If a collage were created to depict the self-management of chronic illness, it undoubtedly would be highly diverse and abstract" (p. 618). Still, there is a general agreement of three primary tasks: medical management, life-role management, and emotional management (Corbin and Strauss 1988). Medical management consists of tangible tasks such as administering medications, interacting with healthcare providers, and adhering to a condition-compatible diet. Life-role management requires adopting new behaviors and/or life roles. For instance, older adults with significant fall-related injuries may require adjustments to their exercise routine or ergonomic adaptations at home or work. Finally, emotional management involves adjusting to the emotional response following a condition onset (e.g., dealing with depressed mood, fear, or hopelessness) (Lorig and Holman 2003).

Self-management interventions promote the acquisition of new skills including problem-solving, decision-making, resource utilization, patient-provider partnerships, and taking action (D'Zurilla 1986). Problem-solving involves a clear definition of the problem, generating possible solutions, and gathering information to select a feasible solution. Information gathering is also a component of the decision-making process. For instance, on a daily basis, older adults with chronic conditions have to consider appropriate responses to symptoms like pain or fevers. Furthermore, self-management skills involve older adults identifying and utilizing helpful resources and developing collaborative relationships with healthcare providers. An example of this skill is an older adult who prepares a list of questions prior to a doctor's visit to ensure a productive, intentional discussion. Finally, taking action is an important self-management skill most often promoted through the development of an action plan and identifying resources to accomplish such a plan (Lorig and Holman 2003). Action plans are specific and delineate resources required for success. For example, an older adult who has experienced weight gain may articulate a goal to engage in regular physical activity. To promote success, the action plan may specify the types of safe exercise to be performed and the best days, times, and location to engage in the exercise.

Efforts to promote self-management among older adults are progressing due to the growing evidence demonstrating at least marginal improvements in physical and mental health outcomes (e.g., pain and depression). For example, participants of an Internet-based arthritis self-management program experienced improvements in pain after 1 year (Lorig et al. 2008), and participants of a culturally tailored diabetes self-management intervention experienced a decrease in HbA1c levels also after 1 year (Rosal et al. 2011). These studies represent just two examples of the promise of self-management.

Theoretical Underpinnings

The development of self-management programs can be attributed to theories that consist of interconnected constructs that explain pathways to health behaviors. With theories, researchers and practitioners can better identify environmental, societal, psychological, physiological, and economic barriers and facilitators of health behaviors. Furthermore, theoretical models depict pathways through which health behaviors occur, ultimately guiding researchers to an understanding of why some individuals living with chronic conditions manage well and others struggle and how to promote self-management through intervention development (Glanz et al. 2015).

Perhaps one of the most influential theories in self-management research and intervention development is social cognitive theory (SCT) (Bandura 1986). Briefly, according to SCT, behavior is influenced by personal factors (i.e., outcome expectations, self-efficacy) and external factors (i.e., one's social or physical environment). Outcome expectations, both positive and negative, refer to the belief that certain behavior will lead to a given outcome, for instance, the belief that regular physical activity could lead to improved weight management. Central to SCT is the self-efficacy construct that reflects an individual's confidence to perform a certain behavior. The more self-efficacious a person feels to perform a specific behavior, the greater likelihood the behavior will be executed. There is a growing body of evidence suggesting self-efficacy is associated with health promotion among older adults living with chronic conditions. Self-management interventions grounded in self-efficacy may improve health outcomes (Bahari 2017), promote mastery of self-management behaviors (Stellefson et al. 2013), and increase confidence to manage pain (Devan et al. 2018). However, more research is needed to better understand differences by gender, ethnicity, and sociodemographic factors.

Another widely applied theory in self-management research is the health belief model (HBM). According to HBM, the threat of developing a chronic condition presents itself through internal and external cues to action such as physical pain or a report of increased prevalence of condition in a given geographic area. The threat is influenced by one's belief about his or her susceptibility to the condition and the severity of said condition. Perceived benefits (i.e., perceptions about the advantages of performing a behavior) and perceived barriers (i.e., obstacles to performing a behavior) predict behavior performance. Also, HBM incorporates self-efficacy by suggesting that one's confidence level to perform a behavior can facilitate (high self-efficacy) or impede (low self-efficacy) behavior performance (Skinner et al. 2015). To illustrate the application of HBM to self-management interventions, a quasi-experimental pilot study to evaluate the acceptability and feasibility of the Heart Health Program with 25 African American older adults is described (Menne et al. 2016). Through education, support, and action plan development, Heart Health promoted behavior change to individuals who are at high risk for cardiovascular disease but lack access to programs and services that contribute to healthier lifestyles. HBM informed the Program's design and implementation. For instance, participants received incentives to reduce the barriers to heart-healthy behaviors and education about the benefits of taking action. As a result, participants who developed action plans expressed their intent to eat healthier, exercise more, and increase mental hygiene (e.g., stress-reducing activities). Also, 63% of participants' action plan components were accomplished (Menne et al. 2016). There are other health behavior theories not covered (e.g., transtheoretical model, theory of planned behavior) that have contributed to the self-management literature. They, too, may help explain predictors of self-management, socio-ecological factors associated with self-management, and modifiable variables that could inform self-management interventions.

National Attention

In the USA, national programs and policies such as the Social Security Act, Medicare, and the Older Americans Act have placed the needs of older adults on the national stage. Due to the unwavering efforts of aging advocates, calls to action for more policies that meet the health needs of older adults' have not waned, in part, because of the unrelenting burden of chronic conditions that negatively affect their well-being. For instance, a goal of Healthy People 2020, an initiative that sets forth health priorities for American citizens every 10 years, was to improve the health status and quality of life of older adults by increasing the proportion of older adults who undergo self-management education (Office of Disease Prevention and Health Promotion 2019). In 2009, aging policies culminated into the American Recovery and Reinvestment Act's prevention and wellness initiative: the Communities Putting Prevention to Work program. The Administration on Aging, in partnership with the Centers of Disease Control and Prevention and the Centers for Medicare and Medicaid Services, awarded $27 million in grants to 45 states, the District of Columbia, and Puerto Rico to disseminate and implement a suite of chronic disease self-management education programs in 2010, 1 year in advance of the first group of baby boomers' 65th birthdays. Grants ranged from $50,000 (Alaska) to $1,190,610 (New York), ultimately reaching nearly 90,000 people, about 64% of whom were aged 60 and older (Administration on Aging 2013).

Self-management language is now reflected in health policies. For example, the 2008 revisions to the Medicare Conditions for Coverage for dialysis units are reshaping dialysis culture. The original Conditions of 1976 lacked emphasis on self-management. Now, dialysis facilities are required to encourage patient participation in care planning (Alt and Schatell 2009). While research is needed to examine the effect of this policy change on patient outcomes, it could mean positive health behavior changes for older adults who represent the fastest-growing segment of the dialysis population. Hopefully, this trend will continue in policies that guide standards of care in other healthcare settings.

Key Research Findings

In public health research, self-management has been described as the critical element needed to reduce the individual, community, and societal burden associated with chronic conditions (Brady et al. 2015; Parekh et al. 2011) because when employed successfully, it can lead to enhanced quality of life; reduction of negative physical and mental symptoms; and adequate utilization and adherence to health care (Brady et al. 2013; Chodosh et al. 2005). Acknowledgment of the Self-Management Resource Center's (SMRC; formally Stanford Patient Education Research Center and The Stanford Arthritis Center) contribution to key self-management research findings over the last four decades is warranted. Their work started with the Arthritis Self-Management Patient Education Research Project, which focused on developing and implementing a patient education program that would improve the health of those diagnosed with arthritis on the assumption that if individuals engaged in an intervention focused on health behavior change, health status would improve (Lorig and Holman 1993; Lorig et al. 1984). While health behaviors and health status improved, a strong association between the two was not observed. Thus, the program was then revised to include self-efficacy enhancing strategies ultimately increasing the effectiveness of the program. As a result, self-efficacy was identified as the core of successful self-management (Lorig and Holman 1993). Arthritis, being among the most common chronic conditions and the leading cause of disability (Centers for Disease Control 2018), served as an exemplar for the development of a suite of programs presently referred to as the Chronic Disease Self-Management Education (CDSME) programs.

In addition to the arthritis self-management program, the CDSME programs include condition- or symptom-focused programs (i.e., diabetes, chronic pain, cancer, HIV); a program for caregivers of people with traumatic-brain injury, post-traumatic stress disorder, dementia, and other diagnosed memory impairments; as well as the MCC-focused program entitled Chronic Disease Self-Management Program (CDSMP). While there is some utility in delivering a condition- or symptom-focused program, the greatest impact has been a result of the well-known and widely disseminated CDSMP. The CDSMP is an evidenced-based peer-led intervention consisting of highly interactive 2.5-h small group (10–20 participants) workshops once a week for six consecutive weeks. The workshops are facilitated by trained laypersons who in many instances are diagnosed with a chronic condition as well. Participants engaged in the program receive a copy of the book *Living a Healthy Life with Chronic Conditions, Fourth Edition* as well as an audio relaxation CD titled *Relaxation for Mind and Body* (SMRC 2019). The weekly workshops focus on teaching individuals ways to deal with pain, fatigue, isolation, frustration, and depression. Furthermore, participants are taught how to develop an action plan to meet intended goals; develop an individualized exercise program; appropriately use medications; solve chronic disease-related problems; and communicate effectively with family, friends, and health-care providers. Participants receive information concerning nutrition and receive guidance on how to make informed decisions about treatment options (Mingo et al. 2015; Ory et al. 2013b). CDSMP has improved health care (e.g., increased communication with physician, medication adherence, and confidence in completing medical forms) and health (e.g., significant improvements in self-reported health status, fatigue, pain, disability, depression, health-related quality of life)(Brady et al. 2013; Ory et al. 2013a) while potentially saving healthcare costs (Ahn et al. 2013; Ory et al. 2013b). To date, CDSMP is offered as community-based in-person program (as described above) in rural and urban settings, Internet-based, and a mailed toolkit. The Internet-based version includes groups of up to 25 people with a variety of health conditions who participate at their convenience for a total of 2 hours a week for six consecutive weeks. Led by two trained lay leaders, the asynchronous online program participants remain highly engaged through internal messaging and discussion boards. The mailed toolkit is a self-directed version of the program where the participant has the autonomy to complete the program at his or her own pace. It is unclear how intervention delivery modalities influence utilization and completion of the program (SMRC 2019). Still, this important body of work has contributed greatly to the self-management literature and the health of older adults.

The majority of the management for chronic conditions occurs external to primary care settings, but it is important to advocate for a collaborative approach because recommendations from physicians may influence patients' willingness to participate in programs similar to CDSMP (Mingo et al. 2013). Healthcare providers can become more active in minimizing this barrier by presenting patients with a prescribed treatment of self-management and facilitate self-management programs within their practice or simply showing knowledge (e.g., being aware of what types and where programs are offered) and unequivocal support for treatment plans that directly encourage engaging in evidenced-based self-management programs. Small changes such as these may have a greater public health impact.

Application: Self-Management and Health Disparities

Health and healthcare disparities prevail in the USA. It is possible that practical adaptations in CDSME programs that embrace cultural norms and preferences may contribute to a reduction in health disparities (Mingo et al. 2013; Gitlin et al. 2008; Goeppinger et al. 2007). For example, African Americans are disproportionately represented in the diagnosis, negative impact, and risk behaviors of chronic conditions. Engaging African Americans in evidenced-based self-management programs could contribute to reducing chronic disease-related health disparities (Mingo et al. 2013; Mingo et al. 2015). To that end, researchers must consider the cultural milieu and unique experiences across the life-course of African Americans that could contribute to changes in health trends.

Although CDSME programs demonstrate effectiveness, African Americans tend to be underrepresented in the access, utilization, and completion of such programs (Mingo et al. 2015). Moreover, African Americans have expressed distinct preferences around program content, structure, and delivery (Gitlin et al. 2008; Mingo et al. 2013; Smith et al. 2015a), suggesting the need for culturally informed adaptations. While research is warranted to identify and gain and in-depth understanding of key factors that contribute to a pathway between CDSME programs and a reduction in health disparities among African Americans, recent efforts have moved the science forward in this direction. For example, national efforts have focused on increasing the dissemination and implementation of CDSME programs among disadvantaged populations by diversifying the types of location delivery sites (i.e., addressing access and acceptability). Findings indicated that this approach was successful in increasing the diversity of CDSME participants. Delivering the program at faith-based organizations and community or multipurpose centers was attractive to African Americans (Smith et al. 2015a). Compared to senior centers, which has deemed to be successful for this target group (Gitlin et al. 2008), attending the CDSME program at a residential facility or community center reduced the likelihood of completion (i.e., attending four out of the six sessions). It is plausible that barriers identified in the health disparities literature such as transportation, competing family responsibilities, or health complications prevent remaining in the program for six consecutive weeks at these particular sites. Yet, senior centers may have a loyal audience that consistently supports programing ultimately encouraging completion. Also, two studies with African Americans living in North Carolina and Pennsylvania, respectively, have introduced culturally relevant adaptations into CDSMP and started a conversation in the literature about its importance (Gitlin et al. 2008; Goeppinger et al. 2007). However, due to the lack of widespread uptake of culturally sensitive adaptations specifically for African Americans, the impact on health disparities is inconclusive. Thus, while CDSME programs have the potential to positively change health trends for African Americans, research is warranted to understand how social, cultural, and environmental factors unique to this target population influence the association between CDSME and reduction in health disparities.

Future Directions

Guidance for Practitioners

A baseline of self-management behaviors, and factors influencing those behaviors, must be established in order for practitioners to determine the need for self-management interventions. Fortunately, there are a number of reliable, publically accessible evaluation tools that can be embedded in psychosocial assessments. Psychosocial assessments are instruments used to evaluate a person's history, health and functional status, emotional health, living conditions, financial resources, and social network characteristics to identify risks, expose unmet needs, and highlight personal and environmental strengths. Psychosocial assessments are most often employed by social workers or case workers in health and social service settings who use assessment data to inform interdisciplinary care plan goals. However, care plans can be undermined when important health and clinical information, such as self-management behaviors, go unassessed (Cagle et al. 2017). The SMRC maintains an accessible list of self-management instruments in English, Spanish, and French, their scoring guidance; psychometric properties; and relevant references (SMRC 2019).

Guidance For Researchers

Before programs like the CDSMP can be implemented in untapped communities and healthcare sites, formative research must be carried out to better understand its feasibility in those settings and its acceptability with their patient populations. For example, healthcare facilities are the second largest delivery site of the CDSMP nationwide (Smith et al. 2015b), but there have been few attempts to implement this program in dialysis facilities. As a precursor to its implementation, Washington and colleagues sought to better understand the relationship between psychosocial factors and kidney disease self-management, how individuals undertaking dialysis define and think about self-management, and their interest in participating in a self-management program (Washington et al. 2016; Washington et al. 2017; Washington et al. 2018a). When surveyed, depression was found to undermine self-management, and 78% of dialysis participants affirmed they would participate in a self-management program if it were offered in their facility. This information is useful because 20% experienced depressed mood, a barrier to self-management, and they evidenced generally low self-management in exercise (range 0–20, mean 2.5), patient-provider communication (range 0–15, mean 2.5), and cognitive symptom management (range 0–30, mean 0.9). Finally, when examining organizational readiness to implement the CDSMP in dialysis facilities, dialysis staff perceived it to be consistent with facility values and agreed they were well-positioned to implement and sustain the program (Washington et al. 2018b). Although these studies are cross-sectional with small samples, when taken together, the findings suggest a self-management program would be beneficial and supported but would require thoughtful implementation considerations. This example, while only one, has implications for developmental self-management research with other chronic conditions.

Policy Implications

It is important for researchers, practitioners, and citizens to continue their advocacy efforts to garner the attention of policymakers who can prioritize healthy aging at the national level. The development of Healthy People 2030 is underway; utilizing the public comment period is one way to ensure older adults' needs, and their caregivers' needs, are folded into its health initiatives. Moreover, patients and providers can collaboratively support legislation that increases the accessibility and availability of programs and services beneficial to the successful management of chronic conditions.

Summary

In summary, there are three points to contemplate. First, defining self-management as one's personal contribution to the direction of his or her health and health care in consideration of his or her context emphasizes the joint contribution of the person and the environment to behavior. Informed by the person-in-environment perspective (Kondrat 2008), this definition contends that individuals are reciprocally engaged in relationships with the physical, social, economic, cultural, and familial world that surrounds them. Second, although 40 years of self-management research has contributed to a better understanding of self-management tasks and behaviors, and informed the development of effective self-management programs that have been widely disseminated, there remains an opportunity to better understand self-management processes among ethnic and marginalized populations. For example, there is a dearth of literature on chronic disease self-management in transgender older adults and effective health promotion interventions that take into account their unique needs. Finally, while it is important to adhere to fidelity protocols of self-management interventions, developers may consider some degree of flexibility to allow for a more person-centered approach. It will require careful identification of their "active ingredients" in relation to outcomes.

Cross-References

- ▶ Aging and Health Disparities
- ▶ Behavioral Gerontology
- ▶ Diabetes Management in Older Adults
- ▶ Healthy Aging
- ▶ Nutrition and Lifestyle
- ▶ Psychological Theories of Health and Aging

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C

Chronic High Blood Pressure

► Hypertensive Cardiovascular Diseases

Chronic Lymphocytic Thyroiditis

► Autoimmune Thyroiditis

Chronic Obstructive Pulmonary Disease (COPD)

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Definition

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities, usually caused by significant exposure to noxious particles or gases (GOLD Update 2019).

The terms emphysema and chronic bronchitis (Medical Research Council Committee on the Aetiology of Chronic Bronchitis 1965) are commonly incorrectly used in defining COPD. Emphysema is a destruction of the alveolus, which are the gas-exchanging surfaces of the lung (also called parenchyma). This pathological term is often used clinically; however, it describes only one of several structural abnormalities present in COPD. On the other hand, chronic bronchitis is defined as the presence of cough and sputum production for at least 3 months in each of two consecutive years (Medical Research Council Committee on the Aetiology of Chronic Bronchitis). This is a clinically and epidemiologically useful term. However, when this definition is strictly applied, it is present in only a minority of subjects living with COPD.

Overview

COPD is caused by a mixture of small airways disease and parenchymal destruction. Chronic inflammation causes structural changes, and it may contribute to airflow limitation and mucociliary dysfunction; in case of alveolar destruction, this decreases lung elastic recoil and gas-exchanging capacity.

In addition, there are systemic inflammatory manifestations, likely as a result of inflammatory processes (Wouters 2007). The systemic inflammation may be present and could play a role in the multiple comorbid conditions found in patients with COPD (Barnes 2016). Many other chronic diseases share the same risk factors, and this may impact patients' health status and survival (Miller et al. 2013).

COPD is a common illness in older adults. Middle-aged and older adults are most likely to be diagnosed. Older people are especially prone to the effects of COPD due to the anatomical and physiological modifications caused by aging. Thus, the main characteristic of older COPD adult patients is the complexity due to an increasing prevalence of comorbidities related to the age and other disabilities that are not related with respiratory disorders, such as physical and mental limitations.

Pathophysiology

The inflammation and narrowing of airways decrease lung function. The destruction of alveoli also contributes to airflow limitation and leads to decreased gas exchange. Emerging evidence also suggests that there is a loss of small airways (Hogg et al. 2017). Alveolus destruction leads to gas exchange abnormalities, which can be expressed in hypoxemia and hypercapnia. A ventilatory drive reduction, hyperinflation, increase of dead space in lungs, respiratory muscle impairment that increases the effort to breathe, and a reduction in pulmonary vascular structure are the most common abnormalities that may lead to gas exchange dysfunction (Jones et al. 2017). This dysfunction gets worse with the progression of the disease.

COPD may present periods of worsening of respiratory symptoms, which are called exacerbations. An exacerbation of COPD is a sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations that is acute in onset and may warrant additional treatment in a patient with underlying COPD. Exacerbations account for the greatest proportion of the total COPD burden on the healthcare system and, therefore, should be prevented reducing the risk of them.

Burden

COPD is a leading cause of disability and death worldwide, imposing a substantial socioeconomic burden due to the need for long-term management (Foster et al. 2006). Indeed, COPD is a major cause of chronic morbidity and mortality, and patients often have important concomitant chronic illnesses at the time of diagnosis. Therefore, multimorbidity development is an important component of COPD in older adults due to most of common risk factors (e.g., aging, alcohol, diet, and physical inactivity) (Lozano et al. 2012).

The prevalence, morbidity, and mortality of COPD vary across countries around the world and also across different groups within countries. The prevalence can vary from 5% to 13% around the world (Soriano and Rodriguez-Roisin 2011). Living in rural or poor areas is consistently associated with airflow obstruction, and lower socioeconomic status is associated with an increased risk of developing COPD (Raju et al. 2019; Townend et al. 2017; Beran et al. 2015). Risk for COPD is affected by long-term cumulative exposure to noxious gases and particles, such as cigarette smoking, fumes, chemical agents, and organic and inorganic dusts resulting from the burning of wood and other biomass fuels. Risk also increases with a variety of host factors, such as genetics, airway hyper-responsiveness, and poor lung growth during childhood (Guerra et al. 2013; Lange et al. 2015).

Moreover, COPD is a disease of age because it is directly related with the cumulative exposure to risk factors. Although the disease is common in older people, the true prevalence among the elderly is unclear and can vary from 25% in a general smoking population to 50% in the elderly smoking population (Lundback et al. 2003). The prevalence also changes across countries. In Norway in people aged ⩾65 was 28% (Waatevik et al. 2013), in the USA population ⩾75 years is 10% (Akinbami and Liu 2011), in Italy the prevalence changes from 7% in the 60–65 year group to 24% in the 80–85 year cohort, and in Spain was significantly higher in subjects aged ⩾70 years (22.9%) (Miravitlles et al. 2009).

In the future, the prevalence and the burden of COPD are projected to increase due to continued exposure to COPD risk factors. Moreover, the increasing longevity of the world's population also affects negatively to the exposure of COPD risk factors. Total deaths from COPD may increase by more than 30% in the next 10 years unless urgent action is taken to reduce major underlying risk factors, especially tobacco use. It is estimated that COPD will become the third leading cause of death worldwide by 2030 (WHO 2019).

Diagnosis

COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease. In this clinical context, spirometry is the best test to diagnose the lung dysfunction (Buist et al. 2007). The presence of a post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of persistent airflow limitation.

The stringent diagnostic criteria requiring a high-quality spirometry for a diagnosis of COPD to be made may increase the rate of underdiagnosis especially in elderly due to the difficulty to achieve the acceptability and or repeatability standards. Likewise, the age, cognitive impairment, disability, multiple grud therapy, and low education are the most common risk factors for a poor quality spirometry (Bellia et al. 2000). Thus, age-related factors and comorbidity-related changes may contribute to remain elderly unrecognized and untreated.

The most characteristic symptom of COPD is chronic and progressive dyspnea. This is a major cause of the disability and anxiety that is associated with the disease (Miravitlles et al. 2014). Cough is also common and may be either sputum-productive or unproductive (Cho et al. 2016). Sputum production is present in up to 30% of patients, and commonly small quantities of persistent sputum are raised with coughing. However, this symptom is often difficult to evaluate because patients commonly swallow sputum instead of expectorating it (Allinson et al. 2016). The color of the sputum is also important; purulent sputum reflects an increase in inflammation and/or the risk of bacterial infection (Soler et al. 2012).

Key Research Findings

There are different types of treatments for COPD. Smoking cessation is the first one that should be considered. Pharmacotherapy, nicotine replacement, plans to band, and counseling may improve the abstinence rates. The effect of using e-cigarettes for smoking cessation is uncertain at present (Stead et al. 2013, 2016), and new evidence shows that the use of e-cigarettes among people with COPD may bring greater risks (Bozier et al. 2019).

Pharmacological therapy can reduce COPD symptoms and the frequency and severity of exacerbations and improve health status and exercise tolerance. Treatment should be individualized and tailored to the severity of symptoms, risk of exacerbations, side-effects, comorbidities, drug availability, and cost. Patient's response, preference, ability, and inhaler technique also should be considered (GOLD Update 2019). Influenza vaccination should also be considered to decrease the incidence of lower respiratory tract infections.

Long-term oxygen therapy improves survival in severe COPD patients with severe hypoxemia (Cranston et al. 2005). For patients with stable

COPD and resting or exercise-induced moderate desaturation, long-term oxygen treatment should not be prescribed routinely. However, individual patient factors must be considered (Long-Term Oxygen Treatment Trial Research Group 2016).

There is strong evidence that pulmonary rehabilitation improves dyspnea, health status, health-related quality of life, and functional exercise capacity in COPD stable patients. It also reduces hospitalizations among patients with a recent exacerbation. There is less evidence regarding the effectiveness of rehabilitation after an acute exacerbation. However, among those patients who have had a recent exacerbation, pulmonary rehabilitation can reduce readmissions and mortality (Lacasse et al. 2015; Spruit et al. 2013). Although there is evidence for its cost-effectiveness (Vogiatzis et al. 2016), the implementation of these programs is very limited (Desveaux et al. 2015). Moreover, among the small proportion of patients who are referred to a pulmonary rehabilitation, 33% do not attend their initial assessment and nearly 40% of those who commence will not complete the program (Steiner et al. 2018). Therefore, there are many challenges with pulmonary rehabilitation. Indeed, in 2015 the American Thoracic Society and European Respiratory Society recommended "a novel Pulmonary Rehabilitation should be developed and studied that will make evidence-based Pulmonary Rehabilitation more accessible and acceptable to patients and payers" (Rochester et al. 2015, p. 1380).

Another challenge is encouraging patients to sustained long-term physical activity. COPD patients are substantially less active than their healthy peers (Vorrink et al. 2011), and this inactivity has been consistently related to a worse prognosis (Gimeno-Santos et al. 2014). Thus, helping patients to adopt a more active lifestyle in the long term is a major goal in COPD management. Unfortunately, achieving and maintaining such behavioral change remain a challenge (Singh 2016). Moreover, the translation to enhanced daily-life physical activity levels after a pulmonary rehabilitation program remains controversial (Mantoani et al. 2016; Lahham et al. 2016). This may be because exercise training in and of itself is not designed to change the complex and multifactorial behavior that contributes to low levels of physical activity (Bauman et al. 2012).

New pulmonary rehabilitation models and long-term behavioral interventions targeting physical activity should be considered. Community-based and low-cost home-based pulmonary rehabilitation programs are effective (Holland et al. 2017). The Urban Training intervention, combining behavioral strategies with unsupervised outdoor walking, was efficacious in increasing physical activity after 12 months (Arbillaga-Etxarri et al. 2018). However, adherence to intervention remains a key issue for patients.

However, in elderly the inactive involvement or the nonadherence to the therapeutic choices (inhaled therapy, oxygen therapy, and pulmonary rehabilitation) is very frequent. The nonadherence rates vary from 50% to 80% (Rand 2005; Oates et al. 2017; Blackstock et al. 2016), and this is a huge problem in the treatment of patients because it can lead to high mortality, morbidity, hospitalizations, and a reduction of quality of life (Khdour et al. 2012). There are several clinical, cultural, social, economic, physiological, and demographical factors related with nonadherence such as cognitive impairment, asymptomatic periods, comorbidities, side effects, lack of belief in benefit of treatment, characteristic of the devices, lack of ability, complexity of treatment, cost of medication, and so on (Osterberg and Blaschke 2005; Hayton et al. 2013).

Future Directions of Research

In general, COPD treatments will widen their scope through advances in interpersonal medicine, which offers a disciplined approach to delivering care that responds to patients' circumstances, capabilities, and preferences (Chang and Lee 2018). In addition, telehealth programs have many potential advantages for health funders, particularly for patients who live further away from major health centers. Future research on pulmonary rehabilitation and physical activity should be based on ecological models that account for the roles of health and disease beliefs, symptoms, emotional characteristics, and social, cultural, and environmental factors (Bauman et al. 2012; Spruit et al. 2013).

Another area of COPD research deserving more attention is to improve the adherence into the different treatments areas where the older adults are especially vulnerable to guarantee the benefits from maintenance medications, a correct and continuous drug therapy, a daily participation in a regular physical activity, and exercise, and so on.

In summary, the future research should focus on the development of new pharmacotherapy treatments, education programs, new pulmonary rehabilitation models, health-related behavioral interventions and strategies to support learning, motivation, self-efficacy, and new ways to improve healthcare providers' engagement with patients.

Cross-References

- ▶ Aging and Health Disparities
- ▶ Aging and Tuberculosis
- ▶ Chronic Disease Self-Management
- ▶ Pneumonia
- ▶ Smoking, Aging, and Longevity
- ▶ Tumors: Non-small Cell Lung Cancer

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Chronobiology and Aging

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Definition

Chronobiology is the discipline which investigates rhythmic processes governed by the circadian clock and the consequences of its malfunctioning.

Overview

Circadian clocks are biological clocks that have synchronizing functions. In essence, they mimic the external light/dark cycle inside of an organism. As such, they optimize metabolism and physiology by tuning organismal metabolism in preparation for activity and rest phases aligned with the daily cycle of light and darkness. Surprisingly, defects of their circadian clock render organisms similarly vulnerable as aging processes. According to the recommendations of the International Agency for Research on Cancer (IARC), which is part of the World Health Organization (WHO), there is limited and sufficient evidence that shiftwork – a major disturbing factor of the circadian clock – represents a carcinogenic risk to humans and experimental animals, respectively (IARC working group on the evaluation of carcinogenic risks to humans 2010). Hence, it was concluded that the circadian clock and aging interact or even interfere (Fonseca Costa and Ripperger 2015). This interference may open up new means to ameliorate aging. As a perspective, reinforcing circadian rhythms in older persons resynchronizes metabolism and physiology with positive consequences for their life.

Key Research Findings

Many organisms exhibit circadian rhythms (Dunlap 1999). These rhythms persist under constant conditions where normal exposure to light and darkness is experimentally suspended, which exposes the underlying circadian clock. This clock generates rhythms of about a day, which are used to govern multiple outputs.

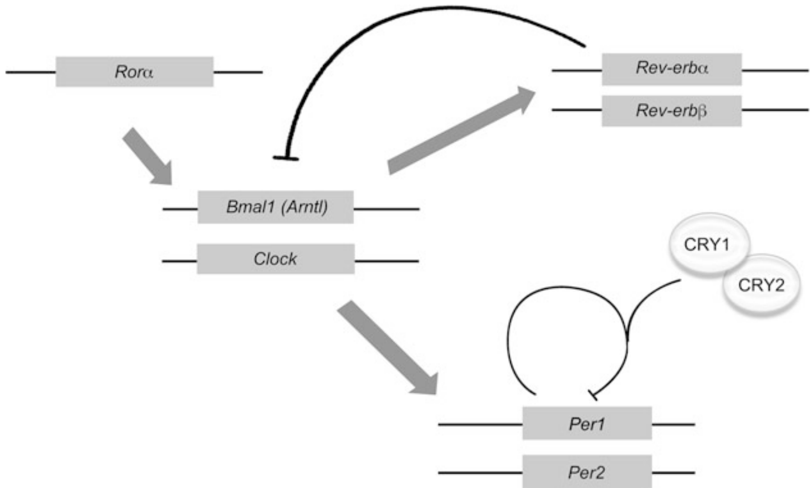
Although being such a widespread phenomenon, it is difficult to demonstrate an effect of the circadian clock on the fitness of survival for an organism, which could have an impact on life expectancy. However, experiments confronting animals with unusual 21 h or 27 h lasting days shortened their life expectancy. The longevity experiments originated from *Drosophila* (Pittendrigh and Minis 1972), but the same principle was found for a variety of organisms including mammalian species such as laboratory mice and primates (Wyse et al. 2010). As a recurring scheme, a nonmatching circadian system with the environmental light/dark period correlated with reduced life expectancy.

Under real-life conditions, the effects of the circadian clocks are masked by the external light/dark cycle, which resets the phase of the circadian system every day (reviewed in Albrecht 2012). In mammals, a bipartite brain structure located above the optical chiasm, the suprachiasmatic nuclei (SCN), serves as a connector between the external light/dark cycle and the peripheral oscillators (Albrecht 2012). Inside cells, there is a molecular oscillator comprised out of transcriptional and posttranslational feedback loops.

In higher organisms, transcriptional and posttranslational feedback loops establish a circadian oscillator as described originally for *Drosophila* (Hardin et al. 1990). A transcriptional repressor, dPeriod, accumulates throughout the night in pacemaker cells of the brain to ultimately repress its own synthesis, following which levels of the protein decline, and a new transcriptional cycle of about 24 h can occur. At least ten genes are involved in the mammalian molecular oscillator, of which four are most central (Fig. 1). The circadian cycle is initiated by binding of BMAL1 and CLOCK to regulatory sites within the *Period* (*Per*) and *Cryptochrome* (Cry) genes to activate transcription. The PER and CRY proteins then accumulate, heterodimerize with each other, and translocate into the nucleus, where they inhibit CLOCK/BMAL1 transcriptional activity, thereby repressing their own synthesis. After the full block of *Per* and *Cry* transcription, their concentration declines, and a further cycle can initiate. Another cycle – based on the competition of nuclear receptors for the same binding site – stabilizes the system. This design facilitates adaptation to tissue-specific regulation by employing further transcription factors as intermediaries.

With age, the amplitude and phase of circadian rhythms in mammals diminish and shift, respectively. The ablation of the SCN region causes hamsters to lose their circadian rhythms under constant darkness conditions (Ralph et al. 1990). At the same token, most other circadian rhythms for metabolism and physiology were blunted or changed phase resembling much older animals. The transplantation of fetal SCN tissue into the ablated site could reconstitute most rhythms (Ralph et al. 1990). Surprisingly, this kind of operation – but none of the other control tissues employed – increased significantly life expectancy of the hamsters (Hurd and Ralph 1998). Hence, a rejuvenation of the central circadian system was beneficial for long-term survival. Similarly, it was observed that mice with a circadian oscillator that perfectly matched 24 h at the age of 14 months lived longer compared to mice with deviating circadian periods (Libert et al. 2012). Taken together, it appears that a perfectly matching and functioning circadian system in the SCN impacts life expectancy.

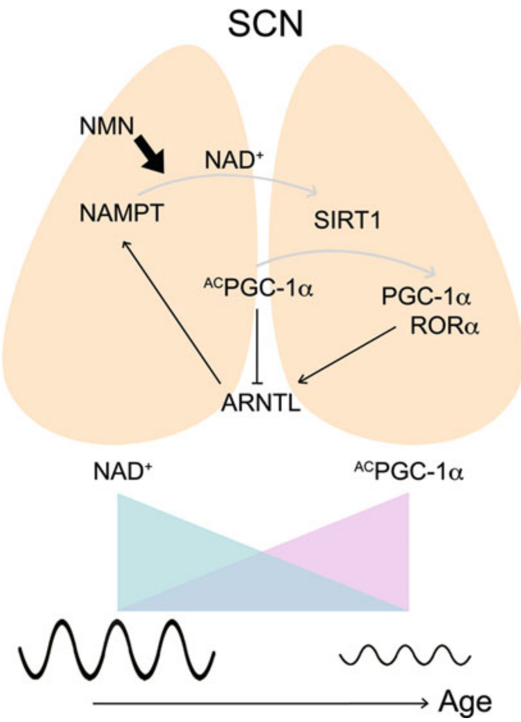
The functioning of the SCN was analyzed in aging mice. A decline of behavior was observed already in middle-aged mice of 12–14 months (Nakamura et al. 2011). The firing activity of neurons in the SCN was higher in resting animals, but their amplitude decreased in older mice. One explanation for the reduction in amplitude of firing is the changing activity with age of ion channels regulating neuronal activity (Farajnia et al. 2015). Surprisingly, the circadian oscillator of the SCN appeared not affected (Nakamura et al. 2011). Bioluminescence rhythms from SCN-containing brain slices expressing a PER2/luciferase reporter were indistinguishable between young and those middle-aged mice. Albeit, a later study found lower amplitudes of reporter gene activity when the mice were kept under prolonged constant dark conditions before the analysis (Nakamura et al. 2015). Hence, aging degraded the functioning of the SCN circadian oscillator, but a recurring light/dark cycle could slow down this effect. Overall, the studies revealed a tight correlation between the declining performances of the SCN neuronal network and the observed changes in locomotor activity.



Chronobiology and Aging, Fig. 1 Interaction of the mammalian oscillator components to yield circadian rhythms. A circadian cycle starts with binding of BMAL1/CLOCK heterodimers to the *Per* genes to activate their transcription. The PER proteins become stabilized and destabilized by the interplay of posttranslational modifications before a sufficient concentration is reached to enter into the nucleus together with the Cryptochrome (CRY) proteins. Here, they suppress their synthesis. The PER proteins degrade, the transcription block is relieved, and consequently a new cycle can occur. At the same time, BMAL1/CLOCK activates transcription of the nuclear receptors Rev-Erbα/β, which repress the *Bmal1* and *Clock* genes by competing with the nuclear receptor RORα. Because the phases of both cycles are roughly 12 h apart, they stabilize each other. (Simplified from Albrecht 2012)

How would the circadian oscillator function changes in the SCN with age? Part of the answer lies in the close relationship between the circadian oscillator on the one hand and the rhythmic activity of sirtuins and their cofactor NAD^+ on the other hand. It was shown that SIRT1 could rhythmically deacetylate components of the circadian oscillator (Asher et al. 2008; Nakahata et al. 2008), while the circadian oscillator regulated the synthesis of NAD^+ via nicotinamide phosphoribosyltransferase (NAMPT) (Nakahata et al. 2009; Ramsey et al. 2009). Changing the levels of SIRT1 in the brain affected the locomotor activity and the ability to respond to phase-setting light pulses of the mice as a proxy for aging (Chang and Guarente 2013). The brain-specific knockout of *Sirt1* resembled in this regard aged mice with reduced amplitude, while overexpression of SIRT1 maintained locomotor activity in a juvenile state. It was proposed that SIRT1 rhythmically deacetylated PGC1α, which acted as a coactivator for RORα on *Bmal1* (Fig. 2). Upon depletion with age of the endogenous concentration of NAD^+, this deacetylation becomes ineffective. As a consequence, the amplitude of the circadian oscillator and consequently NAD^+ production decline. The overexpression of SIRT1 in the brain could protect against this decline of NAD^+ (Chang and Guarente 2013). An independent study showed that the overexpression of SIRT1 in the brain increased life expectancy of female mice by 16% and of male mice by 9% (Satoh et al. 2013). Taken together, the studies suggested molecular changes at the base of the decline of the circadian oscillator in the SCN with age. Such molecular changes may represent targets to interfere with the aging process.

To sum up this part, a strict hierarchy governs the mammalian circadian system. A master clock dictates the rhythm and phases for all peripheral clocks. This tight coupling of the system is, on the one hand, a problem to maintain the system with



Chronobiology and Aging, Fig. 2 **Age-related decline of the circadian oscillator in the SCN.** RORα in concert with PGC-1α activate transcription of *Bmal1*, which is rhythmically repressed by Rev-Erbα/β (see Fig. 1). To fulfill its function as coactivator, PGC-1α has to be deacetylated by SIRT1, which needs NAD^+ as a cofactor. Upon the decline of NAD^+ concentrations in the SCN with age, less BMAL1 can be made, which lowers the amount of NAMPT and the production of NAD^+. Similarly, the amount of SIRT1 influences the circadian oscillator in the SCN. Low concentration of SIRT1 worsens, while high concentration improves circadian rhythms and their output from the SCN. Note that NMN, which acts downstream of NAMPT, could rescue the circadian oscillator from this vicious cycle (see below). (Adapted from Chang and Guarente 2013)

advancing age, but on the other hand, offers the possibility for easy manipulation of the system to rejuvenate its functions.

Examples of Application

From the organization as mentioned earlier of the circadian system in mammals, two different concepts emerge to affect aging. First, it is possible to improve the circadian system by resynchronizing the peripheral circadian oscillators with the central clock in the SCN. Second, drugs can be employed to target directly the molecular circadian oscillator, which affects all circadian oscillators in the organism. This part highlights examples of both strategies.

Light is the major synchronizer of the circadian system via the SCN. Different studies found that older persons are less light responsive than young. For instance, expression of the circadian oscillator gene *Per2* was increased 10 h after early morning exposure to blue (but not green) light in young but not old persons (Jud et al. 2009). The blue light is acting via a specific photopigment, melanopsin, which is located in intrinsically photosensitive retinal ganglion cells projecting to the SCN and adjusting its phase (Hattar et al. 2002). The reason for this lower responsiveness of older persons specifically to blue light might be a yellowing of the lens within the eye (reviewed in Turner and Mainster 2008). This filtering out of short wavelengths progresses slowly but steadily with age (Brøndsted et al. 2013).

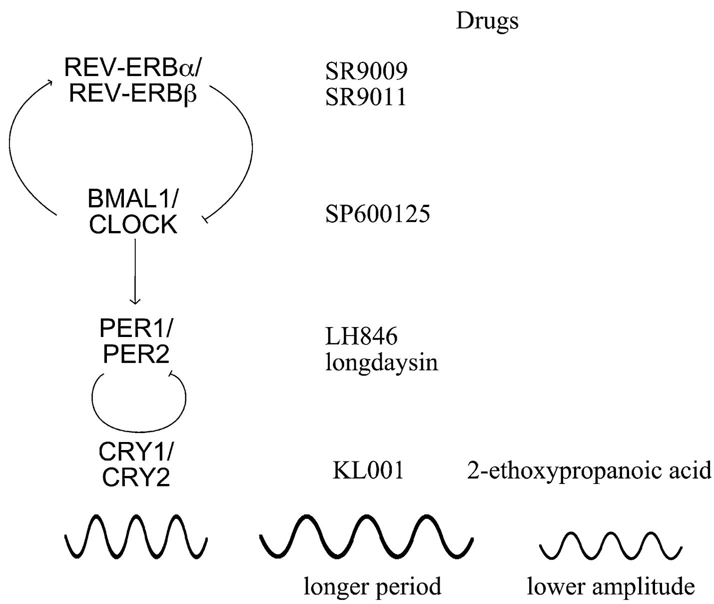
Consequently, a simple way to make old persons responsive to light again would be an increase of the daily light intensity, which was shown to slightly improve the symptoms of dementia in older persons (Riemersma-van der Lek et al. 2008). Alternatively, a chirurgical replacement of the lens can reconstitute the circadian system in older persons, especially if the lens can filter out certain wavelengths (reviewed in Turner and Mainster 2008; Chellappa et al. 2019; Brøndsted et al. 2013). However, short-term exposure to bright light during the day is not sufficient to affect circadian gene expression in humans, and consequently, prolonged exposure periods over multiple days may be more promising (Sato et al. 2017). Also, a recent study suggests that the effect of light is dependent on the individual (Phillips et al. 2019). Hence, further studies on humans are necessary to exploit the full potential of light as an effector of circadian rhythms. Light treatment is employed already to treat mood-related disorders (Maruani and Geoffroy 2019), and it should be rather simple and low risk to adjust the current treatment routines to affect the circadian oscillator. Such a simple light therapy could be supplemented with another approach. It was shown that regular exercise does not only have a positive effect on overall health to fight metabolic disease, but also via the better coordinated muscle - metabolism affects the circadian timing system as well (reviewed in Gabriel and Zierath 2019).

One of the compounds in the body strongly responsive to light is melatonin, which is secreted by the pineal gland (reviewed in Bubenik and Konturek 2011). It was shown that the concentration and amplitude of this substance in the blood are declining with age (Benot et al. 1998). Melatonin, on the one hand, is promoting sleep during the night until it is rapidly degraded and cleared from the blood in response to light (Bubenik and Konturek 2011). As such, the melatonin concentration in the blood perfectly reflects the external light/dark cycle, including the day length, and adjusts the sleep phase accordingly. On the other hand, melatonin has antioxidative properties and as such may be useful to prevent aging (Bubenik and Konturek 2011). The digestion of food yields many potentially harmful radicals. Melatonin quenches a significant proportion of these and at least in some experiments and species increased life span (Anisimov 2003). Taken together, giving melatonin during the night has the potential to reinstate proper sleep and to sequester harmful substances, which may otherwise cause oxidative damage and consequently aging. A beneficial effect of melatonin for humans, however, has to be proven yet.

An effective way to affect the synchrony of the circadian timing system is restricted feeding (Kessler and Pivovarova-Ramich 2019). It was shown that food is a strong phase-setting cue for peripheral oscillators of mice (Damiola et al. 2000). This flexibility would allow the synchronization of the peripheral oscillators to the SCN by simply manipulating the time of food uptake. Hence, the effects of restricted feeding on the circadian clock and overall health were investigated. Mice without functional circadian oscillator tend to develop metabolic syndrome, which is a risk factor for aging. However, when fed only over a short-time window – even with the same caloric input – these mice were protected from the adverse effects of food (Chaix et al. 2019). Studies in humans found a severe uncoupling of the circadian rhythms and the food-uptake rhythms (Gill and Panda 2015). Unfortunately, the population shifts more and more toward high-caloric, palatable diets, which are consumed over a 16-h time interval. The most promising antidote would be time-restricted feeding (TRF), which by contrast to all other restricted feeding regimens does not depend on reduced calorie uptake. However, studies on humans revealed that translation of the mouse results to patients is not so easy (reviewed in Kessler and Pivovarova-Ramich 2019). To sum up, time-restricted feeding not only impacts on circadian oscillator function but also prevents chronic metabolic diseases. However, although there are without any doubt beneficial effects of TRF on chronic diseases, the impact on life expectancy remains to be proven.

Interestingly, restricted feeding provoked an increase of melatonin production in mice and nonhuman primates (Bubenik et al. 1992; Roth et al. 2001). However, this would indicate that it is not the process of food processing that is harmful to the organism and has to be dealt with by melatonin and other antioxidants but the lack of food and consequently the lack of substrates for the metabolic enzymes. A similar phenomenon was observed in the liver, in which the activity of P450 detoxification enzymes was under circadian control to prevent the generation of harmful radicals in the absence of xenobiotic compounds (Gachon et al. 2006). If the circadian component of detoxification was lacking, then the life expectancy was reduced.

Alternatively, drugs could be used to ameliorate the circadian system of older persons. For instance, mice deficient for *Bmal1* have more mTORC1 activity and reduced life expectancy (Khapre et al. 2014). The mTOR inhibitor rapamycin was able to reduce this excess of activity and to increase the life expectancy by 50%. The mTOR inhibitor RAD001 was shown to improve immune functions in older persons (reviewed in Cornelissen and Otsuka 2017). Its effect on the circadian system in the treated patients, however, remains to be investigated. Because part of the mTOR signaling is under



Chronobiology and Aging, Fig. 3 Drugs affecting the phase of circadian oscillators. Indicated are the names of drugs known to interact with the circadian oscillator components on the same levels. Furthermore, there are a plethora of drugs available that target kinases affecting the circadian oscillator. However, their effects may not be as specific as the selected drugs. None of the drugs was tested yet for their effect on life expectancy. (Adapted from Wallach and Kramer 2015)

circadian control, it may be possible to optimize the time of treatment to reduce the amount of drug applied and their potential side effects.

A promising target is nicotinamide mononucleotide (NMN) metabolism, which is part of the NAD^+ metabolism. Again in *Bmal1*-deficient mice, there was less fatty acid oxidation in their mitochondria (Peek et al. 2013). The flux-determining enzyme, the long-chain acyl-coenzyme A dehydrogenase, was not activated by deacetylation by SIRT3 because of the lack of NAD^+. The reason for the lack of NAD^+ was the reduced activity of NAMPT. The addition of NMN could rescue the phenotype because NMN is part of the NAD^+ metabolism downstream of NAMPT (Fig. 2). Cells take up NMN without any problem, and it was demonstrated that supplementing food with NMN could revert the overall age-related physiological decline (Mills et al. 2016). In light of the role of SIRT1 and the NAD^+ metabolism in the SCN (see above), it is tempting to speculate that NMN has a positive impact on both physiology and circadian rhythms. Indeed, it was found that the chronic addition of NAD^+ to the food protected mice from the adverse effects of high-fat diet such as an increased body weight and disturbance of the expression of *Per1* to reconstitute circadian rhythms (Roh et al. 2018).

Many drugs target specific molecules of the circadian oscillator (Wallach and Kramer 2015; Chen et al. 2018) (Fig. 3). However, in general, their influence on life expectancy is not yet investigated. For instance, the clock-enhancing small molecule nobiletin improves the amplitude of *Per2* rhythms and protects against metabolic syndrome (He et al. 2016). As a potent antioxidant, it may have beneficial functions to ameliorate aging.

Future Directions of Research

Both aging and circadian rhythms affect a plethora of processes. Unfortunately, it is impossible to identify the interaction or interference of both for all of these processes. It is challenging to distinguish between the effect of the circadian oscillator on aging and the specific effect of one of its components. For instance, although the *Bmal1*-deficient mice have a whole variety of age-related phenotypes, it turned out those mice in which this gene was inactivated at the age of 3 months had much less of these phenotypes (Yang et al. 2016). Consequently, the lack of BMAL1 may impair some developmental process, which manifests itself later on like an aging phenotype.

Nevertheless, there are some upcoming connections between the circadian oscillator and aging. It was recently found that the composition of the extracellular matrix affected both circadian rhythms and aging (Shin et al. 2019; Streuli and Meng 2019). Similarly, it was found that the metabolism of polyamines was circadian and that their concentration declined with age (Zwighaft et al. 2015). The addition of the polyamine spermidine mimics the effects of caloric restriction, which is beneficial for aging (reviewed in Madeo et al. 2019). It is tempting to speculate that intensive research will unravel further connections soon.

One problem remains, the translation of results from the experimental systems to humans. For instance, the strong effect of melatonin on mice may be rooted in the fact that most laboratory strains of mice have lost the ability to produce melatonin. Hence, in the midterm more of the experiments have to be conducted with humans or human-derived tissue cell culture.

Summary

Two major strategies have a measurable impact on longevity. The first one is caloric restriction and the other one physical activity. Both are related to the circadian system, which, on the one hand, coordinates the efficiency of metabolic processes, and on the other hand, determines the activity and rest phases. In older persons, there is a general decline of the precision of their circadian system affecting metabolism, physiology, and sleep. With the strategies introduced in this review – increasing light intensity, supplementing melatonin, and applying drugs such as mTOR inhibitors, nicotinamide mononucleotide, or nobiletin – it should be possible to rejuvenate the central circadian clock in the SCN and reestablish the synchronization with the peripheral oscillators. This readjustment of the circadian clock will have beneficial effects on health and life expectancy of older persons.

Cross-References

▶ Antiaging Strategies

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Chronological List of Important Aging Studies

► Timeline of Aging Research

Church Attendance and Healthy Longevity

► Religious Involvement, Health, and Longevity

Cinema

► Representations of Older Women and White Hegemony

Circadian Amplitude

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Synonyms

Biological rhythms; Circadian rhythms; Circadian oscillations

Definition

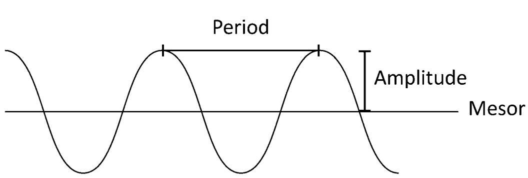
Circadian, derived from two Latin words Circa (around or approximately), and *diem* (day), refers to any process that tends to repeat in a 24-h solar day cycle. Amplitude is the highest point of an oscillation or vibration, measured from the equilibrium position. Taken together, circadian amplitude can be defined as the "difference between the highest point of the oscillation and the equilibrium of a circadian rhythm" or "difference between mesor (mean of the circadian rhythm) and peak of the sinusoidal-shaped circadian rhythm" (Fig. 1).

Overview

Earth, being the only known planet that sustains life, has some amazing features. One of these features includes the 24-h day consisting of concurrent light and dark periods. Therefore, it is critical for the survival of all living organisms inhibiting earth that they adapt to the external changes taking place in its environment. This adaption can be observed in the dramatic fluctuations in the internal environment of living organisms, known as "biological rhythms." These rhythms are observed across the species including single-celled cyanobacteria, algae, fruit flies, rodents (rats and mice), and humans.

Biological rhythms can generally be defined as the natural cycle of changes in living organism's physiology and behavior. There are three main types of biological rhythms:

- Circadian rhythms (repeated in a 24-h cycle),
- Ultradian rhythms (repeated more than once in a 24-h cycle), and



Circadian Amplitude, Fig. 1 Graphical representation of circadian rhythm

- Infradian rhythms (repeated in a cycle of more than 24 h).

Circadian rhythm, any biological process that displays an endogenous, entrainable oscillation of about 24-h solar day, mediates gene expression, metabolism, and behaviors created by the internal clock that governs a range of metabolic physiologies including cardiovascular physiology, metabolism (glucose and lipid), and obesity regulation. The circadian rhythms are regulated by two ways:

- External cues known as *zeitgebers* (*German,* synchronizer) such as light
- Internal cues via clock proteins present almost in every cell and provide transcriptional rhythms based on a 24-h solar day

In mammals, suprachiasmatic nuclei (SCN) are the principal regulator of circadian rhythms. The SCN consists of approximately 20,000 neurons in hypothalamus, above optical chiasm. SCN receive time-of-day signals through retinohypothalamic tract and synchronize the endogenous clock accordingly. SCN further communicates the time-of-day information to peripheral clocks located in heart, liver, lungs, and glands, thereby, synchronizing the rhythmic activities throughout the body to the external environment. SCN also regulate circadian-based release of digestive peptides such as vasoactive intestinal polypeptide and gastrin-releasing peptide. Amplitude reduction and acrophase increase has been observed in rats upon lesioning of SCN (Powell et al. 1980), imitating the normal aging process (See ▶ "Aging in the Short Story").

At the cellular level, circadian rhythms are generated and sustained autonomously in interlocked transcription-translation feedback loops during a 24-h solar day cycle. Clock genes regulate their own cyclic expression, and serve as transcription factors for other genes, referred to as clock-regulated genes. In 1984, Jefferey Hall working in collaboration with Michael Rosbash succeeded in isolation of *period* gene and discovered that its encoded PER protein accumulates during the night and degrades during the day

(Zehring et al. 1984). They hypothesized that PER protein through an inhibitory feedback mechanism led to the blockade of *period* gene activity (Hardin et al. 1990). But the question arouses that how the PER protein moves from its site of production, the cytoplasm, to nucleus to block its gene activity. It was also discovered that the PER protein showed accumulation in the nucleus (Liu et al. 1992) but how did it entered nucleus remained unknown until 1994, when *timeless* gene was discovered by Michael Young that encodes TIM protein, necessary for normal circadian activity (Vosshall et al. 1994). It was reported that TIM binds to PER and move into the nucleus together and block the period gene activity closing the inhibitory feedback loop (Vosshall et al. 1994). Michael Young further discovered another gene, *doubletime*, encoding DBT protein that delay the PER protein accumulation leading to a controlled frequency of circadian frequency to synchronize to the external 24-h solar day cycle (Price et al. 1998). In detail, the transcription activator BMAL1 form a heterodimer complex with CLOCK and binds to the E-box enhancer elements in *period (per1, per2, per3)* and *cryptochrome (cry1, cry2)* and initiates transcription (King et al. 1997; Yoo et al. 2005). Accumulation of PER and CRY proteins triggers suppression of CLOCK/BMAL1 transcriptional activity forming a feedback loop to inhibit their own expression (Griffin et al. 1999; Sato et al. 2006). Subsequently, PER and CRY proteins are degraded (Sato et al. 2006).

Circadian amplitude and circadian rhythm stability are two of the important parameters of circadian rhythms. Although the mechanisms underlying circadian rhythms have been long known now, mechanisms regulating amplitude of circadian rhythms have not been defined in much detail. Coordinated regulation of cycle time including period, phase, and circadian amplitude is necessary for smooth rhythmic physiology (Ramkisoensing and Meijer 2015). REV-ERBα, a core transcription inhibitory component of molecular clock, modulates *Bmal* and BMAL target genes such as *Cry* and *Per* (Cho et al. 2012) by binding to genomic response elements called retinoic acid-related orphan receptor elements (ROREs), for instance, RORα and γ (Takeda et al. 2012). F-box protein, FBXW7, tags REV-ERBα for ubiquitination, which is subsequently degraded (Zhao et al. 2016). Consequently, REV-ERBα-dependent transcription inhibition is reversed, increasing the amplitude of clock genes transcription through an undefined mechanism (Zhao et al. 2016).

Circadian rhythms do not just respond to the daily changes in the external environment but also allow living organisms to prepare living organisms for these anticipated changes. It further ensures that the internal environment remain in synchrony with its external environment as well as the changes in internal environment take place in a coordinated synchrony with each other. Circadian rhythms play a key role in health maintenance, and lack of synchrony in internal environment has been associated with various health issues. For instance, circadian amplitude has been associated to aging, sleep disruption, as well as other diseases (Zhao et al. 2016). With advanced age, significant changes in circadian rhythm parameters have been observed affecting normal physiology such as reduction in circadian amplitude has been reported in normal aging process. In light of the accumulating evidence, disruptions in circadian rhythms are considered to be an early sign of aging-related diseases such as cardiovascular diseases, neurodegenerative disorders, metabolic syndrome, chronic inflammation, and cancer (See ► "Aging and Health Disparities") (Mattis and Sehgal 2016). Stabilized rest – activity routine, calorie restriction along with meal timing, and physical exercise are the widely accepted geroprotectors promoting healthy aging and longevity.

Key Research Findings

In 2017, the Nobel Prize in the category of Physiology or Medicine was jointly awarded to Jeffery Hall, Michael Rosbash, and Michael Young for their breakthrough discoveries revealing the underlying mechanisms of circadian rhythms explaining the adaption and synchronization of internal environment of a living organism to the changes in the external environment caused by the Earth's rotation on its axis (Burki 2017). In the recent years, a significant amount of studies has reported that circadian rhythms play a significant role in normal physiology and homeostasis. Different pathophysiological functions are regulated by the peripheral clocks present in all types of cardiovascular cell types (Beesley et al. 2016; Du Pré et al. 2017). Two clock genes, *NPAS2* and PER2, are reported to be associated to risk factors of metabolic syndrome, which in turn has been reported to be a significant risk factor for cardiovascular diseases and is associated with emergence of myocardial infarction (See ▶ "Cardiovascular Diseases") (Englund et al. 2009). Several physiological factors stimulating myocardial infarction such as blood pressure, vascular endothelial functions, myocardial contractions, metabolism, and glucose homeostasis are reported to be influenced by circadian rhythms (Leu et al. 2015; Virag and Lust 2014). SNPs in important clock genes including *ARNTL, CLOCK, CRY2,* and *PER2* are associated with circadian phenotypes including chronotype and sleepiness in patients with myocardial infarction (Škrlec et al. 2019).

Efficient low amplitude rescue was reported in behavior and clock gene expression in aged animal models, such as rats and flies, upon receiving SCN, principal regulator of circadian rhythms, tissue transplants from young animals suggesting an autonomous and intrinsic control of circadian amplitude and rhythmicity (Cai et al. 1997; Luo et al. 2012). However, the mechanism remained ambiguous until recently. In 2016, a study provides insights into this mechanism reporting that cyclin-dependent kinase 1 (CDK1) mediated phosphorylation of REV-ERBα, a core transcription inhibitory component of molecular clock, is necessary for its recognition for targeted ubiquitination and subsequent degradation (Zhao et al. 2016). Furthermore, hepatic disruption of FBXW7 changes circadian regulated expression of core clock genes complicating the lipid and glucose levels in liver-specific knockout (LKO) mice (Zhao et al. 2016). Together this CDK1-FBXW7 pathway regulating REV-ERBα repression presents a surprising mechanism for reviving the transcription of molecular clock genes and provides a potential therapeutic target to manipulate circadian amplitude (Zhao et al. 2016). As the CDK1 is widely reported to be an evolutionary conserved cell-cycle regulator and also implicated in reviving transcription of clock genes (Zhao et al. 2016) provide clues strengthening the concept of a regulated coordination among cell cycle and circadian rhythms (Hunt and Sassone-Corsi 2007). Likewise, CDK1 inhibitors are reported to modulate expression of clock genes in U-2 OS (human osteosarcoma) cells and mice liver (Iurisci et al. 2009). CDK inhibitors along with CDK inhibitors can act signals to reset the circadian clock and have been reported to modulate gene expression of molecular clock at single cell level in mouse embryonic fibroblast (MEF) cells and also in mice liver at tissue level (Iurisci et al. 2009; Papp et al. 2015).

Aging is a progressive decline in normal physiological features and a vital risk factor for senescence and other common diseases including cardiovascular diseases, dementia, and cancers, leading to death and disabilities. In humans, reduction in circadian amplitude and circadian phase advances in melatonin secretions and body temperature rhythms have been associated with aging (Vinod and Jagota 2017). Moreover, changes in daily rhythms of clock genes, serotonin synthesis and metabolism, antioxidant enzymes, leptin, nitric oxide (NO), and suppressor of cytokine signaling (SOCS) have been also been observed along aging rats (Mattam and Jagota 2014; Vinod and Jagota 2017). Synthesis of NAD1 is mediated through CLOCK-BMAL1 regulated expression of Nicotinamide Phosphoribosyltransferase (NAMPT), thereby, regulating NAD1-dependent enzymes including sirtuins such as SIRT1 (Nakahata et al. 2009). SIRT1 indirectly regulates the molecular clock through interaction with CLOCK-BMAL1 promoting PER2 deacetylation and degradation, deacetylation of BMAL1, PER1/PER2 and CRY1/CRY2, suppress NFκB activity, and counteract histone acetyltransferase (HAT) activity of CLOCK (Miki et al. 2012; Nakahata et al. 2009). Calorie restriction, the widely accepted intervention for lifespan extension, regulate clock gene expression in *Bmal1*-dependent manner, in turn, clock genes promotes longevity through IGF-1-dependent mechanisms in mice (Patel et al. 2016).

β-adrenergic signaling has been observed to amplify circadian rhythms of the heart as intercellular communication within ventricle explants synchronizes both the heart contractions and circadian rhythms in mice (Beesley et al. 2016). Studies monitoring the daily fluctuations in blood pressure showed that atypical fluctuations in blood pressure leads to an increased incidence of cardiovascular complications and determined that stable night-time blood pressure proves to have better predictive index of future cardiovascular diseases as compared to day-time blood pressure or daily mean blood pressure (Kikuya et al. 2005). Inverse dippers, the individuals whose blood pressure rises during sleep, also showed increased incidence of strokes than normal individuals with normal circadian variations of blood pressure suggesting that individuals with disruption blood pressure circadian rhythms are at higher risk of cardiovascular complications including heart failure, myocardial infarction, stroke, and developing left ventricular hypertrophy (See ► "Cardiovascular Diseases") (Takeda and Maemura 2011). *Bmal1,* the transcriptional activator of molecular clock, along with two clock genes, *Cry1 and Cry2,* are shown to be regulator of daily normal fluctuations in the blood pressure; however, their global genetic deletions showed opposite results in mice, as *Bmal1* deletion resulted in loss of blood pressure and hypotension, while compound deletion of *Cry1* and *Cry2* resulted in increased blood pressure and hypertension (Curtis et al. 2007).

Autophagy is an evolutionary conserved process regulating organelle turnover, and protein degradation recycling the cellular components and amino acids that are used for energy production (Rothermel and Hill 2007). Regulated and controlled autophagy is essential for cardiovascular homeostasis and physiology; however, beyond a given threshold, it has detrimental health outcomes leading to cardiac dysfunction and diseases (Rothermel and Hill 2007). The evidence linking autophagy and circadian rhythms dates back to 1972, when the presence of autophagic vacuoles and atrophy of liver following a diurnal patterns in the meal-fed rats in comparison to meal-deprived controls were demonstrated using an electron microscope (Pfeifer 1972). In the following studies carried out in rats, it was observed that autophagy follows diurnal patterns in kidney tubules and heart, as higher number of autophagic vacuoles were observed at morning or late-light phase which declined during evening and late-dark phase (Pfeifer and Scheller 1975), suggesting the presence of peripheral clocks and circadian regulated autophagy playing an important role in tissue and organ repair. AMPK-mediated Unc-51-like kinase 1 activation requires mTORC1 phosphorylation of Unc-51-like kinase 1 (Shang et al. 2011) and was found to be crucial for the autophagy initiation and mitochondrial homeostasis in cardiomyocytes (Kim et al. 2011) linking autophagy and circadian rhythms as both AMPK signaling and mTORC1 are regulated by circadian rhythms (Lee and Kim 2013).

Apoptosis, programmed cell death, involves genomic DNA fragmentation without causing any inflammation. During various cardiovascular diseases, including myocardial infarction and heart failure, apoptosis is the most observed form of cell death (Fliss and Gattinger 1996). In mice, upon irradiation exposure of the small intestine showed circadian rhythm-dependent cell apoptosis with peak initiation of apoptosis observed in the morning compared to the evening hours (Ijiri and Potten 1988). Core clock genes, *Cry1* and *Cry2,* deletions resulted in increased synthesis of tumor necrosis factor-α (TNFα), initiator of extrinsic apoptosis pathway, while ectopic expression of TNFα in mice embryonic fibroblast germline with deleted *Cry1* and *Cry2* showed reduced TNFα production, linking apoptosis to circadian rhythms (Biala and Kirshenbaum 2014). Moreover, NFκB, a major downstream transcription factor of TNFα, was impaired in *Cry1* and *Cry2* deficient cell lines (Lee and Sancar 2011). p53, a key player in intrinsic apoptosis pathway, was reported to directly interact with the molecular clock core components including BMAL1, CRY1/CRY2, and PER1/PER2 (Hamada et al. 2014). RNA interference-based genetic screening identified *BMAL1* as a putative regulator of *p53*, suggesting that *p53* promoter activity may be driven by *BMAL1* (Mullenders et al. 2009*)*. Peroxisome proliferator–activated receptors (PPARs), another key player in intrinsic apoptosis, are involved in rhythmicity of blood pressure and heartbeat rate. PPARγ was reported to activate BMAL1 promoter and showed rhythmic expression in aorta. Genetic knockout-PPARγ vascular endothelial cells and smooth muscle cells showed loss of function and attenuated rhythmicity in blood pressure and heartbeat rate (Wang et al. 2008).

Example of Application

Disruption of circadian rhythms, including reduced or increased circadian amplitude, has been reported numerous times to be involved in deviation from normal physiology leading to diseases and disabilities. Many therapeutic surgeries have been also suggested to prevent or limit the negative effects of circadian disruptions. The most widely studied and observed case of disrupted circadian rhythm is by far the sleep and circadian rhythm disruption (SCRD) including excessive daytime somnolence (EDS), delayed sleep phase disorder (DAPD), advanced sleep phase disorder (ASPD), and seasonal affective disorder (SAD).

The first key step for an effective strategy is to monitor the fluctuations from the normal physiology, in this case, circadian rhythm disruptions. The gold standard for measuring sleeping quality and disruption is polysomnography, a test that record night sleep patterns in human brain waves, blood pressure, blood oxygen level, breathing, and movement of eyes and legs (Wise 2010). Electroencephalography (EEG), a test to detect electrical activity in your brain using small, metal discs attached to your scalp, is a potential alternative but has not yet been approved to be used for this purpose (Vacas et al. 2016). However, monitoring hormones along with other epigenetic, proteomic, and metabolic markers known to fluctuate in a 24-h solar day cycle is a beneficial alternative (Cornelissen et al. 2019). Melatonin, a hormone synthesized by the pineal gland regulating the normal sleep-wake cycle, is reported to be predictor of adverse cardiovascular events in patients with myocardial infarction (Dominguez-Rodriguez et al. 2006). Moreover, technological advances have enabled us to noninvasively measure rhythmic events such as blood pressure, heart rate, and physical activity over a course of several days, providing useful follow-up information and response to therapies (Cornelissen et al. 2019).

The second key step for an effective therapy is "time awareness." Generally, age, sex, and/or other diseases are taken care of while treating a patient, "time" of therapy is unfortunately ignored. Recent studies have highlighted the importance of time in therapies and follow-up in cardiovascular complications. Troponin, type T and C, marker of heart injury/damage, exhibit 24-h solar day cycle, and therefore, a several hour monitoring of troponin levels in a patient can successfully distinguish between an acute coronary syndrome or a minor physiological complication (Fournier et al. 2017). Similarly, corrected QT (QTc) interval, an electrophysiological marker of cardiac repolarization, also exhibits 24-h solar day rhythms, and therefore, monitoring QTc can provide useful insights on the response to therapy or drugs and identification of the risk or adverse cardiovascular events such as ventricular arrhythmias leading to sudden cardiac death (SCD) in patients with heart failure (Du Pre et al. 2017).

The most successful therapy is to prevent/minimize the clock desynchronization augmented by exposure to normal 24-h solar day signals including light intensity and duration, activity, and feeding during the day and night for a prescribed period. Studies have proved the effectiveness of this strategy in clinical outcomes such as reduced delirium (serious mental disturbances leading to confusion and reduced awareness of surroundings following certain diseases and clinical surgeries) and its complexities in intensive care units admitted patients (Oldham et al. 2016). Another treatment strategy is targeted time of drug administration, a most successful example observed in hypertension, associated to most of the cardiovascular diseases (See ► "Cardiovascular Diseases"). In normal physiological conditions, blood pressure shows circadian regulation throughout the day. Negative effects of antihypertension drugs such as hypotension are observed during the day. Most complexities associated with hypertension showed an increased incidence at early morning. Studies have provided evidence of benefits of time of day administration of antihypertensive drugs, such as night-time administration of angiotensin converting enzyme inhibitor reduced nocturnal blood pressure leading to improved cardiovascular outcomes as compared to morning administration (Hermida and Ayala 2009). Similar evidence was produced with other antihypertensive drugs including calcium-channel blockers, angiotensin-receptor-blockers, and β-blockers when administered in a time-specific manner leading to prevention of cardiovascular diseases (De Giorgi et al. 2013).

Future Directions of Research

Circadian rhythms seem to mediate multiple physiologic processes, ranging from cardiovascular functions to behaviors, neuroendocrine functions, and metabolism. Understanding the mechanisms of this mediation will open a horizon of new opportunities for understanding, curing, and therapeutic interventions leading towards healthy aging and longevity. Recent studies have demonstrated the time-of-day dependent circadian rhythms in cardiovascular physiology, along with pathophysiology. Moreover, circadian rhythms have been reported to mediate various renal functions including blood flow, filtration, and sodium excretion. As normal renal physiology holds a key for cardiovascular homeostasis, these findings provide beneficial insights for deep understanding of the kidney disease etiology and design effective treatment strategies.

Therapeutic interventions and translational applications of circadian rhythms including correct timing of the therapy, drug administration along with avoiding and/or minimizing the risks of circadian rhythm disruptions have potential benefits in both patients, in the form of favorable outcomes of a therapy, as well as in healthy individuals, in the form of prolonging their health span and prevention of diseases. The future research on integrating the science of circadian rhythms and therapeutic options has a great potential to improve the treatment and survival of patients with cardiovascular disease. Circadian rhythms can be implicated in cardiovascular therapies in two different ways: (1) As timing of the drug administration and even surgical operations performed at specific time of the day has been proved to have potential benefits, therefore, circadian rhythms can be easily monitored (Montaigne et al. 2018), and drug administration and surgeries can be performed at an optimized time of the day to obtain the most desirable outcomes while reducing the adverse effects of therapies and drugs. (2) They themselves can be targeted for novel therapeutic interventions. Likewise, molecular clock components can be targeted as well, as REV-ERBα, a core transcription inhibitory component of molecular clock, was identified as a therapeutic target leading to improved muscle oxidative function through modulating gene networks controlling mitochondrial biogenesis, physiology, and autophagy (Woldt et al. 2013).

There is a lot to be done on this front in the years to come. The fact that circadian rhythms exhibit vast diversity from individual to individual should not be ignored during application to therapeutic integration and intervention. However, there is a need to raise awareness among public avoid or minimize molecular clock disruptions to promote healthy lifespan and longevity.

Summary

Circadian rhythms help living organisms to anticipate, adapt, and synchronize their internal

biological systems according to the natural changes taking place in external ensuring that the organs to perform right functions at the right time. These rhythms are autonomous, self-sustained, and reported to be crucial for the survival and maintenance of normal physiology. Disruptions in rhythmic parameters such as circadian amplitude and circadian rhythm stability have been observed to be associated with various health complications including cardiovascular diseases (See ► "Cardiovascular Diseases"), aging (See ► "Aging in the Short Story"), age-related neurodegenerative disorders (See ► "Aging and Health Disparities"), metabolic syndromes, and sleep disorders. Integrating the circadian biology with therapeutic interventions have promising results as observed in case of time-specific drug administration studies in hypertension. Calorie restriction, one of the most widely accepted longevity interventions, when coupled with time-specific feeding produces better results in animal studies. Future research combining the scientific knowledge of biology, disease, and chronobiology will open a new horizon of improved drugs, therapies, and discovery of novel therapeutic interventions, ultimately increasing the health span as well as lifespan.

Cross-References

- ► Aging and Health Disparities
- ► Aging in the Short Story
- ► Cardiovascular Diseases

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Circadian Oscillations

► Circadian Amplitude

Circadian Rhythms

► Circadian Amplitude

Circulatory System

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Synonyms

Vascular System

Definition

The circulatory system, or vascular system, is an organ system which carries blood and lymph throughout the body. The mammalian circulatory system is comprised of both a blood vascular system and lymphatic system. The blood vascular system, also known as the cardiovascular system, allows blood to circulate and transport nutrients, wastes, and blood cells throughout the body, whereas the lymphatic system is responsible for returning extravasated material from the blood back to blood circulation. The blood circulatory system helps to fight diseases and maintain homeostasis, pH, and body temperature, while the lymphatic system plays a role in interstitial fluid homeostasis, lipid transport, and immunosurveillance.

Overview

The main component of the mammalian circulatory system is blood, which is a complex structure made up of two major components, including blood cells (erythrocytes, leukocytes, and platelets) and a fluid aqueous phase called plasma consisting of electrolytes, nutrients, lipids, and proteins. All required nutrients are mainly transported in plasma to cells, while waste products including some toxic substances are carried from cells to excretory organs such as liver, kidneys, and lungs. Blood plays an important role in respiration by transporting oxygen from lungs to all cells and carbon dioxide from all cells to lungs to be exhaled out of body. Body fights against foreign invaders and substances with the help of blood leukocytes and circulating antibodies produced by lymphocytes present in blood as a part of plasma protein content. Moreover, blood maintains the homeostasis of vasculature and protects against any damage caused by trauma with the help of platelets and blood clotting factors.

The cardiovascular system includes all blood vessels and the heart which pumps blood to the entire body. This system transports oxygen, nutrients, and hormones to each cell of the body and removes metabolic wastes such as carbon dioxide and nitrogenous wastes. This component of circulatory system is discussed in detail under the entry "Cardiovascular system" in the Cardiovascular Diseases section (See ▶ "Cardiovascular System"). Blood vessels form a closed circulatory system, while the lymphatic system forms a unidirectional transit pathway from extracellular space to blood circulation via venous system. The lymphatic vasculature goes together with blood vasculature in almost all vascularized tissues and organs and is even found in the brain (Louveau et al. 2015). The lymphatic system is composed of lymphatic vessels, lymph nodes (LNs), and associated lymphoid organs. It plays an indispensable role in interstitial fluid homeostasis, trafficking of immune cells, transport of gastrointestinal lipids, and reverse cholesterol transport (RCT).

Lymphatic vessels are classified into capillaries, precollectors, and collectors. Capillaries absorb tissue fluid and solutes from extracellular space. Collecting vessels drain lymph through chains of LNs leading to thoracic duct and right lymphatic trunk and eventually into venous circulation. Lymphatic vessels and lymphatic endothelial cells (LECs) are different from blood vessels and blood endothelial cells (BECs). The discovery of lymphatic specific markers including VEGFC (vascular endothelial growth factor C), VEGFR3 (vascular endothelial growth factor receptor 3), PROX1 (prospero homebox 1), PDPN (podoplanin), and LYVE1 (lymphatic vessel endothelial hyaluronan receptor 1) have made it possible to identify and isolate lymphatic endothelial cells (LECs) (Vuorio et al. 2017). LECs are oak-leaf-shaped with no or discontinuous basement membrane and loosely interconnected with button-like junctions which facilitate entry of fluids and immune cells. Precollector and collector vessels are coated with lymphatic smooth muscle cells (LMCs) and contain intraluminal valves to prevent backflow. The lymphatic vessel segment between two valves forms a contractile unit known as lymphangion. The periodic contraction of smooth muscle cells and several other factors including surrounding skeletal muscle contractions, respiratory cycles, and blood pressure aid to generate unidirectional propulsion of lymph.

The lymphatic system plays an important role in maintaining tissue homeostasis by returning extravasated fluid from tissue surroundings to blood circulation. Lacteal lymphatics uptake and transport lipids from small intestine in the form of chylomicrons, a lipoprotein particle consisting of triglycerides, phospholipids, cholesterol, and proteins. Moreover, lymphatics in other tissues facilitate high-density lipoprotein (HDL)-mediated reverse cholesterol transport. For immunosurveillance, lymphatic vessels uptake tissue patrolling immune cells including antigen-presenting cells and lymphocytes and transport them to lymph nodes. In addition, during inflammation, lymphatics mediate drainage of antigens and cytokines and help to mount innate and adaptive immune responses. Lymphangiogenesis, formation of lymphatic vessels from preexisting lymphatic vessels, can be activated in pathological conditions such as lymphedema, chronic inflammation, transplant rejection, and tumor growth. Vascular endothelial growth factors such as VEGFC and VEGFD can activate VEGFR3 expressed on LECs, which results in migration, proliferation, and differentiation of LECs regulated by transcription factors PROX1 and SOX18 (Brakenhielm and Alitalo 2019).

Increased blood microvascular permeability and inadequate uptake of lymphatic capillaries due to structural and functional alterations of lymphatics due to infection, surgery, medication, and cancer treatment can lead to insufficient lymph drainage and local accumulation of protein-rich interstitial fluid, a condition called as lymphedema characterized by chronic swelling.

Globally, about 250 million people are affected by lymphedema (Carlson 2014). Myocardial edema or cardiac edema has been demonstrated in heart injury as well as in myocardial infarction (MI) and heart failure (HF) (Lota et al. 2017). Lymphatic vessels provide a route for tumors to metastasize. Most carcinomas initially metastasize to lymph nodes and then metastasize further through lymphatic system to the body. Lymphatic vessels mediate transplant rejection, which can be countered by anti-lymphangiogenic therapy to increase the graft survival (Hos et al. 2015). Functional links have been found between lymphatic system malfunction and pathogenesis of obesity, atherosclerosis, and cardiovascular diseases (CVDs). Therefore, lymphangiogenic therapy may form a useful treatment option for atherosclerosis, inflammation, and lymphedema, and anti-lymphangiogenic therapy can be exploited to resolve graft rejection and inhibiting tumor metastasis.

Key Research Findings

Blood

The evaluation of changes in blood composition with age is a complex task, since it is difficult to assess whether the changes in given individual are the result of a disease or it is a phenomenon of normal aging. Blood plasma consists of >90% water and soluble substances including proteins. No dramatic changes are observed in plasma with age. The increase in number of infectious and inflammatory diseases with age may lead to slight changes in serum albumin, antibody concentration, and plasma viscosity. With increasing age, there may be slight decrease in the number of red blood cells and leukocytes, but the peripheral blood platelet count is not changed significantly. There may be higher coagulation enzyme activity with advancing age. Higher plasma levels of coagulation activation markers do not necessarily pose a high risk of thrombosis as centenarians have been shown to have strikingly higher coagulation enzyme activity compared to older controls (age 51–69 years) (Mari et al. 1995). Although erythropoietin levels rise with age, increased incidence of anemia in aging population remains unexplained. Age-related changes in bone marrow and thymus are marked by increase in fat and reduction in hematopoietic tissues and lymphoid mass. These changes as well as changes in differentiation capacity of hematopoietic stem cells may result in age-related anemia and immunosenescence or decline in adaptive immunity (Prabhakar et al. 2009; Wahlestedt and Bryder 2017). Several blood disorders are reported to be linked to pathophysiology of cardiovascular disease (CVD), but reports about gerontological changes in blood leading to CVD are not present. Anemia is associated with risk in proatherosclerotic conditions and heart disease. Hereditary blood disorders like sickle cell anemia and thalassemia result in cardiovascular dysfunction as a consequence of hypoxia and iron accumulation. Blood cell count, hemoglobin levels, and red blood cell parameters represent useful factors in CVD risk scores (Mozos 2015).

Lymphatic System

Aging is the major risk factor in many pathologies, and every physiological function changes with age. Age-associated changes in lymphatic structure and function have been observed in several animal models. Recently, significant disruption of meningeal lymphatic function was observed in aged mice underlining the age-associated cognitive decline. Meningeal lymphatic dysfunction may serve as an aggravating factor in Alzheimer's disease (Da Mesquita et al. 2018). Reduced lymphatic density and lymphatic vessel function have been observed in skin of aged mice (Karaman et al. 2015). In rats, aging-related anatomical and biochemical changes including reduced contractility, enhanced oxidative stress, and impaired permeability in lymphatic collectors have been observed, which lead to impaired lymph transport, fluid homeostasis, and pathogen clearance (Nagai et al. 2011; Zolla et al. 2015). Better outcome of corneal transplants in aged mice as compared to younger mice due to changes in lymphatic vessels and corneal lymphangiogenesis relates age-related decline in immunosurveillance and inflammatory response of lymphatic system (Hos et al. 2008). Age-associated structural and functional changes in lymphoid organs including spleen and lymph nodes can affect functioning of immune cells which can increase incidence and severity of infectious disease in aged population (Turner and Mabbott 2017).

The lymphatic system has been implicated in the pathogenesis of CVDs including obesity, atherosclerosis, and myocardial infarction (MI). Aging contributes to manifestation of CVD. Although the effects of aging on lymphatic system and how these effects can contribute to CVDs have not been studied, some functional links between lymphatic system and pathogenesis of CVDs are summarized below.

Obesity. Obesity is a key factor related to the increased prevalence of metabolic syndrome, a cluster of risk factors which can increase the risk of heart disease, stroke, and diabetes. The association between dysregulated lymphatic vessels and obesity has been shown in several mouse models. The *Chy* (heterozygous mutation in *Vegfr3*) and *Prox1*$^{+/-}$ mice have been characterized by defects in lymphatic vasculature leading to chylous ascites in the abdomen and obesity (Harvey et al. 2005; Karkkainen et al. 2001). Obesity and weight gain have been observed in patients with lymphedema due to cancer treatment (Helyer et al. 2010). Interestingly, *vegfc* deletion in mice resulted only a slow regression in intestinal lymphatic vessels which caused reduced lipid uptake, increased lipid excretion in feces, and resistance to obesity upon high-fat diet (Nurmi et al. 2015). Dysfunctional lymphatic vasculature can lead to obesity as well as obesity can also affect lymphatic function. In high-fat diet-fed mice, high fat lead to adipose tissue expansion which resulted in functional impairment of lymphatic vasculature (Blum et al. 2014). These findings clearly indicate the association between obesity and lymphatic vascular dysfunction. Further studies are needed to find out the underlying molecular mechanisms and causal relationship of obesity and lymphatic function.

Atherosclerosis. Atherosclerosis is a chronic inflammatory disease of the arteries characterized by fatty streaks and plaques filled with cholesterol-laden macrophages (foam cells). Atherosclerosis progression can lead to arterial blockage resulting in ischemia and MI. Removal of cholesterol from the arterial wall has been found beneficial in atherosclerosis regression (Small et al. 1984). RCT (reverse cholesterol transport) is the key player for cholesterol transport, from macrophage transporters ABCA1 and ABCG1 on lipoprotein acceptors such as APOA1 (apolipoprotein A1) in the form of HDL (high-density lipoprotein) particles through bloodstream to liver for biliary excretion. In mice, it has been shown that SR-B1 (scavenger receptor class B member 1) expressed in the lymphatic endothelium facilitates internalization and translocation of HDL, and inhibition of SR-B1 resulted in HDL uptake inhibition, suggesting effective role of lymphatics in RCT (Lim et al. 2013). Therapeutically inhibition of plaque lymphangiogenesis leads to cholesterol retention in the aortae and accelerated atherosclerosis in *Apoe*$^{-/-}$ mice. Moreover, lymphatic function restoration in *Apoe*$^{-/-}$ mice by local injection of recombinant VEGFC growth factor improved lipid clearance and reduced the cholesterol accumulation in skin tissue (Lim et al. 2013; Martel et al. 2013). Lymphatic vessels are present in human coronary arteries and even in atherosclerotic plaques. Increased inflammation and atherosclerotic lesions may lead to enhanced lymphangiogenesis emphasizing the role of lymphatics in excess cholesterol clearance from atherosclerotic sites (Kholová et al. 2011). These observations suggest the role of lymphatics in limiting cholesterol accumulation and possibly plaque formation during atherosclerosis. Further studies should be directed toward targeting HDL transport which could provide better protection against atherosclerosis in humans.

Myocardial infarction (MI) and cardiac transplant. Atherosclerosis can lead to MI, followed by vigorous inflammatory response. Myocardial edema is one of the consequences of cardiovascular conditions such as MI and heart failure. Small changes in cardiac interstitial fluid can lead to reduced cardiac output (Dongaonkar et al. 2010). Cardiac lymphatics have crucial role in countering edema, mounting response in inflammation, and immunosurveillance. Cardiac lymphatic remodeling and lymphangiogenesis have been shown in patients of HF, cardiac inflammation, and cardiac transplantation (Geissler et al. 2006; Ishikawa et al. 2007; Niinimaki et al. 2016). Mouse and rat models of MI have shown activated lymphangiogenesis in infarcted heart. MI in adult mice heart lead to lymphangiogenesis, and ectopic VEGFC treatment augmented lymphangiogenesis leading to improved cardiac function (Klotz et al. 2015). Persistent lymphangiogenesis can lead to transport of immune cells and antigens resulting in transplant rejection. Increased VEGFC expression and lymphatic vessel activation have been observed in rat models of cardiac transplant leading to graft inflammation and rejection. Conversely, pharmacological inhibition of VEGFC leads to better graft survival (Dashkevich et al. 2016). Thus, cardiac lymphatics can be targeted to counter the effects of cardiac injury as well as for immunoregulatory therapy to prevent graft rejection.

Examples of Application and Future Directions of Research

Blood. Blood can serve as a source of biomarkers for various diseases and aging. Chronological age alone as a marker to predict individual's functionality and susceptibility is not good enough. Several biomarkers promise to capture specificity of aging; however, single biomarker to predict correlations is limited by poor specificity. Sebastiani et al. measured 19 blood biomarkers including standard hematological biomarkers in Long Life Family Study (LLF). They correlated them with longitudinal changes in physiological function and risk of cancer, CVD, diabetes, and mortality. Presence of various biomarker signatures and their association with different parameters suggested difference in biological aging patterns (Sebastiani et al. 2017). Serum metabolites can also form associations with metabolic syndrome and cardiovascular disease, for example, a Chinese population study showed that glycine levels are associated with cardiometabolic characteristics and metabolic syndrome in older people (>70 years of age) (Li et al. 2018). Complete blood count (CBC) may also predict potential risk for CVD. A recent population-based study assessed the association of pre-diagnostic CBC with future CVD incidence. White blood cells count showed better prediction of 10-year CVD risk compared to traditional CVD risk factors in general population (Lassale et al. 2018).

Growing evidence suggests that age-related progressive decline in circulating factors including hormones and growth factors which can regulate multiple aspects of blood vasculature, blood flow, atherogenesis, vascular remodeling, and angiogenesis can contribute to vascular aging (Ungvari et al. 2018). Aged rodents seemed to be benefited when exposed to factors found in young blood; particularly GDF-11 (growth differentiation factor 11) could rejuvenate mouse skeletal muscle and cerebral vasculature (Katsimpardi et al. 2014; Sinha et al. 2014). Similarly, exposure of aged mice to young blood could enhance the structure and cognitive function of hippocampus (Villeda et al. 2014). Moreover, progeronic circulating factors may increase with age and impair tissue homeostasis. Decreased hippocampal neurogenesis was observed in young mice when exposed to old blood (Rebo et al. 2016). Similarly, sera derived from calorie restriction (CR) animals increased stress resistance and expression of genes related to longevity in vitro (Allard et al. 2008). Exact nature and mechanisms of progeronic and antigeronic circulating factors remain elusive at this point, and no proven clinical benefits of plasma infusions from young people against normal aging are present. Additional studies including human studies are warranted to find out more novel factors as well as origin of these circulating factors to seek the molecular and cellular impact of these factors on vascular wall.

Lymphatic System. The discovery of lymphangiogenic factors and related signal transduction pathways has made it possible to stimulate or inhibit lymphatic vessel formation to treat lymphedema or inhibit tumor metastasis. Influence of lymphatic vasculature on cholesterol removal and atherosclerotic plaque formation suggests that lymphangiogenesis activation and enhanced HDL transport may be beneficial. However, strategies to enhance HDL cholesterol levels in human could not improve cardiovascular events (Schwartz et al. 2012). Thus, simply increasing HDL levels may not be beneficial; rather targeting actual mechanisms behind RCT may provide better results. Moreover, inducing intimal or adventitial lymphangiogenesis to enhance RCT and reverse atherosclerosis may offer another therapeutic option. However, it remains unexplored.

Therapeutic lymphangiogenesis including *vegfc* gene therapy using adenoviral vectors has shown to reduce edema and inflammation (Zhou et al. 2011). Since VEGFC can also induce angiogenesis leading to blood vessel growth and leakiness, a VEGFR3-specific mutant form of VEGFC (VEGFC-156S) was developed which specifically induced lymphangiogenesis not only in transgenic mouse embryos, as well as when applied viral gene transfer in normal and lymphedema mice (Saaristo et al. 2002). Although increased cardiac expression of VEGFC and VEGFD post MI can induce lymphangiogenesis, it can induce remodeling and dysfunction of lymphatic collecting vessels leading to persistent edema and limited lymphatic transport. Another VEGFR3-specific designer protein VEGFC-C152S, delivered by albumin-alginate microparticles, accelerated cardiac lymphangiogenesis, and lymphatic remodeling was limited leading to attenuated inflammation and lymphatic dysfunction in rat MI models (Henri et al. 2016). These findings suggest therapeutic benefits and potential of VEGFC to induce lymphangiogenesis by protecting against cardiac edema, inflammation, and deleterious effects of MI-induced cardiac remodeling.

Most of the studies regarding the lymphatic system have been carried out in rodent models. To translate these findings into complex human diseases, next step is large animal studies. Large animals have not been utilized to treat cardiac pathologies using aforementioned treatment strategies. Further analysis is needed to find out the exact role of lymphatic vessels in the cardiovascular disease pathogenesis in context of inflammation, obesity, RCT, and immune system regulation. Aging plays a fundamental role in cellular and molecular mechanisms leading to vascular aging and CVD. Aging can affect lymphatic system's structure and function, and lymphatic system is clearly associated with obesity and cardiovascular pathologies. Therefore, lymphatic system with a focus on its role in CVD development with gerontological perspective should be studied. It should lead to development of new strategies to decrease cardiovascular mortality and morbidity.

Summary

The circulatory system is an important organ system which helps to transport blood throughout the body, and lymphatic system as part of the circulatory system circulates lymph. The circulatory system helps to transport nutrients and wastes, maintain body homeostasis, fight diseases, and render immunosurveillance. Blood is the fluid material composed of blood cells and fluid plasma. No significant changes in blood composition are observed with age. Increased incidence of infectious or inflammatory diseases with advanced age and hereditary blood disorders may contribute to age-related changes in blood. Association studies in different populations have associated blood cell count and different hematological parameters including metabolomic biomarkers with risk of CVD, cancer, diabetes, and mortality. In addition to search for biomarkers of aging and disease, recent studies are directed toward finding progeronic and antigeronic factors in blood. Despite antiaging effects of young blood observed in some rodents' studies, further studies are needed to find out specific factors as well as origin of these circulating factors to find the molecular and cellular mechanisms of these factors on vascular wall and CVD development. Lymphatic system forms a one-way conduit for trafficking interstitial fluid and extravasated blood cells, maintaining tissue and blood homeostasis and immunosurveillance. Clinical and experimental research has revealed the role of lymphatics in pathogenesis of diseases including lymphedema, cancer, obesity, atherosclerosis, and myocardial infarction. Experimental studies have uncovered that lymphangiogenesis inhibition can inhibit

tumor metastasis and graft rejection. Insufficient lymphangiogenesis and lymphatic remodeling in several CVDs may contribute to accumulation of atherosclerotic lesions and altered lymphatic drainage capacity. Therapeutic stimulation of cardiac lymphangiogenesis helps to resolve edema and inflammation leading to cardiac recovery. Current studies have focused on VEGFC- and VEGFD-based interventions, and other lymphangiogenesis controlling factors should also be explored. Role of lymphatic system in RCT and therapeutic interventions to target lymphatic vessels in heart and coronary arteries hold substantial promise to counter cardiovascular disease development and progression. Studies designed to uncover age-related changes in lymphatic system and their association with development of age-related decline in structure and function of cardiovascular system may lead to additional strategies to limit or slow down cardiovascular aging and disease development.

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► Cardiovascular System

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Citizen Science

▶ Crowdsourcing and Crowdfunding in Aging Research

Civic Engagement

▶ Volunteering and Health Outcomes Among Older Adults

C

Civic Participation

► Social Participation

Clan Families

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Definition

Clan families are a group of families or households that claim descent from a common ancestor. These types of social groups create a sense of belonging to and with one another based upon claims that manifest into a form of active solidarity with and between clan members. Oftentimes the ancestral connection is to a common DNA ancestor, a supernatural being, totem, or geographical location. Membership into a clan family is acquired through birth, marriage, or adoption, and unlike ethnicity or race, clan membership is easily identifiable because of the family names or the families' or to the ancestors' geographical place of origin (Yang 2019).

Overview

There are different clan systems found in Europe, India, North American, and Africa so clan system rules/customs/traditions can greatly differ. Some common characteristics are that clan families are most often located in villages that are typically comprised of about 100 households or less (Yang 2019). The name of the village oftentimes reflects the dominant clan in that area (Yu 1986).

Clan families were studied by social evolutionists in anthropology in the nineteenth century, and the primary debate centered upon how to designate them into matrilineal and patrilineal forms of a primitive family structure. Clanship during this time was understood as being linked to a totem. Levi-Strauss rejected this idea that there needed to be any necessary connection to an ancestral animal or plant (Burnham 2015). Scholars today assert that the diverse forms of clanships in many parts of the world are understood in relation to two key variables. The first is the extent of the clan family capacity for organized collective action, and the second is their social networking function for a dispersed clan member (Burnham 2015). For example, Schulhoff (2017) found that Indigenous older adults in tribal nursing homes in the United States would use their status as "elder" to address many social problems in reservation communities.

Key Research Findings

Clans are the principal social unit of a tribal organization, and the family is a subcomponent of the clan structure. A tribe can be defined as a social group with territorial affiliation that is ruled by tribal leaders and is united by a common language or dialect, has a common culture, and recognizes a social distance between other tribes or castes. The difference between a tribe and a clan is that a tribe has a territorial limit. A clan does not follow this rule. Another difference is that there can be several clan families in a tribe, depending upon the size, but not vice versa.

Individual members have a strong orientation to the clan family, and the actions of individuals are understood as affecting the reputation of that group. For instance, the Hmong maintain strong family bonds that are based on interdependence rather than independence between its members. As a result, it is expected that older adults will rely on the clan family for assistance and that younger family members will put other family members and the clan family unit before their personal desires. Adult children, in general, identify the importance of providing care to the aging parents in reciprocation for the care that was given to them as children (Gerdner 2006a; Gerdner 2007; Gerdner et al. 2008; Chang and Schneider 2010). Clans in many Asian cultures are the dominant family/political units and primary source of personal identity (Chang and Schneider 2010). Clan families help assist members in solving problems, provide mutual aid, and have a strong spiritual influence on health beliefs and behaviors (Gerdner 2006b). Multiple generations often choose to live in the same household for social and financial support. Clan families traditionally avoid having to depend on outsiders for the care of family members (i.e., older adults and children).

It is important to note that the identity label of "elder" denotes a titled status position within the clan structure that does not entirely depend upon age. Smith (1995) proposes that Hmong older adults, as with many other tribal elders across the globe, do not fit the chronological ages that have traditionally been established for defining "elder." Therefore, an "elder" could be in their early thirties depending upon the clan family's identity labels and role designations.

Future Directions of Research

Future directions for studying clan families would include looking at how clan families in homogenous societies, where there may be little variation by ethnicity, race, language, or landholding (i.e., South Korea), enable the investigation of one dimension of a group's heterogeneity. Secondly, family clans are in villages that are typically comprised of 100 households, or less. The social context of small communities lends itself to examining the topics of cooperation, eldercare, social sanctions, and cultural or social capital, to name a few. Lastly, clan families are organized differently from Western societies so comparative studies would be able to add to many contemporary theories in gerontology and other social sciences.

Cross-References

▶ Family Demography
▶ Family Tree

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Classification of Disabilities

▶ Disability Types

Clerics

▶ Quran on Aging

Climacteric

► Menopause

Climate Change and Aging Studies

► Climate Gerontology

Climate Change and Older Adults

► Climate Gerontology

Climate Change, Vulnerability, and Older People

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Synonyms

Global warming; Sensitivity; Susceptibility; Vulnerability

Definition

Climate change refers to a range of global phenomena created predominantly by burning fossil fuels. These add heat-trapping gases to the Earth's atmosphere (NASA 2019). These phenomena include the increased global temperature trends referred to as global warming that can lead to changes in rainfall, wind patterns, and the frequency of extreme weather events such as tropical cyclones, heatwaves, flooding, and drought, which impact both human health and environment (IPCC 2018; Padhy et al. 2015; Trombley et al. 2017; UNFCC 1994). In contrast to susceptibility, which is a state or fact of being likely or liable to be influenced or harmed by a stimulus (M-W 2019a; Oxford 2019a), vulnerability is a propensity or predisposition to be either physically or emotionally adversely affected (M-W 2019b; Oxford 2019b). This is determined by the characteristics of a person or group that influences their capacity to anticipate, cope with, resist, and recover from the adverse effects of physical events (Wisner et al. 2004; Lavell et al. 2012). Older people are particularly vulnerable to the effects of a changing climate (Kottow 2003).

Overview

The earth's climate system is approaching a threshold, beyond which there will be major and irreversible threats to human physical and mental health (BMA 2018). Rising temperatures, changing sea levels, and more frequent and extreme weather patterns will lead to impacts on human health, environment, and society.

The adverse impacts of climate change are already being experienced. From the mid-1970s to the year 2000 climate change was estimated to have caused over 150,000 deaths and 5.5 million disability adjusted life years (DALYs) per year worldwide (BMA 2018). In developed and developing countries, direct impacts are likely to include deaths, disease, and injury due to:

- Heatwaves (with the greatest impact on older adults, babies and young children, and people with ill-health)
- Flooding and tropical cyclones (including drowning, chemical hazards, contamination of drinking water, and mental stress)
- Increased spread of infections only seen in other parts of the world (such as tick-borne encephalitis, Lyme disease, malaria, and dengue),
- Reduced food safety associated with warmer temperatures greater exposure to ultraviolet radiation with increased risk of sunburn, sunstroke, and skin cancers

- Reduced air quality and increased pollens

Climate change presents the single biggest threat to sustainable development. Urgent action to halt climate change and deal with its impacts is integral to the successful implementation of the UN Sustainable Development Goals (SDGs). In particular, climate change is expected to lead to a widening of health and social inequalities between and within countries, with the effects most severe in developing countries and among the poorest people. The older population is at greater risk due to a combination of exposure and increased psychosocial susceptibility or social vulnerability. Older people are more susceptible to disease (See ▶ "Healthy Aging") and the effects of stresses on the food and water supply, and reduced ability to mobilize (See ▶ "Geographical Gerontology") themselves in an extreme weather event (ASA 2019).

Key Research Findings

The adverse health effects of climate change on the health and well-being of older people are due to their greater physiological susceptibility and social vulnerability. The effects of climate change depend on pre-exposure health status, psychological well-being, and social factors associated with aging and less on the fact of turning 60 or older (Geller and Zenick 2005). People aged 85 and over suffer from physical decline, multiple preexisting chronic disorders that limit mobility, intake of susceptibility-increasing medications, social isolation, possible poverty, and frailty and are, therefore, more likely to develop adverse health impacts from climate change (McGeehin and Mirabelli 2001; Geller and Zenick 2005; Haq et al. 2008).

Accumulated exposure over the life course to air pollution, pesticides, and other neurotoxins can produce greater susceptibility to health threats in older people by heightening inflammatory responses associated with cardiovascular disease, diabetes, dementia, and Parkinson's disease (Cohn and MacPhail 1996; Stein et al. 2008). In the United States, older adults live in areas that will experience higher temperatures, tropical storms, or extended droughts in the future (USGCRP 2014). Poor older people have limited financial resources to cope with heat, relocate or evacuate (See ▶ "Geographical Gerontology"), or respond to increases in the cost of food (USGCRP 2016).

Climate change-related events such tropical cyclones or heatwaves can cause and intensify stress and anxiety, adversely affecting mental health and leading to depression, anger, and even violence. Although everyone is at risk, older people (See ▶ "Geographical Gerontology"), including those with existing mental illness and those with close ties to the land, are especially vulnerable to mental health impacts (APHA 2019).

People and communities differ in their exposure, inherent vulnerability, and adaptive capacity to respond to and cope with climate-related health impacts, which vary across time, location, communities, and among individuals and groups (USGCRP 2016). Factors contributing to exposure of older people include the time spent in risk-prone locations, displacement by weather extremes, economic status, condition of infrastructure, compromised mobility (See ▶ "Geographical Gerontology"), cognitive function, and other behavioral and mental factors.

Psychosocial susceptibility or social vulnerability, and adaptive capacity are tied to many of the same factors, which change across an old person's lifetime and life stage. Locations that experience greater risks include urban heat islands, where cities are significantly warmer than its surrounding rural areas. Exposed older populations in such situations are likely to have limited adaptive capacity due to poor housing conditions, living in rooftop apartments, and are unable to use or to afford air conditioning.

Older people experience different inherent psychosocial susceptibilities or social vulnerabilities to climate-related impacts, especially exposure to extreme ambient temperatures which have been associated with increased hospital admissions for cardiovascular, respiratory, and metabolic disorders. Extreme weather events that compromise the availability and safety of food and water supplies and that interrupt communications, utilities, and emergency services affect older adults (USGCRP 2016). Functional and mobility impairments of older people (See ▶ "Geographical Gerontology") make them less able to evacuate in an extreme weather event. Social and economic factors affect disparities in the prevalence of chronic medical conditions and the incidence of mental health conditions (APHA 2019).

The 2018 Lancet Countdown report on health and climate change noted four key messages (Watts et al. 2018):

1. If global temperatures continue to rise, present day changes in heatwaves, vector-borne disease, and food security, compounded and overwhelming impacts on public health are to be expected: "*Trends in climate change impacts, exposures, and vulnerabilities show an unacceptably high level of risk for the current and future health of populations across the world.*"
2. Increasing greenhouse gas emissions and shortcomings in building adaptive capacity threaten both human lives and the viability of the national public health services.
3. The nature and scale of the response to climate change will be the determining factor in shaping the health of nations for centuries to come.
4. Understanding climate change "*as a central public health issue will be crucial in delivering an accelerated response.*"

Reducing the Climate Vulnerability of Older People

In order to decrease older people's vulnerability to extreme weather events, adaptation measures can be put in place that include (Gamble et al. 2013) the following:

- Registries of and surveillance data on older adults and geographic information systems for identifying them.
- Communities can develop early warning and response systems.
- Community nurses and home health workers could reduce the adverse effects of extreme weather events by educating older people about their vulnerability.
- Vulnerability indices, based on socioeconomic and demographic data, and vulnerability mapping can help planners, emergency managers, and technical support agencies locate vulnerable older individuals
- Educational materials and disaster checklists can be developed and distributed to older people.

The UK Royal Society (2014) developed five principles for building resilience to extreme weather events, which also support the above adaptation measures:

- Resilience building in populations and infrastructure requires responsibility and joint action at local, national, and international levels, by all stakeholders including the public, private sectors, communities, and non-governmental organizations.
- Governments should develop and resource resilience-supporting strategies and tactical measures involving all stakeholders, long-term and system thinking, and including the reconciliation of national and local priorities.
- International policy frameworks on disasters, climate change and its impacts, sustainable development and conservation of the environment should be coherent, mutually reinforcing, and complementary.
- More national and international funds should be directed to resilience-building measures.
- Resilience should be integrated into the global financial system to inform valuations and investment decisions. Organizations should be required to consistently report their financial expenditures for extreme weather events.

Examples of Application

Case Study: Mental Health and Hurricane Katrina

Considerable destruction, devastation, displacement, and death followed in the aftermath of Hurricane Katrina. Over a million people were displaced, thousands were traumatized, 2,000 died, survivors were unable to access basic resources such as shelters, emergency services, and retirement homes, and had to cope with profound loss, disrupted social ties, and resulting surges in violence (APHA 2019). A survey of a random sample of 1043 hurricane Katrina affected residents revealed that the 30-day prevalence rate was 49% for *anxiety-mood disorders* and 26% for *post-traumatic stress disorders (PTSD)*. The prevalence of PTSD and attempts at *self-harm* showed an actual increase, over time, in a long-term mental health impact study of Katrina on a representative sample of 815 pre-hurricane residents. Even 2 years after the hurricane, high mental morbidity was observed (Kessler et al. 2008). Older people may have been more affected, in particular those who already suffer from a mental disorder (approximately 15% of adults aged 60 and over) (WHO 2017).

Case Study: Fatalities in the United States Associated with Tropical Cyclones

In a study of 59 Atlantic tropical cyclones over the period from 1963 to 2012 cyclone-induced direct and indirect fatalities were analyzed as well as cardiovascular failures (Rappaport and Blanchard 2016). Direct fatalities resulted mostly from excessive stormwater, storm surge incidents, and flood events. Indirect fatalities were related to heart attacks, trauma, vehicle accidents, carbon monoxide poisoning, fires, and electrocutions. Hurricane Katrina in 2005 resulted in 520 direct deaths and 565 indirect deaths of which 318 deaths were due to heart attacks and other cardiovascular failures. The number of indirect fatalities increased with age. There were about eight times as many victims who were more than 70 years old as there were victims under the age of 21. For the most part, this disparity comes from the large number of senior citizens who died from heart-related ailments. USEPA (2016) reported that almost half of the Hurricane Katrina deaths were among people aged over 75 and nearly half of the deaths from Hurricane Sandy in 2012 were among people aged 65 and older.

Case Studies: Heat-Related Fatalities During Heatwaves

During a heatwave, most of the additional death and disease are not directly heat related, but are cardiovascular in origin, brought about by the increased cardiovascular challenge associated with thermoregulatory responses to heat stress (Vandentorren et al. 2006). Older individuals are the most vulnerable population during prolonged environmental heat exposure, experiencing worse health outcomes than any other age cohort.

During the New York City heatwaves in July 1972 and August/September 1973, the majority of those who died were 65 years and older (Ellis et al. 1975). Of the 1686 excess deaths in the 1995 Chicago heatwave, 473 or 28% had excessive heat as a contributing cause of death and almost 94% of these excess deaths were found to be related to an underlying cardiovascular cause (Kaiser et al. 2007). The risk of heat-related death was increased for older human beings with known medical problems such as being confined to bed, or being unable to care for themselves, or living alone with no or little social contacts (Semenza et al. 1996).

More than 70,000 additional deaths occurred in Europe during the heat wave in August 2003 of which more than 15,000, 19,000, and 20,000 were estimated for Spain, France, and Italy, respectively (Robine et al. 2007, 2008). Excess mortality varied considerably with age and rose as age increased. Older people confined to bed, with a cardiovascular or neurological disease or mental disorder, living in old buildings without insulation or in the areas with the greatest heat island effects, and with a bedroom located directly under the roof had a higher risk of death (Vandentorren et al. 2006). Another analysis of the heatwave in France concluded that excess mortality in retirement institutions was greater than that in hospitals and that the geographic variations in mortality showed a clear age-dependent relationship with the number of very hot days (Fouillet et al. 2006; Perčič et al. 2018).

Numerous studies have been reviewed investigating the relationship between high ambient temperatures and mortality in Australia (Bi et al. 2011; Climate Council 2016; Wang et al. 2012).

Hot and dry and warm and humid synoptic categories were associated with higher all-cause, circulatory, and cerebrovascular mortality in Sydney and Brisbane, especially for the 65 years and older age group and women. For the week spanning the 2009 heat wave in Melbourne, the greatest number of deaths occurred in those 75 years or older, a 46% increase in deaths occurred in the group of 64–75 years of age but also an unexplained 55% increase in deaths was in the 5–64 age groups.

For Beijing, the heat-related mortality risk for adults aged over 65 in the 21st century was projected from various climate models to rise up to more than 250 percent as compared to the 1980s (Li et al. 2016).

Individuals older than 65 years comprise a majority of the extra emergency room visits and deaths during heatwaves (Semenza et al. 1999). A key factor for enhanced excess mortality of older persons during heatwaves is that evacuation scenarios are difficult for older people with disabilities who may be physically unable or prepared to leave their homes (Kenney et al. 2014).

Case Study: Extreme Weather Events and Mental Health

Extreme weather events can lead to psychological and mental health impacts associated with loss, disruption and displacement as well as cumulative mental health outcomes from repeated exposure to natural and/or manmade disasters (Fritze et al. 2008). The vulnerability of individuals and communities, the appropriateness and swiftness of emergency responses, and the resources available to provide support and rebuild compound the mental health impacts of disasters. Extreme weather events such as Hurricane Katrina shows high rates of depression, trauma, chronic stress, anxiety, co-morbidity with existing psychopathology or medical illness, or dysregulated defenses (Shukla 2013). Such effects are felt most by vulnerable people and those with preexisting serious mental illness, who currently make up for 15% of adults aged 60 and over (Doherty and Clayton 2011; WHO 2017).

A study in Adelaide, South Australia, reported a positive relationship between ambient temperature and hospital admissions for mental and behavioral disorders from 1993 to 2006, The higher the temperature, the higher the admissions for organic mental illnesses such as "dementia; mood (affective) disorders; neurotic, stress-related, and somatoform disorders; disorders of psychological development; and senility." Mortalities due to these disorders also increased during heatwaves in the age group of 65 to 74 years (Hansen et al. 2008).

Future Directions for Research

The vulnerability of older people to extreme weather events such as heatwaves and tropical cyclones has been widely reported. However, more information is needed on the vulnerability of older adults to river flooding, coastal flooding from sea level rise, droughts, wildfires, deterioration of air quality, and contaminated food and water supplies. In addition, strategies are needed for reducing the vulnerability of older people and increasing their ability for adaptation, preparation, and response to emerging climate-related changes.

Indicators for older peoples' overall vulnerability to the effects of climate change – such as personal wealth, gender, age, ethnicity, race, rural or urban residence, property owning or tenancy, education, family and friendship structure, available health and social services, and infrastructure dependence – should be developed to help identify populations and locations that could be targeted for capacity enhancement and communication strategies for reducing vulnerability (Cutter et al. 2003).

Research is needed to better understand the risks posed by climate change to older adults and the appropriate ways to communicate those risks to decision makers, public health and safety officials, and other stakeholders concerned with aging populations (Gamble et al. 2013).

Summary

The earth's climate is warming (IPCC 2018). The adverse consequences of a changing climate include increased weather-related damage to infrastructure, more frequent and severe heatwaves, loss of land to rising sea levels, increased frequency and severity of heatwaves, spatially expanding insect infestation, more wildfires, more droughts and scarcity of water, increase of disease pathogens and invasive pests, a degradation of water quality, and an increase in air pollution and airborne allergens such as pollen and mold (Carnes et al. 2014). At the same time, the number of older people is rapidly increasing from approximately 12% in 2015 to 22% in 2050 (WHO 2017). Growing old in the twenty-first century will bring with it the unique challenge of adapting to changing weather patterns caused by a warmer climate. An interdisciplinary approach is needed to better understand the intersection between population aging and climate change and to reduce the vulnerability of older people, ensuring they reach later life with greater resilience (Haq 2017).

Cross-References

▶ Healthy Aging
▶ Geographical Gerontology

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Climate Gerontology

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Synonyms

Climate change and aging studies; Climate change and older adults; Environmental gerontology; Population aging and climate change

Definition

Climate gerontology is the study of the intersection between climate change and the unique challenges and needs of older people exposed to extreme weather events. This emergent interdisciplinary field has developed from a convergence of three factors: an increase in the number of people living into old age, the rise in the number of climate-related extreme weather events, and an understanding of how a changing climate can influence the quality of life of older people (Haq and Gutman 2014).

Overview

A changing climate will impact human health and well-being (Haq et al. 2008; Bouzid et al. 2013). A warmer planet will cause increased climate variability affecting the number, severity, and duration of extreme weather events (e.g., severe storms, tropical cyclones, flooding, and heat waves) (see ► "Climate Change, Vulnerability, and Older People", ► "Flooding and Older People", ► "Heatwaves and Older People", and ► "Tropical Cyclones and Older People"). Climate change will also have several negative indirect effects such as air pollution, vector-borne disease, and illnesses associated with higher temperatures (IPCC 2018; UN Environment 2019).

To manage the impact of climate change and to meet the UN Sustainable Development Goals (SDG), including SDG 13 (climate action), social dimensions will need to be integrated into climate adaptation and mitigation at the local, national, and international levels.

Older people are not a homogenous demographic group. Some older people lead active and sociable lives and are financially stable; however, there are others who are not. This means that they are less able to cope physically, emotionally, and financially with a climate-related weather event (Filiberto et al. 2019). Some argue that if adverse climate change impacts on older people are to be prevented or minimized, an interdisciplinary study of the convergence of population aging and climate change known as "Climate Gerontology" is needed (Haq and Gutman 2014). By providing the evidence base to "age and climate proof" policies, the study of climate gerontology could ensure older people are more resilient in later life.

As an emerging disciple, climate gerontology meets an apparent need to develop the knowledge base and identify and teach practical skills to address the impact of a changing climate on an aging population. Study in this new discipline would cover the following key areas:

- *Physical Basis of Climate Change*: An examination of the physical and human causes of climate change and climate variability, future trends and impacts of climate change, and current international legal and policy frameworks addressing these.
- *Fundamentals of Gerontology*: The focus here would be on the diversity of the older adult population, rendering it at a point in time simultaneously a vulnerable and potentially resilient population, and including recognition of aging, at the individual level, as a dynamic bio-psycho-social process taking place across time (the life course) in both the developed and developing world.
- *Climate Risks and Impacts on Older People*: The likely climate impacts on older people

from a human, natural, and built environment perspective. This includes the implications of heatwaves, tropical cyclones, and flooding, on health, housing, and transport infrastructure, and on the health care and social services designed to care for older people.
- *Climate Mitigation, Adaptation, and Older People*: How do changing consumption patterns at different life stages contribute to rising greenhouse gas emissions? (Zagheni 2011; Okada 2012; Buchs et al. 2018). How to measure the changing vulnerability of older people and develop adaptive solutions and responses. How to overcome socioeconomic, psychological, and physical barriers to adaptation.
- *Climate Action and Engagement*: How to raise awareness and engage older people in climate change issues. Older people can play an important role in reducing the impact of climate-related weather events as they have local knowledge of their environment. They have also seen the success and failure of past policy measures (Smyer 2018; Hopping et al. 2016).
- *Public Policy, Climate Change, and Population Aging*: The policy response to the convergence of an aging population and climate change. From prevention to emergency response, by hospitals and long-term and social care during climate change-related disasters, to the role of technology and the digital divide that separate the older population from more technologically savvy younger segments.

Key Research Findings

While many older adults live in the developed world, more people are expected to live beyond 60 years of age in the developing world (Pison 2009). An aging population has implications for greenhouse gas (GHG) emissions associated with travel, home heating, and food (Haq et al. 2007; O'Neil et al. 2012; Chancel 2014; Estiri and Zagheni 2019). Smaller households, different lifestyle choices, and higher consumption patterns in later life are having an impact on energy use and greenhouse gas emissions, especially in China, India, the United States, and Europe (see ▶ "Gray Consumption") (Hamza and Gilroy 2011; Menz anbd Welsch 2012; Wei et al. 2018; Yu et al. 2019).

WHO estimate that between 2030 and 2050 there could be 250,000 deaths because of climate change-related increases in health exposure in older people and higher levels of diarrheal disease, malaria, dengue, and coastal flooding (WHO 2014). However, these estimates do not include deaths from the disruption of health services because of extreme weather events (Haines and Ebi 2019). Without development that promotes societies to absorb the shocks and adapt to climate change, the World Bank estimate climate change could force 100 million people into extreme poverty by 2030 (Hallegatte et al. 2015).

Several factors will determine the extent to which a climate-related threat will have a negative impact on older adults (Cardona et al. 2012). These include income, education, state of health and social networks (e.g., family, friends, and the local community groups), and the level of welfare provision (e.g., pensions, healthcare, and social services). These factors will determine whether an older person will suffer a bad outcome, for example, whether they will incur damage or loss of home and belongings or become impoverished, dependent, or abused or neglected (Gutman and Yon 2014).

Human vulnerability is the loss of an individual's ability to absorb shocks, self-organize, and adapt (Adger 2006). Evidence suggests that older people are more affected by climate-related weather events (e.g., heat waves (see ▶ "Heatwaves and Older People"), tropical cyclones (see ▶ "Tropical Cyclones and Older People"), wildfires (see ▶ "Wildfires and Older People"), and flooding (see ▶ "Flooding and Older People")) than other demographic groups. However, the extent of the impact will depend on whether they are 60–74 years old (younger old) or 75+ years old (older old). In addition, sex, health and functional status, and the level of exposure together with individual coping capacities will determine their climate vulnerability (William et al. 2017). There are several indirect effects of climate change such as air pollution, food shortages and water stress, and infectious disease.

Air Pollution

Climate change is affecting air pollution patterns in many world cities (McMichael 2012; Horton et al. 2014). Changes in extreme conditions such as atmospheric stagnation and heatwaves can increase air pollution. One study of China estimated future climate change could increase population-weighted average concentrations of fine particulate matter ($PM_{2.5}$) and ground-level ozone (O_3), by 3% and 4% (Hong et al. 2019).

Air pollution can impact the respiratory health of older people, if they have a pre-existing illness such as lung disease. High associations have been found between air pollutant levels (e.g., nitrogen oxide and particulate matter) and heart and lung disease and pneumonia in older adults. The risk of asthma hospitalization in older people is increased from long-term exposure to traffic-related air pollution (Anderson et al. 2012).

Early evidence suggests high levels of air pollution can facilitate the spread of severe acute respiratory syndrome coronavirus (SARS-CoV-2) (COVID-19) (Marteletti and Marteletti 2020). In particular, fine particulate matter composed of solid liquid and particles may facilitate the survival of the virus in airflow for hours or days (Setti et al. 2020; Zhu et al. 2020). Older people with pre-existing health conditions and those with frailty, who live in assisted living or long-term care facilities, are more likely to develop critical illness and die because of contracting COVID-19 (Fisman et al. 2020).

Food Shortages and Water Stress

The stability of food systems could also be affected by climate change (Lake et al. 2012). This could exacerbate food insecurity in those countries suffering from hunger and nutrition – increasing food inequalities in vulnerable older adults (Trenberth et al. 2014). Indirect impact of climate change on income, access to safe drinking water, and healthcare is also expected to affect access to food.

Infectious Diseases

A warmer planet and changes in weather patterns increase the number of vector organisms such as fleas, mosquitoes and ticks, and nearest hosts (Gamble et al. 2013). As a result, there could be a higher incidence of malaria, lyme borreliosis, dengue fever, and schistosomiasis.

Flooding can increase the risk of waterborne disease such as leptospirosis, norovirus, salmonellosis, and legionellosis due the contamination of water and food (Haines et al. 2006; Kirk et al. 2011). Older people are more vulnerable to gastrointestinal disease from waterborne pathogens because of preexisting medical conditions and biological changes because of the aging process (e.g., changes to the immune and gastrointestinal systems) (Watts et al. 2018). Older adults may also be unable to seek medical attention, which could cause dehydration.

Prospects

A population of healthy older adults means less pressure on health services reducing health and pension costs (Butler et al. 2008). Investment throughout the life course can prevent disease and disability in later life. This requires a health policy that integrates health promotion, disease prevention, with gerontology to achieve a "longevity dividend." This can increase life expectancy and ensure older adults are able to cope with climate change impacts (Olshansky et al. 2012; see ▶ "Longevity Dividend").

The study of climate gerontology can determine which policies need to be developed to reduce the carbon footprint of older adults and to protect them from climate impacts. It can also highlight approaches to harness the knowledge and experience of older people to tackle the climate emergency.

Reducing the Carbon Footprint of an Aging Population

The promotion of greener lifestyles in this demographic group requires appropriate policies to encourage older adults to lead low-carbon lifestyles. Peer-to-peer approaches may be more effective than top-down campaigns (Reed et al. 2008). This should be supported by infrastructure and incentives that make a greener lifestyle in later life a low-cost and easy option.

Protecting Vulnerable Older People

In order to reduce the vulnerability of older people to climate change impacts, a policy approach is needed that focuses on each factor that contributes to a climate vulnerability. This should ensure that older people reach later life with coping skills, savings and social support network, and adequate health and social care. The creation of age-friendly cities can encourage active aging to improve quality of life in old age (Noordzij et al. 2019). Housing and transport should meet the needs of everyone, especially older people who may have mobility restrictions. City infrastructure should be designed to consider the challenges faced in later life, for example, the provision of public toilets, good lighting, sidewalks that are in a good condition, and access to information and social services (Help the Aged 2008).

Mobilizing the Experience of Older People

Older adults have accumulated a wealth of experience and knowledge about their local environment and community over their life course. This knowledge could be harnessed to ensure a community can respond to climate-related hazards (Lloka 2016). Such knowledge and experience are critical in developing local policy responses to an extreme weather event. However, national and local policy makers often ignore the potential role older adults can play in environmental volunteering (Pillemer et al. 2016). Insurance restrictions, health and safety regulations, and lack of access for disabled people are all barriers to volunteering in later life.

Research Challenges

The global population is aging at the time when the planet is heating and causing an increase in the number of extreme weather events. In order to protect the health and well-being of older people in a changing climate, countries need to ensure that older people have access to healthcare, social support systems, and learning opportunities (UNDESA 2019).

A better understanding of the socioeconomic and environmental factors that affect how older adults cope and recover from an extreme weather event is needed. Social protection, the public health system, and infrastructure policies influence an older person's resilience (Otto et al. 2017). Methodological approaches that tackle these factors and determine differences in community resilience across the lifespan are needed. Indicators such as gender, age, ethnicity, race, education, family and friendship structure, personal wealth, rural or urban residence, property owning or tenancy, available health and social services, and infrastructure are required to determine the overall vulnerability of older adults. Research will help target older people who could benefit from activities to increase awareness and capacity to reduce individual vulnerability (Cutter et al. 2003).

In particular, further research is required on the impact of climate-related weather events on older people in developing countries not just related to deaths and disease but highlighting the differences in impact as a function of sex and gender (Green et al. 2019; van Steen et al. 2019). Quantifying exposure to future climate risk and understanding the socioeconomic and institutional factors that contribute to the vulnerability of older adults will be essential for the development of effective prevention strategies (Jones et al. 2018).

Research on how to develop intervention strategies that address the needs of older adults in an extreme weather event is needed (Bukvic et al. 2018). This would range from how to improve early warning systems, evacuation procedures to public awareness about postimpact hazards (Doocy et al. 2013). Research is needed on a range of strategies that emergency responders can use to reduce the impact of climate change and support older people during extreme weather events (Sykes 2017).

Future research should explore how environmental volunteering changes across the life course and the well-being benefits for senior volunteers (Frumkin et al. 2012), also how to mobilize older adults to engage in environmental volunteerism and to adopt low-carbon lifestyles and take part in environmental volunteerism (Haq et al. 2010; Pillemer et al. 2016).

Summary

The intersection between climate change and an aging population needs to be addressed to protect older people and achieve the SDGs (e.g., SDG13 on climate action). This requires additional research on effective preparedness and mitigation strategies, in particular, how to improve early warning systems and strategies to protect older people during and after an extreme climate event in different countries (Doocy et al. 2013; Gamble et al. 2013). Several research challenges exist to better understand the vulnerability and resilience of older people to climate change, and how to provide the evidence to improve the ability of government agencies to prevent and minimize the impact of a changing climate on older adults.

Climate gerontology can contribute to the evidence base to "age and climate proof" policies and help mobilize the contribution of older people in addressing climate emergency while ensuring they reach later life with greater resilience.

Cross-References

- ▶ Climate Change, Vulnerability, and Older People
- ▶ Climate Resilience and Older People
- ▶ Environmental Gerontology
- ▶ Flooding and Older People
- ▶ Heatwaves and Older People
- ▶ Older Adults and Environmental Voluntarism
- ▶ Older Adults in Conflicts and Crises
- ▶ Tropical Cyclones and Older People

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Climate Resilience and Older People

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Definition

Individual climate resilience is the ability of a person to anticipate, reduce, accommodate, and recover from climate-induced hazardous events (IPPC 2014). Older adults are known to be at higher risk for death and disability in extreme weather situations and to be disadvantaged in recovery assistance (Kwan and Walsh 2017; Gutman and Yon 2014). A changing climate and an aging population mean that a greater number of older people may be at risk from the impacts caused by climate-induced weather events such as heatwaves, ice storms, flooding, and tropical cyclones. Older persons require a range of individual resilience capacities if they are to prepare for, avoid, and recover from climate-related threats to health and wellbeing (Haq and Gutman 2014).

Overview

An increase in global average temperature is likely to increase the frequency, severity, and duration of extreme weather events, such as heatwaves (see ▶ Heatwaves and Older people), tropical cyclones (see ▶ Tropical Cyclones and Older People), flooding (see ▶ Flooding and Older People), and sea level rise. Major indirect adverse effects of climate change include temperature-related illnesses and deaths, water stress, air pollution, and vector-borne disease (Haq et al. 2007).

The threat of climate change to wellbeing and quality of life in old age will depend on an individual's ability to cope and withstand and/or recover from difficult conditions or crises and so avoid a bad outcome. Climate change can affect all aspects of life, including social life, health, transport, cost of living, housing, and social care (Mian et al. 2019; Oven et al. 2012). As the population ages, it is important to ensure individuals reach old age with the resilience to adapt to the threats from a changing climate.

Individual resilience is both explicit and implicit in the Sustainable Development Goals (SDGs). In SDG 1 (No Poverty), Target 1.5 states: "*By 2030 build the resilience of the poor and those in vulnerable situations, and reduce their exposure and vulnerability to climate-related extreme events and other economic, social and environmental shocks and disasters.*' Resilience is also a core feature of SDG 13 (Climate Action) in Target 13.1 aim to '*strengthen resilience and adaptive capacity to climate-related hazards and natural disasters in all countries.*"

Extreme weather events force older people to mobilize resources to avoid a decline in their wellbeing (Otto et al. 2017). Their ability to cope is influenced by their mental and physical health, physical strength, degree of disability, income, and social networks (see ▶ Climate Change, Vulnerability, and Older People). An older person's resilience to climate change is also determined by the availability of assets (e.g., education, financial capital, and social relations and networks) and access to services (e.g., transport, communication, emergency relief, and recovery). The importance given by older people to certain factors that can contribute to building resilience vary (Bajekal et al. 2004). Among them are:

- Quality of neighborhood: living in a home and neighborhood that is safe, pleasant with good access to local amenities (e.g., shops, public transport, and green space).
- Social networks and community: having social relationships which offer help and support.
- Material conditions: having sufficient income to meet basic needs and take part in society.
- Health and wellbeing: having good health and mobility, independence in activities of daily living (ADL), and engaging in hobbies and solo as well as collective leisure activities. Having a positive psychological outlook and accepting circumstances which cannot be changed (Gabriel and Bowling 2004; Bajekal et al. 2004).

Key Research Findings

Coping capacity is how adaptable an individual is to deal with the impact of climate change. Improving the coping capacity of older people reduces direct and indirect impacts of climate change. This includes how an individual can recover following a particular event. Older people's ability to cope with the effects of climate change will depend on a combination of individual capacities (e.g., wealth, education, skills, and health), social networks (e.g., family, friends, neighbors, and community institutions such as religious, voluntary groups and charities) and social protection policies (e.g., formal welfare provision such as pensions, health, and social services). This will determine whether they suffer a bad outcome such as damage or loss of home, becoming weaker, impoverished, dependent, or are humiliated or psychologically harmed (Chambers 2006). Inequalities, social injustice, disempowerment, and access to key essential services will shape and further exacerbate coping capacity. Therefore, healthy lifestyles, acquisition of coping skills, strong family and social ties, active interests, and savings and assets, will help ensure that people's reserves are, and remain, strong in later life (Grundy 2006).

Informal support networks play a role in building resilience in later life. Reciprocal relationships and the value of confidants and emotional support contribute to feelings of belonging, security, and wellbeing. A well-functioning formal and informal support network allows individuals to maintain autonomy in old age, even when they have to depend on help from others (Duner and Nostrom 2007). During extreme weather events, links between different networks of care are important to avoid discontinuities that could endanger older people's health and wellbeing. Local knowledge and local caring networks can also assist in the preparedness for extreme weather (Wistow et al. 2015).

Cohen et al. (2016) found that older people in good health could help build community resilience. Opportunities for people to contribute to a community in a crisis should be based on functionality rather than chronological age; even frail older people can be a valuable resource, for example, as a repository of what worked (and did not) in community efforts to mitigate prior extreme weather situations. In turn, physical changes made by the community, such as improving the quality of the housing stock available to older people, will influence their risk of heat (or cold) exposure during extreme weather (Loughnan et al. 2015). Another important element is education of older adults about what they can and should not expect from the management of collective dwellings such as apartments blocks during extreme weather (Kloseck et al. 2014).

Social protection programs contribute to building a person's resilience to climate risks. To strengthen resilience at the individual and household level, it is critical to understand how national systems that span different sectors at the national and subnational level can be transformed to provide reliable and sustainable support structures that reduce vulnerability to livelihood risks in the long term. Doing so might imply different roles for governments, development partners, and NGOs, recognizing there is value in reducing vulnerability by allowing people to anticipate and absorb shocks, at scale (Ulrichs et al. 2019).

Research Challenges

The vulnerability of older people to climate change is shaped not only by physical changes to the climate system but also by demographic, institutional, and sociocultural factors. Further research needs to explore the social, economic, and environmental factors that influence the ability of older people to adapt and recover from extreme weather events. An older person's climate resilience is influenced by policies on social protection, public health system, and infrastructure (Otto et al. 2017). However, a better understanding of the environmental and social interactions that affect the wellbeing of older people is needed. This will require new methodological approaches and data collections, including longitudinal studies that address these factors and the variations in the level of community resilience across the lifespan and connections between ageing population and the resiliency of their community,

Building individual resilience and reducing vulnerabilities are core aspects of the SDGs. The SDGs recognize that threats, disasters, shocks, and stresses present immense challenges, but also pledge that "no one will be left behind." However, in the case of older adults, a greater understanding is required to develop methodologies to determine resilience and establish baselines for measuring hazards and exposure.

Summary

Older adults are at higher risk for death and disability in climate-induced extreme weather situations and are disadvantaged in recovery assistance. A changing climate and an aging population mean that older people may be at risk of climate-induced extreme weather events than other segments of the population. An older person's ability to cope, adapt, and recover from shocks such as heatwaves, ice storms, and flooding is due to several socioeconomic and environmental factors. Individual resilience is integral to the SDGs, but there is a need for further research into how to develop and build individual and community resilience to climate risks among older adults.

Cross-References

- ▶ Baby Boom/Baby Bust
- ▶ Climate Change, Vulnerability, and Older People
- ▶ Climate Gerontology
- ▶ Heatwaves and Older People
- ▶ Tropical Cyclones and Older People
- ▶ Wildfires and Older People

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Climate-Induced Migrants, Aging out of Place

▶ Aging Refugees

Clinical Gerontology

▶ Behavioral Gerontology

Clinical Translation Acceleration

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Synonyms

Early patient access to innovations; Facilitating therapeutic R&D; Healthspan technologies

Definition

Clinical translation acceleration refers to facilitating and speeding up the process of translating fundamental scientific research to its application in clinical practice, creating and utilizing actual medical technologies to ultimate patient benefit. The clinical translation acceleration process may include all the stages of research and development: from studies on cells and tissues, through animal studies and human trials, marketing, production, and distribution, through to securing clinical adoption and patient adherence.

Overview

Increasing the human healthy lifespan (sometimes called "healthspan") is undeniably attractive. An increasing number of potential technologies are coming available to assist in that goal. Less encouraging, especially for those already in the last half of life, is that their arrival can be painfully slow. For example, it is quoted that, for the UK National Health Service (NHS), there is a time gap of 17 years between initial approval and peak usage of new therapies (Hill and Caulfield 2018). Hence, there is an obvious and urgent need to accelerate the process of testing, approval, and adoption of new effective, safe, and affordable therapies (Barker 2016).

The technologies in question are many and varied. Some are quite low-tech and depend on lifestyle change and tracking, using digital aids and online health coaches. Others are applications of more conventional medicine, such as determining the cardiometabolic status of the body and initiating treatments to reduce the risk of developing chronic diseases – from diabetes to dementia. There are drugs – like metformin – that intervene in pathways linked with aging and may therefore lengthen healthy lifespan. The Metformin In Longevity Study (MILES) conducted by Albert Einstein College of Medicine in New York aims to determine if treatment with metformin (1700 mg/day) will restore the gene expression profile of older, glucose-intolerant adults to that of young healthy subjects (MILES 2019).

Prevention of, or delay in, diabetes is of particular importance, as studies show that it is the most common disease "gateway" to the multimorbidity that inflicts frailty on so many seniors (Barzilai et al. 2016). Diagnostics have an important part to play, including sophisticated genetic diagnostics to assess cardiovascular risk (Knowles and Ashley 2018), or identify cancer before any symptoms appear (Narrandes and Xu 2018). Even more "leading edge" are treatments to target and destroy senescent cells (Justice et al. 2019) or to lengthen telomeres (Jäger and Walter 2016). So far, technologies in this last category are only at the earliest stages of animal studies, in vitro testing or human trials.

There are some understandable reasons for expecting delay in bringing such technologies into practice. By definition, forestalling disease and lengthening lifespan generate long-term outcomes, making classic randomized trials with conventional clinical endpoints (such as multimorbidity or death) both lengthy and expensive. There is therefore a strong need to consider means to accelerate development and to develop surrogate endpoints that measure short-term "molecular health" parameters that anticipate longer-term benefit. Likewise, there is a need for markers of safety, since many of the therapies will be used over an extended period. Both for safety and effectiveness, long-term real-world data studies seem an important part of the approach.

An additional barrier is reimbursement, often an add-on step that further lengthens the time to availability. However, there is evidence that some healthy lifespan technologies will be willingly paid by consumers rather than needing payer approval, just as individuals pay for gym memberships or personal trainers. (This is not to discourage health and life insurers paying for such technologies, ultimately in their interest also.)

Development acceleration has been an increasing focus on both sides of the Atlantic, with regulatory authorities and companies pursuing models of the so-called adaptive development. A representative example of this movement is "Medicines Adaptive Pathways to Patients (MAPPS)" being pioneered in Europe (Schulthess et al. 2016). Its goal is to reduce the timeline from trial initiation to patient availability by several years.

MAPPS has four main components. First is the early identification of novel technologies worthy of accelerated development (the so-called PRIME designation). Second is the early dialogue between the innovator, patients, the regulatory authority, health technology assessment (HTA) agencies, and payers to help design an "evidence generation plan" that satisfies the needs of each stakeholder and so speeds the path to subsequent approval, reimbursement, and adoption. The third is the concept of "conditional approval" (which can be coupled with conditional reimbursement) whereby the technology is approved with a lesser evidence base than historically required but only for those groups of patients that appear to have the greatest benefit/risk ratio. The fourth plank of MAPPS is the collection of real-world data (via patient registries and digital outcome tools) to confirm or refine the understanding of the clinical value in routine use. This is in contrast to classical clinical trials, given their narrow patient populations defined by strict inclusion/exclusion criteria and structured clinical monitoring. There is growing recognition that real-world data is both vital to understand the performance of technologies in routine practice and also a way of uncovering unexpected benefits of therapies already in use, by applying machine learning to major health databanks.

MAPPS is now one of the routine development routes available through the European Medicines Agency, and comparable efforts are underway in the USA, with the FDA pledged to provide earlier access to new treatments provided safety is not compromised (Food and Drug Administration 2018). However, so far the main target of accelerated access has been drugs for acute disease, such as cancer and rare conditions, rather than technologies to extend healthy lifespan, unconnected with a specific diagnosed disease. Given the "time lag" point mentioned above, we may need to develop MAPPS in new directions for the latter, with particular attention to surrogate endpoints and real-world data monitoring.

Notably, as we seek to accelerate the development of medical technologies, our goal should not be mere extension of life, maintaining or increasing the present levels of old-age multimorbidity and frailty. Along with approaches to reduce the risk of cardiometabolic disease (diabetes, cardiovascular conditions, etc.), there will be the need for therapies for the diseases that frequently strike people in their second half of life, such as osteoarthritis and dementia. Improving cardiometabolic status will reduce risks in these areas, but it won't eliminate them.

These so-far intractable later-in-life conditions are also beginning to yield to bioscience. Cell therapy for arthritic joints (Negoro et al. 2018) and various routes to intervene in the diverse mechanisms underlying dementia (Shetty et al. 2018) are appearing, although results are so far mixed, in both cases. In fact, the first trial of a "senolytic" agent targeted idiopathic pulmonary fibrosis (Justice et al. 2019), a defined disease rather than overall healthy lifespan. Given the long-term course of such diseases, clinical metrics should be envisioned, elaborated, and evaluated, including leading indicators of efficacy.

Future Directions of Research

A critical question for the accelerated development and adoption of new medical technologies for healthspan improvement will be determining the strength of evidence for their effectiveness and safety. There is an obvious need to give priority to clinical trials to provide robust evidence for their efficacy and safety. Prioritizing and fast-tracking such well-evidenced approaches will help bring effective life-saving therapies and improve the quality of life for as many people as possible, as rapidly as possible. This requirement for good evidence holds true for any therapies and for healthspan-improving therapies in particular. Yet, regarding the latter, the question remains what constitutes adequate "evidence" of efficacy and safety for healthspan-improving interventions: there is as yet no formal and agreed clinical definition of degenerative aging and of its modification to improve healthspan (Stambler 2017a). Hence, the need to prioritize the best evidence-based treatments will go hand in hand with the need to develop robust outcome metrics. Together these tasks represent critical strategic areas for scientific and policy research (Stambler 2017b).

The development of evidence-based diagnostic criteria for the efficacy and safety of healthspan-extending interventions will require us to be able to objectively measure the aging processes. Various testing modalities (in vitro, in vivo, in situ, in silico) should be investigated and the correlations (or noncorrelations) between them established. Scientific, regulatory, and ethical challenges will need to be addressed for many of these.

There is often a deficit of cross talk between the biologists, physicians, and bioinformaticians involved in these methods, often due to the narrowness of training of specialists. In vitro testing modes often suffer from logistical obstacles in supply, transportation and utilization of live cells, and deficits in appropriate analytical equipment. Animal testing also frequently faces logistical difficulties and deficits of facilities and equipment. In addition, there are often unfavorable public perceptions and regulatory hurdles for animal trials.

In vivo human trials, of course, face particular challenges. There is a need to develop and disseminate clearer guidelines for the ethical, safety-assured human testing of aging-ameliorating and healthspan-improving therapies, taking into account the specifics of the field (Newman et al. 2016). Different kinds of incentives may need to be conceived to attract test subjects to participate in lengthy aging amelioration and healthspan improvement studies, while protecting their safety and privacy.

Because of the long timescales associated with healthspan-improving interventions, we need early biomarkers of efficacy that – over time – can be correlated with actual clinical outcomes (Reiman et al. 2011).

Overall, there is a need for intensive scientific effort to establish the efficacy and safety of potential aging-ameliorating and healthspan-improving therapies, using robust and objective metrics, if we are to accelerate the development and deployment of such technologies.

Summary

The area of healthy lifespan (or "healthspan") is now one of lively research and venture investment, and we can anticipate a widening range of technologies that promise delay of disease, prevention of frailty, and promotion of youthful vigor into our 70s, 80s, 90s, and beyond. But in parallel with the clinical science, there will be a need for active work between industry, patient organizations, regulators, and healthcare payers to reduce the delays and obstacles in clinical translation that will otherwise frustrate the promise.

Cross-References

▶ Longevity Activism
▶ Longevity Advocacy
▶ Regulation of Geroprotective Medications

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Clinical Translation of Geroprotective Drugs

► Regulation of Geroprotective Medications

Clinical Trial Design for Older Cancer Patients

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Synonyms

Cancer trial design; Clinical trial studies; Clinical trials

Overview

The world's population is aging, and it is estimated that by 2050, the number of people aged 65 and over will be 15% of the global total, which was just 5% in 1950 (United Nations 2019). Cancer is strongly associated with aging, so it is not a surprise that the majority of new diagnoses and cancer deaths occur in people over the age of 65 years (Hurria et al. 2014).

Despite statistics from all over the world showing a growing number of older patients with cancer, older adults are still underrepresented in cancer clinical trials. Because they may respond differently to cancer treatments compared to their younger counterparts (Hurria et al. 2015), this inevitably raises serious questions with regard to the efficacy and tolerability of cancer drugs in older people and, given the heterogeneity of the group, how to accurately define older patients and recruit them to clinical trials. The need to pay greater attention to geriatric oncology and to clinical trials in this population is therefore obvious.

Key Research Findings

Implications of Underrepresentation of Older Patients in Cancer Trials

Older adults have historically been underrepresented in cancer clinical trials due to various reasons including restrictive eligibility criteria, trial design, physician recommendation, transportation or caregiver issues, perception of aggressive therapy, “excessive” visits, financial aspects, and limited expectation of benefit (Lichtman 2012a, b). It has also been observed that older patients are more likely to experience severe toxicities resulting in treatment discontinuation and receive a reduced dose which could dilute or affect the true benefit of the treatment and are more likely to have comorbidities that can result in death from non-cancer causes. All these issues have resulted in age limitations and strict trial inclusion criteria which have excluded large numbers of older patients from clinical trials (Wildiers et al. 2013).

A review of the patient information leaflets of 24 cancer drugs approved between 2007 and 2010 showed that only 33% of the trial participants were aged 65 years or more (Scher and Hurria 2012). From 1997 to 2000, of the 59,000 patients participating in 495 National Cancer Institute (NCI) trials, only 32% were older adults (while in the general population, this age group contains about 60% of cancers). Another study (Le Saux et al. 2016) showed that since the creation of the International Society of Geriatric Oncology (SIOG), the proportion of phase III trials reporting at least one analysis dedicated to older patients has grown: 46.7% between 2011 and 2014 versus 19.3% between 2001 and 2004. However, this evidence can only be considered as preliminary because the data was mostly extracted from subgroup analyses.

It has also been noticed that underrepresentation of older adults in cancer clinical trials has significant clinical implications. Aging affects drug pharmacokinetics and metabolism (Wildiers et al. 2003). Also the biology of certain cancers is changed with age. These factors, combined with the comorbidities expected in an older population, may lead to substantial differences in the efficacy and safety of cancer treatments (Wildiers et al. 2013). While there is an increased understanding that chronological age and physiological age can differ substantially, many older patients receive less aggressive treatment (especially chemotherapy) than recommended by guidelines due to the questions of tolerability and benefit (Hurria et al. 2014, 2015).

Several international organizations such as the European Organisation for Research and Treatment of Cancer (EORTC), SIOG, Cancer and Aging Research Group (CARG), and American Society of Clinical Oncology (ASCO) have held debates on research priorities in geriatric oncology which has led to discussion on how to select the most appropriate endpoints relevant to the older population, clinical trial design, and wider eligibility criteria.

Suitable Endpoints in the Older Population

Endpoints are essential to assess the effectiveness of therapy in clinical trials. Well-established and standard clinical endpoints exist for randomized controlled trials (RCTs) in oncology. While such endpoints as overall survival (OS) and disease-free survival (DFS) in the curative/adjuvant setting are gold standard, they may not be the most appropriate measures in the older population.

Overall Survival (OS)

OS is a distinct and easy approach to measure endpoint, but its relevance in older adults is complicated by non-cancer-related deaths. It also does not take into account the importance of quality-of-life (QoL) parameters from the patient’s perspective.

Disease-Specific Survival (DSS)

DSS is an endpoint that indicates better how many patients die as a result of disease and how many die as a result of other causes, although this can be subjective as the cause of death may be difficult to evaluate. As DSS can evaluate the "true benefit" of an anticancer therapy on cancer mortality, trials should ideally report DSS in addition to OS (Wildiers et al. 2013).

Coprimary Endpoints

Coprimary endpoints enable researchers to capture more than efficacy alone, and multiple single endpoints can be chosen as coprimary endpoints of equal importance. However they require a larger sample size if the trial objective is to have positive results for at least one or all coprimary endpoints, and the type I or II error, respectively, must be adjusted for multiple testing (Wildiers et al. 2013).

Composite Endpoints

A composite endpoint in a RCT is when multiple single endpoints are combined so that an event is triggered if any of the endpoints occur. Those endpoints enable other parameters of special interest, such as QoL or the ability to carry out daily tasks, to be incorporated. All components of a composite endpoint should be analyzed and reported separately because the separate reporting of endpoints is essential to facilitate cross-study comparisons or to generate assumptions for future trial designs. The major advantages of a composite endpoint are the simple statistical design based on a single endpoint (i.e., the composite one) and the resultant increase in statistical efficiency.

An interesting example of a composite endpoint in older population is therapeutic success which combines efficacy, toxicity, and patient compliance with treatment and is defined as a patient receiving at least three cycles of chemotherapy at the planned dose (without dose reduction) and schedule (no treatment delay beyond 2 weeks) and having a response (either complete or partial) without experiencing grade 3 or 4 toxicity according to the common toxicity criteria. Therapeutic success is particularly interesting as an endpoint in the metastatic setting to compare toxicity, which in this kind of treatment should ideally be low, against a supposed treatment benefit. However, in the adjuvant setting, higher levels of toxicity may be generally more acceptable if there is a considerable survival benefit.

Treatment Failure-Free Survival and Time-to-Treatment Failure

Treatment failure-free survival (TFFS) and time-to-treatment failure (TTF) are well-known composite endpoints. TFFS is defined as the time that elapses between random assignment and early treatment discontinuation because of any reason including disease progression, death resulting from any cause, or any other event of interest. While TTF is similar, only disease-specific and treatment-related deaths are considered events.

TFFS and TTF are both interesting endpoints in cancer trials for older adults because they enable toxicity to be taken into account rather than just concentrating on efficacy. As older patients often prefer quality over quantity of life, it is important to be able to capture treatment discontinuation due to toxicity. However, they also have their limits, treatment breaks or "chemotherapy holidays," that are unrelated to toxicity, or disease progression should also be taken into consideration and not just being viewed as treatment failures. Similarly, early treatment discontinuation should not be seen as a failure in situations where significant toxicity is followed by positive disease outcomes (Wildiers et al. 2013).

QoL-Related Endpoints

The major goal of cancer treatment is to improve or maintain QoL. Especially in the palliative setting, the main aim should be to reduce the symptoms, loss of functionality, pain, and deterioration of overall QoL arising from progressive disease. HRQOL is impaired in cancer patients compared to the general population, but the impact on specific HRQOL domains varies by age. Within the cancer population, some HRQOL components improve with age, while others deteriorate. Optimal care for older cancer patients should target HRQOL domains most relevant to this population (Quinten et al. 2015).

Health-related QoL (HRQOL) is a multi-dimensional parameter that focuses on the impact of health status on QoL, and it is a major concern for patients with cancer. HRQOL can be influenced by both symptoms due to cancer and treatment-induced toxicity. It has been shown that while younger patients with children may prioritize survival over quality of life, older patients are less willing to compromise their HRQOL for an increase in survival potential (Wildiers et al. 2013; Yellen et al. 1994).

As a measure of outcome, HRQOL is appropriate in trials for older adults and should be captured in all trials of palliative and adjuvant chemotherapy in older populations regardless of the primary endpoint of the trial. Given its complexity it is fraught with issues on how it can be optimally measured – it is not well-defined how the different measures of QoL, such as physical, emotional, and social functioning, can be combined into one score and how they can be made relevant to older people and which cutoffs are suitable endpoints (Quinten et al. 2019).

In an attempt to provide an instrument that focuses on HRQOL issues that affect older people with cancer, the EORTC QoL Group developed a questionnaire module specific to older population to supplement its general QLQ-C30 core questionnaire (Wheelwright et al. 2013).

Preservation of Functional Capacity/Independence

An endpoint closely related to HRQOL which should be a major aim of older patient cancer management is the preservation of independence and function. Incorporating this measurement into outcome events is highly valuable as survival has been shown to be linked with functional capacity (Reuben et al. 1992; Wildiers et al. 2013).

Cognitive Function

Another important endpoint for older patients can be cognitive function. It has been proven that cognitive deficits may affect a patient's quality of life and their compliance to treatment.

Surgical Trial Endpoints

A relatively large number of older cancer patients do not receive standard surgery as they are considered unfit for surgery due to an inaccurate estimation of their surgery-related risk. The preoperative assessment of cancer in the elderly (PACE) assesses operative risk and is recommended for all older patients prior to surgery (Audisio et al. 2008).

Improving Cancer Trial Design in Older Patients

Age Limits

In registration clinical trials drugs that are intended to be used across the entire adult age spectrum should have outcomes evidence across the same age range. Therefore, studies should include older patients without an upper age limit and a minimum cohort of all older patients. Failure to do so results in a selection bias toward younger patients or to older patients who may have been eligible for the trial on the basis that they are fitter. As a result the trial conclusions are unable to be generalized across the entire population.

Another issue is the characteristics of the therapy under investigation because some standard treatments (control arm) are not suitable for unfit or frail older patients, or even those who are fit, because of their expected high toxicity risks. Examples include bone marrow transplantation, major surgery, or concurrent chemoradiotherapy. Therefore, specific trials in the frail or older patient that modify a chemotherapeutic or biologic regimen and compare it against supportive or palliative care may be a better approach. One example is EORTC 75111 (Wildiers, Lancet Oncol 2018) where the standard treatment for first-line HER2+ metastatic breast cancer (taxane, trastuzumab, pertuzumab) was not selected because frail patients were likely to be excluded. It was rather decided to explore two experimental regimens with low toxicity profile, and the combination of metronomic cyclophosphamide with trastuzumab and pertuzumab at the end appeared to be an effective regimen with low toxicity.

Phase III Versus Phase II Trials

Phase III studies are gold standard in clinical research regardless of age, but usually phase III RCTs are reserved for younger populations. There is also probably some kind of reluctance from the pharmaceutical industry to develop large trials in older patients due to an enhanced risk of toxicity or other adverse events that could hamper drug development, despite that an aging global population can offer huge market potential.

The ability of phase II trials to also provide insight into the efficacy and toxicity of cancer drugs in older adults may provide a reasonable solution as randomized phase II study in older unfit patients could quickly establish if a drug is too toxic compared to the results of a phase III study in younger and fitter patients. Similarly, if a phase II study in older unfit patients shows efficacy and toxicity results in line with a previous phase III study in younger patients, there may not be a need to repeat the phase III trial again in the older unfit population.

Pharmacokinetics and Phase I Trials

Aging organs can heavily affect the pharmacokinetics of drugs and the metabolic process which often can cause enhanced drug toxicity compared to that seen in younger patients. Pharmacokinetic and phase I studies specific to these populations should be designed for new drugs and could run parallel to standard phase I trials or shortly thereafter, assuming the results of standard studies have shown promise.

Future Directions of Research

Randomized Controlled Trials, Observational Cohort Studies, or Both?

Randomized Controlled Trials (RCTs)

RCTs are defined as quantitative, comparative, and controlled experiments in which a group of investigators study two or more interventions by administering them to groups of individuals who have been randomly assigned to receive each intervention (Stolberg et al. 2004).

RCTs have always strict inclusion and exclusion criteria which limit the heterogeneity of each study arm. Patients in RCT are randomly assigned to one intervention (control) or another (comparison) so that the only known major variable is the exposure to the intervention being tested. While this is very good for quality control, the results of randomized trials have the potential to establish a new standard of care that may not necessarily be applicable across broad populations, particularly in older adults (Mohile and Wildiers 2012).

Observational Cohort Studies

It has been recommended by experts that observational cohort studies should be developed to increase the much needed evidence in geriatric oncology. An observational cohort study prospectively follows a group of patients who have specific features in common over a defined period of time. The information collected in observational cohort studies is prospectively defined for outcomes, sample size, and duration of follow-up. Observational cohort studies have the potential to provide timely and cost-effective data on efficacy, safety, and compliance in real-life older patients (Mohile and Wildiers 2012).

Single Versus Multicenter Observational Cohort Studies

Large, multicenter observational cohort studies are preferred because they have the ability to provide useful data about the consequences of specific treatment decisions, while single-center cohort studies in older patients provide only limited meaningful information as individual treatment centers tend to use the same (potentially biased) approach. Because there are different treatment approaches toward older cancer patients between centers and countries, it is vital that these studies collect similar, if not identical, data across different tumor types and settings to enable the creation of large databases and cross-trial comparison.

Overcoming Bias in Observational Cohort Studies

Observational studies can provide important, unbiased, and accurate information on the toxicity of new drugs or therapies in the general older population, but special caution is required when an evaluation of efficacy compared to other treatment strategies is the goal. The sheer fact that treatments are not randomly assigned in observational cohort studies means that they are subject to bias and that the causal effect from treatment may not be entirely accurate.

To obtain meaningful results from observational cohort studies, it is vital to design the study carefully. One way to help overcome issues with bias and still collect valuable additional data is to establish a RCT and to include ineligible patients, or those who declined, in a parallel observational cohort study. Integrating patients into an adjunct observational cohort study would increase the quality of the RCT because the patient selection would be better described.

If well designed observational cohort studies can be used to collect data relevant to older populations including efficacy, safety, adherence to treatment, patient-reported outcomes, HRQOL, resource utilization, patterns of care, and cost. They can enhance the quality of RCTs and potentially inform and guide RCTs that compare different treatment approaches in older patients with cancer. Finally, as older cancer patients with comorbidities are usually excluded from RCTs, observational cohort studies can evaluate the relationship of comorbidities or underlying health problems with cancer treatment outcomes (Mohile and Wildiers 2012).

Despite an aging world population, older adults are still underrepresented in clinical trials which leads to selection bias and difficulty in drawing conclusions on the effects of interventions in this population of patients. The oncology community is more and more aware of this issue, but the challenge is in designing trials that capture the heterogeneity of an entire population, particularly the older and frail.

We need separate trials for older patients with cancer which incorporate pharmacokinetic studies, appropriate endpoints, and appropriate control arms. OS remains a crucial endpoint, but DSS should be recorded in all cancer trials with older patients to capture deaths from causes other than cancer. Composite endpoints allow additional parameters, such as QoL, preservation of functional capacity, and independence.

Randomized or single-arm phase II trials in older adults can provide important information on efficacy and toxicity. Large observational cohort studies have been recommended, ideally alongside a RCT, to capture data on ineligible trial patients such as the older and unfit.

C

Summary

Despite the demographic trends showing a growing number of older patients diagnosed with cancer, older adults are still underrepresented in cancer clinical trials which have significant clinical implications. Therefore, better clinical trial designs are crucial to understanding the impacts of new therapies on older individuals and for improving care for this growing population of cancer patients. To ensure the best effectiveness of therapy in clinical trials, valuable endpoints must be used. The most appropriate measures in the older population of patients are not only endpoints like overall survival or disease-specific survival but also composite endpoints such as treatment failure-free survival (TFFS) and time-to-treatment failure (TTF), quality-of-life-related endpoints, and cognitive functions measures.

Cross-References

▶ Aging and Cancer: Concepts and Prospects
▶ Epidemiology, Aging, and Cancer
▶ Geriatric Interventions
▶ Monitoring and Clinical Research in Oncogeriatrics
▶ Prediction of Outcomes Among Cancer Patients
▶ Quality of Life
▶ Survival Analysis

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Clinical Trial Studies

► Clinical Trial Design for Older Cancer Patients

Clinical Trials

► Clinical Trial Design for Older Cancer Patients

Cluttered Nest

► Crowded Nest

Codehydrase I

► Nicotinamide Adenine Dinucleotide (NAD+) in Aging

Codehydrogenase I

▶ Nicotinamide Adenine Dinucleotide (NAD+) in Aging

Coenzyme I

▶ Nicotinamide Adenine Dinucleotide (NAD+) in Aging

Cognition

▶ Working Memory

Cognition and Frailty

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Overview

Frailty represents vulnerability to poor health outcomes, resulting from multiple determined decrease in the ability to respond to stress. Two approaches predominate in quantifying frailty: the deficit accumulation or frailty index approach and syndromic or frailty phenotype approach.

The deficit accumulation model postulates that frailty is a health state representative of organism homeostasis. A frailty index score is the proportion of health deficits present out of a number of health deficits assessed (Mitnitski et al. 2001). For example, using Comprehensive Geriatric Assessment (routine in geriatric care), of 50 items that might be assessed, a person in whom 15 were recorded as deficits would have a frailty index score of 15/50 = 0.30. Conversely, the frailty phenotype identifies five features: weight loss, low grip strength, physical inactivity, slow walking speed, and fatigue. Having none of these indicates "robust," presence of one or two is deemed "pre-frail," while three or more indicates "frail." (Fried et al. 2001).

C

Key Research Findings

Frailty and cognition have been linked in cross-sectional and longitudinal analyses (Armstrong et al. 2016; Godin et al. 2017; Kelaiditi et al. 2016; Wallace et al. 2019), typically where frailty is evaluated as a predictor for cognitive impairment (Buchman et al. 2014; Robertson et al. 2013; Song et al. 2014). The majority of these investigations have employed the frailty index or frailty phenotype. Frail people are more likely to have subjective cognitive decline (Hsieh et al. 2018), mild cognitive impairment (MCI), and dementia (Kojima et al. 2016). More severe frailty is associated with worse cognition and more rapid cognitive decline (Auyeung et al. 2011; Boyle et al. 2010). Frailty predicts MCI (Boyle et al. 2010) and AD incidence (Buchman et al. 2007) and conversion from MCI to AD (Boyle et al. 2010; Samper-Ternent et al. 2008). Frailty occurs in tandem with cognitive decline; several studies demonstrate correlation in their change over time (Armstrong et al. 2016; Buchman et al. 2014). Emerging evidence suggests the relationship between frailty and cognition is independent of dementia status (Bunce et al. 2018; Chen et al. 2018). Some authors describe a state of "cognitive frailty," combining MCI and phenotypic physical frailty, though this remains controversial.

Evidence is less clear on how frailty and cognitive decline are causally related and/or how they work together to produce dementia and other adverse health outcomes. Several shared mechanisms related to aging have been suggested; popular hypotheses include the role of hormones, neuropathology, chronic inflammation, and immunosenescence. Hormonal pathways are of particular interest because aging, frailty, and dementia show consistent but paradoxical sex differences: although women live longer than men, on average they are frailer at any age and have a higher incidence of dementia. Estrogen levels have been linked with cognition across the life course (Morgan et al. 2018). Likewise, female rodents treated with estradiol show improved memory performance (Frick et al. 2018). Alzheimer's neuropathology (amyloid and tau protein aggregates) has been associated with frailty and cognitive decline (Buchman et al. 2014; Wallace et al. 2018). Recent reports suggest that frailty and neuropathology work synergistically to give rise to dementia (Wallace et al. 2019).

Summary

Given that frailty is associated with cognitive decline, relevant clinical applications include screening for frailty in people with memory complaints. In such cases, frailty interventions may slow decline and improve quality of life (Apóstolo et al. 2018).

Future research should focus on longitudinal evaluations of frailty as measured by the deficit accumulation approach; most studies investigating frailty and cognition have employed the phenotype, which has ceiling effects, excludes the most frail people due to performance-based measures, and has unreliable modifications (Theou et al. 2015). Experimental evaluations of shared mechanisms should shed light on the natural history of dementia and improve our understanding of frailty. Implementation of frailty interventions in people at risk of cognitive impairment is needed.

Cross-References

- ▶ Biology of Frailty
- ▶ Dementia
- ▶ Epidemiology of Frailty
- ▶ Measurement of Frailty
- ▶ Vascular Dementia

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Cognitive Aging

► Cognitive Processes

Cognitive Assessment

► Montreal Cognitive Assessment

Cognitive Behavioral Therapy (I)

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Definition

Cognitive-behavioral therapy (CBT) refers to a collection of therapies which emphasize the individual's ability to alter the relationship between a stimulus and the response through their cognition (Ellis 1973).

Overview

From the CBT perspective, mental health challenges are believed to be sustained through these cognitive factors (Hofmann et al. 2012). Research examining CBT's effectiveness for the older population has increased in the last decade, and the most recent findings are reported here.

Key Research Findings

Research into CBT-based interventions has focused on three key mental health challenges, depression, anxiety, and insomnia (See ► "Mental Disorders"), for older adults. Depression is one of the most prevalent mental health challenges for older adults (World Health Organization 2015), so it is not surprising it has been the target of a considerable amount of research. A review into the effectiveness of CBT in older adults found it effective for older adults experiencing symptoms of major depression and dysthymia (Zalaquett and Stens 2006). There is similar support for CBT regarding anxiety disorders (Schuurmans et al. 2009). Furthermore, CBT aims to reduce symptoms of depression comorbid with anxiety for older adults (Weitz et al. 2018; Wuthrich et al. 2016). The third key area of CBT research for older adults is insomnia due to the changes in sleep patterns in aging (Buysse 2004). Again, CBT has been effective in reducing insomnia, and there is some evidence treatment for insomnia reduces clinical markers of risk of disease (Carroll et al. 2015; Morin 2010). Medication in conjunction with CBT has also been found effective for depression, anxiety, and insomnia (Cherukuri et al. 2018; Rosnick et al. 2016; Wuthrich et al. 2016).

Methods of delivering CBT in older adults also vary. While many CBT approaches are offered face-to-face, other methods are increasing in availability as many older adults have difficulty with mobility (Webber et al. 2010). Home-delivered, telephone-delivered, and online approaches have been found effective for reducing anxiety and anxiety symptoms (Barrera et al. 2017; DiNapoli et al. 2017; Gratzer and Khalid-Khan 2016; Scogin et al. 2018). CBT can also be offered in a group-based format and remain effective (Graham 2013; Wuthrich et al. 2016). CBT is also effective for a diverse older adult population, including rural, ethnical older adults (DiNapoli et al. 2017; Scogin et al. 2018), individuals with dementia (Tay et al. 2018), and older adults with attention deficit hyperactivity disorder (Solanto et al. 2018).

Unfortunately, there are some limitations with the use of CBT. The most revealing is the lack of non-Western studies examining CBT for older adults. Only one study, examining CBT in older Chinese adults with generalized anxiety disorder, was found for this review. This is problematic as populations become more diverse and there being a need to adapt therapies to different cultures (Lau and Kinoshita 2019). Mental health wise, most studies focus on older adults showing symptoms of a mental health disorder rather than those being diagnosed with a clinical disorder making it difficult to know if CBT would work for those who need it most (Cuijpers et al. 2009).

Future Directions of Research

Further research is needed to improve the universality of CBT for more diverse populations and mental health challenges. This does not just relate to the increase practice of CBT in non-Western countries, but also in recognition that Western countries are becoming more diverse and mental health issues more prevalent, both which are now appearing in the clientele (Cuijpers et al. 2009). Another direction is examining the different aspects of CBT to understand why some approaches are effective and others are not for older adults. Considering there are limited financial resources for helping older adults, any potential redundancies in therapy must be removed to use resources better (Jeste et al. 1999).

Another potential area of future research is discovering what aspect of CBT is effective and for whom. As mentioned, CBT is a group of interventions based on the same concept; the techniques involved though may vary. Potential differences between studies for older adults could be less about CBT and more about the techniques used. This could explain why some CBT interventions can focus on similar issues but have different outcomes (Beissner et al. 2009; Goode et al. 2018). This leads to the broader difficulty of knowing if it was CBT or the counselling experience in general which led to client improvements (McLaughlin and McFarland 2011). There is evidence CBT is effective in targeting specific cognitions, but its effectiveness compared to other therapies varies (Spinhoven et al. 2018).

Finally, the use of technology with CBT must be further investigated for older adults as they are one of the populations facing the most limitations regarding mobility. While this includes the general use of computers and phones, virtual reality is another option to explore. Virtual ability would allow the use of CBT techniques, such as in vivo exposure, from the home. Also, older adults can have a reduced ability to create mental images, an important ability for several CBT techniques, which can be counteracted using virtual reality (Grenier et al. 2015).

Summary

In summary, CBT is an umbrella term for many different therapies based on the same concept. It has been shown to be effective for older adults, but the research is limited, and the population examined is also limited. As a result, there are many possible directions for future research which will help us further understand how CBT can help older adults.

Cross-References

► Mental Disorders

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Cognitive Behavioral Therapy (II)

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Synonyms

Cognitive behavioral treatment; Cognitive impairment intervention; Cognitive rehabilitation therapy

Definition

Cognitive behavioral therapy (CBT) refers to a class of interventions based on the theoretical rationale that affect and behavior are maintained by cognitive factors (Beck et al. 1979; Hofmann et al. 2012). Today's CBT can be traced back to the work of Aaron Beck and Albert Ellis. Along with their colleagues, both Beck and Ellis attributed behavioral problems and psychiatric disorders to maladaptive cognitions (Beck et al. 1979; Ellis and Harper 1961). CBT adopts the behaviorism rationale that thoughts and behavior are the direct result of previous experiences and learning (Beck et al. 1979). Therefore, symptoms of disorders such as anxiety and depression are maintained by cognitions, and changing these cognitions leads to symptom reduction or remission.

Overview

CBT uses many therapeutic strategies to change the cognitions that are causing problems in a patient's life. Patients play an active role in therapy, working to test and challenge their cognitions and change their behavioral patterns (Hofmann et al. 2012). Patients must be educated on the theory behind CBT to play this active role (Beck et al. 1979). The therapist's role is to help patients think and act in a more adaptive way that reduces symptoms (Beck et al. 1979). Common techniques used in CBT are monitoring cognitions; recognizing the connections between cognition, affect, and behavior; challenging distorted automatic thoughts; introducing reality-oriented interpretations of cognitions; and behavioral techniques (Beck et al. 1979). The main goal of CBT is to reduce symptoms and improve functioning by correcting misconceptions, irrational beliefs, and reasoning biases (Hofmann et al. 2012; Peng et al. 2009). CBT can be used to treat many disorders, including: substance use disorders, psychotic disorders, depression, anxiety disorders, eating disorders, and insomnia.

CBT is most commonly used to treat anxiety, depression, and insomnia in older adults. These disorders and their symptoms are often co-occurring in older adults and may be attributed to normal aging. Anxiety, depression, and insomnia in older adults are associated with decreased quality of life, high frequency of coexisting conditions, increased dependence on services, diminished cognitive functioning, and substance abuse (Ho et al. 2015; Stanley et al. 2003; Wetherell et al. 2013). Older adults usually receive pharmacotherapy for these disorders, but CBT may be a safer and preferred treatment option considering drug side effects and interactions (Landreville et al. 2001). CBT is also usually short term and cost effective which may be ideal for older populations (Chand and Grossberg 2013). Some older adults have difficulty applying the cognitive techniques and adhering to a protocol, leading to higher dropout rates (Hendriks et al. 2008). Other considerations for using CBT in older adult populations include cognitive impairment, severe symptoms, severe medical illness, or sensory loss (Chand and Grossberg 2013). Current research is investigating the efficacy of CBT in older populations, specifically looking at factors unique to this group.

Key Research Findings

CBT has proven effective in the treatment of anxiety in older adults (Hendriks et al. 2008). CBT for anxiety appears to improve symptoms of worrying and depression most significantly (Hendriks et al. 2008; Stanley et al. 2003, 2009). There is a lack of improvement in General Anxiety Disorder (GAD) severity measures and the effect sizes tend to be small where there is significance (Gould et al. 2012). Current research suggests that CBT for anxiety has promise and may be a good alternative to medication for older adults (Hendriks et al. 2008). Medications are commonly used with CBT for treatment of anxiety disorders and can boost response, prevent relapse, and eventually, the addition of CBT can allow older adults to taper off their medication (Mohlman et al. 2005; Wetherell et al. 2013). Many older adults with GAD report some form of sleep disturbance (Bush et al. 2012). CBT for insomnia has been shown to improve many factors of sleep, including quality and duration (Bush et al. 2012). CBT for anxiety may be useful in improving some aspects of sleep disturbance such as perception of sleep quality and ability to fall asleep (Bush et al. 2012). CBT for insomnia has also been shown to be effective in subjects with comorbid medical or psychiatric conditions (Geiger-Brown et al. 2015). Older adults often experience a variety of co-occurring conditions. For example, many older adults with depression have another physical or psychological diagnosis. CBT has been shown to be effective in treating co-occurring conditions such as anxiety and depression with lasting effects (Wuthrich et al. 2016). Follow-up measures have showed that symptom reduction can be maintained for months after therapy has ended, but more studies are needed in older adult populations (Geiger-Brown et al. 2015; Hendriks et al. 2008; Wetherell et al. 2005, 2013). There has been a shift toward making CBT more accessible for older adults allowing therapy to be accessed over the phone or computer, in group settings, and at home (Brenes et al. 2015; Ho et al. 2015; O'moore et al. 2018; Rybarczyk et al. 2005; Wetherell et al. 2005; Wuthrich et al. 2016; Zou et al. 2012).

Future Directions

A major concern with respect to CBT for older adults is access to therapy. Some patients are less likely to benefit from or access therapy due to physical or cognitive impairment, cost, transportation, and limited availability (Wetherell et al. 2005). Future studies should examine the efficacy of modified CBT for older adults. Modification may involve adding specific techniques such as motivating strategies, accounting for sociocultural elements unique to older adults, utilizing emerging technology such as virtual reality, and modifying delivery of CBT using self-help, community-based education, and group programs (Bélanger et al. 2011; Grenier et al. 2015; Hendriks et al. 2008; Laidlaw et al. 2004). Refining treatment for older adults will also improve response to treatment (Wetherell et al. 2005). Future studies should identify the specific mechanisms of CBT that older adults respond to and look at the effect that common comorbid conditions have on outcomes.

Summary

CBT is a form of psychotherapy that focuses on correcting maladaptive cognitions to reduce symptoms. CBT has shown to be effective in treating depression, anxiety, and insomnia in older adults. More studies are needed to test the efficacy of CBT and create interventions that target problems specific to older adults.

Cross-References

▶ Cognitive Behavioral Therapy (I)
▶ Depression and Antidepressants
▶ Geriatric Anxiety Inventory
▶ Geriatric Mental Health
▶ Insomnia, Sleep Disorders, and Healthy Aging
▶ Mental Health Services
▶ Mood Disorders
▶ Psychotherapy

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Cognitive Behavioral Treatment

► Cognitive Behavioral Therapy (II)

Cognitive Compensatory Mechanisms

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Synonyms

Cognitive strategies; Compensatory techniques

Definition

Compensatory cognitive mechanisms allow individuals to mitigate the impact of cognitive deficits arising from neurologic injury or disease.

Overview

Compensatory cognitive mechanisms can be broadly conceptualized as ways individuals are able to "work around" deficits arising from neurologic injury or disease (Hampstead et al. 2014). However, many of these same "compensatory" approaches also enhance functioning in cognitively and neurologically intact individuals (both defined as an increase in the amount of information that can be processed and in terms of cognitive efficiency). It is important to distinguish between neuroimaging-based evidence suggesting functional changes that arise following disease/injury versus those arising from interventions that teach such compensatory mechanisms (e.g., mnemonic strategies). Therefore, we briefly review extant evidence of neurophysiologic changes arising from "normal" aging and multiple disease/injuries and then highlight interventional work in these same populations. Although external compensatory aides are known to be effective (e.g., notebooks, calendars, and smartphones) (Cicerone et al. 2011), we intentionally limited the latter to studies involving internal compensatory techniques, which we subsequently refer to as mnemonic strategies.

Key Research Findings

The aging brain undergoes a series of physical and functional changes that are generally regarded as "normal" (i.e., nonpathological). A number of theoretical models emerged from the study of such normal aging and posit that older adults maintain cognitive performance by engage additional brain regions relative to younger adults. The Hemispheric Asymmetry Reduction in Old Adults (HAROLD; Cabeza 2002) and Compensation-Related Utilization of Neural Circuits Hypothesis (CRUNCH; Reuter-Lorenz et al. 1999; Reuter-Lorenz and Cappell 2008) are two such examples that integrate evidence of altered brain "activation" to explain enhanced or even stable cognitive functioning in older adults. An important caveat of such models is that they were developed prior to recognition that pathological processes (e.g., accumulation of beta-amyloid) occur decades before the onset of cognitive deficits and, as a result, such functional changes may reflect unmeasured disease pathology. Compensatory neural recruitment has been reported in several other populations beyond "normal" aging. For example, hyperactivation is commonly reported in the right prefrontal cortex following traumatic brain injury (TBI) relative to controls (e.g., Turner et al. 2011; Gillis and Hampstead 2015). Similarly, patients with multiple sclerosis (MS) have shown prefrontal hyperactivation within the context of comparable cognitive performances relative to controls (Forn et al. 2006); a finding that suggests increased neural "effort" that maintains cognitive abilities. There is also evidence of both hypo- and hyper-activation and connectivity in those with the clinical phenotype of mild cognitive impairment (MCI; Gigi et al. 2009; Sperling 2007; Hampstead et al. 2011; Mormino et al. 2011) that more recent findings may emerge as a function of biomarker profile (e.g., hyper- in amyloid positive but tau negative individuals and hypo- in amyloid and tau positive individuals, Schultz et al. 2017).

Thus, there is consistent evidence of neurophysiological change that arises from neurologic injury and disease. Such changes may reflect: (1) an innate compensatory response that maximizes cognitive functioning, (2) disruption associated with cognitive decline, and/or (3) aberrant findings that are unrelated to cognition. Intervention-related studies can directly test these effects and manifest as (a) reduced activation following mnemonic strategy training that would suggest increased processing efficiency or (b) increased activation that signals either a "restorative" (i.e., re-engagement of "normal" brain regions/networks) or "compensatory" (i.e., recruitment of novel regions/networks that are not engaged in neurologically intact individuals when given comparable training). Regardless, such inherent changes form the foundation on which intervention-related changes should be interpreted.

Examples of Application

Mnemonic strategies are known to be beneficial in neurologically intact adults. For example, young adults demonstrated a marked increase in memory test performance that was accompanied by greater functional connectivity (especially involving the prefrontal cortex) after 6 weeks of mnemonic strategy training (Dresler et al. 2017). Such strategies have also yielded promising memory improvement in mixed neurologic samples (Stringer 2011) and are recommended for mild memory deficits following TBI and stroke (Cicerone et al. 2011). Comparable memory improvement (Chiaravalloti et al. in press) and functional connectivity between the hippocampus and neocortical regions (Leavitt et al. 2014) have been reported following mnemonic strategy training in those with multiple sclerosis. We (Hampstead et al. 2008, 2012, in press) and others (e.g., Belleville et al. 2011; Simon et al. 2018, in press) have also reported increased activation in the lateral frontoparietal cortices as well as the hippocampus following mnemonic strategy training in those with MCI. In contrast, cognitively intact older adults showed both increased and decreased activation (Belleville et al. 2011; Hampstead et al. 2012, in press). Perhaps most striking are the long-term effects of cognitively oriented treatments in older adults, as reflected by the ACTIVE trial data (Rebok et al. 2014). Thus, there is consistent evidence that mnemonic strategies improve memory test performance, an effect that appears driven by (re)engagement of frontoparietal regions involved in cognitive control and complex attention and their interaction with the hippocampus.

Future Directions of Research

As noted above, the ramifications of altered activation and connectivity in neurologic populations requires considerably more investigation. While the evidence suggests mnemonic strategy training is beneficial across a range of populations, individual differences are likely and work is needed to determine intervention-specific parameters as they relate to dosing (e.g., how much, how long, for whom) and persistence of any benefits. Related to the latter, biomarkers will inevitably become increasingly important as they are identified and become available in standard clinical practice. Finally, the combination of mnemonic strategy training and other interventions, whether pharmacologic or nonpharmacologic, are important to investigate. For example, we (Hampstead et al. 2017) and others (Woods et al. 2018) are currently combining cognitively oriented treatments with noninvasive brain stimulation with the goal of evidencing greater and more persistent effects.

Summary

Cognitive compensatory mechanisms may arise both in response to sudden (e.g., TBI) and progressive (e.g., aging, neurodegenerative disease) cognitive deficits. There appears to be an innate relationship between evidence of neural change (e.g., activation, connectivity) and the behavioral manifestation of improved and/or sustained cognitive performance across populations. Moreover, additional changes can be evidenced through intentional training of such compensatory mechanisms (i.e., mnemonic strategies). Future work should focus on understanding the compensatory vs. restorative effects of altered neurophysiology across neurologic populations as well as fundamental treatment parameters (e.g., dosing) necessary to evidence adaptive change.

Cross-References

- ▶ Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE)
- ▶ Aging Mechanisms
- ▶ Cognitive Training
- ▶ Communication Technologies and Older Adults

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Cognitive Disability

▶ Impairment

Cognitive Disorders in Older Patients with Cancer

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Synonyms

Cancer-related cognitive impairment

Definition

Cognitive difficulties such as attention and memory disorders are frequently reported by cancer patients with central nervous system (CNS) tumors but also in patients without CNS tumors. The concept of "Cancer Related Cognitive Impairment" (CRCI) in non-CNS cancer patients refers to cognitive impairment of memory, executive functions, attention, and information processing speed (Joly et al. 2015; Lange et al. 2019c).

Overview

Although CRCI is mainly mild and transient and often decrease in 6–12 months posttreatment (Janelsins et al. 2017), some cancer survivors reported long-term cognitive impairment (Koppelmans et al. 2012). Some patients can also experience cognitive difficulties before exposure to cytotoxic treatments and suggest the involvement of other factors, such as cancer itself, psychological, biological, and genetic parameters (Olson and Marks 2019; Lange et al. 2019c). In practice, patients experience difficulties regarding concentration, retrieval of memory information, and the memorization of information while processing. The impairment also concerns the capacity to process information quickly and to adapt behavior to new situations that could be an important problem in older patients with cancer. These cognitive difficulties are usually assessed by neuropsychological tests or self-report questionnaires of cognitive complaints (Lange et al. 2019a). Based on a multidisciplinary group of neuropsychologists, oncologists, geriatrics, neurologists, and neuroscientists, the International Cognitive and Cancer Task Force (ICCTF) aims to assess and better understand the phenomenon of CRCI.

CRCI can be induced by the cancer and/or by the treatments (mainly described with brain irradiation and with cytotoxic drugs). It has been mainly studied after chemotherapy in young breast cancer patients. Besides adding to the other side effects of the different treatments, these difficulties have a negative impact on quality of life (Boykoff et al. 2009). Although aging is associated with cognitive decline and is a risk factor for cancer, few studies have assessed cognition in older patients with cancer (Ahles et al. 2002; Mandelblatt et al. 2013; Lange et al. 2014; Loh et al. 2016). Nevertheless, cognitive impairment linked to the age can have important impact on adherence of medications in the case of oral treatments. Furthermore, in this group of frail patients, cancer treatments can induce cognitive decline among and autonomy lost.

Briefly, it is known that chemotherapy can have a negative impact on cognition in several cancer patient populations such as in breast, colorectal, hematological, and testicular cancer patients (Joly et al. 2015). Other treatments such as targeted therapies (Mulder et al. 2014; Joly et al. 2016), immunotherapy (Joly et al. 2019a), and more debatable, hormone therapies (Joly et al. 2015), could also induce cognitive difficulties. In most of the cases, several months to years after chemotherapy, results of anatomical and functional imaging studies show decrease in gray matter volume and white matter density, as well as changes in patterns of activation and in resting state metabolism, notably in frontal regions involved in executive and memory processes, and were usually related to cognitive impairment or cognitive complaints (Li and Caeyenberghs 2018; Chen et al. 2018; Lange et al. 2019c).

To better understand physiopathology of these cognitive disorders, the direct impact of the different used treatments (chemotherapy and targeted therapies) and the influence of different parameters (such as aging, mood, and stress), animal models have been developed (Winocur et al. 2018). Most of the studies conducted in animals established a direct deleterious role of chemotherapy on cognitive functioning (learning spatial memory, behavioral flexibility, or executive functions), involving reduced neurogenesis and systemic and/or central inflammation (Joly et al. 2015).

Although there are still no preventive measure available, various methods of CRCI management are being studied and assessed (medication, cognitive, physical, and behavioral). Preliminary findings have demonstrated beneficial effects, particularly with nontherapeutic approaches such as cognitive training, mainly on cognitive complaints (Chan et al. 2015).

Key Research Findings

Specificities of Older Patients with Cancer

More than half of patients newly diagnosed for cancer are over 65 years old (National Cancer Institute 2020). Due to increase of life expectancy and therapeutic management, the number of older patients with cancer substantially increases. This group of patients is especially heterogeneous regarding frailty and toxicity of cancer treatments is a major issue in these patients (Hurria et al. 2011; Jayani et al. 2020).

Although aging is a risk factor for cancer and cognitive disorders and despite the potential impact of these cognitive disorders on patient's autonomy, overall, few studies focused on the assessment of impact of cancer treatments on cognitive functioning in older patients with cancer (Ahles et al. 2002; Mandelblatt et al. 2013; Lange et al. 2014; Loh et al. 2016). The impact of cancer and chemotherapy on cognitive functioning and quality of life depend on several factors cognitive functioning, which could be lower in elderly than in younger patients. Furthermore, cognitive status before treatment could be associated with worse prognosis. A recent study based on the Montreal Cognitive Assessment (MoCA) score in older patients with cancer (mainly breast and prostate cancers) showed that cognitive impairment is an independent risk factor of death during 2 years following cancer treatment initiation in older patients, regardless of the presence of other well-characterized medical or geriatric risk factors (Libert et al. 2016).

Main Studies in Older Patients with Cancer

The largest study in breast cancer included 344 survivors over 60 years old without dementia or neurological disease and healthy controls (Mandelblatt et al. 2018). In this study, neuropsychological tests, cognitive complaints questionnaire, and biological tests were performed before treatment and at the 12th and 24th months post-treatment. Results showed that frailty was associated with baseline scores of attentions, processing speed and executive functions, and self-reported decline. Survivors treated with chemotherapy had significantly lower longitudinal cognitive performances on the domain of attention, processing speed, and executive functions than other groups. This effect was largely observed in patients with the allele e4 of the Apolipoprotein E (ApoE e4) – which is associated with cognitive impairment related to Alzheimer's disease, brain trauma, and aging. An association was also found between this genotype and lower learning and memory scores after hormone therapy start.

The second largest prospective study in older patients with breast cancer patients concerns 118 patients over 65 years old (Lange et al. 2019b). Forty nine percent of patients had objective cognitive decline after adjuvant treatment, a proportion higher than that reported in younger patients (15–25%). More precisely among patients who experienced cognitive decline, 12% of patients declined without cognitive impairment, 31% without initial cognitive impairment developed impairment, and 6% experienced accelerated cognitive decline. Furthermore, the oldest patients were more likely to have cognitive decline with chemotherapy, particularly with docetaxel.

These results have probably underestimated the cognitive dysfunctions because patients who participated to these studies were well educated, had little comorbidity, and were screened according to the result of Mini-Mental State Examination (MMSE) score. In real life, older patients present more frequently neurodegenerative disease, poor health status, or geriatric frailties.

Cognitive functioning is also a challenge in patients with prostate cancer that represents the most frequent cancer in male older patients. There is still a debate on the impact of androgen deprivation therapy (ADT) on cognition. According to a systematic review and a meta-analysis included 26 articles, patients receiving ADT were not more likely to experience cognitive impairment in comparison to non ADT users or healthy controls in the pooled analysis of the two prospective studies (Sun et al. 2018): one showed a pronounced increased risk between ADT and cognitive impairment whereas the second study found no association. More prospective studies are needed to assess precisely the impact of these treatments. Furthermore, novel oral agents targeting the androgen signaling axe (Abiraterone acetate and Enzalutamide) are nowadays available and are largely prescribed to older patients with metastatic prostate cancer in addition to first generation of ADT, and some preliminary results suggest that these treatments could have a cognitive impact (Gonzalez et al. 2015; Thiery-Vuillemin et al. 2018).

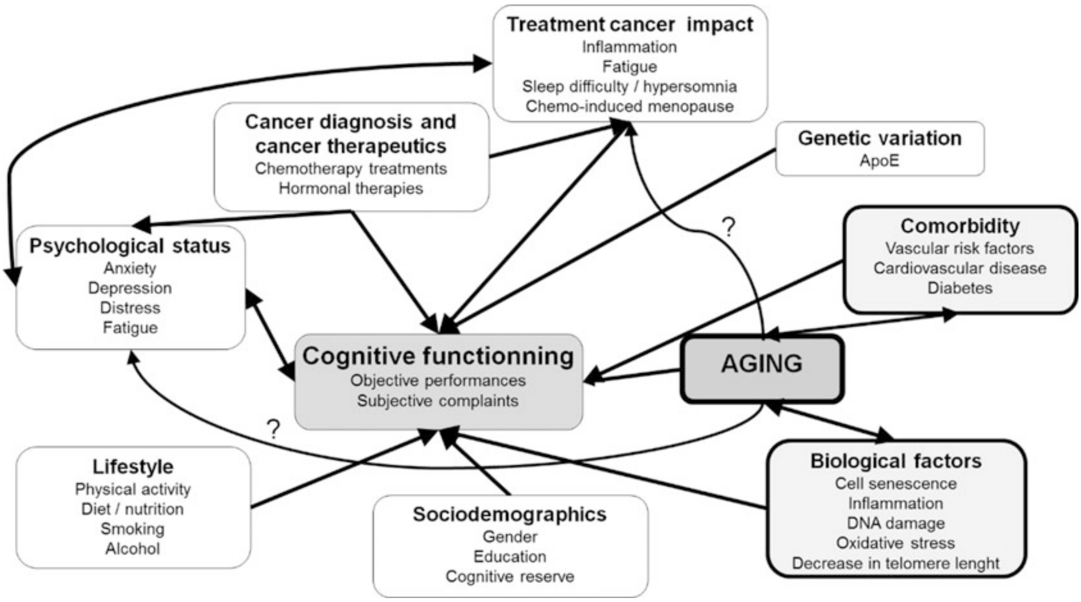
Possible Contributors to Cognitive Difficulties in Older Patients with Cancer

Many factors are involved in cognitive disorders particularly in older patients with cancer (Fig. 1; Lange et al. 2014). Aging, neurodegeneration, biological processes underlying cancer, the impact of cancer treatments, and cognitive decline appear to be linked, leading to the phase shift hypothesis, i.e., that cancer treatments may accelerate the aging process (Ahles et al. 2002). According to this hypothesis, age-associated decline in cancer patients is not only parallel but is greater than that of older adults with no cancer history. An additional hypothesis, postulates that only vulnerable populations exhibit the accelerated aging pattern (Mandelblatt et al. 2014a).

Cognitive frailty, comorbidities (mainly cardiovascular diseases), psychological status, fatigue, biological factors, and tolerance to cancer treatment are factors, closely related to aging that may contribute to increase cognitive alterations (Joly et al. 2019b). Aging may potentially induce inflammation modifications and several studies confirmed the role of the inflammatory environment (e.g., tumor necrosis factor-α or interleukin 6) in the occurrence of cognitive alterations (Joly et al. 2015; Carroll et al. 2019). Furthermore, genetic factors, such as the ApoE e4, constitute risk factors for chemotherapy-induced cognitive decline in breast cancer survivors (Mandelblatt et al. 2018). In addition to physiological toxic effects of cancer treatments, combinations of biological and medical factors such as side effects of surgical experience and anesthesia also could play a role (Joly et al. 2015).

Future Directions of Research

Overall, little information is available about the effect of treatment on the cognitive functioning of older patients with cancer or whether cancer treatments-associated cognitive difficulties affect older patients' ability to perform their daily activities. Additional research is needed to apprehend the impact of cancer treatments on these patients and to define risk factors. Regarding oncologic practice, assessment of cognitive functioning before



Cognitive Disorders in Older Patients with Cancer, Fig. 1 Possible contributors to cognitive difficulties in older patients with cancer (issued from Lange et al. 2014)

treatment and more detailed cognitive assessment of cognitively frail subjects would help oncologists to choose the most appropriate therapy.

Recommendations in Practice to Assess Cognition in Older Patients with Cancer

While the ICCTF recommends using some neuropsychological tests to the assessment of cognitive domains the most impaired (Wefel et al. 2011), in clinical practice, especially with older patients, these tests are unable to establish the differential diagnosis between CRCI and neurodegenerative disease. Early detection of cognitive disorders is a challenge in older patients to detect the subgroup of patients at risk having a cognitive decline with cancer treatments (that is particularly true with adjuvant treatment and could help in decision-making). The Comprehensive Geriatric Assessment can help oncologists in the global care of older frail cancer patients. However, this multidimensional, multidisciplinary diagnostic approach, that assesses dependence, comorbidities, mood state, and social support, includes only screening test to detect dementia.

Cognitive functioning is often assessed by screening tests such as the MMSE, which is not enough sensitive to detect subtle cognitive dysfunctions of CRCI. In the absence of a neuropsychologist to perform a comprehensive cognitive assessment, another quickly administered screening test, the MOCA (Nasreddine et al. 2005), could be used as an alternative because it is more sensitive to executive function deficits (consisting of 11 items: visuospatial/executive, naming, memory, attention, language, abstraction, orientation) (Lange et al. 2019a). Thus, a recent study conducted in cancer patients older than 70 years old who were candidates to a first-line of treatment showed that the MoCA seems to be most relevant than the MMSE to screen for cognitive impairment (Rambeau et al. 2019). When cognitive difficulties are observed with the MOCA, a detailed cognitive assessment with a neuropsychologist could be proposed as an additional criterion in order to make treatment decision-making. Furthermore, guidelines exist in prostate cancer patients and the International Society of Geriatric Oncology (SIOG) now recommends using the mini-Cog to assess cognitive functioning (Droz et al. 2017).

Early detection of cognitive difficulties is also a major issue before starting oral treatments that take an increasing place in cancer management. These patients are at risk of nonadherence and treatment discontinuation (Lange et al. 2014). Indeed, a prospective study in cancer patients initiating a first oral treatment, who more than half of patients were over 70 years, showed that beyond depression, cognitive difficulties on working memory and short-term memory were associated with nonadherence (Dos Santos et al. 2019). Thus, dedicated follow-up by home nurses or therapeutic education of the patient and his caregiver can be organized.

Cardiovascular disease and diabetes are also classically associated with cognitive disorders in patients even before any adjuvant treatment. Thus, including a comprehensive assessment of comorbidities (e.g., cardiovascular disease, chronic kidney disease, and obesity) and co-medications must be encouraged (Hurria et al. 2011; Mandelblatt et al. 2014b).

Finally, 6–12 months after the end of treatment, patients who report cognitive difficulties which affect their daily life should be referred to a neuropsychologist to a comprehensive cognitive assessment (Vardy et al. 2017).

Summary

In summary, there is a growing body of evidence that cancer therapies may impact cognitive function although very few studies have concerned cognition in older patients with cancer. Furthermore, few studies have directly investigated older patients with cancer, even though age is a risk factor for cancer and cognitive impairment.

Cross-References

▶ Aging and Cancer
▶ Aging and Cancer: Concepts and Prospects
▶ Cancer Diagnosis
▶ Cancer Screening
▶ Chemotherapy Toxicity
▶ Cognitive Processes
▶ Epidemiology, Aging, and Cancer
▶ Geriatric Assessment for Older Adults with Cancer
▶ Mini Datasets for Research in Geriatric Oncology

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Cognitive Function

► Working Memory

Cognitive Functioning

► Cognitive Processes

Cognitive Impairment

► Dementia
► Impairment
► Intellectual Disability (Cognitive Disability)
► Saint Louis University Mental Status Examination and Older Adults

Cognitive Impairment Intervention

► Cognitive Behavioral Therapy (II)

Cognitive Inhibition

► Inhibitory Deficit Hypothesis

Cognitive Intervention

► Cognitive Training

Cognitive of Aging

► Neuropsychology

Cognitive Processes

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Synonyms

Cognitive aging; Cognitive functioning; Mental abilities

Definition

Cognitive processes refer to the mental abilities needed to perceive, attend to, process, manipulate, retain, retrieve, and use information to carry out necessary daily activities. Cognitive aging is the study of changes in these cognitive processes in old age. Intact cognitive functioning allows an older adult to perform daily activities, which could include taking care of oneself and a spouse, driving (especially in unfamiliar places), remembering doctor’s appointments, making decisions on important matters such as end-of-life directives, learning a new skill (e.g., how to use a new cell phone), and navigating a new environment.

Overview

As the aging population increases rapidly, it has become imperative that we understand the impact that advancing age has on cognition. The present entry reviews the fundamental cognitive changes that occur with healthy aging. Although many cognitive abilities such as fluid intelligence, working memory, and divided attention have been shown to decline with old age (See ▶ "Prevention of Age-Related Cognitive Impairment, Alzheimer's Disease, and Dementia"), processes such as crystallized intelligence, semantic memory, and language ability, in fact, stay constant or even increase with age (Harada et al. 2013).

Key Research Findings

Crystallized and Fluid Intelligence

Crystallized intelligence refers to the ability to utilize our general knowledge, vocabulary, skills, and semantic memories. Fluid intelligence involves the use of executive function, memory, and processing resources to problem-solve and reason. Research has shown that fluid intelligence declines with age, while crystallized intelligence remains constant or even increases with age. Specifically, Salthouse (2012) found that crystallized intelligence improve at a rate of 0.02–0.003 standard deviations per year during a person's 60s and 70s (See ▶ "Intelligence (Crystallized/Fluid)").

Speed of Processing

Speed of processing refers to the time required to complete a cognitive or a motor task. An age-related speed decline beginning in a person's 30s that continues throughout the lifespan is well documented (Salthouse 2010). This slowing process may limit the amount of time spent on important information, especially if it is presented later rather than earlier in a sequence or a conversation. Slowing will also reduce the amount of information retained in general by older adults because early information may be lost by the time later processes take place. Thus, the age-related decrease in speed of processes has implications in older adults' overall cognitive functioning, even though many cognitive tasks may not appear to have a speed component (See ▶ "Speed of Processing").

Attention

Attention is a multifaceted concept, and its meaning depends on the context in which it is used. With these different aspects of attention, the findings in aging and attention are mixed and complex. Healthy older adults showed wide range of performance in attentional tasks. It is still unclear if all aspects of attention are affected by normal aging. This entry focuses on selective attention, sustained attention, divided attention, and task switching.

Selective attention is the ability to selectively focus on relevant information while ignoring irrelevant information. Researchers used a variety of paradigms to measure selective attention in different domains, and these different ways of measuring selective attention led to different results (Zanto and Gazzaley 2014). One of the most prominent paradigms of selective attention is the Stroop task (Stroop 1935), in which participants are required to name the colors of the printed words rather than the words themselves. Studies often report age-related declines in the Stroop task (Drag and Bieliauskas 2010), although findings are not entirely consistent throughout the literature (Verhaeghen and Cerella 2002).

Sustained attention refers to the ability to maintain focus or vigilance over time. This area of research has been relatively understudied compared to other functions in cognitive aging. Staub and colleagues (2013) conducted a review based on 27 studies on the effects of aging on sustained attention. Their review showed conflicting results in the field: older adults performed comparably, impaired, or improved in comparison to younger adults. The lack of consensus of how sustained attention is defined and the way of assessing it contribute to these discrepancies.

Divided attention is the ability to concurrently process information or attend to two or more sources. In general, older adults show significantly impaired performance compared to young adults in divided attention, especially when the tasks are complex (Drag and Bieliauskas 2010).

Older adults also show difficulty when asked to switch rapidly among different tasks. These age-related declines are usually observed when switching between tasks requires activation and maintenance of two mental task sets (Verhaeghen and Cerella 2002). These deficits may be related to general slowing in older adults or their inability to disengage from one task and refocus on another task (Drag and Bieliauskas 2010). However, age-equivalent performance is often found when the switching task sets are actively maintained (Verhaegen and Cerella 2002; Zanto and Gazzaley 2014).

Memory

The human memory system is an active cognitive process that allows information from the environment to be encoded, maintained, stored, and retrieved. People tend to remember information to which they attend and are motivated to remember. The memory system is complex and can be subdivided into separate components. The effects of aging on memory are not uniform in size or universal across different domains and components of memory (Lustig and Lin 2016).

Working memory describes a system in which information is retained for a brief amount of time, usually less than 15 seconds (Baddeley and Hitch 1974). Working memory includes a phonological loop that registers sound-based information, a visual-spatial sketchpad that encodes visual and spatial information, and an executive function unit that integrates information into meaningful knowledge (See ▶ "Working Memory"). Older adults have been found to exhibit significantly smaller working memory span, with this age-related effect becoming greater with active manipulation of information (Bopp and Verhaeghan 2005).

Long-term memory includes everything you could remember from a few minutes ago to the first few years of your life. In contrast to working memory, it has an unlimited storage and is coded based on semantics (meaning). Long-term memory can be further subdivided into explicit (declarative) and implicit (nondeclarative) memory. Explicit memory is deliberate and conscious, while implicit memory is often described as unconscious. Explicit memory is further subdivided into episodic memory and semantic memory. Episodic memory refers to personal events that can be retrieved with time information, while semantic memory refers to a person's general knowledge about the world and vocabulary. Episodic memory (fluid intelligence) declines with age, while semantic memory (crystallized intelligence) usually stays rather constant or even increases with advancing age (Park et al. 2002). This dissociation is apparent when older adults have trouble recalling past events, such as what they did last summer, but have no trouble recalling capital cities of countries and giving definitions of words (vocabulary) that they know (See ▶ "Short-Term/Long-Term Memory").

According to dual process models of memory, two processes – recollection and familiarity – underlie recall and recognition (Yonelinas 2002). Recollection is a slow, attention-demanding process, entailing conscious retrieval of episodic information, such as recognizing someone and vividly recalling where and when you met this person. Familiarity is an unconscious, relatively automatic process that is recruited more rapidly, such as thinking that you know someone but cannot remember details of when you might have met. There is wide consensus that recollection declines with age, while familiarity stays rather constant or even increases (Chung and Light 2009). Thus, older adults are more likely to make false memory errors than young adults, especially in situations where they are forced to make a memory judgment quickly or with little contextual support, i.e., basing their decision purely on familiarity rather than recollection.

Language

Language is a cognitive domain that involves both fluid and crystallized intelligence. Overall, language functioning stays rather intact in old age. As reviewed in the semantic memory section above, vocabulary (a form of crystallized intelligence) stays constant or even increases as people grow older. However, research has shown that even though older adults maintain their ability to name objects until late old age (around age 70), this ability starts to gradually decline thereafter (Zec et al. 2005). Another aspect of language that may be disproportionately affected by age is verbal fluency, i.e., older adults' ability to come up with words for a word-finding paradigm or generate examples for specific categories (Salthouse 2010; Singh-Manoux et al. 2012). This decline may be due to age-related declines in fluid intelligence and speed of processing. Furthermore, older adults report more tip-of-the tongue (TOT) experiences, i.e., word-finding issues despite confidence that they know the word, than young adults, likely due to difficulties in phonological retrieval rather than semantic representations (Burke et al. 2008) (See ► "Language and Communication Disorders").

Reasoning and Problem-Solving

Older adults do not usually show declines in reasoning if the problems are presented in and can be solved in familiar ways. Reasoning, however, does seem to decline when unfamiliar materials are used (Singh-Manoux et al. 2012). Research has also documented declines in abstract thinking and mental flexibility, especially after age 70 (Salthouse 2010; Oosterman et al. 2010; Wecker et al. 2005). For example, older adults may exhibit higher levels of functional fixedness than young adults, i.e., difficulty in thinking of alternate usage of familiar objects or tools or thinking outside of the box during problem-solving. Older adults have also been found to perform worse on inductive reasoning tasks that involve verbal and mathematical manipulations (Singh-Manoux et al. 2012). These declines in thinking may be directly related to age-related changes in executive functioning, i.e., a person's capabilities to behave independently, appropriately, and purposively. Executive functioning can include a wide range of measures, including self-monitoring, planning, organizing, and reasoning. Older adults' performance on these measures tends to stay relatively constant with advancing age, unless they are presented with paradigms that are speeded or unfamiliar (Harada et al. 2013).

Visuospatial Skills

In general, older adults show a decline in visuospatial abilities compared to young adults (Drag and Bieliauskas 2010). However, it is important to note that visuospatial information is complex and likely more heterogeneous than verbal stimuli. Thus, the larger observed age-related deficits could both imply a higher sensitivity to aging effects in the domain or the complexity of the measure itself. For example, older adults often show lower scores on the performance subtest of the Wechsler Adult Intelligence Test than on the verbal subtest (Goldstein and Shelly 1981). Visuospatial tasks that involve speed, mental rotation, visuospatial construction, and copying of complex figures have been found to be significantly affected by aging. The more complex the task, the more likely an age effect would be observed. This finding is consistent with the frontal aging hypothesis, which suggests that tasks that require high levels of frontal lobe functioning, e.g., executive functioning and working memory, are more sensitive to aging effects (Drag and Bieliauskas 2010).

Summary

Cognitive processes change with advancing age, although these changes are not universal across different cognitive domains, nor are they homogenous among older adults. The outcome of an individual's developmental trajectory is a complex interplay among genetic dispositions, environment, life experience, and personal choices. Although selective cognitive processes do decline with age, many cognitive processes stay intact and even improve with aging. The cognitive domains in which we often see declines include fluid intelligence, speed of processing, controlled attentional processes, working memory, episodic memory, specific language and reasoning abilities, and certain visuospatial functions. Areas that show intact functioning in healthy aging include crystallized intelligence, semantic memory (e.g., vocabulary and general world knowledge), automatic and familiar processes, language, and general reasoning abilities.

Cross-References

- ▶ Intelligence (Crystallized/Fluid)
- ▶ Language and Communication Disorders
- ▶ Prevention of Age-Related Cognitive Impairment, Alzheimer's Disease, and Dementia
- ▶ Short-Term/Long-Term Memory
- ▶ Speed of Processing
- ▶ Working Memory

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Cognitive Rehabilitation Therapy

▶ Cognitive Behavioral Therapy (II)

Cognitive Strategies

▶ Cognitive Compensatory Mechanisms

Cognitive Therapeutic Training

▶ Reality Orientation

Cognitive Training

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Synonyms

Cognitive intervention

Definition

Cognitive training is targeted intervention aimed at improving specific mental abilities such as memory, attention, speed of processing, or executive function. Two major types of cognitive training are process-based, which includes repeated practice of targeted exercises, and strategy-based, which involves learning strategies and techniques.

Overview

Cognitive training is one particular type of cognitive intervention designed to improve core abilities within targeted domains such as attention, speed of processing (See ► "Speed of Processing"), executive function, or memory (See ► "Cognitive Processes"). There are two major types of cognitive training: process- and strategy-based (Lustig et al. 2009). Process-based techniques target improving specific cognitive domains through repeated practice or drills of cognitive exercises. Many different process-based cognitive training programs exist and target domains such as attention, speed of processing, working memory (See ► "Working Memory"), as well as basic perceptual abilities and various aspects of executive function. Strategy-based cognitive training focuses on learning and practicing strategies (e.g., mnemonics for memory) to improve a domain of cognitive function such as reasoning, problem solving, or memory. For older adults, cognitive training is typically designed for those with age-related cognitive decline or mild cognitive impairment (See ► "Mild Cognitive Impairment"). Most cognitive training programs are not designed for individuals who have dementia (See ► "Dementia") although there are cognitive remediation techniques for that purpose (See ► "Behavioral Interventions in Dementia").

Cognitive training is distinct from more general cognitive intervention approaches such as cognitive stimulation, which applies a variety of stimulating activities such as puzzles or games (e.g., crosswords, Sudoku). Cognitive training is also distinct from cognitive engagement, which involves learning new hobbies, skills, or intellectual activities (Park et al. 2014; Stine-Morrow et al. 2008). Cognitive stimulation and engagement interventions are more broad and general in nature and encourage activity and engagement rather than directly targeting improvement of a core cognitive ability. Ultimately, the goal of cognitive training programs for older adults is not only to improve the targeted cognitive functions but also to enhance everyday function and to avoid, or at least delay, cognitive decline including dementia.

Key Research Findings

Many cognitive training techniques exist, each targeting specific cognitive abilities. Clearly, the efficacy of different cognitive training techniques varies. Among older adults, process-based and strategy-based cognitive training techniques consistently improve the targeted cognitive ability (e.g., processing speed, attention, memory, or reasoning) as evidenced across more than 30 years of research including hundreds of clinical trials and meta-analyses thereof (Au et al. 2015; Edwards et al. 2017b; Hill et al. 2017; Hindin and Zelinski 2012; Kelly et al. 2014; Kueider et al. 2012; Lampit et al. 2014, 2015; Mewborn et al. 2017; Sprague et al. 2019). Nevertheless, cognitive training is not without critics.

A criticism of cognitive training is that transfer to improvement beyond the abilities targeted by the intervention is not evident (Noack et al. 2009;

Reijnders et al. 2013). It is common that cognitive training does not show strong evidence of broad transfer to various other cognitive domains. For example, in one of the largest US studies of cognitive training to date, the Advanced Cognitive Training in Vital Elderly (ACTIVE) study, cognitive training enhanced the targeted domain but did not improve other aspects of cognition (e.g., speed of processing training did not enhance memory): However, such transfer was not expected (Ball et al. 2002). At the same time, how cognitive outcomes in studies of cognitive training are categorized makes a difference. In a 2014 meta-analysis of 51 studies of cognitive training among older adults, Lampit and colleagues found improvements from cognitive training relative to controls across domains of nonverbal memory, verbal memory, working memory, processing speed, and visuospatial skills, but not for attention or executive function. A subsequent reanalysis of the attention and executive function outcomes indicated that aspects of executive function such as set shifting and inhibition are improved by cognitive training, while updating is not (Webb et al. 2018). In general, cognitive training programs typically improve the targeted outcome and also improve cognitive outcomes in the same domain, but do not necessarily affect multiple cognitive domains.

A more important question is whether cognitive training transfers to improved everyday function (i.e., instrumental activities of daily living (IADL)). However, everyday function is not typically measured as an outcome in cognitive training studies. A systematic review conducted in 2017 indicated that only about 10% of published randomized trials of cognitive training evaluated everyday function as an outcome (Sprague et al. 2019). Across cognitive training studies among older adults actually measuring everyday function as an outcome, results are overall positive (e.g., Edwards et al. 2017b; Kelly et al. 2014; Sprague et al. 2019). Perhaps the best evidence for far transfer to improved everyday function comes from studies of cognitive speed of processing training in the useful field of view (UFOV) paradigm. Across eight different randomized trials, UFOV cognitive training consistently improved IADL function including both performance-based and self-report indices (Edwards et al. 2017b). At the same time, it is important to note that the effects of cognitive training on everyday function may not be immediately evident, but can emerge over time. This may particularly be the case when the study sample is initially healthy. As an example, in the ACTIVE study, although improvements from cognitive training on self-ratings of IADL were not evident initially, at the 5-year assessment, those randomized to reasoning and those who received speed of processing training booster sessions showed less functional decline across time relative to controls (Willis et al. 2006). At 10 years post intervention, those randomized to either reasoning, speed of processing, or memory training all showed less IADL decline as compared to controls (Rebok et al. 2014). Overall, it is likely that some types of cognitive training show far transfer to improved everyday function, while others may not. Effects of cognitive training on everyday function may not be immediately evident, but emerge over time. Increasingly, evidence indicates that cognitive training can enhance functional outcomes (Edwards et al. 2017b).

Another common criticism of cognitive training is that results may be due to expectation effects. Critics assert that cognitive training effects can be attributed to the expectations of participants or a placebo effect since study participants are aware they are completing an intervention. Such an effect would be evident by cognitive training effects being larger relative to no-contact control groups as compared to active-control conditions. However, evidence from several systematic reviews of cognitive training demonstrate that effects are *not* larger when compared to no-contact control conditions yet are clearly evident relative to active controls (Edwards et al. 2017b; Hill et al. 2017; Lampit et al. 2014; Mewborn et al. 2017). Further, direct investigation of expectation effects on working memory training indicates that cognitive training gains cannot be attributed to participant beliefs (Tsai et al. 2018).

Perhaps the most pressing concern is whether cognitive training can prevent or delay cognitive impairment or dementia. A 2017 National Academies of Sciences report concluded that there is moderate evidence to support cognitive training as a treatment to prevent cognitive decline and dementia (National Academies of Sciences 2017), with cognitive training showing stronger evidence than other treatments such as management of cardiovascular risk factors or dietary supplements. Few studies have been designed to quantify the longitudinal effects of cognitive training on subsequent incidence of cognitive impairment or diagnosis of dementia, although several are underway (e.g., Maintain Your Brain and Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)). To date, only one intervention has shown reduced risk of dementia in a randomized clinical trial, namely, UFOV cognitive training.

Examples of Application

UFOV training, which is also known as cognitive speed of processing training, is a process-based perceptual/cognitive training technique. This bottom-up approach is grounded in the information degradation theory (Humes et al. 2013), which posits that age-related changes in the brain cause perceptual processing errors that negatively affect cognition. Dr. Karlene Ball initially developed the UFOV training paradigm and was one of the first scientists to demonstrate that older adults' cognition can be enhanced through targeted practice (Ball and Sekuler 1987; Sekuler and Ball 1986). Ball and Roenker further developed the UFOV cognitive training program (Ball et al. 1990) leading to its inclusion as one of three cognitive training programs investigated in the ACTIVE trial (Ball et al. 2002).

Data analyses from ACTIVE indicated that those randomized to UFOV training (a.k.a. speed of processing training) were 29% less likely to meet criteria for dementia across 10 years (Edwards et al. 2017a). Those who completed additional booster sessions of UFOV training were up to 48% less likely to meet dementia criteria. The ACTIVE study results and evidence from 17 other randomized clinical trials demonstrate numerous benefits of UFOV cognitive training among older adults with and without mild cognitive impairment such as improved speed of processing and attention (Edwards et al. 2017b). In addition to the aforementioned beneficial effects of UFOV training on IADLs (Edwards et al. 2002, 2005, 2009a; Lin et al. 2016; Rebok et al. 2014; Wolinsky et al. 2015), research has demonstrated that UFOV training results in safer and prolonged driving mobility among older adults (Ball et al. 2010; Edwards et al. 2009, 2009b; Roenker et al. 2003). In addition to these everyday functional benefits, UFOV training results in maintained health and well-being (e.g., Wolinsky et al. 2006, 2009a, b, 2010). Interestingly, emerging evidence indicates UFOV training may improve gait speed and balance (e.g., Smith-Ray et al. 2014).

Similar to other cognitive training programs, UFOV training does not seem to transfer to improved neuropsychological outcomes other than speed of processing and attention, but positively enhances well-being, health, and quality of life longitudinally (Edwards et al. 2017b). Perhaps of the utmost importance, UFOV training may longitudinally reduce dementia risk (Edwards et al. 2017a). Even small effects to delay functional impairment and dementia are clinically meaningful in that if an intervention could delay the onset of Alzheimer disease by only 1 year, there would be a reduction of 9.2 million cases over the next 35 years (Brookmeyer et al. 2007).

Future Directions of Research

A significant barrier to progress in the cognitive training field is that the majority of published reviews of cognitive training research equate approaches and types, despite the fact that different cognitive training approaches can vary greatly and have quite unique effects. Cognitive training programs differ substantially in goals, abilities targeted, techniques used, and underlying mechanisms (Green et al. 2019). To advance and clarify findings in the field, we must be more careful in our terminology and descriptions of such interventions (Green et al. 2019). More careful, considered categorization of cognitive outcomes, particularly by parsing executive functions into relevant component abilities, is also needed to clarify results (Webb et al. 2018). Further, systematic reviews and meta-analyses should focus on evaluating the evidence for specific cognitive training programs, given that effects vary by approach.

The Institute of Medicine (2015) recommended that cognitive training research should focus on addressing the following questions: (1) Has the training program been evaluated relative to an active-control group whose members have the same expectations of cognitive benefits as do members of the experimental group? (2) Has the training program demonstrated transfer of training to other laboratory tasks that measure the same cognitive construct as the training task? (3) Has the training program demonstrated transfer of training to relevant real-world tasks? Further, international experts in cognitive training provided several excellent methodological guidelines for advancing cognitive training research (Green et al. 2019). This report indicates that feasibility, mechanistic, efficacy, and effectiveness studies of cognitive training are all necessary and valuable, with recommended methodology for such studies described.

Moving forward, a priority is determining if cognitive training can delay the risk of cognitive impairment or dementia. In the 2017 National Academies of Sciences report, several recommendations for future research were advanced for interventions aimed at preventing dementia in general, and cognitive training in particular (National Academies of Sciences 2017). Future research on cognitive interventions should investigate optimal dosage, delivery, and timing in order to maximize benefits. These factors are likely to vary by the type of cognitive training. For example, it may be most effective to intervene prior to any signs of cognitive impairment for strategy-based cognitive training programs. A challenge to cognitive training, as with any behavioral intervention, is promoting adherence. It could be that social engagement may help to promote adherence, and a recommendation was to examine if including a social aspect promotes adherence (National Academies of Sciences 2017).

Given that cognitive training may not broadly enhance cognition, investigations should determine if multimodal approaches the most effective (National Academies of Sciences 2017). Multimodal approaches could include a variety of cognitive training exercises targeting multiple cognitive domains. As an example, a recent study showed that combining UFOV cognitive training with other attention training techniques produced greater improvements in speed of processing and attention (Van Vleet et al. 2016). Multimodal techniques may also combine cognitive training with other intervention approaches such as those that indirectly enhance cognition by reducing anxiety or improving physical function (e.g., mindfulness, yoga, aerobic exercise, diet). It is likely that the best combination of cognitive interventions may vary on an individual basis, given that the trajectory of cognitive aging differs across persons. The best approach may be targeting the cognitive performance domains that are weakest for each individual and addressing other underlying individual factors that are likely to increase risk of cognitive decline or dementia (e.g., anxiety, depression, cardiovascular health, diet). Finally, identifying mechanisms of efficacious cognitive training is needed. What the key elements or combinations thereof that determine cognitive training efficacy remains unclear.

Summary

Cognitive training has been investigated as a way to promote cognitive and functional health among older adults for well over 30 years. Evidence across hundreds of clinical trials indicates that cognitive training improves the targeted cognitive domain. Although relatively few of these studies have examined the impact on everyday function, overall results indicate that cognitive training may also enhance everyday function. Interestingly, cognitive training is the only cognitive intervention shown to reduce risk of dementia in a randomized clinical trial. Cognitive training is a promising technique deserving of future investigation. Well-designed and statistically powered studies with sufficient sample sizes are needed, and longitudinal follow-up over many years is required to ascertain effects on incidence of cognitive impairment and dementia.

Cross-References

- ► Cognitive Processes
- ► Executive Function
- ► Information-Processing Theory
- ► Reality Orientation
- ► Speed of Processing
- ► Working Memory

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Cognitive-Behavioral Therapy (CBT)

▶ Psychotherapy

Cohabitation

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Synonyms

Consensual union; De facto marriage; Living together

Definition

Cohabitation refers to couples who live together in intimate relationships without being married (Brown 2017; Chevan 1996). In one of the first studies of older cohabitors, Chevan (1996: 657) defined cohabitation as a "heterosexual couple whose members are not married to each other and who live in the same household in a close relationship." The definition is now more inclusive to also include same-sex couples. Whereas today cohabitation is commonly viewed as normal and desirable by most Americans, it was once stigmatized and described in disapproving terms such as "living in sin" and "shacking up" (Brown 2017).

Overview

The United States has experienced dramatic demographic changes in family life over the past several decades, including a declining proportion of adults who are married, high levels of divorce, and a rise in cohabitation (Cherlin 2010; Kennedy and Ruggles 2014). These patterns of change in union formation and dissolution are particularly evident in the second half of life (Brown and Wright 2017; Cooney and Dunne 2001). Since 1980, the share of middle-aged adults who are unmarried has increased by 50% (Kreider and Ellis 2011). Today's older adults (defined as those ages 50 and older) have a wider array of partnership options from which to choose and are increasingly opting to take advantage of their ability to form nonmarital relationships, including cohabiting unions. The baby boomers were the first cohort to have large numbers cohabit as young adults, and as they have entered their later years, the number of cohabitors aged 50 and older has quadrupled since 2000 (Brown et al. 2006; Stepler 2017). Research on the implications of cohabitation among older adults is limited, but suggests that cohabitation and marriage may offer similar benefits for well-being.

Key Research Findings

The Rise of Later Life Cohabitation

Although the share of older adults in the United States who are married has declined, a growing number are involved in nonmarital relationships (Calasanti and Kiecolt 2007). Over the past few decades, the United States has seen a swift increase in the number of adults aged 50 and older who are cohabiting (Brown and Wright 2017). In 2000, there were about 951,000 older cohabitors, and this figure increased to roughly 2.3 million by 2007 (Stepler 2017). Yet, the rise of cohabitation in later life has accelerated especially quickly in the past decade. According to a recent estimate, there are approximately four million cohabitors aged 50 and older, a 75% increase since 2007 (Stepler 2017). The recent growth in cohabitation has been faster among older adults than for younger adults (Brown and Wright 2017), such that today nearly one of every four cohabiting couples includes at least one partner aged 50 or older.

One of the key factors driving the growth of later life cohabitation is that a greater proportion of older adults is eligible to cohabit. The share of adults in the US population who are currently married is at an all-time low (Cherlin 2010), and this retreat from marriage is apparent among older adults. Today, more than one-third of adults aged 50 and older are unmarried (Brown and Wright 2017; Lin and Brown 2012) Thus, there is a greater proportion of older adults for whom cohabitation is an option. Several recent patterns in intimate relationships have played a role in the increasing number of older people who are unmarried and available to cohabit.

First, there has been a small increase in the number of never married persons, particularly among men (Lin and Brown 2012). Second, despite recent stability in the overall divorce rate in the United States, the gray divorce rate (i.e., divorce among people ages 50 and older) has doubled over the past couple of decades (Brown and Lin 2012). In 1990, the divorce rate among those aged 50 and older was 4.9 divorced persons per 1,000 married persons, but by 2015 the rate had risen to about 10 per 1,000 (Brown and Lin 2012; Brown and Wright 2017). Thus, among those who divorced in 2010, 1 in 4 was at least 50 years of age, whereas only 1 in 10 were 50 or older in 1990 (Brown and Lin 2012).

Third, the declining remarriage rate in the United States also has contributed to a greater number of older adults who may form cohabitations. The overall remarriage rate has sharply declined over the past several decades and is stable for older adults (Wu 2017). The reduction in the remarriage rate among US adults leaves a larger pool of people eligible to cohabit. Rather than getting remarried, an increasing share of divorced older adults are forming cohabiting relationships (Brown et al. 2018). Indeed, researchers have found that the likelihood of single older adults forming a cohabiting union is nearly the same as their odds of remarrying (Brown et al. 2012; Vespa 2012). Overall, demographic changes in US family life over the past few decades, particularly in marriage, divorce, and remarriage, have led to a higher number of unmarried older adults who are eligible to cohabit.

The rise in cohabitation goes beyond there simply being a greater share of older adults who are eligible to cohabit. More people are choosing to enter cohabiting relationships. Today, about 14% of unmarried older adults are in cohabiting relationships, doubling from just 7% in 2000 (Brown and Wright 2017). Research on cohabitation attitudes among older adults suggests that recent cohorts of older people are more accepting of cohabitation than previous cohorts (Brown and Wright 2016). In 2012, 46% of older adults reported favorable attitudes regarding cohabitation, compared to just 20% in 1994. This increase in favorable attitudes is largely driven by cohort replacement. The baby boomers were the first cohort for whom large numbers cohabited as young adults, and they tend to be more supportive of cohabitation than cohorts born earlier (Brown and Wright 2016). In other words, older adults today are more supportive of cohabitation because baby boomers, who hold more favorable attitudes toward cohabitation, have entered their later years and replaced previous, less supportive generations. Coupled with the greater share of older adults who are eligible to cohabit, this shift toward more favorable attitudes suggests that the growth in later life cohabitation is likely to continue into the future.

Why Do Older Adults Cohabit?

Much of the early research on later life cohabitation in the 1990s focused on the benefits of cohabitation for older adults and identified a variety of social and economic factors that may contribute to the increasing popularity of cohabitation among older adults (Chevan 1996). Economically, there are potential Social Security benefits to cohabiting. Although marrieds often enjoy higher Social Security benefits, cohabitors maintain Social Security and pension benefits that would end in the event of a remarriage (Chevan 1996). Among cohabiting women, those who receive entitlement income have lower odds of marrying than those who do not receive such income (Vespa 2013). Cohabitation may be attractive to people who are near or below the poverty line because older adults who cohabit are able to pool their resources and achieve economies of scale without having to marry (Chevan 1996). Thus, older cohabitors can live together in an intimate relationship, with flexibility to combine their resources in a way that works for them (Brown and Wright 2017).

Cohabitation also provides older couples with the ability to define their own relationship scripts (Brown and Wright 2017). Scholars have argued that cohabitation can be viewed as an incomplete institution in which there is no clear set of norms or expectations guiding the behaviors of cohabiting partners (Nock 1995). The ambiguity and uncertainty of the roles of cohabitors can present challenges, but also offer couples an opportunity to actively create their own norms and expectations for their relationships (Brown and Wright 2017; Vespa 2013). Cohabitation also does not come with many of the legal obligations attached to marriage. For instance, cohabitors do not have any legal responsibilities related to their partner's medical expenses (Brown and Wright 2017). Moreover, cohabiting couples do not have a legal attachment to their partner's assets. Cohabitation may appeal to some older adults because it offers greater flexibility to remain financially independent than marriage, more so ensuring that assets are passed to children rather than a partner (Brown and Wright 2017; Chevan 1996).

Gender also may play a role in the desirability of cohabitation among older adults. Repartnering, through both remarriage and cohabitation, in later life is much more common among men than women (Brown et al. 2018; Schimmele and Wu 2016). Older women have a smaller pool of potential partners because, on average, women live longer than men and they tend to partner with older men. Previous research also suggests older women and men have different preferences for repartnering. Qualitative studies have found that women are less interested in repartnering than men (de Jong Gierveld 2002; Talbott 1998; McWilliams and Barrett 2014). Cohabitation may be favorable to older men because they are often interested in finding a partner to provide them with care (McWilliams and Barrett 2014), and it offers a live-in partner who can offer social support (de Jong Gierveld 2002). Women are typically less enthusiastic about repartnering because they have provided care to a previous husband and children and prefer not to repeat the experience (Talbott 1998). For many older women, cohabitation may be appealing because there are fewer caregiving obligations than in marriage (Talbott 1998; McWilliams and Barrett 2014). Indeed, prior research has shown that caregiving is less likely among older cohabitors than spouses (Noël-Miller 2011).

Cohabitation as an Alternative to Marriage

A large body of literature on family life has explored the role of cohabitation in the lives of adults in the United States. For many younger adults, cohabitation seems to serve as a prelude to marriage or an alternative to being single. Older cohabitors, however, are unlikely to report having plans to marry their partners (King and Scott 2005). Rather, mounting evidence suggests that later life cohabitation may be a long-term alternative to marriage (Brown et al. 2012; King and Scott 2005). Older cohabiting individuals report higher levels of relationship quality, on average, compared to younger cohabitors (King and Scott 2005). Moreover, whereas relationship quality tends to be higher among married than cohabiting younger adults, remarried and cohabiting older adults appear to have comparable levels of relationship quality (Brown and Kawamura 2010; Lewin 2017). Brown and Kawamura found similarities in levels of relationship quality between cohabitors and remarrieds across several positive and negative dimensions, including openness, interaction, emotional satisfaction, pleasure, criticism, and demands. The only difference uncovered was that remarrieds were more likely than cohabitors to report that their relationships are very happy.

Cohabiting unions in the second half of life also tend to be fairly stable. A recent study reported that the average duration of later life cohabitations was approximately 10 years (Brown et al. 2012). Comparatively, over half of all cohabiting unions among younger adults end through marriage or separation within 2 years, and the majority end via breakup (Kennedy and Bumpass 2008). Among older cohabitors, the most common reason for relationship dissolution is the death of one of the partners (Brown et al. 2012). Only a small share of later life cohabiting unions lead to marriage or separation. The stability of these cohabiting unions tends to be unique to older adults. Overall, prior studies have shown several similarities between remarried persons and cohabitors, suggesting that later life cohabitation and remarriage may be comparable.

The Profile of Older Cohabitors

The profile of older cohabitors is noticeably unique from that of the remarried and unpartnered. Most partnered older adults (both remarrieds and cohabitors) are men, whereas the majority of unpartnered individuals are women (Brown and Wright 2017). Cohabitors tend to be younger than the remarried and unpartnered, on average, with a median age of 60 years. The median ages of the remarried and unpartnered are 63 and 68 years, respectively (Brown and Wright 2017). Compared to the remarried, a higher proportion of cohabitors are racial/ethnic minorities, though a greater share of unpartnered than cohabiting older adults are minorities (Brown and Wright 2017). In terms of marital history, almost 90% of older cohabiting individuals have been previously married (Brown et al. 2006; Brown and Wright 2017). Prior to entering their cohabiting unions, the vast majority (85%) of previously married cohabitors were divorced rather than widowed (15%) (Brown and Wright 2017).

Cohabitors tend to be somewhat economically disadvantaged compared to the married, though they often fare better than the unpartnered. On average, the remarried are more educated than cohabitors, as approximately one-fifth of remarrieds have a college degree or more, compared to just over one-fifth of cohabitors (Brown and Wright 2017). About one-fifth of unpartnered persons have at least a college education. A higher proportion of cohabitors are employed than either remarrieds or unpartnereds (Brown and Wright 2017). Nearly two-thirds of cohabiting older adults are working, compared to a little over half of remarrieds and just more than one-third of unpartnered individuals (Brown and Wright 2017). The difference in employment is likely related to the younger median age of cohabitors in comparison to their counterparts. Although a greater share of cohabitors is working, they do not appear to reap the economic benefits enjoyed by remarried older adults. On average, cohabitors have lower household incomes and are less likely to own their homes than the remarried (Brown et al. 2006; Brown and Wright 2017). Similarly, cohabiting older adults are much more likely to report being in poverty than the remarried (Brown et al. 2006; Brown and Wright 2017). Cohabitors have higher household incomes, on average, and are also more likely to own their homes than the unpartnered (Brown et al. 2006; Brown and Wright 2017). These patterns are consistent with prior research that has shown wealth to be positively linked to forming a cohabiting union (Vespa 2012). Nonetheless, although cohabitors tend to have higher average household incomes than the unpartnered, a greater proportion of cohabitors than unpartnereds report being below the poverty line (Brown and Wright 2017).

Finally, cohabitors fare poorly in terms of social ties compared to both the married and unpartnered. Across the groups, they are the least likely to report having friends or relatives in the neighborhood and the lowest levels of religiosity (Brown et al. 2006). When cohabiting women have friends or relatives nearby, they have higher odds of ending their cohabiting unions through breakup and are less likely to marry (Vespa 2013).

Cohabitation and Well-Being

It is well established that partnership status is linked to health and well-being. On average, married people tend to fare better than the unmarried on both physical health and psychological well-being (Hughes and Waite 2009). Typically, married individuals report lower levels of depressive symptoms than unmarried people, as well as higher average levels of self-rated health (Williams and Umberson 2004; Hughes and Waite 2009). In the middle and later years, married people tend to have fewer chronic conditions and mobility limitations than the unmarried (Hughes and Waite 2009; Lin and Brown 2012).

Very few studies have examined the health and well-being of older cohabitors. A cross-sectional study using data from the 1990s found higher levels of depressive symptoms, on average, among older cohabiting men than married men (Brown et al. 2005). Levels of depressive symptoms were particularly low for married men, whereas the psychological well-being of cohabiting men, married women, and cohabiting women were similar. More recently, Wright and Brown (2017) used longitudinal data to explore several dimensions of psychological well-being among older cohabitors and found no differences in psychological well-being by partnership type among women. The results for men showed that the psychological well-being of cohabitors is comparable to or better than the married. Future research should investigate the psychological well-being of cohabitors using additional outcomes and larger samples of cohabitors.

The physical health of older cohabitors has received slim attention, and it is unclear how they compare to their married counterparts. On the one hand, it is possible that cohabiting older adults have poorer well-being than the married. According to the resource perspective, marriage should be advantageous to spouses' well-being because it affords economic, social, and psychological benefits that amplify their physical and psychological well-being (Zhang et al. 2016). Given that cohabitors tend to be economically disadvantaged and typically have fewer social ties and less social support than the married, they may experience lower levels of well-being (Brown et al. 2006). It is also possible that any differences in health between cohabitors and marrieds could be attributable to the consequences of marital dissolution (Williams and Umberson 2004). Although remarriage reduces the negative health consequences of marital dissolution, remarried adults in midlife still report poorer health than the continuously married (Hughes and Waite 2009). With both groups being currently married, these findings suggest that marital dissolution plays an important role in health. With almost all older cohabitors having been previously married (Brown et al. 2006; Brown and Wright 2017), the chronic strains of marital dissolution may influence their health (Zhang et al. 2016). Whether this is the case is unclear because previous studies have not examined cohabitors. Moreover, whereas remarriage offsets the detrimental consequences of marital dissolution, it is unknown whether that is also true of cohabitation.

On the other hand, the well-being of older cohabitors may be similar to the married. As previously discussed, later life cohabitation appears to operate as an alternative to marriage (Brown and Wright 2017; King and Scott 2005). Thus, it is possible that cohabitation offers benefits that are akin to remarriage, and these may extend to well-being. Cohabiting Blacks do not experience a mortality disadvantage compared to their married counterparts, and the mortality disadvantage of cohabiting White women and men decreases with age (Liu and Reczek 2012). Older marrieds and cohabitors also appear to have comparable psychological well-being (Wright and Brown 2017). Future research should provide further insight into the well-being of cohabitors by investigating their physical health.

Example of Application

Although researchers have addressed relationship quality among older cohabitors (Brown and Kawamura 2010; King and Scott 2005; Lewin 2017), little is known about whether cohabitation is associated with relationship quality similarly across subgroups, especially race. Previous research suggests that there may be fewer gains to marriage for Blacks than Whites (Liu and Reczek 2012). Using data from the 2010 to 2012 Health and Retirement Study, a nationally representative sample of a continuous cohort of individuals over age 50, unpublished analyses suggest that there are no differences in relationship quality between remarried and cohabiting White older adults. Older Black cohabitors, however, appear to enjoy higher levels of positive relationship quality than their remarried counterparts. Research on marriage has shown that the benefits of being married are largely extended only to those in higher quality marriages, whereas those who are in poorer quality marriages enjoy few benefits or are worse off than if they divorced (Zhang et al. 2016). Thus, it is essential to further consider relationship quality and subgroup variation because of the potential implications for the well-being of older cohabitors.

Future Directions for Later Life Cohabitation Research

One key task for future research on later life cohabitation is to further investigate the dynamics of cohabiting relationships. For example, remarkably little is known about the extent to which older cohabiting couples pool and share their resources or keep their finances separate. Chevan (1996) argued that cohabitation may be attractive to older adults in poverty, or close to it, because they can combine their resources to achieve economies of scale. Yet, cohabitation may also be attractive to some older adults because it potentially offers greater financial independence than marriage (Brown and Wright 2017; Chevan 1996). These economic dynamics may have consequences for cohabitors and public policy because more than one-fifth of older cohabitors report being in poverty (Brown and Wright 2017).

There has been a shortage of research on same-sex older cohabitors, and much of the scholarship on same-sex cohabiting relationships has focused on health. Older same-sex cohabiting men are comparable to different-sex married men on physical health, though they fare worse on psychological distress (Gonzales and Henning-Smith 2015). Same-sex and different-sex cohabiting men have been found to be similar in their health (Baumle 2014). Same-sex cohabiting women are at a health disadvantage compared to different-sex married and cohabiting women (Baumle 2014; Gonzales and Henning-Smith 2015). When same-sex cohabitors enjoy health advantages, it appears to often be due to higher levels of socioeconomic status (Liu et al. 2013), as same-sex cohabitors are socioeconomically similar to different-sex marrieds and better off than different-sex cohabitors (Baumle 2014). Future research should extend these studies by further investigating additional aspects of same-sex cohabiting relationships.

Researchers should also address how later life cohabitation influences parent-child relationships. Older cohabitors are less likely than the married to receive care from their partners (Noël-Miller 2011). Thus, it is possible that cohabitors need other sources of care, such as their adult children. Few published studies have examined the parent-child relationships of older cohabitors. Divorce among parents is negatively associated with relationship quality and frequency of contact between parents and their children, especially among fathers (Kalmijn 2013). Forming new intimate relationships may further undermine parent-child ties, particularly among men (Kalmijn 2013). Little is known, however, about the association between older adult cohabitation and parent-child relationships. Likewise, the extent to which adult children are willing and do provide care to their cohabiting parents has been largely unexplored. If cohabitors are lacking sources of care, more of the caregiving burden may fall to societal institutions (Brown and Wright 2017).

With changes in the union formation and dissolution behaviors of US adults over the past few decades, there is more variation in the family life courses of today's older adults, highlighting the need to consider the broader marital biographies of older cohabitors. Almost all older cohabitors are previously married, and the vast majority of them are divorced (Brown and Wright 2017), but some are also widowed or never married. Are there well-being differences for cohabitors who were divorced compared to those who were widowed or never married? Moreover, cohabitation is just one of many relationship options available to older adults today, and other types of nonmarital relationships, such as dating and living apart together (LAT), are perhaps more common than cohabitation (Brown and Shinohara 2013; Lewin 2017). Future data collections and research on the family lives of older adults would benefit from greater attention to these complex marital biographies and emerging forms of nonmarital relationships.

Summary

Many of the most sweeping changes in family life are occurring among older adults (Brown and Wright 2017; Cooney and Dunne 2001), including growth in the share of older people who are cohabiting. Mounting evidence suggests that cohabitation may provide many of the same benefits as remarriage and serve as a viable alternative to remarrying (Brown and Wright 2017). Research on this segment of the population remains limited, as scholars have only begun to scratch the surface in developing our understanding of cohabitation among older adults. Although our insight on later life cohabitation has greatly expanded in the past decade, researchers should extend prior work by considering the relationship dynamics of later life cohabiting couples, as well as the implications of cohabitation for well-being, parent-child relationships, and same-sex couples. Studies should also further investigate subgroup variation in the ramifications of cohabitation. Given that cohabitation in the second half of life is likely to continue growing in the future (Brown and Wright 2017), it will be important for scholars to shed additional light on older adult cohabitation.

Cross-References

▶ Co-residence
▶ Family Demography
▶ Family Formation and Dissolution

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Cohort Analysis

► Age-Period-Cohort Models

Cohort Sequential Study

► The Longitudinal Aging Study Amsterdam (LASA): An Overview

C

Cohort Study

► Cross-Sectional and Longitudinal Studies

Cohort Study of Centenarians in Hainan, China (CHCCS)

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Project Goals/Missions, Uniqueness

Hainan Province, an island in the South China Sea, is one of the provinces with the highest life expectancies in China (76.3 years in 2010) (Li et al. 2016). CHCCS is designed to interview all centenarians (as possible) in Hainan. Most centenarians in Hainan are ethnic minorities and have lived on this island for all their life, which has facilitated collecting a wide range of health indicators of centenarians in this special environment tropical island and providing a relatively reliable gene bank for longevity gene research.

The CHCCS was designed for three main objectives:

First, to assess the physical and mental health of Hainan centenarians in the context of their socioeconomic conditions from past to present. It is especially important for developing countries like China to understand the impact of resource shortages on their past health and longevity.

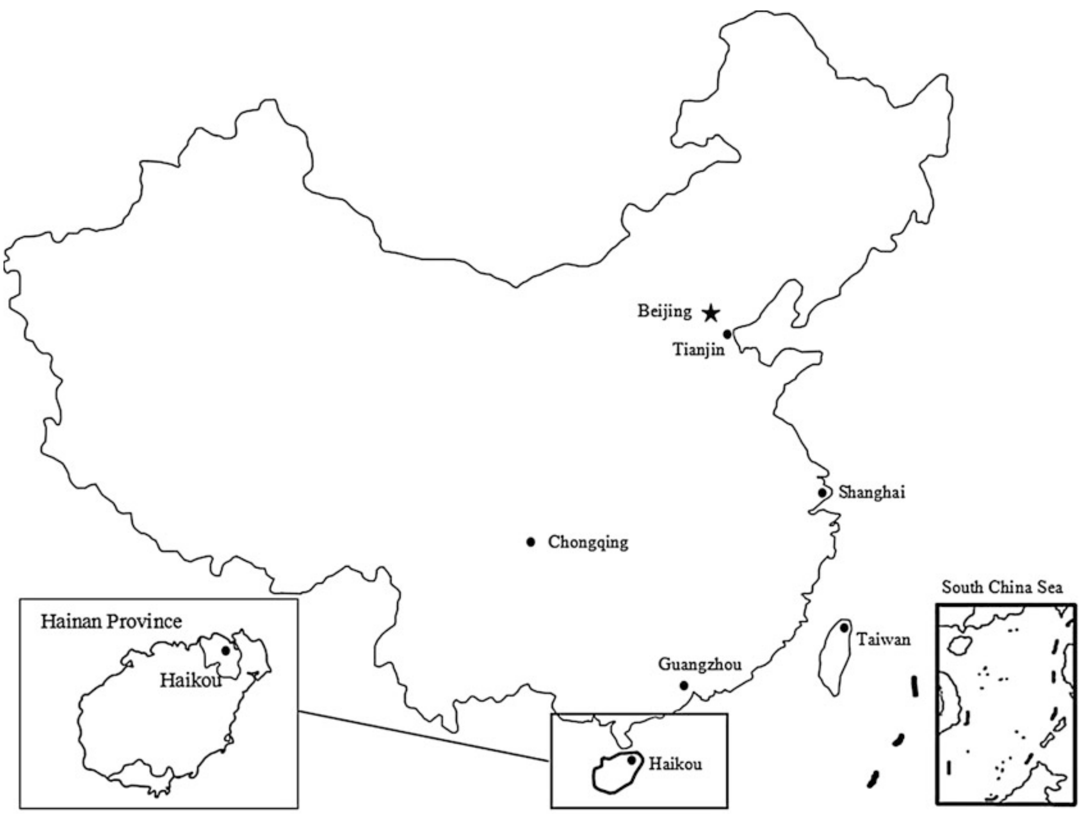
Second, to identify the factors associated with longevity in the framework of the aging psychosocial model.

Third, to propose and develop healthy aging indicators that can be used for population-wide health interventions in the future.

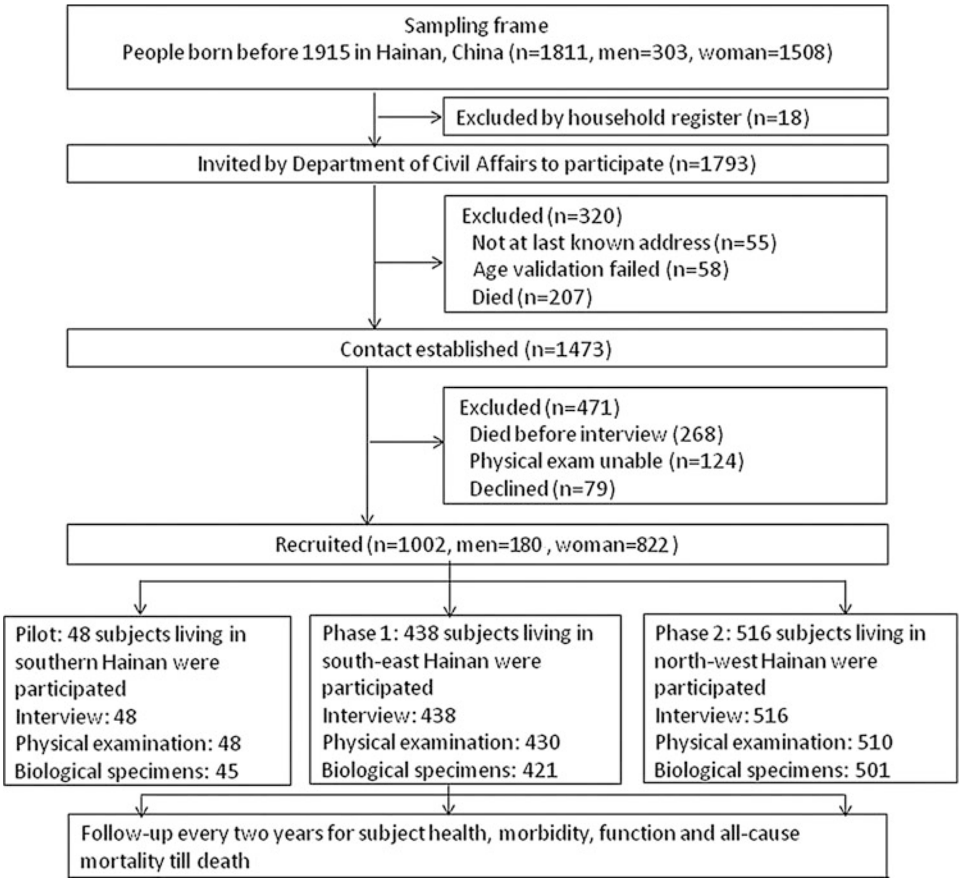
Sampling Procedure and Interviews

The CHCCS was designed to interview all centenarians (as deemed possible) in Hainan Province (Fig. 1). The sampling frame of the CHCCS includes the list of all males and females claiming to be a centenarian in Hainan Province in 2013, provided by the Hainan Provincial Civil Affairs Bureau. By February 2014, there were 1,811 self-claimed centenarians in total, and 1,473 of them in 18 cities and counties of Hainan Province were identified in June 2014 when the CHCCS started. By December 2016, 268 centenarians had died, 203 refused to participate, and 1,002 participated in the study, with a response rate of 83.2% (also see Fig. 2).

The criteria for recruiting study participants are as follows: male or female (1) who self-claimed to be aged 100 or older by June 1, 2014; (2) was willing to participate in the study with informed consent; and (3) was able to complete the questionnaire via face-to-face interview, physical health examination, and blood tests. The following participants were excluded from the CHCCS: (1) personal identification information (e.g., names, sexes, dates of birth) was not complete, or ID card showed their age was below 100 years old at the beginning of the interview; (2) the interviewee refused to comply with the requirements of the study, including the collection of



Cohort Study of Centenarians in Hainan, China (CHCCS), Fig. 1 Location of Hainan province. (Note: The boundary does not reflect any endorsement of the Publisher and any third party)



Cohort Study of Centenarians in Hainan, China (CHCCS), Fig. 2 Participants recruitment in CHCCS

physical or biological samples. In order to ensure accuracy of the data and to avoid participants overstating their age, an age verification process was implemented before participants were included in the study. It is an unprecedented challenge to recruit all centenarians for epidemiological study as much as possible, including detailed questionnaires and extensive clinical examinations. During the interview, the Department of Civil Affairs of Hainan Province provided substantive coordination with the local government agencies to ensure the implementation of CHCCS.

To collect a wide range of health-related samples and indicators from the interviewee and to facilitate their participation, the eligible individuals were given the choice of completing the interview and the examination either at home or at the community health service centers (public clinics). The home-based option was mainly for participants who have difficulties in mobility or live far away from the clinic. For the clinic-based option, the subject was interviewed and examined by well-trained doctors. The CHCCS project team consists of experienced geriatricians, cardiologists, otolaryngologist, dentists, gynecologists, a sonographer, and trained nurses with an average of 5 years of practice in the Hainan Branch of the Chinese PLA General Hospital. Among these two options, there is a nurse who speaks the local dialect to help with translation. The interview took approximately 45 min.

The pilot study was initiated in January 2014, followed by baseline interviews and examinations in 2014. The baseline survey was suspended during the winter as participants were potentially vulnerable to the Hainan climate. Figure 2 shows a flow chart for the recruitment of participants. The CHCCS was approved by the Ethics Committee of the Chinese People's Liberation Army General Hospital (Beijing, China).

Major Questions Designed in the Surveys and the Data Quality

To ensure comparisons with other similar studies, including the CKB (Zhengming et al. 2011), CLHLS (Zeng 2012), and other national and international epidemiological studies of centenarian populations, the CHCCS used standardized and validated instruments for data collection (Table 1). These instruments were pretested on a convenience sample of 48 sampled participants who resided in Sanya suburb, and the instruments were slightly simplified before use. In sum, there are 911 items from the questionnaire, including sociodemographics, anthropometric measures, socioeconomic status, lifetime lifestyle, present medical history, family medical history, functional disability, disease conditions, cognitive function, and biomedical measures including blood and DNA. About 720 items are from laboratory tests.

Major data collected from the interviewee in the CHCCS are shown in Table 2. Initially, 8 ml fasting blood was drawn from interviewees by nurses using four vacutainer tubes (2 ml each), two of which were purple top anticoagulant tubes containing ethylenediaminetetraacetic acid (EDTA) and the other two were yellow top serum-separating tubes (SST). Thereafter, the interviewees were given free breakfast and then prepared to complete the interviews and other physical examinations. In the face-to-face interviews, detailed information on the standardized structured questionnaire were collected by the local interviewers, including social demographics, personal and family disease histories, functional status, cognitive and mental health status, lifestyles, dietary habits, sleep quality, leisure and physical activities, economic status, social support, health service use, and reproductive histories (for females only). Clinical examinations were then conducted by the study group, including blood pressure, anthropometric indices, geriatric syndromes, and visual and hearing acuity as well as the administration of 12-lead electrocardiography, ultrasonography, an equipped dental examination, and a gynecological examination. Biological specimens including hairs and saliva were also collected. To ensure the quality of the data, all biomedical data were immediately delivered to the hospital and stored in refrigerated containers on the same day.

Major Findings

The overall profile of the CHCCS has been published in the international journal of epidemiology (He et al. 2018).

Although 203 participants were unable to be included in the study, participants and non-participants were similarly distributed according to age and gender ($P = 0.27$ and 0.56, respectively; Table 3), which suggests that the CHCCS samples are highly representative of the self-claimed centenarians in Hainan Province.

Excluding those with more than 25% missing questionnaire data, 1002 self-claimed centenarians ranged in age from 100 to 115 years, with an average age of 102.77 ± 2.75 years (102.45 ± 2.26 years for men and 102.84 ± 2.84 years for women). Among them, 82.2% ($n = 822$) of the participants were women. Compared with men, women are more likely to be widowed (87.0% vs. 67.2%), illiterate (96.6% vs. 67.2%), living with families (87.3% vs. 80.6%), and have a BMI <18.5 (61.3% vs. 39.4%).

Vitamin D and Healthy Outcomes

- The prevalence of functional dependence (FD) among the participants was 71.2%. Vitamin D deficiency, lack of tea consumption, lack of outdoor activities, visual impairment, and fracture are symptoms of FD. Participants with the lowest quartile of serum 25-hydroxy vitamin D (25OHD) concentration were approximately three times more likely to suffer from FD than the highest quartile in multiple logistic regression models (OR = 2.88; 95% CI 1.75–4.73; $P = 0.001$). For every 1 ng/ml decrease in

Cohort Study of Centenarians in Hainan, China (CHCCS), Table 1 Contents of the baseline data collection in the CHCCS

Components	Measurements
Face-to-face interview	
Sociodemographics	Marital status, occupation, educational attainments, household structure, personality
Functional capacity	Unintentional weight loss, vision and hearing, basic and instrumental activities of daily living (ADLs [Mahoney and Barthel 1965] and IADLs [Lawton and Brody 1969])
Cognitive function	Mini-mental state examination (MMSE [Katzman et al. 1988])
Mental health	Geriatric Depression Scale (GDS-15 [Burke et al. 1991]), WHO-5 Well-Being Index (Heun et al. 2001), stress, sense of isolation
Behaviors	Smoking and passive smoking, alcohol consumption, tea consumption, physical activity, sexual life
Habitual dietary	11-Item Semi-Quantitative Food Frequency Questionnaire
Sleep quality	Pittsburgh Sleep Quality Index (PSQI [Buysse et al. 1991])
Quality of life	EQ-5D (Rabin and De-Charro 2001)
Family information	Family structure, family harmony, family disease history
Social support/relations	Subsidy, social networks, social activity, companionship, reciprocity
Environment	Drinking water supply, occupational exposure, passive smoking exposure, cooking and heating fuels
Economic status	Previous and current income
Health service use	Outpatient attendance, emergency treatment, hospitalization, health insurance coverage
Reproductive history	Age of menarche, menstrual history, pregnancy history, hormone-replacement therapy history
Medical/clinical examination	
Health conditions	Medical and surgical history, comorbidity, medication
Anthropometric measurement	Weight, height, demi-span, waist, hip, thigh, calf, biceps circumference
Falls	Fall history, location, and outcomes
General pain	Visual analogue scale (VAS [Price et al. 1983])
Physical function	Timed up-and-go test, chair standing, one-leg standing, grip strength
Physical examination	Resting blood pressure, heart rate, auscultation for the heart and the lung, visual and hearing acuity, detecting pitting ankle edema, joint movement, spinal formation, cervical, axillary, and inguinal lymph node
Electrocardiogram (ECG)	12-Lead ECG
Ultrasonography	Carotid, thyroid, cardiac, pleural, visceral, femoral, calf ultrasonic examination
Dental examination	Tooth count, degree of mouth cleaning, periodontal disease
Biological specimens	
Blood analysis	Fasting blood test and DNA sampling
Saliva DNA	Production, component, and DNA of saliva
Hair analysis	Trace elements detection
Feces examination	Morphology of feces, intestinal flora detection via 16S rRNA sequence and whole-genome sequence analysis
Gynecological check-up	Thin prep cytology test (TCT)

25OHD concentration, the risk of FD increases 6% (OR = 1.06; 95% CI 1.04–1.08; $P = 0.001$), so serum 25OHD levels are significantly associated with FD in Chinese centenarians (Yao et al. 2018b).

- The prevalence of depressive symptoms among the sample was 32.2% (95% CI 29.7–34.7%). Serum vitamin D levels were lower in participants with depressive symptoms than in those without (20.8 ± 8.7 vs. 23.7 ± 9.7, ng/

Cohort Study of Centenarians in Hainan, China (CHCCS), Table 2 Summary of clinical measurements collected at baseline in the CHCCS

Variables	Number of measurements	Equipment used	Method
Standing height	Once	Manufactured instrument	
Sitting height	Once		
Hip circumference	Once	Standard tape measure	Around the maximal girth of the hips
Waist circumference	Once		Horizontally around the smallest circumference between ribs and iliac crest, or at naval if no natural waistline
Weight	Once		
Resting pulse rate	Twice	Omron HEM-7200	
Resting blood pressure	Three	Omron HEM-7200	Seated blood pressure, 1 min apart, after a 3-min rest
12-Lead electrocardiography (ECG)	Once	GE MAC 5500	12-Lead ECG was performed by specialized technicians
Ultrasonography	Once	Philips CX50	Carotid, thyroid, cardiac, pleural, visceral, periumbilical fat, femoral, calf ultrasonic examinations were conducted by experienced sonographer
Audiometry	Once	MADESEN Xeta	
Equipped dental examination[a]	Once		Count tooth and evaluate oral hygiene and periodontal disease
Complete blood count[b] (CBC)	Once	Sysmex XT4000i	
Comprehensive metabolic panel[c] (CMP)	Once	Roche cobas 8000	
Lipid profile[d]	Once		
Markers of immune system[e]	Once		
Markers of carcinoma[f]	Once	Roche cobas 8000	
Hormone test[g]		Roche cobas 8000	
Hepatitis B antigen (HBsAg)	Once		

[a]Evaluation of oral hygiene included dental plaque, odontolith, saprodontia, and gums bleeding on probing
[b]White (leukocytes) and red blood cell (erythrocytes) counts, and platelets (thrombocytes)
[c]Electrolytes, serum glucose, blood urea nitrogen, creatinine, serum calcium, serum total protein (TP), serum albumin, bilirubin, alkaline phosphatase (ALP), aspartate amino transferase (AST), and alanine amino transferase (ALT or SGPT)
[d]Total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides
[e]Anti-cardiolipin antibody (ACL), complement component 4 (C4), immunoglobulin A (IgA), immunoglobulin E (IgE), immunoglobulin G (IgG), and immunoglobulin M (IgM)
[f]Carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), cancer antigen 125 (CA 125), cancer antigen 19-9 (CA 19-9), cancer antigen 15-3 (CA 15-3), cancer antigen 724 (CA 724)
[g]Estradiol (E2), follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), progesterone (PROG), testosterone (TES)

mL). Therefore, Vitamin D deficiency was an independent risk factor for depression after controlling for the potential covariates (odds ratio = 1.47, 95% CI = 1.08–2.00; $P = 0.014$). What's more, there is negative relationship between serum vitamin D level and depressive symptom; it remained significant after adjusting for a wide range of other covariates. The multivariate adjusted odds ratio of depressive symptoms for the lowest versus highest

Cohort Study of Centenarians in Hainan, China (CHCCS), Table 3 Participants and nonparticipants by sex, CHCCS

Characteristic	Total	Men	Women	*P*
Address known, *n*	1,473	262	1,211	
Dead, *n* (%)	268	49 (18.2)	219 (81.7)	0.81[a]
Alive, *n* (%)				
Refused or incapable	203	33 (16.2)	170 (83.7)	0.56[b]
Participants	1,002	180 (18.0)	822 (82.0)	
Age (mean ± standard deviation)				0.27[c]
Nonparticipants ($n = 471$)[d]	102.7 ± 2.6	102.6 ± 2.5	102.7 ± 2.6	
Participants ($n = 1{,}002$)	102.8 ± 2.8	102.5 ± 2.4	102.9 ± 2.8	

[a]The chi-square test was used to examine the gender differences between dead and alive participants
[b]The chi-square test was used to examine the gender differences between nonparticipants and participants
[c]*t*-Test was used to examine age differences between nonparticipants and participants
[d]Nonparticipants included those who had died, out-migrated, or refused to participate

quartiles of vitamin D level was 1.73 (95% CI 1.10–2.72), and the adjusted odds ratio with 5 ng/mL decrement of serum 25OHD level was 1.10 (95% CI 1.01–1.19) (Yao et al. 2018c).

- The overall prevalence of vitamin D deficiency among these 943 centenarians was 39.9% (376 subjects) and the mean serum vitamin D concentrations were 22.7 ± 9.5 (ng/mL). Female centenarians had a higher prevalence of vitamin D deficiency than male (44.0% vs. 21.7%, $P < 0.001$). Multivariate logistic regression analysis showed that female, urban residency, lower body mass index, higher serum parathyroid hormone levels, no fish consumption, and reduced sun exposure time were significant and independent determinants of vitamin D deficiency. No significant associations of vitamin D deficiency with ethnic, education, geographic location, tea drinking, alcohol use, or smoking were found in this study (Yao et al. 2018a).

Plans for Future Research

The social, psychological, physical, and health status of centenarians have not yet been fully elucidated. In addition, the underlying mechanisms of longevity among centenarians is still not clear. Therefore, the future research plans of the CHCCS will focus on the following three areas:

- Exploring health-related biomarkers among centenarians (providing more than 100 biomarkers related to disease, functional status, health, and death categories, especially among unique geographical and ethnic characteristics).
- Exploring the role of social, behavioral, environmental, and genetic factors in determining the life span of participants, especially to discover key molecules in the biopsychosocial framework based on the "gene-phenotype-health outcomes" approach and to elucidate the pathogenesis and mechanisms of disease.
- Developing aging-related health indicators for improving population health interventions in the future.

Summary

Hainan Province is a historically closed island with a low proportion of immigrants, where its long-lived population has a high degree of homogeneity, thus making it conducive to studying factors determining human longevity. The CHCCS is the first province-wide study on centenarians in China. Although the CHCCS has many advantages over other similar studies, several points should be emphasized. First, the age of the participants is mainly self-reported. Although self-reported ages have been verified by the national modern household registration system since the mid-1950s, the accuracy of many centenarians' age remains questionable. Thus, more formal checks and protocols are needed to further validate these ages. Second, due to their relatively low cognitive function, it cannot be ruled out that these centenarians may have recall biases when answering questions, especially for their childhood or early adulthood. Third, in future follow-up waves, sample attrition may be a challenge due to withdrawals or losses to follow-up in the coming years – in addition to high rates of mortality.

Cross-References

► Chinese Longitudinal Healthy Longevity Survey (CLHLS)

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Cohousing

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Synonyms

Collaborative housing; Community; Housing choice; Intentional living; Loneliness

Definition

A recent New South Wales State Government funded study conducted by the Institute for Sustainable Futures (ISF) at the University of Technology Sydney (UTS), looked at the appropriateness of the cohousing model for older people (See ► "Aging in the Right Place"), and, while acknowledging the many definitions and variations, and citing Williams (Williams 2005), defined cohousing as, simply, "Cohousing is a form of community living that contains a mix of private and communal spaces, 'combining autonomy of private dwellings with the advantages of community living'" (Riedy et al. 2018, p. 5).

The features that make cohousing different from other forms of housing (See ▶ "Housing") is its focus on community living. Cohousing or collaborative housing is "co-designed" with residents, to encourage community interaction and connectedness. They are usually initiated and run by the residents (See ▶ "Autonomy and Aging"; ▶ "Senior Entrepreneurship") all who have a common desire, commitment, and purpose to live more communally. They can be small, two to three households, but are usually larger multi-unit developments. This entry discusses the value of cohousing as an alternative choice for older people as they grow older.

Overview

The ability to choose where one lives is an inalienable human right and remains one of the key decisions for people as they age. Where and, more to the point, how to live come into play as family situations change, people leave full-time employment, and houses become too big and hard to maintain. In much of the Western world, people overwhelmingly opt to stay in their own homes as they get older (Productivity Commission 2015) and are emotionally attached to them (Daley and Oates 2017). Clearly there are advantages to staying put, but there are internal and external forces that can cause a reconsideration of this decision, especially with ever-increasing age, and, equally, there are a number of advantages for older people if they move from their often very large homes (See ▶ "Home Equity Conversion"), for their own well-being and for societal reasons.

The Grattan Institute, using data from the Australian Housing and Urban Research Institute (AHURI), suggests that it is "Way of life" (See ▶ "Aging in Place and Quality of Life") issues that dominate the decision to consider moving, or "downsizing," (See ▶ "Accommodation Downsizing") but that "availability of type" came up as the key problem for 70% of the people looking to downsize (Daley 2017). One of the reasons for this lack of "availability of type" may be because there are only really two options for older people if they seek to move into accommodation specifically for older people. These are commonly referred to as "retirement villages," (See ▶ "Retirement Villages") for more independent living, and "residential aged care," (See ▶ "Aged Care Homes") for higher levels of care. But these options are not popular. In Australia, for example, retirement villages attract only about 5.7% of people over 65 (Property Council of Australia 2014) and residential aged care, even less (Australian Bureau of Statistics 2015). These two options are clearly not preferred by older people. The pull factors are not strong enough to move away from the family home (See ▶ "Residential Happiness and Quality of Life").

But what if there were other options that were able to bridge the gap between these often more isolating living environments and the family home? What if there was an option where people could live with a group of their friends and stay in their own home (See ▶ "Social Integration")? Would this encourage more people to move? The idea of getting together with a group of friends and living with them is a popular dinner conversation for people as they grow older (See ▶ "Social Participation") and cohousing, with its focus on community living while maintaining privacy, has the potential to become one such alternative and has many advantages for older people.

Key Research Findings

The UTS ISF report concluded that: "Cohousing has the potential to help seniors to age with dignity..." and "...can help to address policy challenges such as an ageing population, rising health care costs and housing affordability" (Riedy et al. 2018, p. 8) (See ▶ "Affordable Housing").

But it is more than that. With loneliness being identified as a key factor in the health and well-being of older people (Lunsted et al. 2010) with data suggesting the effect of loneliness on one's health equates to smoking a pack of cigarettes a day (ibid.), there are bottom-line health benefits to an approach that can provide the sense of community and connectedness that cohousing offers. The colocation of a group of people also makes the delivery of various care services a lot easier (See ► "Aging in Place: Maintaining Quality of Life for Older Persons at Home"). While this is true of other forms of accommodation for older people, the difference here is that people are in their own homes in cohousing and not in a specific retirement or care institution. Data from the Australian Government have determined that the cost of providing care in peoples' own homes is also far cheaper (Australian Institute of Health and Welfare 2018). While very high care may be better delivered in an environment specifically set up for that, it is clear that there is bottom-line value providing a level of care in the "own home" cohousing approach. And it opens up all sorts of sustainability advantages, not just the economic and social ones highlighted, but colocating a group of purposeful residents committed to sharing means that environmental benefits would also accrue (ISF 2018) (See ► "Corporate Social Responsibility and Creating Shared Value").

So why isn't it more popular? The UTS ISF report, through focus groups, identified potential barriers and found there was a general lack of awareness about cohousing. Even when explained, while attractive, participants were generally unsure about the practicality of such an arrangement, identifying legislative, financial, and social issues. How does inheritance work? What if we lose friends?

Summary

While more established in Europe and to a certain extent in the USA, cohousing is still in its infancy as a choice for older people in many parts of the world. The potential benefits for older people mean that it could provide an attractive option for them and a significant solution to many of the issues facing people as they get older. As discussed, it helps alleviate alienation and isolation by creating community bonds within the development and ideally keeps people close to their local community. It gives people personal, social, and financial security. It provides a missing link between the more formal older person-specific housing and the family home. It uses land more responsibly and frees up larger houses for others. It is sustainable. At the very least, it provides another option for people as they decide where and how they want to live as they grow old.

Cross-References

- ► Accommodation Downsizing
- ► Affordable Housing
- ► Aged Care Homes
- ► Aging in Place and Quality of Life
- ► Aging in Place: Maintaining Quality of Life for Older Persons at Home
- ► Aging in the Right Place
- ► Autonomy and Aging
- ► Congregate Housing
- ► Corporate Social Responsibility and Creating Shared Value
- ► Home Equity Conversion
- ► Housing
- ► Joint Tenancy and Tenancy in Common
- ► Residential Happiness and Quality of Life
- ► Retirement Villages
- ► Senior Entrepreneurship
- ► Social Integration
- ► Social Participation

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Collaborative Housing

▶ Cohousing

Collateral Demographic Dividend

▶ Demographic Dividend

Colorectal Adenocarcinoma

▶ Tumors: Colorectal

Colorectal Cancer

▶ Tumors: Colorectal

Combined Caregiving Careers

▶ Double-Duty and Triple-Duty Caregivers

Combined Caregiving Roles

▶ Double-Duty and Triple-Duty Caregivers

Coming-of-Age Novel

▶ Reifungsroman/Vollendungsroman/Bildungsroman

Communalism

▶ Familism

Communication Technologies and Older Adults

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Synonyms

Digital divide and older adults; Digital exclusion at old age; Digital technology and aging

Definition

Information and communication technology (ICT) is the general term used to describe all media utilized in the communication of information (Chandler and Munday 2016). Older adults may conceptualize ICT as both the tools and the tasks completed while using them (Hill et al. 2015). These tasks can be categorized as transportation and mobility technology (e.g., ride-share services), health and wellness technology (e.g., pedometer and other exercise tracking devices and applications, online medical portals, medical alert buttons), socialization technology (e.g., social networking, email and messaging programs, online dating services), educational and informational technology (e.g., massive open online courses, search engines), and instrumental or functional technology (e.g., online banking or shopping).

Overview

Recent estimates suggest a rapid increase in ICT use among the older adult population worldwide (see ▶ "Digital Participation"). In 2016, 67% of US adults over the age of 65 reported Internet use, as compared to only 12% in 2000 (Anderson and Perrin 2017). Of these individuals, 17% reported using the Internet once daily, 51% reported multiple uses per day, and 8% reported constant Internet use. There is a notable age effect even among older adults, with 82% of relatively younger cohorts (65–69 years) reporting regular Internet use, but only 44% of the oldest old (80+ years) acknowledging Internet use (Anderson and Perrin 2017). These patterns extend to other forms of ICT; there has been an increase in the proportion of older adults utilizing smartphones (42%), tablets (32%), and social media (34%) from 2013 to 2016, while e-reader usage has remained stable (19%; Anderson and Perrin 2017). Approximately 18% of older community-dwelling adults use Skype or other video-chatting services (Teo et al. 2019). These rates are roughly commensurate with international statistics (Konig et al. 2018), which purport a median computer and Internet use rate of 49% across European nations, with Croatia citing lowest older adult use (27%) and Denmark citing the highest (83%). Older adults appear to utilize ICT for a variety of purposes. While most seniors use digital technology for informational (i.e., knowledge seeking, education, viewing pictures and videos) and social activities (e.g., writing emails or messages), a smaller proportion also employ ICT for instrumental purposes, such as online banking, shopping, or healthcare and legal activities (Schehl et al. 2019; Hunsaker and Hargittai 2018).

Despite growing familiarity with and use of ICT in the older adult population, the number of seniors engaged with communication technology continues to lag significantly behind that of the general population, 90% of whom regularly use the Internet and associated technologies (Anderson and Perrin 2017). Referred to as the digital divide, this age effect has been explained as older adult disengagement from ICT due to limitations in access, knowledge, ability, or motivation (Siren and Knudsen 2017). Digital exclusion has a negative impact on all facets of successful aging. Among nonusers, it appears to exacerbate existing age-related problems such that those with limited education or occupational history; declining cognitive, physical, or functional abilities; poor health; or a paucity of social connections least likely to be capable of or invested in learning new technologies, despite the potential for greatest gain. In contrast, those who are already socially supported, educated, and able are more likely to expand these strengths through ICT. One older adult drew a pertinent parallel between the modern digital divide and historical literacy and education gaps:

> If you...can't use a computer these days it's like...not being able to sort of read or write 50 years ago). (Hill et al. 2015, p. 418)

Key Research Findings

Factors Impacting Communication Technology Use in Older Adults

Demographic Factors

As previously noted, age affects the use of ICT even within the older adult population. Individuals born during or after the second World War are more likely to utilize the Internet, likely because those born before this date retired prior to widespread implementation of the Internet and associated technologies and devices in the workplace (Gilleard and Higgs 2008). Indeed, computer use as part of one's occupation predicts internet use postretirement (Friemel 2016; Konig et al. 2018). The role of early-life technology exposure in predicting late-life ICT use is also exemplified by the positive relationships between education (Konig et al. 2018), employment (Siren and Knudsen 2017), income (Konig et al. 2018; Arcury et al. 2018), and Internet use among seniors; those older adults with the financial resources to access novel technology as it is developed are understandably more motivated and likely to use it. Socioeconomic status (SES) also interacts with other demographic factors to predict ICT use. In older adults of minority race and ethnicity, lower SES reduced the odds of ICT use for health information (Yoon et al. 2018), with some studies estimating racial differences in use of up to 24% (Anderson and Perrin 2017). Studies of sex differences have produced mixed results (Hunsaker and Hargittai 2018), with the earlier finding of lower use among women diminished after controlling for other socioeconomic variables (Friemel 2016; Konig et al. 2018). A more nuanced analysis of technology use might provide some insight into the complexity of gender differences; while older men are more likely than older women to partake in informational and instrumental activities using ICT, both sexes are equally likely to use digital technology for social networking purposes (Schehl et al. 2019).

Social Factors

As part of Rowe and Kahn's model of successful aging (1987), social engagement is a critical predictor of health across the lifespan. The development of digital ICT has expanded opportunities for not only information gathering but also social interaction and support that is unhindered by tangible limitations such as distance, transportation, weather, and physical impairments (see ► "Social Isolation"); however, a variety of social factors predict older adult ICT use, contributing to the digital divide. Partners' use of the Internet, as well as household familiarity, predicts engagement with ICT (Konig et al. 2018), as does simply living with a spouse (Vroman et al. 2015). Other forms of "social capital," or social integration and network (Choi and DiNitto 2013) predict the extent to which digital technology is used and for what purpose; individuals with limited social capital due to personal factors (e.g., anxiety) and behaviors (e.g., less religious service attendance, less engagement in community volunteering) are less likely to utilize ICT. Additional, macro-level socio-ecologic factors, such as the extent to which a region has technological infrastructure including broadband connections, density of technology, and affordable access to tools and means, may impact use (Konig et al. 2018), resulting in significantly higher use in urban areas and developed countries.

Psychological Factors

A combination of general and technology-specific psychological factors appears to predict ICT use in older adults. Individuals who describe themselves as lonely (see ► "Loneliness") tend to cite lack of access to digital technology, as opposed to a lack of interest, as the primary reason for limited use (Helsper and Reisdorf 2013). In contrast, older adults who describe themselves as shy cite low interest as opposed to access limitations. Furthermore, lower depressive and anxiety symptoms and higher global cognitive ability are associated with more Internet use (Hamer and Stamatakis 2014; Choi and DiNitto 2013); this relationship is likely reciprocal, with greater Internet use also promoting improved mental and cognitive health (Hunsaker and Hargittai 2018). Regular senior digital technology users describe themselves as being satisfied, persevering, physically and emotionally independent, and having a positive outlook on life (Vroman et al. 2015).

While general locus of control, or the extent to which one feels control over one's behavior and fate, does not appear to impact engagement with ICT (Helsper and Reisdorf 2013), poor technology self-efficacy and confidence does. Among older adults, only 26% of those using the Internet also say that they feel confident using smartphones, computers, or other electronic devices to access it (Anderson and Perrin 2017). Additionally, 73% endorsed needing assistance from others to set up and demonstrate the use of new electronic device purchases (Anderson and Perrin 2017). This combination of personal knowledge and skills and sense of support from others, also known as perceived behavioral control, predicts engagement in informational, social, and instrumental online activities in older adults (Schehl et al. 2019; Chu 2010). Older nonusers rate themselves as intimidated and anxious around technology (Vroman et al. 2015) and report high levels of "computer stress" (Arcury et al. 2018). In contrast, those with higher self-assessed general abilities (e.g., vocabulary, numeric ability, problem-solving), technology-specific skills and knowledge, and confidence in ability to learn the technology are more willing to adopt novel ICTs (Berkowsky et al. 2018). These technology self-efficacy variables may better account for the digital divide than cohort itself; a recent study suggested that, though age and other demographic variables predict Internet use, the effect was fully moderated by perceived skill and motivation variables, such as willingness to take a course in technology or a desire to become better at ICT use (Siren and Knudsen 2017).

Beliefs About ICT

The majority of research surrounding older adult beliefs and biases about technology has been qualitative in nature, making it difficult to generalize to the larger population; nonetheless, consistent themes have emerged to support the idea that the perceived value and positive and negative impacts of ICT on quality of life shape use among older adults (Berkowsky et al. 2018). Most older consumers hold positive views of ICT, with 58% rating its impact on society as beneficial, 33% rating its impact as neutral, and only 4% rating its impact as primarily deleterious (Anderson and Perrin 2017). Among these benefits is the idea that ICT allows older adults to overcome the physical barriers of distance, mobility, time, weather, and transportation access to continue participation in social and cultural activities (Hill et al. 2015). In contrast, many older adults harbor concerns that technology is fallible and error-prone, particularly in the hands of a relatively unskilled user unable to identify and resolve issues as they arise (Hill et al. 2015). Fear of a breach in the security of the device and their associated personal information is a major deterrent to use among older adults (Hill et al. 2015). Older adults may also have biases about the broader cultural context created by technology, as it compares to their personal experiences in early life; some seniors describe technology as "de-skilling" younger generations' ability to write, problem-solve, live independently, or become comfortable in their own company. Furthermore, the forced evolution of etiquette and boundaries due to ICT (e.g., taking a phone call or text in a public location or using social networking while out to dinner) may be difficult for some older adults to accept (Hill et al. 2015).

The Relationship Between ICT and Health ICT use has shown promise to improve mental and physical health in the aging population (see ► "Health 3.0"). Data from the Health and Retirement Study (HRS) indicate that ICT use and Internet comfort may lower the risk for late-life depression by up to 20–28% (Cotton et al. 2012). Specifically, the use of video-chatting technologies by older adults, even as compared to email, social networking, and instant messaging, may lower risk for depressive symptoms by up to 50% (Teo et al. 2019). When social intimacy is grossly limited by physical and practical factors, the enhanced sense of connectiveness with others through ICT likely contributes to this effect (Cotton et al. 2012). Given the known negative health effects of depression and loneliness, particularly for older adults, it is possible that future research may determine that ICT elicits additional benefits.

Several health factors do, however, affect ICT use in older adults. Although health literacy, knowledge, and attitudes, along with medical decision-making ability, predict Internet use in American older adults, health status (i.e., overall medical severity) may not (Arcury et al. 2018). Dementia constitutes a caveat to this finding; while individuals with new-onset depression or other medical diagnosis appear to use ICT with the same or increased frequency, individuals diagnosed with dementia tend to reduce use (Levine et al. 2018). Longitudinal research is needed to determine whether diminished use occurs as result of mood, behavioral, or cognitive symptoms associated with dementia or rather because dementia is simply more prevalent in the oldest old (those who statistically use ICT less). Nonetheless, cognitive and functional deficits do appear to create barriers to effective ICT use for older adults. In a study of working older adults aged 60–79, ICT experience and willingness to work with a computer were undermined by age-related deficits in task-switching (Ogata et al. 2012). Similarly, in the population of US older adults receiving Medicare benefits, Internet use has been growing in almost every demographic group, with the exception of those with functional impairments (Greysen et al. 2014). In fact, individuals diagnosed with a new dementia (−26%), a decline in functional status (−10%), a decline in mobility or physical ability (−3%), or relocation to a nursing facility (−31%) decrease in likelihood of using these technological advances (Levine et al. 2018).

Examples of Application

Although ICT use appears to be less frequent in those with Alzheimer's or another neurodegenerative dementia, digital technology itself has allowed for improved assessment, diagnosis, and treatment of these diseases. ICT has allowed for the development and validation of novel assessment tools, including imaging and video processing technology-assisted evaluations for functional (Sacco et al. 2012) and behavioral symptoms (Romdhane et al. 2012) in Alzheimer's dementia, and affective symptoms in those without it (Gros et al. 2016) (see ▶ "Mobile Data Collection with Smartphones"). ICT has provided new frameworks and modalities for cognitive rehabilitation or cognitively stimulating therapies targeting dementia(see ▶ "Telemedicine"). These studies have demonstrated that, though moderated by technological knowledge and comfort of the patient, the introduction of ICT assistive devices or training tools results in improved cognitive outcomes, quality of life, and ability to age in place (D'Onofrio et al. 2016).

Summary

Although still apparent in the oldest old, the digital divide is rapidly diminishing in older adults, through better understanding of the factors that predict use and nonuse, improved interface design and education, and expanded benefits for the aging population. Increased technological reach, in combination with the aging of a more technologically literate older adult population, has also addressed this critical barrier for older adults. Digitalization may present an intimidating challenge for many older adults; however, embracing ICT may allow for broadened connections, increased knowledge, continued empowerment and autonomy, and cognitive and functional benefits, ameliorating the effects of aging.

Cross-References

▶ Ableism and Ageism
▶ Digital Participation
▶ Health 3.0
▶ Loneliness
▶ Mobile Data Collection with Smartphones
▶ Social Isolation
▶ Telemedicine

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Community

▶ Cohousing

Community Health for Older Adults

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Synonyms

Community-based geriatric care; Population health, Public health

Definition

The term, community health, is conceptualized broadly as the social, physical, economic, and environmental characteristics of a geographically defined community (e.g., city, neighborhood, or state) or a population-defined community (e.g., persons over 65 years). Considered as a field within the discipline and practice of public health, the purpose of community health is to address public health problems that impact the well-being of members of that community (Newton 2013: 197). Not only does community health refer to the health status of a group of persons (i.e., the community), but the concept encompasses "…actions and conditions that promote, protect, and preserve the health" of the individuals within the designated community (McKenzie et al. 2012: 7). In defining community health of older adults, this population may be older adults in a geographical locality or older adults as members of a defined community (e.g., older African Americans with dementia).

Community-health actions can be implemented by private or public organizations or individuals. For example, a health fair for older adults sponsored by a federally qualified health care clinic is a community health program that promotes health and well-being of a group of individuals within a community. A nonprofit community-based organization (e.g., Alzheimer's Association) that focuses on community-wide education and services related to brain health and well-being of persons with dementia and their care partners is also a community health program as this organization provides community-based health education, influences policy, and supports research. A similar term, population health, refers to the health status of people living in the community but differs in that they are not organized or identified by locality (e.g., all persons over 65 years) (McKenzie et al. 2012).

Overview

Community health for older adults encompasses an array of age-related issues, programs, and services focusing on social, physical, economic, and environmental factors and individual and community interactions with systems in those environments. Community health is a process that emphasizes behavioral and environmental strategies that target individual health behaviors; identifies environmental, social, and disease causal factors; and conceptualizes health as greater than the individual (Kelly 2009). An effective community health effort to optimize successful aging requires a coordinated community effort implemented by persons knowledgeable about geriatric issues, syndromes, and resources. Having knowledge of the aging process and age-related changes relevant to specific older adult populations identified for community health interventions is essential. While it is well-known that the number and longevity of older adults has been rising for decades, less is known about related health and lifestyle changes. The number of older adults with chronic condition is increasing. Numbers of Medicare beneficiaries with documented chronic conditions are at high levels across disease spectrums, including: dementia (10%); arthritis (30%); cancer (8%); chronic obstructive pulmonary disease (11%), depression (17%); and diabetes (27%) (Centers for Medicare and Medicaid Services 2018). Such illness can create functional limitations, major lifestyle changes, co-morbid illnesses, social isolation, and needs for support, particularly when the older adult's goal is to remain in the community. Because longevity is increasing, health and social service professionals must be aware of the needs of those they serve and resources available in their communities to support optimal well-being. Needs can be health and/or social, including: economic, housing, transportation, and personal care (McKenzie et al. 2012). Whether the focus is on an individual, group, or community, interventions must be accessible and targeted to meet prioritized needs, including asking the older adults to identify their needs.

Community health programs are often locally based efforts that provide geriatric health education and promotion and treatment of age-related chronic conditions specifically designed for persons in the defined target community most in need (Gourley et al. 2015). Offering a geriatric health screening event through churches is a strategy that identifies potential health concerns and provides educational and prevention-focused information to individuals and the community (See ► "Neighborhood Social Environment and Health"). Emphasizing a community-engaged focus (i.e., collaborating with members with lived experiences related to target community) in interventions and research can also enhance outcomes by integrating members' insights and experiences (Fortuna et al. 2019). For example, Fortuna et al. (2019) partnered with certified peer specialists to offer a peer-delivered mobile health (mHealth) intervention for older adults with serious mental illness (SMI) using eModules and a smartphone app (See ▶ "Mobile Health"). Reported outcomes for this approach include improvements in self-efficacy, hope, quality-of-life, self-management, and feelings of empowerment (Fortuna et al. 2018a).

When developing intervention strategies with the goal of promoting health for older adults, factors that may impact the population and the intervention must be taken into consideration (McKenzie et al. 2012):

- *Physical environment*: Size, environment, and past and current industrial development
- *Social and cultural characteristics*: Beliefs, traditions, prejudices, economic assets and challenges, political climate, religious and spiritual influences, and socioeconomic status
- *Community organization*: Determining the way in which a community organizes and prioritizes its resources
- *Individual profile*: Those actions taken by individual older adults to promote the health of themselves and their community (e.g., getting an annual flu vaccination).

Community health strategies to promote and preserve health for older adults are multifaceted and include the following.

Primary Care and Prevention

With the number of older adults increasing and the number of geriatricians and health care providers specializing in the care of older adults declining (American Geriatrics Society 2017), the primary responsibility for providing health education, promotion, and treatment falls to providers in primary care settings. While physical health needs can be met, social and personal care needs may go unnoticed if not included in assessments conducted by an interprofessional team. Siegler et al. (2015) report that most health care providers lack knowledge of available resources and mechanisms for patients to access needed services. Norman et al. (2018) report that providers find service coordination difficult. Integrating person-centered care teams into primary care settings eases the navigation through complex health systems for older adults and caregivers (Lafortune et al. 2015) (See ▶ "Person-Centered Care for Older Adults"). Along with addressing social needs, primary care providers can engage in community health prevention and promotion strategies by integrating geriatric-specific assessment, education, and intervention in the areas of vaccinations, fall prevention, diet, physical activity, oral health, and brain health (See ▶ "Preventive Care"). As an example, the Rapid Geriatric Assessment (Morley 2017) assesses for frailty, sarcopenia, anorexia, and cognitive function, provides literacy appropriate patient materials and encourages follow-up testing and/or treatment with the older adult's health care team.

Treatment and Interventions

Managing acute and chronic medical conditions within a geriatric population can be approached from a community health perspective (See ▶ "Ambulatory and Outpatient Care"). While treatment of the individual is the core of care provided, strategies to promote quality-of-life and prevention of disease progression can be introduced into care plans involving the patient, caregivers, and other health care team members for conditions and needs, including: cardiovascular disease, hypertension, diabetes, cancer, psychiatric and behavioral health (e.g., depression and cognitive impairment), and advance care planning and palliative care. Such interventions should be delivered with cultural competence and humility and designed to meet the needs of the older adult population being treated. Building on an ongoing assessment of needs and concerns using a team approach, older adults can be supported as they navigate community-based, acute, post-acute, and long-term care systems.

To further optimize older adult well-being and health, public, nonprofit, and for-profit community-based programs and services supplement the care received to enable older adults to maintain and improve health and function (See ▶ "Home and Community-Based Services"). Four general areas include:

- *Nutrition and home-related service.* Often provided through programs funded by the Older Americans Act and state and local agencies, congregate and home-delivered meals, homemaker/chore services, and senior center-based programs provide access to resources that empower older adults to remain in the community, particularly for those with the greatest needs (Siegler et al. 2015) (See ▶ "Older Americans Act"; ▶ "Congregate and Home-Delivered Meals").
- *Home health services.* Typically provided by an interprofessional team, including nursing, occupational, speech, and physical therapy, and social work, health care and social services provided to older adults in-home or via telehealth delivery promotes a range of positive health and social outcomes for older adults. Outcomes reported include: decreased social isolation, continued independent living, increased sense of security, improved self-management of medical regimens, and decreased emergency and hospital-based care admissions (Husebø and Storm 2014; Miner et al. 2017).
- *Adult day services.* Aimed at enabling older adults to live in their own or caregivers' homes, adult day services typically provide day-time services that promote a safe and stimulating environment for older adults who can benefit from supportive care (See ▶ "Adult Day Services"). Health, social, psychological, and behavioral outcomes for both the older adult and the caregiver have been reported (Ellen et al. 2017).

Community health workers. A recent addition to the geriatric workforce, community health workers serve as extensions of health care systems to provide such services as health system navigation, outreach, and care management to improve access and integration of care and decrease the fragmentation and disparities that exist (Kaur 2016). Community health workers serve as liaisons between the older adult community and the community- and health care-based organizations that provide care and services. Employed in public health centers, social service agencies, and health systems, community health workers provide prevention and health promotion education, advocacy, and build capacity for those older adults in a geographic or defined community (Rapkin 2015). Another emerging group within the workforce is peer specialists. As members with ties to the target community who have lived experience with the health and social issues being addressed, peer specialists' ability to engage with community members is reported to positively influence: health behavior change, inpatient service use, relationships with providers, and sense of empowerment, activation, and hopefulness (Chinman et al. 2014; Fortuna et al. 2018b). As noted, the inclusion of certified peer specialists in delivering a technology-supported intervention for community-dwelling older adults informs and guides the use of peers and technology in serving older adults (Fortuna et al. 2018a, b, 2019).

Examples of Application

There are many innovations of community health programs designed primarily for older adults. Community health programs for older adults are focused on health promotion, health education, and prevention and/or treatment. Examples of these programs include the Program of All-Inclusive Care for the Elderly (PACE), home-based primary care (HBPC), and Independence at Home (IAH) (See ▶ "Program of All-Inclusive Care for the Elderly (PACE)"). Started in the 1970s as an alternative model to nursing home care, PACE was developed as a community-based care model to deliver comprehensive medical and social services for frail community-dwelling older adults (Cortes and Sullivan-Marx 2016). Through an interdisciplinary team-based care approach, PACE provides preventive, primary care, acute, chronic care, and long-term services and supports for older adults to help them remain living at home and delay placement into residential long-term care (Cortes and Sullivan-Marx 2016). PACE participants, most of whom are dually eligible for Medicare and Medicaid, tend to be the most frail and vulnerable population of community-dwelling older adults with chronic medical conditions, functional limitations, or cognitive disabilities and have higher cost of care due to their needs (Bloom et al. 2011). The effectiveness of PACE in improving health outcomes and quality of life of older adults, lowering health care cost, and decreasing nursing home placements and hospitalizations have led to the PACE Innovation Act being legislated in 2015 to expand this program (Cortes and Sullivan-Marx 2016).

Home-based primary care (HBPC) is the practice of delivering primary care services to older adults in their home. In response to the evolving health care policies and growing population of older adults with increasingly complex health care needs, different models of HBPC have proliferated. Models vary in terms of clinical and nonclinical staffing, funding source, institutional support, range of services, and geographical boundaries of services (DeCherrie et al. 2012). Often aimed at reducing emergency department visits and hospitalizations, HBPC services can include management of acute issues, post-acute care, chronic conditions, and health maintenance. HBPC models enable health care professionals to assess older adults in their own home and social environment, functional limitations, safety, and nutritional status (DeCherrie et al. 2012). The Veterans Health Administration (VHA) has been implementing its HBPC program since the 1980s, using an interdisciplinary team to deliver a comprehensive range of services for patients with complex health care needs (DeCherrie et al. 2012). Independence at Home (IAH) is an HBPC initiated by the Centers for Medicare and Medicaid Services (CMS) Innovation Center as a demonstration project. IAH targets Medicare beneficiaries with multiple chronic conditions and functional limitations, who can be high risk and high cost patients (Rotenberg et al. 2018). Primary care service is delivered by interdisciplinary teams to older patients in the home (Rotenberg et al. 2018).

Screening and Assessment

Preventive services are critical for older adults' health, not only to prevent morbidity and mortality but also for early detection and intervention of chronic disease, health maintenance, and overall quality-of-life. Timely screening and assessment can identify specific deficits or decline and prompt appropriate intervention or accommodation. Screening instruments and assessments tool are available for many types of health issues/conditions (FRAIL scale, Simplified Nutritional Assessment Questionnaire (SNAQ), Rapid Cognitive Screen (RCS), and Michigan Alcohol Screening Test-Geriatric Version). Not all-inclusive, the following discussion highlights several major geriatric syndromes and issues:

Frailty is defined as "state of increased vulnerability from age-associated decline in reserve and function resulting in reduced ability to cope with every day or acute stressors" (Lee et al. 2018: 2), while frailty phenotype consists of fatigue, weakness, slow gait, low physical activity, and weight loss (Walston et al. 2018) (See ▶ "Frailty Screening"). Frailty prevalence rates range from 4% to 59% among community-dwelling older adults (Collard et al. 2012). Identifying and addressing frailty can prevent adverse health outcomes for older adults, such as falls, disability, morbidity, and hospitalizations (Lee et al. 2018).

Older adults at nutritional risk or malnourished can experience weakness, sarcopenia (muscle weakness), cachexia, poorer wound healing, infections, lower immunity, and increased risk of morbidity (Laur and Keller 2017) (See ▶ "Nutrition Issues in Geriatrics"). Conversely, older adults with obesity have higher risk of functional impairment, morbidity, increased utilization and cost for health care, and mortality (Batsis et al. 2017). Nutritional screening can identify significant weight changes, underweight or overweight status, changes in appetite, or imbalance intake (Laur and Keller 2017) so that appropriate dietary or behavioral interventions can be recommended. Decrease in appetite and food intake has been linked to depression, cognitive impairment, and social isolation among older adults (Landi et al. 2016); hence the importance of nutritional screening to detect changes in appetite and food intake to prevent anorexia of aging (See ► "Anorexia of Aging"). A relatively novel approach, the use of wearable activity device, a type of mobile health (mHealth) technology, has been evaluated and found to be feasible and acceptable among older adults to support behavioral change for weight loss (Batsis et al. 2016) (See ► "Wearable Technology"). Benefits cited by older adults include the ability to self-monitor, obtain real-time feedback on activity, and motivation (Batsis et al. 2016).

Cognitive screening is used to detect cognitive impairment or decline in older adults, which can indicate a medical or neurological disorder. Early detection of cognitive impairment or decline among community-dwelling older adults can lead to proper diagnoses, and in the case of mild cognitive impairment or dementia, planning to address home safety, driving and other risk issues, plan for long-term care services, address financial or legal matters, receive pharmacological management to address symptoms, and non-pharmacological interventions to improve functioning (Ismail et al. 2010).

Alcohol is the most commonly used substance among older adults, with an estimated prevalence rate of 62% (Han and Moore 2018) (See ► "Alcohol Consumption and Health"). Prescription drug misuse is increasingly prevalent among older adults, particularly opioids prescribed for pain management and benzodiazepines (Han and Moore 2018). Age-related physiological changes render older adults more vulnerable to the negative impact of substance abuse, such as worsened medical conditions, harmful interaction with prescribed medications, overdose, falls, injuries, accidents, and hospitalizations (Han and Moore 2018) (See ► "Substance Abuse and Addiction"). Screening for alcohol and drug abuse among older adults can be challenging, yet critical to prevent adverse health outcomes.

Key Research Findings

Due to the wide array of community health programs and services for older adults, research encompasses a broad range of programs, services, and outcome evaluations. PACE program research, for example, reports that participants experience significant decreases in hospitalizations, readmissions, and potentially avoidable hospitalizations (Segelman et al. 2014; Meret-Hanke 2011); decrease of emergency department visits and skilled care placements; and functional improvement (Fretwell et al. 2015). A systematic review on home-based primary care programs for community-dwelling homebound older adults reported significant decrease in emergency department visits, hospital and long-term care admissions, improved screening for geriatric syndromes and vaccination rates, improved quality of life and satisfaction of care among the older adults and their caregivers, and initiation of end-of-life discussions (Stall et al. 2014). A study of the BRIGHTEN program (Bridging Resources of a Geriatric Health Team via Electronic Networking), a virtual multidisciplinary primary care team-based intervention, showed that this program was effective in reducing depressive symptoms and improving mental health in a diverse group of community-dwelling older adults, suggesting evidence of benefit of integrating behavioral services into primary care services (Emery-Tiburco et al. 2017). A review of 76 studies on adult day services found participation in these services resulted in positive health, social, and behavioral outcomes for the older adults, and generally high satisfaction with service among older adults and caregivers (Ellen et al. 2017). A systematic review of community health worker interventions to improve health care access among ethnic minority older adults yielded positive outcomes, including higher rates of preventive screenings and follow-up, and improvements in diet and physical activity (Verhagen et al. 2014).

Gaps and barriers in health care service delivery, which inform how community health programs and services can be improved for older adults, is well studied. For example, older adults who fail to follow-up with their primary care physician after a hospital discharge have greater likelihood of readmission within 90 days (Hardman and Newcomb 2016). Older adults who live in rural settings face additional barriers in terms of accessing primary care services, such as lack of transportation, geographical distance of outpatient clinics, poor health coverage, long wait times, and shortage of physicians in the community (Hardman and Newcomb 2016). A study of Medicare home health patients identified factors associated with increased risk of hospitalization including history of multiple hospitalizations, taking five or more medications, depressive symptoms, frailty symptoms, functional limitations, heart disease, urinary tract infection, chronic obstructive pulmonary disease, and skin wounds (Lohman et al. 2018). Results can inform home health agencies and other community-based health providers to identify older adults with higher risk of hospitalization and increased their monitoring or services. In sum, research on community health for older adults cover myriad topics related to the different aspects of geriatric health care and issues.

Future Directions of Research

While considerable research exists across the spectrum of community health programming for older adults, a clear research agenda is lacking. Included in the Medicine/Public Health Initiative (developed by the American Public Health Association and the American Medicine Association) are goals calling for research agendas that focus on interdisciplinary teams studying health problems and integrating health promotion into community-based care interventions (Gourley 2018). Such goals can be extended to community health for older adults to establish an agenda for research that includes a range of education and intervention-focused strategies to determine their efficacy. Used to improve access to health care providers, management of health care directives, and quality-of-life for older adults (including social isolation), areas to be further studied include: (1) evaluate and standardize processes for helping older adults navigate the current health care system and evaluate the knowledge of health professionals in engaging patients in decision-making (Elliott et al. 2018); (2) determining the financial and health outcomes impact of community health programs and services on utilization of emergency care, hospital admission-readmission, and care transitions; (3) role and legal and ethical implication of technology, including social assistive devices, tablet- and smartphone-based resources, and motion mapping (i.e., wearable sensors that can aid in assessment, early detection, and intervention/management of psychiatric symptoms, movement and fall risk, and physical activity)) (Collier et al. 2018; Fortuna et al. 2018a; Vahia and Ressler 2017). Such research can further provide evidence-based strategies for the role of community health workers and care managers in helping older adults and their care partners manage their health and chronic conditions.

Summary

Community health for older adults is a broad concept that encompasses public health, educational, and service delivery components. Promoting common understanding among health care professionals, the community, and older adults themselves through person-centered health education, health promotion, and interventions has the potential to significantly change the experience of aging as well as traversing the often-fragmented health care system. Calling for the creation of age-friendly health systems and dementia-friendly communities can improve the responsiveness from and access to services and providers who understand the needs of the older adult (Sanford et al. 2019).

Cross-References

▶ Adult Day Services
▶ Alcohol Consumption and Health
▶ Ambulatory and Outpatient Care
▶ Anorexia of Aging
▶ Congregate and Home-Delivered Meals
▶ Frailty Screening
▶ Home- and Community-Based Services (HCBS)
▶ Neighborhood Social Environment and Health

▶ Nutrition Issues in Geriatrics
▶ Older Americans Act
▶ Person-Centered Care for Older Adults
▶ Preventive Care
▶ Program of All-Inclusive Care for the Elderly (PACE)
▶ Wearable Technology

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Community Housing

► Social Housing

Community Involvement

► Social Participation

Community Nutrition Program

► Congregate and Home-Delivered Meals

Community Participation

▶ Social Participation

Community-Based Geriatric Care

▶ Community Health for Older Adults

Community-Based Long-Term Care

▶ Program of All-Inclusive Care for the Elderly (PACE)

Companion Pets

▶ Pet-Raising and Psychological Well-Being

Compassion

▶ Altruism

Compassionate Release

▶ Older Prisoners

Compensatory Techniques

▶ Cognitive Compensatory Mechanisms

Complex Family Structures

▶ Family Diversity

Complexity of Family Relationships

▶ Family Diversity

Compliance

▶ Exercise Adherence

Comprehensive Care

▶ Comprehensive Digital Self-Care Support System (CDSSS)

Comprehensive Digital Self-Care Support System (CDSSS)

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Synonyms

Comprehensive care; Digital support for the aging; Self-care support

Definition

Comprehensive digital self-care support system (CDSSS) is defined as a self-care support system that employs varied digital technologies to provide a common platform for individuals (a) to acquire and integrate data and knowledge about their personal health (physical and mental) from varied sources and (b) to communicate with relevant entities in their self-care network to gain social and emotional (or empathetic) support for managing own health, thereby promoting holistic, preventive care.

Overview

The aging population, both within the USA and across the globe, is growing rapidly. By 2035, in the USA, the aging population (people above the age of 65) will be 78 million and will outnumber children (those below the age of 18) (US Census Bureau 2018). Given that the aging population uses much more healthcare resources than the younger population, the burden on our healthcare system, which is already staggering with high costs, will be prohibitive (Osborn et al. 2014). The use of healthcare resources is projected to increase, not just because of the rapid growth in the aging population but also due to the steady increase in chronic disease incidence among the aging (IoM 2012; McPhail 2016).

All of these imply the need to empower the aging population in ways that would help them develop a deeper understanding of their own care (Kahana et al. 2018), i.e., by the provision of more comprehensive and integrative care with a focus on *self-care* (Leenerts et al. 2002; Rowe et al. 2016). It also implies the need for more innovative and cost-effective solutions to reduce their utilization of healthcare services – specifically, solutions that leverage community and home-based resources and support. Indeed, there is a critical need for a **comprehensive digital self-care support system** (CDSSS) for the aging – one that utilizes new digital technologies, adopts a comprehensive or holistic perspective to care, focuses on prevention and self-care, emphasizes support resources from communities and other entities outside the formal healthcare system, and simultaneously helps improve the quality of life and reduce the healthcare costs.

Partly in response to this, in recent years, variations of such digital self-care support systems have emerged. By and large, these support systems have tended to cater to the need for self-management support and the need for chronic disease management (Gustafson et al. 2008; Gustafson et al. 2013). While self-care is sometimes interchangeably used with self-management (Jerant et al. 2005; Cimprich et al. 2005; Ryan and Sawin 2009), self-care has a broader focus on prevention, i.e., self-care also involves tasks undertaken by healthy individuals to prevent the onset of chronic diseases (Clark et al. 1991).

Studies show that informed health consumers – patients who are educated and understand their illnesses better – tend to comply more with their treatment (Jankowska-Polańska et al. 2016), ask their physicians the right kinds of questions (Sommerhalder et al. 2009; Oh and Lee 2012; Kahana et al. 2014), and overall fare better than those whose health literacy and knowledge regarding one's own health is low (Gustafson et al. 2008).

Despite these studies, there is a lack of in-depth understanding of what a comprehensive digital self-care support system (CDSSS) for the aging should be comprised of, their key functions, and their deliverables. While rapid advancements in digital technologies (e.g., mobile technologies, blockchain, social media, digital sensor, cloud computing, etc.) allow for the development of more versatile and multidimensional self-care support systems, most current systems are narrowly focused (e.g., on one disease) and not necessarily tailored for the aging population that is already struggling with a fragmented care system.

CDSSS-Related Needs of the Aging Population

The Centers for Disease Control and Prevention (CDC) estimates that 90% of our nation's 3.3 trillion-dollar annual healthcare expenditures are spent on individuals with chronic diseases, mostly the aging population. It is a very significant and critical burden for our economy. Six out of 10 adults in the USA have one chronic disease, and 4 out of 10 adults have more than one chronic disease (CDC 2018).

Another important issue, closely associated with chronic conditions among the aging, is comorbidity (Machlin and Soni 2013; Ward and

Schiller 2013; Bayliss et al. 2014). Increasingly, it is becoming evident that an individual with one chronic condition is more susceptible to other chronic conditions. For example, obesity, which is now classified as a chronic disease, is a risk factor for heart disease, stroke, cancer, chronic respiratory diseases, and diabetes (Bauer et al. 2014). It also appears that both heart disease and several cancers have the same set of risk factors (e.g., inflammation) and biological mechanisms (Prasad et al. 2012; Kitsis et al. 2018), which is a similarity that is seen with almost all other chronic conditions (Tu et al. 2018). All of this implies the critical need for **prevention-focused care**. Importantly, most chronic diseases are shaped to a great extent by individual's lifestyle choices and hence are preventable (Bauer et al. 2014; Tu et al. 2018).

The increase in chronic diseases has led the pharmaceutical industry to develop more powerful drugs. Such drugs with higher potency can induce severe drug-to-drug interactions and more severe and damaging side effects (Hajjar et al. 2007; Maher et al. 2014). In the USA, the proportion of people over the age of 65 who takes 5 or more medications has been rapidly increasing; one report estimates that it tripled from 12.8% to 39% between 1988 and 2010 (Charlesworth et al. 2015). Polypharmacy and complex medication regimen increase the likelihood of poor medication adherence, cognitive impairments, adverse reactions, and increased healthcare costs (Hajjar et al. 2007; Maher et al. 2014). Chronic conditions also result in patients receiving treatment from multiple specialty care providers that in turn leads to fragmented and disconnected care (Bayliss et al. 2014). To reduce the associated treatment burden and the potential harm that such fragmented care may cause among the aging population, there is a critical need for a more **comprehensive and integrative** approach to delivering care (Tinetti et al. 2012; Bayliss et al. 2014).

In this current fragmented healthcare delivery environment, self-care has been getting increasing attention, especially for managing multiple chronic conditions among the aging. While self-care has been shown to have positive impact on treatment outcomes and well-being of the aging population, a comprehensive and integrated approach with focus on self-care and healing has been difficult to achieve within our current healthcare model (Leenerts et al. 2002; Bayliss 2003). The key ingredient to realizing such a comprehensive approach to care is to have the ability to put the aging individual at the center of the care network (Epstein et al. 2010) and to provide an environment that would allow them with access to an appropriate set of resources (which includes knowledge and tools to collect and assess information on one's own health). This will enhance their ability to "take charge" of their own health. While many patient-centered models and patient-centered medical homes (PCMH) have adopted this as their central philosophy, implementing it within practices has been challenging (Nutting et al. 2009). A self-care support system that is rooted in the **community and home setting** could play an intermediary or supportive role for the healthcare system that aims to put the patient at the center.

Self-care has often involved tacit knowledge that people sometimes inherit from their parents or acquire from others around them; however, recent interest in alternative care has spurred an increased level of knowledge sharing on the Internet regarding self-care practices (Silva 2017), moving it from tacit to explicit knowledge. Adoption of self-care practices can be difficult for someone new to it. Further, self-care practices are also difficult to evaluate as what may be effective for one person may not be effective for another (or may not be needed altogether). This requires proper education and training for (a) understanding one's own body and the health issues and (b) finding an effective solution to alleviate the symptoms or to treat it. Home-based and mobile digital health monitors and trackers offer some insights into our body's functioning; however, self-care calls for more than that. Indeed, the key ingredient for effective self-care is the ability to actively *listen to one's body*. An integrated approach – that helps bring together information from personal health monitors, health providers, and peer communities via a knowledge sharing and knowledge creation platform (Nambisan and Nambisan 2009) – could provide the required **education and training for self-care** for the aging population.

Another important factor that goes hand in hand with chronic diseases is declined mental well-being, exacerbated by social isolation and loneliness among the aging (Shankar et al. 2017). Social support has been found to improve treatment outcomes, improve mental well-being, reduce stress, and help in developing and achieving health-related goals (Uchino 2004; Siedlecki et al. 2014; Cornwell and Laumann 2015). Moreover, *providing* social support could be just as important as, or even more important than, *receiving* social support in reducing mortality rate among the aging (Brown et al. 2003). As emphasized in the social science literature, reciprocity is important in relationship bonding, and such bonding is important for psychological and emotional well-being of the individual (Buunk and Schaufeli 1999). Similarly, in addition to social support, receiving empathy has also been found to be important for better mental well-being and for better treatment outcomes (Kim et al. 2004). To provide **social and emotional support** to geographically dispersed population, many healthcare organizations and public health agencies have been establishing online patient forums. However, these online forums have also been following a fragmented approach, i.e., focused on individuals with a specific disease rather than on the aging with multiple comorbidities.

Finally, the aging population also face needs associated with technology use. Recent surveys show an increase in the extent of technology use by the aging population (PEW Research Center 2017); however, there are still considerable barriers when it comes to using new technologies (Charness and Boot 2009). Data **privacy and security**-related issues have been found to be important in making older adults reluctant to use new technologies (Yusif et al. 2016). Similarly, usability issues have also, albeit to a lesser extent, been found to impact the use of new technologies (Lee and Coughlin 2015). Another critical factor relates to user's perceived experience in using the technology-based product (or service) – specifically, **positive experience** (e.g., fun) enhances the extent of use. Prior studies indicate that the aging population actively seek fun experiences (Karahasanović et al. 2009; Tingley 2018) and that fun experiences are critical for better mental well-being. In a study that surveyed older adults who used social media, it was found that fun or hedonic experiences have a statistically significant impact on mental well-being (Nambisan et al. 2014).

Key Research Findings

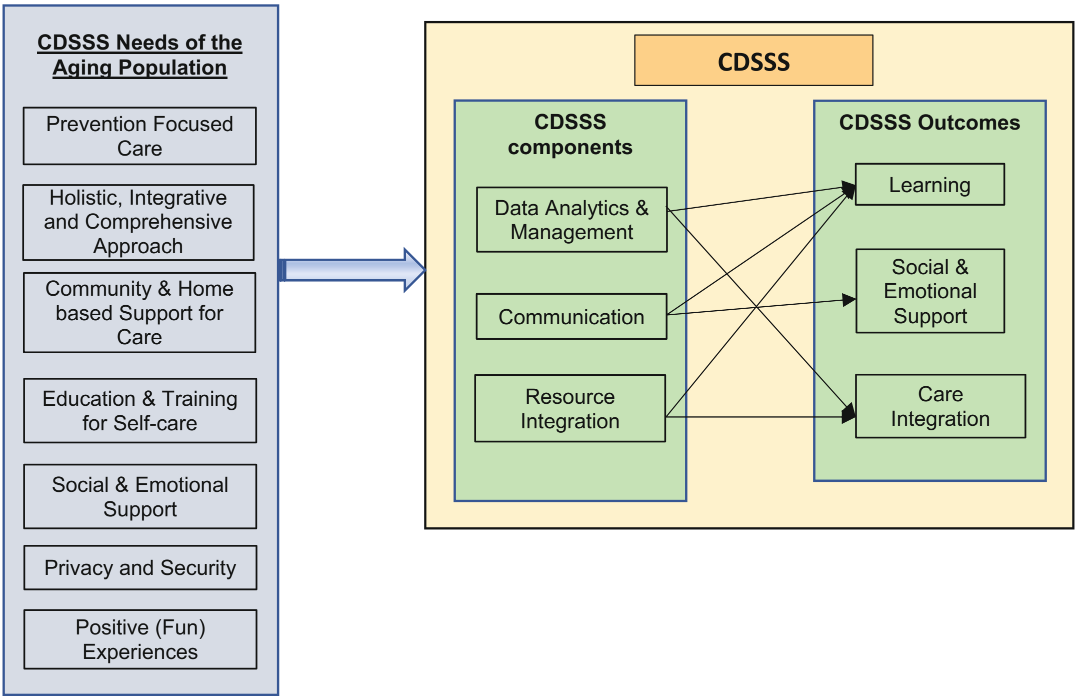
The above discussion indicates the critical need for a comprehensive, integrative, holistic, data and evidence-based digital self-care support system for the aging population. Specifically, the core needs of the aging population are (a) prevention-focused care; (b) holistic, integrative, and comprehensive approach to care; (c) support for community and home-based care; (d) education and training for self-care; (e) social and emotional support; (f) data privacy and security; and (g) positive (fun) experiences. Designing such a comprehensive system calls for drawing on ideas and concepts as well as empirical studies from varied disciplines to evaluate the effectiveness of various design aspects. The CDSSS framework presented below takes an initial step in this direction by identifying the key structural components and deliverables and relating them to the above needs (see Fig. 1).

Designing of a Comprehensive Digital Self-Care Support System (CDSSS)

Structure of a CDSSS

There are three main components in a CDSSS: (a) data analytics and management, (b) communication, and (c) resource integration.

Data Analytics and Management The first component of a CDSSS, *data analytics and management*, involves the use of varied digital technology-based devices, tools, and techniques to acquire, analyze, and learn from a wide range of personal health data. This includes digital health trackers and monitors that help acquire different types of data (e.g., weight, blood pressure) as well



Comprehensive Digital Self-Care Support System (CDSSS), Fig. 1 Comprehensive digital self-care support system (CDSSS) framework

as research-based health questionnaires (e.g., PROMIS scales) (Spiegel et al. 2014) that allow individuals to gather perceptual data on daily health issues (e.g., sleep pattern). However, such personal health data are useful only when individuals are empowered to analyze them and personalize the associated learnings. Data analytic tools with visual or graphical outputs can support such learning, i.e., how different types of personal health data may relate to or are associated with one another. For example, the PatientsLikeMe forum allows its users to analyze and learn from not only one's own data but others' as well (Frost and Massagli 2008; Wicks et al. 2010). As increasing numbers of people (both young and old) start using digital health trackers (as evidenced from the popularity of the term "digitized self"), such data analytics and data integration capabilities will become an essential component of CDSSS. Further, as healthcare organizations promote the use of online patient portals, the ability of CDSSS to connect with or tap into data from such portals will also assume significance. Indeed, the adoption of patient portals could be enhanced by patients' active use of a health information management system such as CDSSS at home (Nambisan 2017b).

Communication The second component of CDSSS, *communication*, facilitates individuals' interactions with relevant others in their self-care network – including homecare providers, personal physicians, as well as peers pursuing similar self-care goals. For example, online forums allow individuals to create and share experiential knowledge on self-care as well as factual knowledge regarding specific monitoring devices, treatments, and diseases – all of which could drive behavioral change. Such online forums and communities have been an integral part of many successful digital self-care applications such as the Comprehensive Health Enhancement Support Systems (CHESS) at UW-Madison (Gustafson et al. 2008) and PatientsLikeMe (Frost and

Massagli 2008). Many health trackers and apps such as Fitbit also provide online support forums for users to interact with one another and to exchange information. Beyond providing a venue for learning, online forums also provide an environment for extending and gaining social support and empathy (Nambisan 2011), both of which are important and necessary elements of self-care (Wicks et al. 2010). While it could be argued that one's health is an individual responsibility, people who surround us (e.g., formal caregivers, informal caregivers, friends, family, etc.) influence how we perceive health-related issues and make decisions regarding our lifestyle choices. A successful CDSSS should thus provide a robust communication module that can help bring together all the people who are part of in the individual's self-care network, i.e., those promoting and facilitating self-care for the aging individual.

Resource Integration The third crucial component of CDSSS, *resource integration*, involves bringing together diverse types of resources to promote actions on the part of the individual that advance comprehensive or holistic self-care. For example, therapeutic and non-therapeutic knowledge (i.e., knowledge generated outside of the formal healthcare or medical system) are needed to guide individual's choices and decisions regarding self-care. In addition, resources other than knowledge (e.g., relational resources) available in the healthcare setting, community setting, and home setting need to be integrated, in such a way that the individual can make full use of these resources. Thus, a CDSSS component that curates and integrates such different types of resources in ways that make them action-oriented assumes critical significance as the aging individual pursues self-care goals.

CDSSS Deliverables

As noted previously, prior studies have shown a wide range of positive outcomes associated with the use of CDSSS including improved quality of life and treatment outcomes. However, these are all secondary outcomes. The primary outcomes associated with CDSSS would be (a) learning, (b) social and empathetic support, and (c) self-care integration. These, in turn, could lead to a host of secondary outcomes, and more broadly, to the effectiveness of self-care.

Learning The first and most important outcome of CDSSS is *learning*. Learning is critical to address the education and training needs mentioned earlier and also to meet the needs related to preventive care. CDSSS can facilitate learning in different ways. Bandura's social learning theory (Bandura 1978) has been used to analyze diverse learning contexts for types of population groups and age groups. Bandura's theory not only explains learning behavior but also connects learning, behavior, and how our environment influences our varied self-care outcomes. A CDSSS can provide a shared learning environment; for example, online forums allow individuals to connect with other across care specialties and demographic differences and to share experiences, thereby promoting learning. Similarly, data analysis and visual data presentation tools can facilitate "learning by doing." Behavioral change requires a change in attitude as well as a change in subjective and normative factors (Ajzen and Fishbein 1973). Individuals can be predisposed with certain attitudes, for example, regarding health information seeking or regarding dietary habits. Persuasive strategies such as peer-to-peer information exchange and data visualization tools can help in absorbing new knowledge and correcting wrong perceptions (White and Dorman 2001). As such, communication and data integration capability of the CDSSS assumes importance. Lave's situated learning theory posits that learning is situated and that knowledge presented in authentic contexts, where the learner can get involved, is better than "out of context" environment (Lave 1988). A CDSSS that is rooted in the home context (where much of the care happens) and complements that with the ability to integrate resources (e.g., knowledge) acquired from relevant others will thus facilitate more in-depth learning; as such, resource integration would contribute to learning. Thus, all the three components of the CDSSS – communication, data integration, and resource integration – will contribute to individual learning in self-care.

Social and Emotional Support As previously noted, social and emotional support needs of the aging population continue to be unmet; hence, one of the main deliverables of a CDSSS should be social and emotional support. Positive experiences within social forums have been found to impact mental well-being (Nambisan 2017a); and, among older adults, such positive experiences would be critically shaped by the presence of close friends and family in the network and related online activities (e.g., viewing pictures of grandchildren) (Nambisan et al. 2014). Currently, many digital support systems provide online social support, mostly comprising of interactions with people with the same disease or condition. However, for the aging, a more integrated social support comprising of close friends and family in the community would be more appropriate and effective. Further, as noted by Ryan and Sawin (2009), self-regulation is an important precursor for self-care behaviors. Self-regulation involves behaviors related to goal setting, monitoring, evaluation, and reflective thinking. A recent study showed that social networking platforms can be used for self-regulation, especially for the searching and the self-evaluation steps of self-regulation, to achieve weight management goals (Nambisan 2015). Social support potentially aids in self-regulation, especially for people with external locus of control; hence, social support from those in an individual's personal network (who might exercise the most influence) could potentially facilitate self-regulation and thereby shape behavioral change (a precursor to prevention focused self-care). Thus, the communication component of the CDSSS will play a critical role in delivering social and emotional support to individuals.

Care Integration Another key deliverable of the CDSSS relates to the integration of care-related resources (including resources at home and in the community) and data (including provider data and data generated by the patient and the community) that would in turn facilitate the delivery of more *comprehensive and integrated care* to the aging individual. Systems theory or systems perspective, when applied to healthcare, implies the need to view human body, diseases, and the associated care, as a complex system comprised of a multitude of interrelated and interconnected parts, wherein a change in one part can impact other parts, and thereby, the whole system (Wang et al. 2014; Rebhan 2017). A robust CDSSS would adopt such a "whole system" perspective, which will help individuals discover and acknowledge these interdependencies (e.g., how a specific disease or its treatment may impact other parts of the body) and allow them to take that into consideration while making specific self-care decisions. However, for this to happen, timely and effective integration of data and resources from varied sources – from healthcare providers, from the patient, and from the home and the community – is warranted. Thus, both the data integration and the resource integration components of the CDSSS will play a key role in contributing toward care integration.

Directions for Future Research

Future research should focus on designing and evaluating a CDSSS that will meet the unique needs of the aging. Importantly, as noted here, design of a CDSSS will need to be informed by ideas and concepts from varied fields and disciplines including communication, sociology, and consumer psychology. As such, future research may focus on identifying specific concepts/constructs from different disciplines (e.g., shared learning, trust, empathy, user experience) and evaluate their value as design attributes for CDSSS development. Further, empirical studies that evaluate the extent to which specific features and components of CDSSS cater to the needs of the aging population are also warranted. Such studies will need to integrate digital technology-related attributes and non-technology and contextual attributes in evaluating the effectiveness of

CDSSS. Importantly, such studies would also need to adopt mixed-method (quantitative and qualitative) techniques to derive insights on the design and effectiveness of CDSSS for the aging.

Conclusion

The rapidly emerging "aging population" crisis and the increasing need for more comprehensive and preventive care imply the significance of CDSSS. The core objective of the CDSSS should be to provide a *learning environment*, rooted in the home and community contexts, which would help individuals to "listen to their bodies" and make informed self-care decisions. While advances in digital technologies indicate the promise and potential to develop such CDSSS, a deeper understanding of the underlying individual and community-level concepts and issues is critical to design and deploy them successfully. Future research that builds on the ideas and concepts presented here could thus inform not only on CDSSS development but also on their evaluation and related practices.

Cross-References

▶ Chronic Disease Self-Management
▶ Consumer Health Informatics
▶ Managing Long-Term Conditions: Wearable Sensors and IoT-Based Monitoring Applications

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Comprehensive Distancing

► Acceptance and Commitment Therapy

Comprehensive Geriatric Assessment

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Synonyms

Multidimensional Geriatric Assessment

Definition

The comprehensive geriatric assessment (CGA) is a multidimensional, interdisciplinary diagnostic process focused on determining the medical, psychological, and functional capabilities of older persons for developing a coordinated and integrated plan for treatment and long-term follow-up (Pilotto and Martin 2018). Due to its usefulness in exploring multiple domains of health, CGA is indeed the multidisciplinary geriatric tool of choice to determine the clinical profile, pathological risk, and residual skills to define the personalized therapeutic and care plan and to facilitate clinical decision making for older subject.

Overview

The observations of high rates of institutionalization in the frail older population and the inadequacy of provision for readily recognizable and remedial problems in this high-risk group led to the development of one of the cornerstones of modern geriatric care – CGA (Rubenstein 2004). The concept is that the early identification of individuals at greatest risk for complications and unfavorable outcomes would enable a more adequate treatment plan and a better allocation of the resources available to the multidisciplinary team.

CGA differs from the standard medical evaluation for its concentration on frail older people with complex problems, emphasis on functional status and quality of life, and use of interdisciplinary teams and quantitative assessment scales. Moreover, CGA can vary in intensity from screening assessment (focused on identifying older persons' problems performed by primary care/community health workers) to thorough diagnostic assessment and management of these problems carried out by a multidisciplinary team with geriatric training and experience. CGA is both a diagnostic and therapeutic process, seeking to ensure that problems are identified, quantified, and managed appropriately. Common to these interventions are several key features (see paragraph "key components of the CGA") that have been attributed with their effectiveness.

During the last 35 years, the clinical models of CGA have evolved to meet differing needs becoming the foundation of "progressive" geriatric care, meaning that CGA is successfully performed at varying levels of intensity in different settings including acute hospital care, day hospitals, rehabilitation units, nursing homes, and home-care services (Pilotto et al. 2017).

The Key Components of the CGA

The key components of different models of CGA include a coordinated multidisciplinary assessment, geriatric medicine expertise, identification of medical, physical, social, and psychological problems, and the formation of a plan of care including appropriate rehabilitation. The core domains of the CGA are functional status, mobility, gait speed, cognition, mood and emotional status, nutritional status, comorbidities and polypharmacy, geriatric syndromes (fall risk, delirium, urinary incontinence, dentition, visual or hearing impairments), disease-specific rating scales (i.e., parkinsonism, dementia), goals of care, and advanced care planning. A patient's social and environmental situation also is evaluated, with a focus on the social interactions network, social support needs and resources, financial concerns, and environmental adequacy and safety.

The CGA uses validated geriatric scales and tests to produce an inventory of health problems, which can then serve to develop an individualized geriatric intervention plan (citation) (Pilotto et al. 2017). An interdisciplinary team approach is employed in most CGA programs to assess patients, interpret results, and pool expertise in working toward common goals. In many settings, the CGA process relies on a core team consisting of a physician (usually a geriatrician), a nurse, and a social worker (Pilotto and Martin 2018). When appropriate, specialists in several other disciplines either take part in the basic assessment or act as consultants with an "extended" team of physical and occupational therapists, nutritionists, pharmacists, psychiatrists, psychologists, dentists, audiologists, podiatrists, and opticians. Program setting, the availability of resources, and caseload influence the size of the core and extended team. At present, CGA programs are moving towards a "virtual team" concept in which members are included as needed, assessments are conducted at different locations on different days, and team communication is completed via telephone or electronically (Pilotto et al. 2018d).

Key Research Findings

CGA in Hospital

The organization of CGA in hospital is commonly divided into two types. The first is delivered by a multidisciplinary team in a ward, i.e., Geriatric Evaluation and Management Unit (GEMU) or Acute Care for Elders (ACE) unit, with direct control over the delivery of the team recommendations (Rubenstein et al. 1984). The second is a multidisciplinary team assessing patients and delivering recommendations to nongeriatric specialists (internists or surgeons), and this is known as the Inpatient Geriatric Consultation Service (IGCS) (Applegate et al. 1990). The first randomized clinical trial (RCT) conducted on 123 older patients from the same GEMU showed that CGA was effective on reducing mortality, nursing home admission, rehospitalization rates and costs (Rubenstein et al. 1984). These findings were further confirmed in RCTs carried out in a community rehabilitation hospital (Applegate et al. 1990). A first meta-analysis including 28 RCTs confirmed that across all CGA programs there was an 18% reduced mortality risk for patients in the CGA programs, a 25% increased likelihood of living at home at follow-up, a 41% increased chance of cognitive improvement, and overall a 12% reduced hospital readmission risk (Stuck et al. 1993).

More recently, a meta-analysis of 22 RCTs of 10,315 participants in six countries with inpatient CGA by mobile teams (general ward setting) or in designated wards (GEMUs, ACE units, or rehabilitation wards) found that patients who received CGA were more likely, after the follow-up period, to be alive and in their own homes and less likely to be living in residential care, compared with usual care (Ellis et al. 2011). An updated meta-analysis of 29 RCT recruiting 13.766 participants across nine countries confirmed that older patients were more likely to be alive and in their own homes at follow-up if they received CGA on admission to hospital. Moreover, data were uncertain to show a difference in effect between wards and mobile teams as well as a clear evidence for cost-effectiveness due to imprecision and inconsistency among studies (Ellis et al. 2017).

CGA in Community/Outpatient Consultation

Home geriatric assessment programs and outpatient geriatric consultation share a preventive viewpoint; their aim is to detect modifiable risk factors and worsening health conditions, in order to prevent or reduce disability, healthcare use, and related costs. Despite some differences, most programs of home assessment and outpatient geriatric assessment involve a visiting nurse trained in geriatric care, a physical therapist, a social worker, a psychologist, and, when appropriate, specialty referrals. The progressive refinement of organizational models revisiting past experiences of outpatient geriatric assessment has led to the development of specialized team management programs integrated within primary care activities and practices.

A substantial body of evidence based on multiple meta-analyses suggested that home assessments appeared to be consistently effective in reducing functional decline, admissions to long-term care facilities, and overall mortality in the general older population (Pilotto and Panza 2017). In this context, preventive home visit programs appeared to be effective on the risk of LTC admission, provided the interventions are based on multidimensional CGA, including multiple follow-up home visits and targeting persons at lower risk for death (Stuck et al. 2002). More recently, a meta-analysis of 21 RCTs found that multidimensional home CGA programs were effective in reducing functional decline if a clinical examination was conducted and in reducing mortality in patients age $\leq$77 years old. However, the home visits did not significantly prevent nursing home admissions, and, like other meta-analyses for home CGA, a great heterogeneity across studies limited the full interpretation of results (Huss et al. 2008).

Some innovative approaches to outpatient CGA have proposed a specialized team management with some of the more successful components of older models adapted to programs within primary care practices. One of these approaches is the Geriatric Resources for Assessment and Care of Elders (GRACE), including home-based CGA and long-term care management by a nurse practitioner and social worker who collaborate with the primary care physician and a geriatrics interdisciplinary team. In RCTs of low-income older patients, those randomly assigned to the GRACE intervention had better health-related quality-of-life and fewer emergency department (ED) visits compared to those assigned to usual care

(Counsell et al. 2007). Guided Care (GC) is an enhanced model of primary care integrating a nurse intensively trained in chronic care into primary care physician practices to provide CGA and chronic care management to older at-risk patients with multiple chronic conditions and complex needs. In RCTs on multimorbid older patients, those randomly assigned to GC reported improved satisfaction rates and had less health care utilization compared to those randomly assigned to usual care at 8 months (Boult et al. 2011).

Despite controversies over the effectiveness of multifactorial interventions, various CGA-based preventive programs in the community and in general practice are currently implemented in many healthcare systems throughout the western world. Only new studies with rigorously scientific methodology will allow better interpretation of evidence in the field of the interventions aimed at maintaining self-sufficiency among community-dweller older people.

CGA in Specific Settings or Clinical Conditions

Emergency Department

There are a few RCTs addressing the emergency care of older people, mainly focusing on post-discharge support with relatively few addressing the care of older people inside the ED itself. Indeed, some CGA programs for patients discharged to home from the ED were found to be effective at reducing emergency room visits and hospital admission (Caplan et al. 2004). Recently, the CGA delivered into one ED was associated with a statistically significant improved discharge rates from the ED and reduction in hospital readmissions in older people (Conroy et al. 2014).

Orthogeriatrics

Comanagement with a geriatrician may be beneficial for hip fracture patients in reducing complications, mortality, readmissions, and delirium. Models range from a limited consultation or liaison service through integrated orthogeriatric units. A systematic review and meta-analysis conducted on 18 RCTs on various orthogeriatric care models (routine geriatric consultation, geriatric ward with orthopedic consultation, and shared care) found that orthogeriatric collaboration was associated with a significant reduction of in-hospital and long-term mortality; length of stay was also significantly reduced, particularly in the shared care model, although heterogeneity limited this interpretation (Grigoryan et al. 2014). A recent review on the optimal setting and care organization in the management of older adults with hip fracture reported that differences in the trials interventions, populations, and outcomes hamper the ability to define which model, setting, and care organization may be optimal or better than the others in terms of short- and long-term outcomes. Patients receiving a CGA-based approach, however, demonstrated better overall outcomes compared to patients receiving a traditional non-CGA based approach (Giusti et al. 2015).

Preoperative Assessment

Geriatric conditions are often associated with adverse surgical outcomes. Therefore, objectives, priorities, and life expectancy need to be assessed in frail older adults to determine whether surgical management is preferable to alternative approaches. A systematic review evaluating the impact of preoperative assessment on postoperative outcomes in older patients undergoing elective surgery showed that CGA reduced postoperative complications and the time to be “fit for discharge,” while total costs were unchanged (Partridge et al. 2014). Another systematic review of 54 studies in older patients, although with a substantial heterogeneity in methods, measures, and outcomes, reported that preoperative cognitive impairment was associated with postoperative delirium, while frailty was associated with a 3- to 13-fold increased risk of discharge to a long-term care facility (Oresanya et al. 2014). Therefore, individualized preoperative optimization strategies in older age should target CGA-based functional, cognitive, and clinical conditions and that communication of realistic risk estimates is probably essential to guide individualized clinical decision-making.

Cognitive Impairment and Dementia

A previous meta-analysis of Stuck et al. showed that across all CGA programs there was a 41% increased chance of cognitive improvement (Stuck et al. 1993). These findings were substantially confirmed also in a recent large meta-analysis in which older patients were more likely to experience improved cognition if treated with a CGA approach (Ellis et al. 2011). Several studies conducted in different settings confirmed these findings. For example, both in academic geriatrics practice and in community-based practices, a model of nurse-practitioner comanagement resulted in improvements in quality of care in older subjects with dementia, falls, and urinary incontinence (Reuben et al. 2013). Moreover, the use of a CGA-based multidimensional prognostic index (MPI) was effective in assessing the risk of hospitalization and all-cause mortality in outpatients evaluated in a tertiary care center for cognitive impairment (Gallucci et al. 2014) as well as in hospitalized demented patients aged 65 years and older (Pilotto et al. 2009) demonstrating the prognostic role of CGA in older patients with dementia. Finally, recent data reported that the degree of frailty modifies the association between Alzheimer's disease pathology and Alzheimer's dementia, i.e., individuals with even a low level of Alzheimer's disease pathology might be at risk for dementia if they have high amounts of frailty (Wallace et al. 2019). These results strongly suggested that individualized multidomain interventions target physical, nutritional, cognitive, and psychological domains could delay the progression to dementia and secondary occurrence of adverse health-related outcomes, such as disability, hospitalization, and mortality.

The CGA-Based Multidimensional Prognostic Index

An increasing body of evidence indicates that the prognosis of older patient is strongly related to the presence of concomitant diseases and to the degree of physical, cognitive, biological, and social impairment. A large systematic review identified eight prognostic indices for mortality meeting the requirements of accuracy and calibration required to be used in a hospital setting (Yourman et al. 2012). The Multidimensional Prognostic Index (MPI) was the only CGA-based predictive tool to be included in the list, showing good discrimination and accuracy that were maintained both at 1-month and 1-year of follow-up (Pilotto et al. 2008). Further multicenter studies showed that MPI was a significantly more accurate predictor of all-cause mortality than other frailty indices commonly used in clinical practice (Pilotto et al. 2012), an independent predictor of in-hospital mortality and the length of hospital stay (Volpato et al. 2015), and sensitive to clinical changes of patients' health status during hospitalization (Volpato et al. 2016). A systematic review reported that MPI demonstrated the highest validity, reliability, and feasibility (evaluated through the QUADAS score) compared to other tools used to identify frail older patients (Warnier et al. 2016). Moreover, a recent reflection paper published by the European Medicines Agency (EMA) reported that while a complete evaluation of frailty to support its management requires a CGA, which is the "*gold standard*" in clinical practice, "*the MPI is able to extract information from CGA to categorize frailty in three subgroups with excellent prognostic value*" (Committee for Medicinal Products for Human Use 2018).

Very recently the investigators of the MPI_AGE international multicenter project demonstrated a significant association between MPI score and survival time and risk of hospitalization in a population-based cohort with a very long-term follow-up up to 12 years (Angleman et al. 2015; Pilotto et al. 2018). Moreover, the CGA-based MPI performed at hospital admission was very accurate in predicting in-hospital mortality and postdischarge one-year mortality, nursing home admission, need for home-care services and hospital re-admissions in 1140 older patients hospitalized in acute wards of nine hospitals in Europe and Australia (Pilotto et al. 2018).

CGA and Clinical Decision Making

Despite clinical recommendations to incorporate patients' prognosis in clinical decisions (Gill 2012), a recent observational study demonstrated that several barriers, i.e., uncertainty in predicting prognosis, difficulty in discussing prognosis, and concern about patient reactions, may limit the implementation of these recommendations (Schoenborn et al. 2016). Results from the MPI_AGE European project demonstrated, however, that the CGA-based MPI may be useful to evaluate whether specific treatments, i.e., statins in secondary prevention of diabetes mellitus (Pilotto et al. 2015) or coronary artery disease (Pilotto et al. 2016a), anticoagulants in atrial fibrillation (Pilotto et al. 2016b), and antidementia drugs in demented older subjects (Pilotto et al. 2017), are cost-effective in the older patients accordingly to their individual prognostic profile (Pilotto et al. 2015, a, b, 2017). Moreover, a study from France demonstrated that the CGA-based MPI was useful to evaluate outcomes among older patients undergoing transcatheter aortic valve implantation (TAVI) (Bureau et al. 2017), as subsequently confirmed in a multicenter international survey (Ungar et al. 2018). Very recently, a study from Germany reported that the CGA-based MPI were significantly associated with use of indicators of healthcare resources, including the grade of care, the length of hospital stay, and discharge allocation (Meyer et al. 2018). All these studies suggested that with full access to prognostic information derived from CGA-based predictive tools, physicians are better equipped to make clinical decisions that are aligned with their patients' needs in terms of safety and efficacy.

Future Directions of Research

In light of the existing information on the beneficial role of the CGA, it is important that further evidence is collected at an intersectorial level and in settings additional to the hospital. There is a need of better understanding how the information driven by CGA can be translated into tailored interventions and care plans both in the hospital and in home-care services. Furthermore, the performance of a CGA should occur in a professionalized and standardized manner in order to achieve its maximum potential; therefore, teaching the CGA at an undergraduate, postgraduate, and healthcare professional levels should be improved and evaluated (Roller et al. 2018). In light of the upcoming dramatic increase of the oldest-old population, additional research is also needed to establish self-administered CGA tools as prognosis screening instruments to be readily used in clinical settings (Pilotto et al. 2018c). Finally, the use of new technologies (ICT, app tools, ambient and wearable sensors, domotics, and robotics) should be encouraged to assess multidimensional assessment and management to improve clinical decision-making in older subjects (Pilotto et al. 2018d).

Summary

The CGA is a multidisciplinary diagnostic and treatment process that identifies medical, psychosocial, and functional capabilities of older adults in order to develop a coordinated plan to maximize overall health with aging. At present, no standard criteria are available to readily identify patients who are likely to benefit from the CGA. Specific criteria used by CGA programs to evaluate patients include age, medical comorbidities, psychosocial problems, previous or predicted high healthcare utilization, change in living situation, and specific geriatric conditions. Evidence coming from RCTs and large systematic reviews and meta-analyses suggests that the healthcare setting may influence the effectiveness of CGA programs. Home CGA programs as well as the CGA performed in hospital have been shown to be consistently beneficial for several health outcomes. The effectiveness of CGA programs may be modified also by particular settings or specific clinical conditions, with tailored CGA programs in older frail patients evaluated for preoperative assessment, admitted or discharged from emergency departments and orthogeriatric units or with cognitive impairment and dementia. The CGA, capable to effectively exploring multiple domains in older age, is indeed the multidimensional and multidisciplinary tool of choice to determine the clinical profile, the pathological risk and the residual skills, as well as the short- and long-term prognosis, i.e., the Multidimensional Prognostic Index (MPI), to facilitate the clinical decision making on the personalized care plan of older subjects.

Cross-References

▶ Cardiovascular Diseases

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Comprehensive Geriatrics Assessment

▶ Geriatric Interventions

Compulsory Retirement Age

▶ Mandatory and Statutory Retirement Ages

Computerized Physician Order Entry

▶ Computerized Provider Order Entry

Computerized Provider Order Entry

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Synonyms

Computerized physician order entry; Electronic prescribing (e-prescribing)

Definition

To replace paper, computerized provider order entry (CPOE) systems allow providers such as physicians, nurse practitioners, or other ordering authorities to electronically order medications, tests, or other medical procedures for an individual patient (Taieb-Maimon et al. 2018). In hospital setting, this term tends to be used instead of e-prescribing which usually refers to electronic prescription of medications, because the scope of CPOE is broader than e-prescribing. It may also include other types of medical orders (Ahmed et al. 2016).

Overview

Globally, CPOE has been taken up by many countries such as the USA, Australia, Canada, and England (Samadbeik et al. 2017; Scott et al. 2018), with majority of research evidence from the USA (Scott et al. 2018). In the USA, 77% of all prescriptions were completed electronically in 2017 (Surescripts 2017).

Due to comorbidities and physiological changes, older people commonly use a large number of medications (Qian et al. 2016), have greater healthcare demands, and need long-term treatments (Tommelein et al. 2016). Thus, they are more vulnerable to potentially inappropriate prescriptions (Dalton et al. 2018). It is estimated that at least one potentially inappropriate prescription occurs in about 25–56% of hospitalized older people (Hamilton et al. 2011), nearly 30% of older people living in community (Morgan et al. 2016), and almost 50% in residential aged care homes (Stafford et al. 2011). Computerized provider order entry systems have been shown to reduce inappropriate prescriptions and aid in the prevention of adverse drug events for older people (Dalton et al. 2018). These beneficial effects on care quality have become one of the key driving forces for the introduction of CPOE, in addition to efficiency and cost saving.

Key Research Findings

Development History

In 1971, the first CPOE system was developed in the USA with rudimentary functions which allowed physicians to quickly order medications with a few clicks (OHSU 2015). In the 1980s, additional features were added to CPOE systems, including simple decision support, e.g., alerts for known adverse interactions and automatic reordering (OHSU 2015). The 1990s saw the rapid development of commercial CPOE systems; however, the uptake was slow with less than 10% of the US hospitals had fully operational CPOE systems in 2002 (Ash et al. 2004). Since CPOE became a core requirement in the Meaningful Use of Electronic Health Records, the usage rate of CPOE in the US hospitals has increased significantly from 14% in 2010 to 64% in 2016 (Castlight and Leapfrog 2016).

E-prescribing is a unique type of CPOE. While CPOE systems allow orders to be transmitted to a pharmacy information system and nursing services within a hospital, e-prescribing allows an outpatient department (e.g., emergency department), clinic, or other health services outside of a hospital to transmit prescriptions to retail pharmacies (StratisHealth 2009).

The development of e-prescribing includes four overlapping phases: adoption, utilization, quality, and optimization (HealthTechZone 2018). Beginning in 2005, the US health industry was focused on the adoption of e-prescribing (HealthTechZone 2018). To encourage the use of a qualified e-prescribing system, in 2009 the US government established an Electronic Prescribing Incentive Program (Centers for Medicare and Medicaid Services 2018). Although the program has ended in 2013, e-prescribing continues with the meaningful use (Centers for Medicare and Medicaid Services 2018). The development of CPOE has entered the third phase, focusing on improving the quality of prescription (HealthTechZone 2018).

Research on CPOE

There are an increasing number of research on CPOE. Much of the research was conducted in the USA, and a small number of studies were conducted in residential aged care homes. Scott et al. (2018) conducted a systematic review of 20 studies involving the use of CPOE to reduce potentially inappropriate medication prescriptions. Their review showed that 14 (70%) of these studies were conducted in the USA, 4 (20%) in Canada, 1 (5%) in Italy, and 1 (5%) in the Netherlands. Eight (40%) of these studies were conducted in hospitals, nine (45%) in primary care, and only three (15%) in residential aged care homes.

Dalton et al. (2018) also conducted systematic review on the effectiveness of CPOE to reduce potentially inappropriate prescription. Their review included eight controlled trial studies. Except for one study that was conducted in Italy, all the other studies were conducted in the USA (87.5%) in hospital settings.

In an earlier review conducted by Clyne et al. (2012), 14 studies on using CPOE to reduce inappropriate medication use and polypharmacy in older people were included. Of these studies, 12 (85.7%) were conducted in the USA, and 2 (14.3%) were in Canada. Six studies (42.8%) were conducted in ambulatory care, four (28.6%) in hospitals, and four (28.6%) in residential aged care homes.

Barriers to Implementation

Although the world is embracing CPOE, the implementation of CPOE is still a daunting task. Research has identified barriers to implementation including disruptive changes in the workflow during the implementation (Adams et al. 2008), low training support (Elliott et al. 2016), lack of integration with other systems (Elliott et al. 2016), poor user interface (Graber et al. 2015; Taieb-Maimon et al. 2018), and physician resistance due to perception of loss of autonomy (Kruse and Goetz 2015). Among these, disruptive changes and low training support are the top two barriers (Kruse and Goetz 2015).

Benefits

The benefits of CPOE include reduced number of errors, reduced number of inappropriate orders of medications, decreased adverse drug events (ADEs), improved patient safety, improved efficiency, enhanced physician-patient communication, and cost saving.

Reduced Number of Errors Related to Poor Handwriting

As pharmacists do not have to interpret illegible handwritten orders (Elliott et al. 2016), the number of errors related to poor handwriting has been reduced by CPOE (Stürzlinger et al. 2009).

Reduced Number of Inappropriate Orders of Medications

With specific alerts embedded into a CPOE system, the number of orders of potentially inappropriate medications for hospitalized older people decreased quickly (Mattison et al. 2010).

Decreased Adverse Drug Events

Adverse drug events are harms caused by inappropriate medications (Bhavsar et al. 2017). Due to high chance of multiple chronic conditions, older people are at high risk of experiencing ADEs, nearly seven times more often than the other population groups (Lucado et al. 2006). It is estimated that over half of the ADEs are preventable (Von Laue et al. 2003) and up to 60% of ADEs identified during hospitalization actually occur at the time of ordering (Nebeker et al. 2005); therefore, the CPOE systems play a critical role to prevent ADEs.

A systematic literature review of 50 studies found that the CPOE systems were capable of preventing ADEs (Charles et al. 2014). A more recent study has also found that higher e-prescribing usage rate was linked to lower ADE rate (Bhavsar et al. 2017), because it can help overcome common risk factors of ADEs, such as the lack of communication between concurrent prescribers (Green et al. 2007) and inappropriate medication orders (Mattison et al. 2010).

Improved Patient Safety

Safety benefits of CPOE have been perceived by physicians, nurses, and pharmacists. A study conducted in an Australian residential aged care home found that the physicians perceived e-prescribing as beneficial to the safety of older people because the changes they made to prescriptions could be synchronized to the system used in the residential aged care home, ensuring that nurses had access to correct medication list (Elliott et al. 2016). Nurses who worked in the residential aged care home also felt that e-prescribing had safety benefits because it helped to avoid transcription errors and delays associated with a hybrid paper-electronic medication management system (Elliott et al. 2016). As the pharmacists did not have to interpret handwritten orders, they also saw the safety benefits that e-prescribing had to offer (Elliott et al. 2016).

Improved Efficiency

Computerized provider order entry has shown efficiency gain in residential aged care homes (Elliott et al. 2016; Subramanian et al. 2007), because no paper-based prescription forms need to be faxed among nurses, physicians, and pharmacists who work in different locations (Elliott et al. 2016).

Enhanced Physician-Patient Communication

In a survey study investigating older people's perception of e-prescribing, more than 80% of them preferred e-prescribing, and more than 90% were satisfied with their physicians, because the system had led them to enjoy an increased communication with their physicians regarding medication-related topics (Schleiden et al. 2015).

Cost Saving

A study conducted in six hospitals in Massachusetts in the USA found that a CPOE system could save a hospital up to US $2.7 million per year, despite the onetime implementation cost of US $2.1 million and the annual maintenance cost of US $ 435,000 (Adams et al. 2008). An average hospital could expect full payback in about 26 months (Adams et al. 2008).

Unintended Adverse Consequences

It is now well recognized that health information technology including CPOE may introduce unintended adverse consequences (Vélez-Díaz-Pallarés et al. 2017), with more than 60% of the technology-based medication incidents related to CPOE (Samaranayake et al. 2012). A study investigated prescription errors associated with CPOE among hospitalized older people in Spain (Vélez-Díaz-Pallarés et al. 2017). It found that during the 6 months of using the CPOE system, 107 errors were introduced by the system (Vélez-Díaz-Pallarés et al. 2017). Almost all these errors were related to human-machine interactions due to wrong or partial entries (Vélez-Díaz-Pallarés et al. 2017).

Use Errors

Due to a lack of attention in human-computer interaction, use errors such as selection of a wrong patient by slipping off a dropdown list may occur (Graber et al. 2015; Taieb-Maimon et al. 2018). Research has found that improvements in human-computer interface design such as highlighting selected patient and adding patient photo can draw the attention of users and significantly improve the recognition of wrong patient error (Graber et al. 2015).

Alert Fatigue

Out of the intention to improve patient safety, a growing number of alerts have been built in CPOE systems to alert providers for drug-drug interactions, dose check, allergy, laboratory test value, etc. (Vanderman et al. 2017). However, these alerts caused fatigue to providers and were overridden 49–96% of the time (Van Der Sijs et al. 2006). Alert fatigue has become the most common complaints about CPOE (Ash et al. 2007).

To reduce alert fatigue, mitigation strategies have been developed. Riedmann et al. (2011) developed a context model for prioritizing drug safety alerts. This model contains 20 factors grouped into 3 categories: characteristics of the patient or case (e.g., diagnosis), characteristics of the organizational unit or user (e.g., experienced users may receive less intrusive alerts regarding certain drugs), and characteristics of the alert (e.g., less serious ADEs may be presented in a less intrusive way) (Riedmann et al. 2011). Vanderman et al. (2017) implemented a simple, non-interruptive, age-specific alert function to identify inappropriate prescription at the point of CPOE in an ambulatory care setting. They found a significant decrease in the incidence of the most frequently prescribed inappropriate medications for older patients receiving care (Vanderman et al. 2017).

Inefficiency

Due to lack of system interoperability, use of hybrid paper-electronic systems, and legal requirements, end users have experienced inefficiency with CPOE systems. As physicians usually look after older people living in different residential aged care homes, they may have to learn to use different information systems for medication prescription when visiting each residential aged care home (Elliott et al. 2016). This impedes work efficiency.

If e-prescribing is in place but medication administration records are still on paper, nurses would have to print out the electronic prescriptions for transcribing into paper-based medication administration records (Rochon et al. 2005). Even though the medication administration records are in electronic systems, manual transcription may still be required because of a lack of interoperability between the e-prescribing system used in a physician's office and the electronic system used in a residential aged care home (Bollen et al. 2005).

The legal requirement may also impede work efficiency. One study conducted in an Australian residential aged care home identified that physicians had to wait for nurses to print out paper copy and sign on it, because electronic signature was not acceptable by law (Elliott et al. 2016).

Future Directions of Research

Despite the increasing adoption and implementation of CPOE systems in healthcare, the relevant research of CPOE use in residential aged care homes is still limited. More research needs to be conducted in this setting where more vulnerable older people were concentrated. Although improvements have been made in CPOE systems to mitigate the unintended adverse consequences, ongoing monitoring is required as newer systems may introduce new types of unintended adverse consequences. Prospective studies need to be conducted to analyze in detail how these unintended adverse consequences occur and to establish strategies to prevent them (Vélez-Díaz-Pallarés et al. 2017). As the true impact of CPOE on care outcomes is still unclear, large-scale multicenter randomized controlled trials are needed (Dalton et al. 2018).

Summary

Computerized provider order entry systems allow orders of medications, tests, or other medical procedures to be made electronically. Due to comorbidities and physiological changes, older people are particularly at risk of inappropriate prescriptions; therefore, they are the major beneficiaries of the CPOE systems. Despite the ample benefits of CPOE, unintended adverse consequences including use errors, alert fatigue, and inefficiency may also occur, hindering the benefits it promised. Therefore, ongoing monitoring and responding mechanisms need to be in place to prevent the unintended adverse consequences and maximize the benefits of CPOE.

Cross-References

▶ Electronic Health Record
▶ Health 2.0
▶ Health Information Exchange

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Computer-Mediated Counseling

▶ Cybercounseling

Confinement

▶ Older Prisoners

Confucian Culture and Filial Piety

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Synonyms

Confucianism; Filial obligations; Filial responsibilities

Definitions

Filial piety, which is rooted in the traditional Confucian ideal of familial interdependence, is a family value in Confucian culture based on the principles of hierarchy, obligation, and obedience. Filial piety stipulates that children are obligated to obey their parents and provide old-age support to them. Filial piety also stresses the importance of adult children's obligation to continue the family lineage through male offspring as a form of ancestor worship (Ikels 2004). Traditionally viewed as a virtue, filial piety is no longer unanimously considered a central value of family life, and its expectations and practice have decreased in contemporary Confucian societies.

Overview

Recent research has shown both continuations of and deviations from traditional filial piety practices concerning marriage and family in East Asia where Confucian culture originated (Raymo et al. 2015). Examples of continued practices of filial piety include nearly universal marriage (Xu et al. 2014), son preference (Hesketh et al. 2011), and intergenerational transfer (Cong and Silverstein 2011). Examples of deviations from the traditional practices include delayed age at first marriage (Yu and Xie 2015a), rise in nonmarriage and divorce (Yu and Xie 2015b), fertility decline (Raymo et al. 2010), and change in multigenerational co-residence (Ma and Wen 2016).

Key Research Findings

Affected by such joint forces as economic growth, urbanization, and demographic transition, patterns of intergenerational support have become more complexed. This is most evident in the case of grandparenting in China. The traditional notion of filial piety emphasizes upstream support from adult children to their old-age parents and does not charge grandparents with primary responsibility for the care of grandchildren (Short et al. 2001). Grandparents also have the authority to intervene if they perceive inappropriate child rearing by adult sons and daughters-in-law (Cong and Silverstein 2008). However, due to high level of female labor force participation, massive rural-to-urban migration, and shortage of public childcare resource, among others, Chinese grandparents are increasingly engaged in caring for grandchildren (Xu 2019). Based on recent nationally representative data, it is estimated that more than one third of the Chinese grandparents have provided care to their grandchildren in the past year (Luo et al. 2018). In rural China, full-time custodial grandparenting is on the rise as millions of rural children are left behind by their migrant parents who seek better job opportunities in cities (Silverstein and Cong 2013). Some scholars have proposed a model of intergenerational time-for-money exchange to explain such a departure from the traditional filial piety: grandparents spend time providing grandchild care to allow their adult children to seize economic opportunities and as a result contribute to the material well-being of the grandparents through reciprocal transfers of money or living necessities (Cong and Silverstein 2008; Lee and Xiao 1998; Sun 2002).

On the other hand, Chinese grandparents may still adhere to the obligation of supporting their own old-age parents or parents-in-law. Thanks to prolonged life expectancy and reduced infant mortality, extended Chinese families that comprise four generations, co-residential or not, are no longer rare. A recent study estimated that in 2011, nearly 29% of the middle-aged or older Chinese adults were grandparents in lineages that comprised four generations with at least one grandchild under the age of 16 and at least one living great-grandparent (Xu 2019). Among them, about 10% provided informal care to the great-grandparents only, and another 15% cared for both great-grandparents and grandchildren.

Gerontologists and health researchers are increasingly interested in the potential aging and health implications of new patterns of grandparenting in Asian populations who used to or continue to embrace filial piety. There is a growing theoretical consensus that low-to-moderate intergenerational caregiving is a productive activity of older adults, whereas intensive custodial grandparenting has a detrimental health effect. However, empirical evidence is mixed in mainland China (Luo et al. 2018; Xu 2019), Taiwan (Wang et al. 2018), South Korea (Choi and Zhang 2018), and Vietnam (Giang et al. 2018).

The obligation of continuing the patrilineal family lineage as prescribed by filial piety remains a popular notion in Confucian societies, but it has also faced new challenges. In China, for example, marriage remains more or less universal as nearly 80% of the respondents aged 16 or older were married and only 1.2% were divorced according to a nationally representative survey in 2012 (Xu et al. 2014). However, the rate of premarital cohabitation, once perceived as a threat to family harmony and stigmatized in Confucian culture, has increased to nearly a third among the most recent marriage cohort in 2012 (Xu et al. 2014). In addition, late entry into marriage is no longer a rare phenomenon, especially for the most educated women and the least educated men (Xu et al. 2014). Similar trends are also observed in Japan, Korea, and Taiwan where filial piety is valued to varying degrees (Raymo et al. 2015).

Not only is age at first birth is delayed, but extremely low fertility rate has prevailed in East Asian societies. As of 2010, the total fertility rate in East Asia ranged from as low as 0.9 in Taiwan to as high as 1.6 in mainland China (Raymo et al. 2015), all well below replacement level, which runs counter to the notion of "more children would bring more happiness" in filial piety. An obvious consequence is that the share of working-age population will drop in the long term and the entire society will be in a social and economic crisis of providing old-age support (Westley et al. 2010). It is worth noting that the extremely low fertility rates may be caused by such socio-economic factors as the high cost of raising children and increased female labor force participation rather than by any ideational change (Raymo et al. 2015).

Despite fertility decline, there is evidence that son preference persists in China and South Korea (Hesketh et al. 2011). Because South Korea is a high-income country and China is establishing a new pension system to cover its huge rural population (Chen et al. 2019), raising a son to provide economic support at old ages may no longer be a major driving force behind the lingering son preference. The cultural pressure of filial piety to continue the family lineage through male offspring is likely an important contributing factor. Caught between low fertility and son preference, some families in China and South Korea resort to illegal sex-selective abortion, resulting in imbalanced sex ratio (Chen et al. 2013; Yoo et al. 2017).

Future Directions of Research

Originated in East Asia, Confucian culture and filial piety have spread to other parts of the world thanks to international immigration (Nagata et al. 2010). Recent research has suggested that similar notions also exist in western populations and affect marriage and intergenerational relationships in the context of aging (Latham et al. 2015; Polenick et al. 2015). Future comparative research is needed to understand the role of filial piety in shaping population aging and health across Asian and non-Asian societies. Future research should examine how continuation of and deviation from the traditional filial piety affect demographic patterns and intergenerational relationships at both the micro- and macro-level.

Summary

Confucian culture and filial piety are long-lasting as a set of fixed values and norms, but their practices are evolving in an ever-changing world. Observed departures in practice from filial piety in East Asian marriage and family are not entirely driven by shifts in cultural values or believes, but are resulted from a compromise between traditional ideation and current socioeconomic reality. Cultural pressure alone no longer ensures the traditional elderly support from adult children who are facing new challenges because of dramatic social, demographic, and economic changes. The burden of providing not only financial but also personal care to an increasingly aging population has to be shared both within and across families to better serve the well-being of both the young and old generations.

Cross-References

- ▶ Confucian Stages of Life
- ▶ Filial Piety and Responsibilities Among the Chinese
- ▶ Intergenerational Exchange and Support
- ▶ Intergenerational Family Dynamics and Relationships
- ▶ Intergenerational Family Structures
- ▶ Multigenerational Families
- ▶ Parenting and Grandparenting

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Confucian Stages of Life

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Definition

Confucian stages of life refer to the conception and stages of life experienced by the Chinese sage, Confucius (551–479 B.C.), who is widely seen as the founder of Confucianism in China. Confucius reflected upon the different stages he went through in his life in an autobiographical paragraph, now collected in Chapter 2 Section 4 of the Confucian classic the *Analects*. This paragraph becomes an important reference for Chinese people when they are projecting their personal development. Confucius sees human beings as moral agents, and life a moral journey. The further one travels in life, the closer one approaches moral maturity and even perfection, if he determines to cultivate himself in values. With continuous moral efforts, agedness just promotes an individual to a more advanced state of moral being. The Confucian conception and stages of life forms a meaningful counterpoint to the obsession of youthfulness and physical vibrancy in modern culture.

Aging in Modern Culture

In modern society, aging is usually understood as the undesirable process of the decline of one's life. Aging often implies the loss of one's youthful appearance, bodily strength, and vitality, and in media representations, the old body is symbolically derogated to be having lesser value than a younger vibrant one (Rodan et al. 2014). Beauty and healthy food industries constantly remind us to slow down or reverse the unpleasant effects of aging brought to our faces and bodies. It is suggested in some cosmetic advertisements that women's skins show signs of early aging when they reach 20 years old, and hence they have to start antiaging care for their skin then (Covino 2004; Malkan 2007).

In a culture that venerates youthfulness and body strength, senility is often the synonym for agedness and the old body (See ► "Ableism and Ageism"). The cultural disparagement of the aging body unnecessarily creates psychological tensions and anxiety on the part of the modern older adults (Aronsohn 1984; Tulle 2008). This becomes an even more acute problem when the average life span of the world population increases. People are likely to live with their "abject bodies" for a more extended period of time than ever before (Covino 2004). Aging, however, does not have to be associated with the withering of one's life. If we shift the focus away from physicality and appearance that inevitably deteriorate with time to other modes of performativity that develop with time, then growing old can actually be a fulfilling experience. Ancient China was a case in point that revered older people for the knowledge and wisdom they embodied.

Traditional Chinese Perspective of Agedness

Traditional China was a society that placed high virtues on maturity and old age over immaturity and youth. Chinese culture was known for having high respect for older adults and emphasized longevity as a cultural value (Sung 2007). In the "postfigurative," past-oriented culture, borrowing Margaret Mead's concept (1970), of premodern Chinese society, the older generation was the source and authority of social knowledge and deemed important assets of the society. The reverence for the older adults in China was also related to the Confucian conception of the potential moral development of an individual's life toward the state of sageness as one ages. With continuous efforts, getting older makes one closer to perfection as a moral agent, which is regarded as a more advanced state of being in Confucian culture (Tang 1963). From the traditional Chinese perspective, aging did not necessarily imply a depreciation of the value of life toward the end, but a moral culmination. This is revealed in the life-order of Confucius who spent his life in learning and moral pursuits.

Confucian Stages of Life

The Epigram by Confucius

The autobiographical reflection of Confucius, who was regarded as a sage and the paragon of all teachers, greatly shaped traditional Chinese understanding of life and perspective of aging. An ideal Chinese life, as Confucius exemplified, passed through different stages of progressive moral development to the eventual fruition in values and even religiosity. Confucius' discussion of his personal development can be found in the epigram in Chapter 2 Section 4 of the *Analects* (Slingerland 2003). The *Analects* is one of the most important classics of Confucianism. It is a posthumous work documenting Confucius' words, thought, and teaching compiled by his disciples. Confucius' autobiographical paragraph is read as,

> The Master said, "At fifteen, I set my mind upon learning; at thirty, I took my place in society; at forty, I became free of doubts; at fifty, I understood Heaven's Mandate; at sixty, my ear was attuned; and at seventy, I could follow my heart's desires without overstepping the bounds of propriety." (Slingerland 2003, p. 9)

This paragraph is rather short. Nonetheless, it embodies the rich experience and wisdom of the Chinese sage and deserves further exegesis.

The Construction of Life-Order

It would be instrumental to deploy the concept of "life-order" – how to organize life – to make sense of Confucius's reflection. The problem of "life-order" or "life-conduct," *Lebensordnung*, is for certain not new in Western thought (Bormuth 2006). The famous American thinker Ralph Emerson (1860) already discussed "the conduct of life," and posed questions like "How shall I live?" and "What to do?" in the nineteenth century. The problems related to *Leben*, life, and *Lebenswelt*, life-world, are also the solemn concern of many modern German thinkers from Edmund Husserl (1970), Max Weber (2004) to Jurgen Habermas (1987). The Western attention to the conduct of the unconsecrated life, as opposed to life observing religious creeds and the dictates of church, began with the secularization and modernization of European society. Yet, as read from Confucius' autobiographical remark, *Junzi*, the educated gentlemen in China took the construction of a meaningful and orderly life seriously in the foundation period of Confucianism around 500 B.C.

Confucianism as a body of thought and cultural worldview is well-known for its this-worldly orientation (Weber 1951). Confucianism preaches the goodness and moral capacity of human nature (Tang 1963). Since the inception, it endorses the positive value of human life and discourages pondering afterlife. As Confucius told his disciple Zilu, "You do not yet understand life—how could you possibly understand death?" (Slingerland 2003, p. 115) Under the influence of Confucian secularism, one's lifespan is regarded as the only proper domain for the actualization of values and meanings. How to conduct life in an orderly manner and carve out its meaning to the fullest possible hence has long been the preoccupations of Chinese people. Yet, to plan and conduct one's secular life in a systematic manner is a difficult undertaking because it puts high demands on an individual. Historically, Chinese gentlemen drew the inspiration of their construction of life-order from Confucius, whose life is widely regarded as the exemplar of a purposeful and fulfilling life (Tu 1976).

The Stages of Confucius's Life

As seen from the epigram cited, Confucius' life-course went through different stages which normally last for a decade. The decennary age benchmarks mentioned by Confucius should however not be taken as arbitrary milestones. They are at most nominal, and Confucius referred to them just as self-description and approximation, as many interpreters of the passage and the authoritative contemporary Neo-Confucian scholar Mu Qian (1985, pp. 24–26) suggest, of the different stages he passed by himself. Confucius never asked his disciples to follow his footsteps in their pursuits because life-order is a very individualized matter. Yet, the direction and the developmental stages of Confucius' life-conduct remain normative for those who aspire for a meaningful and autonomous life in China.

"At fifteen, I set my mind upon learning": According to Confucius, an individual should begin by laying down the orientation of his life when he approaches adulthood and works diligently toward the purpose he assigns to himself, if he wants a fulfilling existence. Otherwise, he would be disoriented and wasting the precious time of his life. In this first stage of adult life, Confucius made up his mind to become a learned person. He was so immersed in learning all through his life that he sometimes forgot to eat and grew old without noticing the passage of time (Slingerland 2003). Confucius said "I am not someone who was born with knowledge. I simply love antiquity and diligently look there for knowledge" (Slingerland 2003, p. 71). Making up one's mind in value orientation and being industrious all along are what the construction of life-order should start off with.

"At thirty, I took my place in society": When Confucius reached 30, he felt that he was relatively established. Taking his place in society means both the higher accomplishment of his learning and the fact that he was better recognized by the society, after he submitted to "the rigors of study and ritual practice until these traditional forms have been internalized" (Slingerland 2003, p. 9). Hitherto, Confucian concluded his first stage of adult development satisfactorily by attaining fundamental internal coherence regarding his quest and action, and assimilating the moral code of the society (Qian 1985). At the very first stage of adulthood, it is important that different aspects of one's life cohere to the purpose one appoints to himself.

"At forty, I became free of doubts": Even if one is able to maintain internal coherence of his quest and action, he is likely to face challenges from outsides, doubts of others, and setbacks of one's endeavors that may throw him into mental disarray. Hence, in the second stage of mature life, an individual not only acquires a deeper understanding of the meaning of his enterprise. He but keeps his perseverance even in unfavorable situation (Qian 1985). He is able to overcome the mundanity that wavers his resolution and distracts his strivings with wisdom, and becomes more dedicated to his cause than ever before. A higher integrity of an individual's thought and deeds can be expected. When one is free of doubts, his energy is better conserved. His thought will be fully elaborated in action and his action will be better unified with his thought (Tang 1963). Unification of thought and action is always an aspiration of the learned in China. But it is much easier said than done. Most people would have to spend their whole life to come close to the state of integrity and hence personal freedom.

"At fifty, I understood Heaven's Mandate": Understanding the Heavenly Mandate is a further stage from being free of doubts. This is also the threshold of becoming *Junzi*, gentleman, a developmental stage, according to Qian's (1985) interpretation, not accessible to everyone, and it is futile to force upon that. For average people, going through the first few stages until the point of freeing of doubts already guarantees meaningful existence in the moral and cultural universe, and consumes the energy of a lifetime.

Understanding Heaven's Mandate goes well beyond the ready reach of the scope of knowledge and vision of ordinary people, and stretches toward the divine domain of the Way and the obligation it bestows on an individual. Only very few people through their learning and piety in their endeavors will be able to feel the Heaven's Mandate in their lives, and approach the realm of religiosity in Confucianism (Qian 1985). The appropriation of this realm of being is guided only by pious practices in worldly preoccupations but not faith. The revelation of Heaven's Mandate cannot be planned, nor expected. It is not by nature a reward of one's effort either. These however should not sway his dedication to the moral pursuit of his life (Qian 1985).

"At sixty, my ear was attuned": The ear is deployed as a metaphoric receptor of not only sound, but wise words and the Heaven's Mandate. Confucius said his ear was attuned at 60 means that he was receptive to the teachings and deeds of the Sage Kings before him, and able to see the Way and perceive Heaven's Mandate on different things and people (Slingerland 2003). He not only better comprehended the demand of the Heaven's Mandate and fulfilled his calling to it, but was able to see the Heaven's Mandate on others too (Qian 1985, p. 25). In addition to his own, he is able to help other to realize their Heaven's Mandate at the same time.

"At seventy, I could follow my heart's desires without overstepping the bounds of propriety": This is the culmination of Confucius's life. At this stage, he had fully assimilated Heaven's Mandate into the practices of his daily life. The Heaven's Mandate had been integrated so well in his life that he did not feel its weight any more and could act spontaneously without disregarding it. This is the highest state of autonomy of Chinese life, in which the social and cultural world and the higher order cosmic force meet and harmonize within one's moral practice (Qian 1985). Such state is the highest ideal of Confucianism—*Tian Ren He Yi*, the union of the Heaven and human. Confucius died at the age of 72, after arriving at the pinnacle of Confucian secular religiosity – transcendence and religiosity in the absence of religious belief (Yu 2016).

Summary

In Confucian perspective, life is imbued with moral potential and moral development culminates in the full autonomy of an individual (Tang 1963). The positive meaning of aging is an individual may achieve a more advanced state of moral being when he becomes older, in which he is also able to help other to recognize their meanings in lives. If the journey of life is understood this way and lives out orderly with a sense of inner purpose, then getting old would be a much less dreadful process because the gradual weakening of bodily function is compensated by a deeper individual actualization and value fulfillment. The further down the road of self-cultivation in values, the closer one will be to moral perfection and autonomy, and even religiosity.

Nevertheless, a fulfilling experience of life is by no means at one's fingertips. It requires devotion and incessant efforts in self-cultivation. An individual should start with the construction of life-order when he approaches adulthood. He has to commit to causes and values he assigns to himself as his lifelong calling, and organize the different aspects of his life around them. With perseverance and self-discipline, he would accomplish a higher state of inner coherence and development as he further matures. He will then be largely free from external impositions, no matter that is the modern obsession of youthfulness or emphasis of physicality and appearance over virtuousness or others that would exhaust him, and remains autonomous.

If our culture steers the focus of our life from our bodies and youthfulness to inner development and self-cultivation as in Confucian preaching, then the meaning of growing older can be positively enriched (See ▶ "Aging Well"). A renewed understanding of older age would become ever more important, as the average lifespan of the world population increases and most countries are now facing the issues of aging population. A hopeful and developmental projection of elder age empowers the older adults, who are usually prompted by our culture to see aging as a declining process, and is instrumental in promoting a new mode of aging culture that would make the extended last stage of life more rewarding for individuals. Our society would also be benefited if we see older adults as more a resource than liability.

Cross-References

▶ Age Stereotypes
▶ *Bushen* and Longevity in Chinese Culture
▶ *Yangsheng* and Longevity in Chinese Culture

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Confucianism

▶ Confucian Culture and Filial Piety

Congestive Heart Failure

▶ Heart Failure

Congregate and Home-Delivered Meals

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Synonyms

Community nutrition program; Meals on wheels; Senior meal program; Seniors

Definition

The Congregate Nutrition Program and the Home-Delivered Nutrition Program are the key nutrition programs provided through the Older Americans Act under Title III (US Department of Health and Human Service et al. 2019a). Both programs provide adults ages 60 years and older with healthy meals and health and wellness programming. The Congregate Nutrition Program provides these meals in group settings such as faith-based locations and senior centers, while the Home-Delivered Nutrition Program serves meals to the homes of older adults who live alone (US Department of Health and Human Service et al. 2019a).

Overview

General Description

The Older Americans Act Title III provides nutrition services to older adults (US Department of Health and Human Service et al. 2017; Kowlessar et al. 2015) including the congregate meal (CM) and home-delivered meal (HDM) programs. The purpose of the Older Americans Act (see Older Americans Act) is to reduce food insecurity and hunger, support socialization, promote health and well-being of older adults, and delay adverse health conditions (see Diet, Longevity, Quality of Life) by providing community-based nutrition and wellness services (US Department of Health and Human Service et al. 2017; Kowlessar et al. 2015). These programs are funded through state-level grants provided by the Administration for Community Living's Administration on Aging (US Department of Health and Human Service et al. 2019). About 44% of CM program expenditures and 30% of HDM program expenditures are federally funded (Lloyd and Wellman 2015). In order to receive this federal funding however, states must commit a 15% match (Colello 2018). The HDM program also receives funding through Medicaid Waiver programs, which differ by state, as well as meal funding as part of transition care from hospitals, rehabilitation centers, or nursing homes back to the community (Lloyd and Wellman 2015). HDMs can also be provided through private pay services. The remaining expenditures are funded through public and private sources within each state (Lloyd and Wellman 2015). The CM program location is community-dependent and includes such places as senior centers, community centers, churches, or libraries. HDM programs provide a similar service as the CM program but to those who face obstacles in leaving their home and aims to provide a safety check. An individual must be classified as disabled, homebound, frail, or isolated to receive HDMs (Lloyd and Wellman 2015).

The CM and HDM programs are not entitlement programs (see Entitlement Program) nor do they require a means test. The Older Americans Act Title III is intended to serve: (1) those aged 60 years and older; (2) those younger than 60 years and disabled who are living in older adult housing; (3) adults who are disabled and residing at home and attending the CM site or with older adults; (4) and volunteers who work during meal hours at the CM site (US Department of Health and Human Service et al. 2017; Kowlessar et al. 2015). Participants are encouraged to make a voluntary contribution toward the cost of their meal; however, participants will not be denied the meal if they are unable or unwilling to do so. A recent study reported the majority of CM participants (81%) had contributed toward their meal while about one-half (58%) of HDM participants contributed (Mabli et al. 2017).

Meals Description

The meals provided through the CM and HDM programs are required to: (1) follow the current Dietary Guidelines for Americans; (2) provide at least one-third of Dietary Reference Intakes; (3) comply with state and local food codes; (4) be appealing for consumption; and (5) be adjusted to meet the special dietary needs as related to health, religion, and cultural/ethnic needs of participants (Lloyd and Wellman 2015; US Department of Health and Human Service et al. 2019). Each state Department on Aging is responsible for implementing these nutritional standards in a way that best meets the needs of the older adults in their state (US Department of Health and Human Service et al. 2019a). This enables flexibility and variability between states. For example, one state may choose to focus the menu on a chronic health issue affecting the majority of that state's older adult population, while another may choose to base the menu on nutrient analysis (US Department of Health and Human Service et al. 2019a).

Nutrition, Health, and Wellness Programs

In addition to a healthy meal, both programs offer other nutrition services including nutrition screening and assessment, nutrition education, and nutrition counseling. These programs also connect participants to other community-based and in-home services such as transportation, homemaker and home-health aide services, chronic disease self-management programs, fall prevention programs, physical activity programs, and home repair and modification (US Department of Health and Human Service et al. 2019a). HDM participants are more likely to utilize these additional program services (i.e., personal care, home health visits, case management, and housekeeping) than CM participants (Mabli et al. 2017).

Program Participation

Despite a growing older adult population, CM participation has been steadily declining while HDM participation is increasing. From 2006 to 2016, the number of CM served nationally declined about 9% (US Department of Health and Human Service et al. 2019b). Meanwhile the number of HDMs served between 2006 and 2016 grew about 17.5% (US Department of Health and Human Service et al. 2019b). Although the number of CMs served has declined, the number of older adults receiving these meals classified at "high nutritional risk" has increased from 14.2% in 2006 to 21.7% in 2016 (US Department of Health and Human Service et al. 2019b). The percent of those receiving HDMs classified at "high nutritional risk" also increased over a 10-year period rising from 43.1% to 57.7% (US Department of Health and Human Service et al. 2019b). The decline in CM participation is likely due to funding. When adjusted for inflation, CM and HDM program funding has decreased. Since federal support is limited to 44% of the operating needs, many states have needed to close meal sites, decrease the number of days a meal site is open, and establish waiting lists, thus reducing the number of older adults served (Lloyd and Wellman 2015). Currently, a CM is cheaper than a HDM. The average CM costs about $10.69 while the average HDM is $11.06; these costs include both donated and purchased resources (Ziegler et al. 2015). However, the CM paid cost ($9.30/meal) is higher than the paid cost of the HDM ($9.00/meal) (Ziegler et al. 2015). Many factors influence these costs including location of meal preparation site (e.g., central kitchen); region (e.g., west is most expensive, while south is least expensive); program size, with smaller programs costing more; urban versus rural community; and meal delivery method (Ziegler et al. 2015). These findings suggest it would be a better use of resources to enroll older adults in the CM program versus the HDM program. This would require reaching older adults and encouraging them to attend the CM program before they become homebound.

Meal Program Participants

A recent national assessment sponsored by the Administration on Aging examined the impact of CM and HDM participation to those not enrolled in either program. Most CM participants (41.2%) were between ages 75 and 84 years, while most HDM participants (43.1%) were ages 85 years and older (Mabli et al. 2017). Women accounted for about two-thirds of participants in both programs (Mabli et al. 2017). Over three-quarters of CM participants (76.5%) and over one-half of HDM participants (59.7%) had a high school education or higher (Mabli et al. 2017). Nearly half of CM (46.5%) and HDM (52%) participants were widowed (Mabli et al. 2017). About 60% in each group lived alone (Mabli et al. 2017). One-third of CM participants (36.7%) and HDM participants (35.3%) rated their health as "good" (Mabli et al. 2017). The majority in each group reported consuming three meals daily and about one-half in each reported having a "good" appetite (Mabli et al. 2017).

The majority of CM participants (82%) and HDM participants (85%) received meals three times or more weekly (Mabli et al. 2017). CM consumption accounts for about 41% of CM participants' daily energy intake while HDMs consumption accounts for 38% of daily energy intake among HDM participants (Mabli et al. 2017). Over three-quarters of CM participants (79.1%) and HDM participants (76.8%) rated the meal program in which they participated as "very good" and "excellent," respectively (Mabli et al. 2017). Most participants in both programs were classified as "poor" or "near poor"; however, the majority in both meal programs were classified as "food secure" (Mabli et al. 2017).

Key Research Findings

Health, Diet, and Nutrition Outcomes

Participation in the CM and HDM programs improves self-reported health, nutritional intake, food security, and maintains participants' independence (see Improving Nutrition in Old Age). Mabli and others (2017) found CM participants consumed a higher quality diet (65.5 points out of 100) than nonparticipants (59.4 points out of 100) as measured by the Healthy Eating Index-2010 (US Department of Agriculture 2018). The significantly higher scores were attributable to higher consumption of total dairy, total fruits, and total vegetables and lower consumption of refined grains by the CM participants (Mabli et al. 2017). Likewise, HDM participants tended to have more adequate nutrient intakes than nonparticipants; however, no significant differences in overall dietary quality were detected between groups (Mabli et al. 2017). Similarly, Wright and others (2015) reported significant improvements in nutritional intake for energy and protein as well as nutritional status among HDM participants. Finally, about two-thirds (67.6%) of CM participants found the program helpful compared to 82.7% of HDM participants (Mabli et al. 2017). The majority in both programs said participation helped them eat healthier foods, improved their health, and remain independent (Mabli et al. 2017).

Health Care Utilization Outcomes

Meal program participation had mixed outcomes on health care utilization. CM participation resulted in fewer hospitalizations and nursing home admissions while HDM participation did not. Among those with limited income and living alone, CM participants had lower incident of hospital admission than nonparticipants (Mabli et al. 2018). No significant differences between groups were detected among those with higher incomes or who were living with other family members (Mabli et al. 2018). In addition, CM participation was associated with lower nursing home admission rates; 3.7% of CM participants were admitted compared to 6.0% of nonparticipants (Mabli et al. 2018).

The results of HDM participation on health care utilization are mixed. Mabli and others (2018) found HDM participants were more likely to experience an emergency room visit resulting in a hospital admission than nonparticipants (18.0% compared to 8.1%). In addition, a higher percentage of HDM participants (14.3%) were admitted to a nursing home than nonparticipants (5.2%) over a 12-month period (Mabli et al. 2018). Furthermore, more HDM participants were admitted (31.6%) or readmitted (8.7%) to the hospital compared to nonparticipants (21.9% and 3.3% respectively) (Mabli et al. 2018). Finally, monthly Medicare expenses were higher for HDM participants ($1695) than nonparticipants ($1195) (Mabli et al. 2018). These findings are contradictory to that of Thomas and Mor (2013) who suggested that if more older adults participated in the HDM program, the result would be an increase in the number of older adults who would be able to remain in their homes and lower nursing home related Medicaid programming costs. Sands and others (2012) also reported a lower nursing home placement among Medicaid recipients who received five HDMs weekly than those who did not receive the meals. Finally, another study by Cho and others (2015) showed participation in the HDM program resulted in fewer hospital readmissions at three and 6 months; however, it was not known the influence that medication management services that were received had on these lower readmission rates.

Socialization Outcomes

The CM and HDM programs are also designed to provide the opportunity for socialization. CM participants report better socialization outcomes than nonparticipants (Mabli et al. 2017). Loneliness levels were similar across groups; however, less CM participants screened positive for depression than nonparticipants (Mabli et al. 2017). CM participants also reported higher satisfaction with their socialization opportunities than nonparticipants (Mabli et al. 2017). Conversely, HDM participants report more loneliness and less satisfaction with their socialization opportunities than nonparticipants; these outcomes were not significant though (Mabli et al. 2017). However, others have reported positive social outcomes related to HDM participation. For example, Thomas and Dosa (2015) reported HDM participation significantly lowered feelings of isolation among those living alone and reduced worry about being able to remain in their home. Another study by Wright and others (2015) reported significant improvements in loneliness and emotional well-being.

Food Security Outcomes

The impact of program participation on food security was mixed. Mabli and others (2017) found a lower percentage of older adults living in food insecure households among CM participants (15.5%) than nonparticipants (19.5%); however, this difference was not significant. These results are similar to those detected among HDM participants and nonparticipants. However, a significant difference in food insecurity was detected among HDM participants who received less than five meals weekly compared to nonparticipants (25.8% vs. 15.9%, respectively) (Mabli et al. 2017). Similarly, Wright et al. (2015) reported HDM participation improves food security. A smaller study in Georgia also was found that among older adults wait-listed for HDM, the odds of becoming food secure after 4 months were higher for those receiving meals than those who did not (Lee et al. 2011).

Future Directions of Research

The series of CM and HDM evaluations sponsored by the Administration on Aging provide valuable insight as to the impact of the CM and HDM programs at a national level. In order for these programs to advocate for more funding, further evidence as to the benefits they offer to participants as well as health care utilization costs is needed. A challenge, however, is that each state has autonomy over how the programs are implemented. This poses challenges when evaluating the program's impact. One strategy is to conduct ongoing standardized program evaluation across states. This can be achieved by selecting validated, easy-to-administer research tools examining nutritional risk, diet quality, food security, socialization, and health care utilization. In addition, the mixed results regarding HDM participation on hospitalization rates and nursing home placement warrants further exploration. Moreover, the number of participants classified at "high nutritional risk" has steadily increased. It is important communities encourage older adults to enroll in these nutrition programs before their nutritional status declines. This requires better marketing of the CM and HDM programs and services. Qualitative assessments (e.g., focus groups, surveys, interviews) regarding motivators and barriers toward program participation and menu selection are needed in order to better market these programs and services towards prospective and current participants.

Summary

The CM and HDM programs are the largest community nutrition programs for older adults. The information presented here indicates participation results in improved nutritional status, dietary quality and independence. Continued programming evaluation using validated and reliable assessment tools would strengthen the understanding of these impacts across states.

Cross-References

▶ Artificial Nutrition at Old Age
▶ Older Americans Act
▶ Vetek (Seniority): The Movement for Longevity and Quality of Life

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Congregate Housing

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Synonyms

Independent living units; Naturally occurring retirement communities; Retirement housing; Seniors or age-specific housing; Sheltered housing; Supportive housing

Definition

Congregate housing usually refers to multiunit housing that offers some supportive services, filling a place in the housing continuum between housing without services and supportive housing with personal care services, like assisted living. While this type of supportive housing exists worldwide, the term congregate housing is specific to a particular type of housing with services in the United States which is funded and regulated by the federal government. In all countries, the terminology used to describe the housing often varies according to the target population. For younger people with disabilities, congregate housing may be called group homes or sheltered housing, while for older adults, the terms retirement housing and independent living may be used. Living units are usually apartments with a kitchen and bathroom, while common areas often include dining areas as well as social and recreational spaces (Carder 2012).

Overview

In the United States, federal funding of purpose-built multifamily housing for low-income older people started in 1959 through Section 202 of the Housing Act. In 1978, Congress authorized the Congregate Housing Services Program (CHSP) to "provide meals and other supportive services needed by frail elderly residents and residents with disabilities in federally subsidized housing" (US Department of Housing and Urban Development 2019a). The services aim to maintain independence and delay placement in long-term care facilities. In addition to meals, services may include housekeeping, transportation, and case management. About 100 sites continue to be funded by the CHSP, but no new sites have been added since 1995.

Another US program that seeks to maintain the independence of both older adults and those with disabilities living in government-funded housing is the Service Coordinator Program (SCP), which started in 1990. Service coordinators funded by the SCP work in buildings to connect residents with community services, rather than providing services in the building (US Department of Housing and Urban Development 2019b). Evaluation shows that service coordinators can be beneficial to both residents and housing managers (Sheehan and Guzzardo 2008).

Instead of adding services to housing built specifically for older adults, programs may bring services to buildings or neighborhoods with high percentages of older adults, called naturally occurring retirement communities (NORCs). Development of formal programs to reach older adults in these communities has been geographically uneven; New York developed the first NORC with a Supportive Service Program (SSP) in 1986. By 2001, 35 NORCs had professionally staffed supportive service programs in the United States, and by 2011 this number had grown to 80 programs in 25 states (Guo and Castillo 2012). Funding through Title IV of the Older Americans Act for about 50 demonstration projects was available from 2002 through 2010 (Greenfield 2013). Some programs have since successfully obtained other sources of funding (Community-Centered Solutions for Aging at Home 2013), while others have ceased operations.

Often NORCs (and congregate housing more broadly) have been seen as only applicable to multifamily housing. However "horizontal," or community, NORCs exist in addition to the traditional "vertical" NORCs (Bronstein and Kenaley 2010). As population aging progresses globally, NORCs are being recognized in other countries (Gorczca and Grabinski 2018; Jiang Lou and Lu 2018).

Linking community services with housing is accomplished now in some communities through the Village model instead of the NORC supportive services model (Greenfield and Davitt 2012). Villages are consumer-directed organizations that aim to provide members with opportunities for social and civic engagement as well as access to services that can support aging in place. Research to date suggests that villages may be an effective way for older adults living independently to receive some of the instrumental and emotional support benefits of the congregate model (Graham and Stark 2017; Graham and Kurtovich 2018).

Summary

There is an ongoing need to help older adults age in place in a wide variety of housing situations. This may create opportunities for "aging-in-place housing specialists" to work with residential property managers (Ewen Lewis Carswell Emerson Washington and Smith 2017). Access to necessary services and the affordability of both housing and services will continue to be challenges as housing and service providers as well as older adults themselves continue to collaborate and innovate.

Cross-References

▶ Affordable Housing
▶ Care Coordination

▶ Care Needs
▶ Productive Aging
▶ Retirement Villages
▶ Supportive Housing

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Connected Home

▶ Smart Homes

Conscious Aging

▶ Aging: An Islamic Perspective

Conscious Capitalism

▶ Corporate Social Responsibility and Creating Shared Value

Consensual Union

▶ Cohabitation

Consequences of Pneumonia in Older Adults

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Synonyms

Catastrophic disability; Immunosenescence; Pneumonia; Post-influenza pneumonia; Post-pneumonia cognitive decline; Post-pneumonia myocardial infarction; Post-pneumonia sequelae

Overview

In most industrialized countries, pneumonia (often classified as influenza and/or pneumonia) is the only infectious disease in the top 10 causes of death (Statistics Canada 2018). In contrast to the developing world where pneumonia frequently kills children, in industrialized nations most of these deaths are in older adults (55+ years). Pneumonia is an insidious infection as it accelerates the development of seemingly unrelated chronic health conditions and can precipitate a decline in health and independence. Older adults who are hospitalized for community-acquired pneumonia have an increased risk of mortality (unrelated to pneumonia) in the next 5 years and increased risk of subsequent hospitalization (Yende et al. 2007). One study of American Medicare recipients reports that those who acquire pneumonia during a hospital stay have 2-year mortality rates that are twice as high as those who do not acquire pneumonia and they accrue an extra $15,000/year in health-care costs, primarily due to the development other chronic inflammatory conditions (Thomas et al. 2012). Having pneumonia in mid- to late-life is associated with increased risk of developing cardiovascular disease (Singanayagam et al. 2012; Corrales-Medina et al. 2015a), depression (Davydow et al. 2013, 2014), metabolic disorders (Yende et al. 2007), and dementia (Shah et al. 2013; Tate et al. 2014). Older adults who are hospitalized for pneumonia, even those who had no functional impairments, are likely to become impaired in the activities of daily living (Davydow et al. 2013). These post-pneumonia sequelae are the reason that the Ontario Burden of Infectious Disease Study lists pneumonia as the most economically costly infectious disease due to years of life lost and reduction in health-adjusted life years (Kwong et al. 2010).

Disturbingly for those of us who are getting older, or care for an older adult, is that this increase in mortality and declining health is independent of comorbid conditions. This means that having pneumonia in mid- to late-life reduces the years of good health in otherwise healthy, active older adults. Although pneumonia can be devastating to older adults in perfect health, it is even more problematic for those with pre-existing conditions. Individuals with chronic conditions such as cardiovascular disease, lung disease, diabetes, frailty, or cognitive decline are at increased risk of acquiring pneumonia and have poorer outcomes after hospitalization (Shea et al. 2014). There is a strong case to be made that age is less of a risk factor than the presence of multiple chronic conditions and frailty (Hak et al. 2004; Shea et al. 2014). Since socioeconomics and health are inextricably linked, individuals of lower socioeconomic status are more likely to have risk factors such as multiple chronic conditions and therefore are more likely to be hospitalized for influenza/pneumonia (Crighton et al. 2007; Grantz et al. 2016).

Key Research Findings

Severe Pneumonia Can Result in Widespread Organ Damage

Studies on the consequences of pneumonia have generally focused on events that occur in the airway. Yet, considerable clinical and laboratory evidence indicates that during severe pneumonia that results in bacteremia (~20% of hospitalizations), the responsible bacteria can gain access to and cause long-lasting damage in other vital organs. One of the most striking examples is the heart, where opportunistic pathogens such as *Streptococcus pneumoniae*, the leading bacterial cause of community-acquired pneumonia, kill cardiomyocytes, impair heart function, and prime permanent cardiac scarring in damaged heart tissue that presumably impairs contractility in survivors (Brown et al. 2014; Alhamdi et al. 2015; Gilley et al. 2016). Notably, the incidence of adverse cardiac events coincides with severity of infection, with individuals requiring admission into an intensive care unit having the highest rates of heart failure. As it is older adults who are most susceptible to severe pneumonia, it is also older individuals who are most susceptible to concomitant adverse cardiac events. Overall, ~20% of adults hospitalized for pneumococcal pneumonia experience an adverse cardiac event during hospitalization, and these individuals are fourfold more likely to die than those with pneumonia alone (Musher et al. 2007). Importantly, hospitalization for pneumonia and severity of pneumonia are also linked to greater incidence of adverse cardiac events and mortality in convalescence. This extends for a period of up to 10 years post-infection (Corrales-Medina et al. 2011, 2012, 2015a, b). Thus, the negative consequences of severe pneumococcal pneumonia on the heart are considerable and both acute and long-lasting.

Two other critical organ systems that can become damaged as result of severe pneumonia that results in invasive disease include the central nervous system and kidneys. *S. pneumoniae* and *Haemophilus influenzae*, also a common cause of bacterial pneumonia, are neurotropic and capable of crossing the blood-brain barrier to cause bacterial meningitis. In addition to having a 17–30% mortality rate, survivors of these types of bacterial meningitis typically have lifelong cognitive impairments (Erdem et al. 2014). Acute kidney injury also occurs during severe *S. pneumoniae* infection and is similarly linked to elevated mortality rates (Murugan et al. 2010; Lin et al. 2016). Thus, the notion that bacteria are restricted to the airway during pneumonia is not necessarily accurate. Moreover, the presence of bacteria in the bloodstream allows for disseminated organ damage, and this in turn has a harmful effect on not only hospital outcomes but also long-term survival and quality of life, as many of these individuals must now deal with the sequelae of these serious infections. Fortunately, effective vaccines against the most virulent version of *S. pneumoniae* and *H. influenzae* protect against invasive disease. Moreover, the influenza vaccine confers indirect protection against severe pneumonia by preventing co- or secondary infections. Thus, these disease states can potentially be avoided.

Cognitive Decline/Dementia

Life-threatening infections such as sepsis or inflammatory events (e.g., acute respiratory distress syndrome) are associated with cognitive decline that is evident even years after the event (Hopkins et al. 1999; Mikkelsen et al. 2009, 2012; Ehlenbach et al. 2010; Iwashyna et al. 2010). It has also been demonstrated that individuals with some degree of cognitive impairment or dementia have an accelerated decline in cognitive capacity after surgery, injury, or infections (Abildstrom et al. 2000; Holmes et al. 2003; Shah et al. 2013). What is surprising is that having pneumonia is strongly associated with cognitive decline even in cognitively intact individuals. This was explored in a well-controlled study by Tate et al. In this study, older adults took various cognitive tests every 6 months and were followed for at least 6 years. Approximately 7% of the participants ($n = 221$) developed pneumonia severe enough to be hospitalized but not severe enough to require an ICU stay (i.e., was not perceived as life-threatening). Those who had pneumonia were two times as likely to develop dementia over the 3 years of follow-up (HR = 2.3, CI: 1.6–3.2) than those who did not. Disturbingly, only individuals who showed no evidence of any cognitive impairment were included in this study, demonstrating that post-pneumonia cognitive decline occurs in otherwise healthy, cognitively intact individuals (Tate et al. 2014). Consistent with other studies (El Solh et al. 2006; Davydow et al. 2013), hospitalization for pneumonia is much more strongly associated with cognitive decline than hospitalization for any other reason (Tate et al. 2014). The general consensus is that between 20% and 38% of older adults hospitalized for pneumonia will develop dementia or become cognitively impaired earlier than expected (Torres et al. 2004; Tate et al. 2014; Girard et al. 2018), but since many of these studies have a relatively short follow-up period (<6 years), this may be an underestimate.

The mechanisms by which pneumonia precipitates cognitive decline or dementia are currently speculative. Elevated levels of serum cytokines and changes in behavior and cognition have been evident for decades. Older adults hospitalized for pneumonia have more pronounced and protracted inflammatory responses than younger adults (Bruunsgaard et al. 1999), and these increase in inflammation and delay in returning to homeostasis may contribute to poor outcomes including cognition (Yende et al. 2008, 2011). Indirect evidence for the role of soluble mediators in inflammation in post-pneumonia cognitive decline comes from observations that the risk of functional decline post-pneumonia is proportionate to severity of the infection (Torres et al. 2004). Further support for the risk of elevated cytokines contributing to cognitive was found in patients with Alzheimer's disease. Those with the greatest decrease in cognitive scores post-infection had the highest levels of serum IL1β (Holmes et al. 2003). Mechanistic evidence is lacking, but some studies have suggested that during neurodegeneration, microglia are primed to induce inflammatory responses and a secondary insult such as infection causes them to produce high levels of inflammatory cytokines, which perpetuate the state of inflammation (Cunningham et al. 2009). Along such lines, studies with animals have shown that exposure to bacterial cell wall products, which are highly inflammatory, alone results in the death of neurons in the dentate gyrus of the hippocampus (Orihuela et al. 2006).

Severe Pneumonia Can Unmask Underlying Metabolic Dysregulation

It is unclear whether having pneumonia in mid- to late-life increases the risk of developing diabetes or whether having pneumonia unmasks preexisting conditions since metabolic dysregulation is a well-known risk factor for pneumonia (Kornum et al. 2008, 2010; Foltran et al. 2013). The observation that diabetics are more susceptible to pneumonia was made over a decade ago, and recent evidence indicates that this is due to hyperglycemia rather than comorbid conditions such as obesity (Kornum et al. 2007; Hirata et al. 2013; Alexopoulos et al. 2016). In fact, even in nondiabetics, careful management of hyperglycemia during hospitalization reduces mortality from life-threatening infections (van den Berghe et al. 2001, 2003). The mechanism by which blood glucose affects antibacterial immunity is unclear, although decreases in phagocytosis and cellular recruitment to the site of infection have been reported (MacRury et al. 1989; Martinez et al. 2016a, b). Older adults are at higher risk of developing metabolic disorders and often have higher blood glucose levels, even in the absence of diabetes (Dharmarajan et al. 2016) which contributes to both susceptibility to pneumonia and outcome. Blood glucose levels at admission to hospital are a predictor of mortality, even in nondiabetic patients, and the elevation in blood glucose need not be extreme to increase mortality risk (Bagshaw et al. 2009; Lepper et al. 2012; Salonen et al. 2013; Akirov and Shimon 2016; Koskela et al. 2014; Schuetz et al. 2014; Akirov and Shimon 2016). This increased risk of mortality extends to as long as 5 years after release from the hospital at which time very few deaths are from pneumonia (Koskela et al. 2014; Akirov and Shimon 2016). To determine whether preexisting and subclinical dysregulation of glucose metabolism contributed to pneumonia outcome, hospitalized patients had their postprandial levels of glucose measured during their entire hospital stay. Those with the highest spikes of blood glucose after a meal (even if fasting glucose fell in the normal range) had increased mortality 12 months after admission (Koskela et al. 2014). These data suggest that pneumonia uncovers rather than causes metabolic dysregulation in older adults.

C

Dysregulated Inflammatory Responses May Contribute to Post-Pneumonia Health Impairments

The inflammatory response is essential for surviving severe acute infections; however, excessive or prolonged inflammation causes pulmonary epithelial hyperpermeability and immunopathology and, in the case of pneumonia and influenza, is often the actual cause of death (Matthay et al. 2012). Levels of inflammatory markers are substantially higher in older adults and in frail inpatients (Palmer et al. 2019), and furthermore they are correlated with prognosis and adverse outcomes of pneumonia. For example, C-reactive protein (CRP) is elevated during acute infection and pneumonia and predicts adverse outcomes (Verschoor et al. 2014; Ticinesi et al. 2017). Similarly elevated interleukin (IL)-6 levels at either baseline or 1 week post-admission are predictive of 28-day mortality (Takahashi et al. 2016). It is likely that the ability to resolve inflammation following critical illness is a major determinant of prognosis. Studies have shown that patients with persistently high levels of CRP 3 months following discharge exhibit the poorest mobility (Griffith et al. 2016), and high CRP levels prior to discharge are a significant predictor of readmission (Gulcher et al. 2016). Available evidence suggests that older adults have excessive and prolonged inflammatory responses which contribute to mortality and post-influenza and pneumonia health impairments (Yende et al. 2008, 2011); however, mechanistic links between these inflammatory processes and outcomes of pneumonia and influenza have yet to be established.

Summary

Older adults have unacceptably high rates of hospitalization for pneumonia, ranging from >270/100,000 in 50–65-year-old to >4000/100,000 in those older than 85 (Storms et al. 2017). Of these hospitalizations between 20% and >30% are severe enough to require an ICU stay (Storms et al. 2017). Although having a pre-existing healthy condition or frailty increases the risk of hospitalization for pneumonia, even healthy older adults are likely to experience life-changing changes in health and independence as a result of infection. In fact, 5-year mortality rates for those hospitalized for pneumonia are as grim as those hospitalized for congestive heart failure, stroke, or major fracture (Yende et al. 2007).

The majority of pneumonia in older adults is caused by *Streptococcus pneumoniae* or results from post-influenza pneumonia, and consequently vaccination should be aggressively pursued to prevent not only the primary infection but also the long-term health consequences. Vaccination is admittedly less effective in older adults than children and young adults (Rudnick et al. 2013; Leventer-Roberts et al. 2015), although there is good evidence that even when it does not prevent infection, it improves outcomes by reducing time in the ICU and heart attacks and increases the chance that the patient will be able to live independently post-discharge (Arriola et al. 2017). Because contact with children is a major risk factor for infection, effective vaccination strategies should include vaccinating whole communities (Loeb et al. 2010).

Vaccination may be the only strategy we have to prevent hospitalization for pneumonia; however, it is clearly not sufficient. In the immediate term, preventative strategies such as vaccination for influenza and pneumococcal pneumonia should be aggressively pursued in order to minimize these health consequences. Older adults who have had pneumonia should be considered at risk for developing other, seemingly unrelated, health issues. In the longer term, further research is required to understand the mechanisms by which pneumonia accelerates or exacerbates age-related health issues. Dysregulated inflammatory responses and an inability to resolve inflammation are potential mechanisms by which pneumonia and declining health may be linked.

Cross-References

▶ Aging and Health Disparities
▶ Dementia
▶ Frailty in Clinical Care
▶ Human Immune System in Aging
▶ Influenza Vaccination in Older Adults
▶ Myocardial Infarction
▶ Pneumonia
▶ Prevention of Age-Related Cognitive Impairment, Alzheimer's Disease, and Dementia

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Conservatorship

► Guardianship

Consortium on Health and Aging: Network of Cohorts in Europe and the United States (CHANCES)

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Overview

The Consortium on Health and Ageing: Network of Cohorts in Europe and the United States (CHANCES) project is a collaborative large-scale integrating project funded by the European Commission within the Seventh Framework Program and coordinated by the Hellenic Health Foundation.

CHANCES aims at combining and integrating ongoing prospective cohort studies in order to produce evidence on aging-related health characteristics and determinants of healthy aging in Europe and the United States and their socioeconomic implications. Fourteen cohorts participate in the project, covering populations from eighteen EU member states, four associate countries, and three additional countries. The combination of these different studies would lead to an integrated approach to the study of health in the older people.

Sample

Target Population

For the purpose of this project, the limit of 60 years of age is selected to define the older people. However, most cohorts included in the consortium include subjects aged 50 or over, and separate analyses are conducted on health-related characteristics and determinants in subjects aged 50–59, 60–69, and 70+ years.

Sample Design

Three types of studies are included in the consortium: (i) longitudinal (cohort) studies which were primarily established to address health issues related to aging and aging-related conditions (these studies have detailed and repeated assessments of chronic conditions and disabilities and other characteristics related to aging) (e.g., occupational status); (ii) longitudinal (cohort) studies which were established for purposes other than the investigation of aging-related conditions but include a sufficiently large number of older people to justify specific analyses (these studies have more limited information but include large and diverse populations); and (iii) cross-sectional studies which would allow to identify associations between aging-related conditions and relevant health outcomes, to be tested in the longitudinal studies. The combination of these different types of studies would lead to an integrated approach to the study of health in the older people.

Sample Size

The CHANCES project has a large overall sample size that provides blood samples for repeated overtime assessment of biomarkers that either alone or in combination may turn out to be important predictors of health in the older people. The CHANCES project includes many cohorts with validated information on social, environmental, lifestyle, and nutritional factors and with longitudinal assessment of health characteristics. Several cohorts have included a second assessment of health determinants, thus allowing a more accurate measurement of the determinants of interest, as well as an estimation of changes over time. A similar opportunity is provided for the assessment of biomarkers of nutrition, aging, and health.

Fourteen cohorts and cohort consortia were included in the project: the Cohort of Swedish Men (COSM), the EPIC-Elderly Study, the ESTHER Study, the HAPIEE Study, the MORGAM Study, the Northern Sweden Health and Disease Study, the Rotterdam Elderly Study, the Seneca Study, the SHARE Study, the Swedish Mammography Cohort (SMC), the Tromsø Study, the Zutphen Elderly Study, as well as two studies conducted in the United States – the Nurses Health Study and the National Institutes of Health-AARP (formerly known as the NIH-AARP Study).

Previous research, although very important, has been hampered by sample size limitations and restriction to particular population groups with narrow ranges of exposures and inherent difficulties for generalization. The various cohorts participating in CHANCES provide a wide coverage of the European and North American populations, as well as a large overall sample size which facilitates the statistical documentation of findings and allows consideration of an extended list of factors that may modify the association between social, environmental, lifestyle, and nutritional factors and health in the elderly. The participation of North American cohorts, conducting parallel analyses to those carried out in Europe, is extremely valuable in order to explore further the consistency and generalizability of findings to non-European populations. Furthermore, all CHANCES cohorts are already established longitudinal studies.

The CHANCES project has additional advantages. Not only does it offer a large overall sample size, but it also provides in a sizable part of the populations under study blood samples for repeated overtime assessment of biomarkers that either alone or in combination may turn out to be important predictors of health in the older people. If such biomarkers or combination of biomarkers were shown to be powerful predictors or correlates of aging, they would provide a powerful proxy of aging in studies assessing the anti-aging potential of lifestyle and nutritional interventions or even medication.

Objectives

The CHANCES project aimed to combine and integrate on-going studies in order to produce evidence on aging-related health characteristics and determinants in Europe, addressing five main types of health-related characteristics:

1. Occurrence (incidence) of chronic conditions, disabilities, and mortality
2. Presence (prevalence) of chronic conditions and disabilities
3. Health-related determinants (risk factors) of chronic conditions and disabilities
4. Aging-related characteristics as determinants of chronic condition, disabilities, and mortality
5. Social and economic implications of chronic conditions, disabilities, and mortality in the elderly

CHANCES focuses on four major groups of chronic conditions and disabilities which account for a large proportion of the morbidity and mortality burden in the elderly population: (i) cancer; (ii) diabetes and cardiovascular diseases; (iii) fractures and osteoporosis; and (iv) cognitive function and Alzheimer's disease. Health-related determinants of interest comprised of (i) socioeconomic factors (e.g., education, income), (ii) environmental factors (e.g., occupational exposures), (iii) lifestyle factors (e.g., tobacco smoking, alcohol drinking), and (iv) nutritional factors (e.g., BMI, dietary patterns). Aging-related determinants included (i) biomarkers and (ii) genetic profiles of aging.

Using the above-indicated data from CHANCES cohorts, the following aims target at: (a) Estimating incidence of the indicated health outcomes and associated cause-specific mortality, (b) estimating prevalence of the health conditions indicated above and related disability, (c) identifying health- and aging-related determinants of these conditions and of the resulting disability and mortality, and (d) evaluating the social and economic implications of chronic conditions, disabilities, and mortality in the elderly (where applicable).

To achieve the above objectives, each cohort provides relevant data. Combining the different types of studies required harmonization of data across the diverse participating cohorts with respect to outcomes and exposures of interest. This major work is carried out by the THL

(National Institute for Health and Welfare (Finland)), CHANCES partner. Through a web-based WIKI space, accessible to CHANCES consortium and collaborators, descriptions of the participating studies, definitions of harmonized variables, and conversion rules form the different studies, and the characteristics of the harmonized data are fully documented (see ► "Big Data") (Boffetta 2015).

Outcomes: Health Conditions and Mortality

The following outcomes were included: lung function; prevalence of hypertension, incidence, and family history of coronary heart disease, stroke, and diabetes; prevalence and incidence of cancer (by organ of origin); prevalence and incidence of fractures and osteoporosis; prevalence and incidence of depression, cognitive impairment, and dementia; multi-morbidity; mortality (by cause); disability and frailty; quality of life; and self-perceived health (Boffetta 2015; Boffetta et al. 2014).

Exposures

Lifestyle (including tobacco smoking, drinking status, physical activity); anthropometry (including weight, height, waist/hip circumference); socioeconomic status (including education, marital status); medical history (including use of drugs, reproductive history); dietary factors (including total energy intake, intake of specific macro and micronutrients, foods and food groups, ethanol intake); and blood biomarkers (including ApoA1, ApoB, CRP, GGT, glucose, glycated hemoglobin, total and HDL cholesterol, triglycerides, vitamin D; oral glucose tolerance test; biomarkers of oxidative stress (hydroperoxides), antioxidant status (biological antioxidant potency), and redox status (total thiols)) (Boffetta et al. 2014).

In order to assess in particular the role of biomarkers of aging on the indicated health outcomes, a list of biomarkers to be measured in a common fashion by five CHANCES partners was established, and measurements of electrolytes Ca, Mg, Na, Cl, and K, the oxidative stress markers reactive oxygen metabolites, biological antioxidant potential, and total thiols in proteins, 25-hydroxy vitamin D, gamma glutamyl transferase, creatinine, high sensitive C-reactive protein and the B vitamins folate and vitamin B12, alanine aminotransferase, uric acid, urea, ROM, TTL and H-index, I-Index, and L-index were undertaken in subsamples of five CHANCES cohorts which agreed to provide blood samples for their participants.

To emphasize the importance of cognitive disorders among the elderly, an Alzheimer's Disease (AD) registry with validated cases and suitable controls was created in Umeå (Sweden) which enables the investigation of the association between certain biomarkers such as inflammatory markers, protein and metabolic patterns, serological analyses, and analysis of specific substances and AD incidence (see ► "Alzheimer's Disease").

Statistical Analyses

Taking into account the inherent differences across cohorts in measurement of exposures/outcomes, statistical analyses for the different research hypotheses are carried out by means of meta-analysis. Given the large number of different cohorts participating in CHANCES and considering the different policies for data sharing in each of them, two approaches are used for the pooled data analyses, which are coordinated by ad hoc writing groups. The first is to share individual-level data after signing a data transfer agreement. The second approach is to analyze the data locally in the participating centers using program scripts provided by the writing groups and to share the results of the local analyses for a meta-analysis (Boffetta et al. 2014).

Directions of Research

Research Topics Investigated Within the CHANCES Project by Outcome of Interest

Cancer Incidence: Smoking, vitamin D, food groups/dietary patterns, alcohol consumption, socioeconomic position, disability-adjusted life years (DALY), and population attributable fractions for major determinants (see ► "Healthy Aging").

Cardiovascular Diseases and Diabetes: Prediction models and adapted prediction scores, HbA1c levels, smoking, alcohol consumption, education, obesity, dietary patterns, vitamin D, DALY, and population attributable fraction for major determinants (see ► "Exercise and Healthy Cardiovascular Aging").

Fractures and Osteoporosis: Socioeconomic status, weight and weight changes, DALY, population attributable fraction for major determinants, and excess mortality following hip fractures (see ► "Frailty and Social Vulnerability").

Cognitive Decline and Alzheimer's Disease: Cardiovascular diseases, lipid intakes, dietary patterns, sedentary behavior, lifetime smoking, and DALY.

Disabilities and Mortality: Adapted prediction scores, HbA1c levels, smoking, alcohol consumption, education, self-perceived health, physical activity, obesity, dietary patterns, vitamin D, telomere length, DALY, population attributable fraction for major determinants, and predictive value of potential frailty criteria (see ► "Disability Measurement").

Genetic: Telomere length, lifestyle factors, and height (see ► "Telomeres") (Boffetta et al. 2014).

The CHANCES project produced novel and strong scientific evidence on the determinants of healthy aging in Europe, including modifiable behaviors, nutritional factors, and/or other exposures. Projects developed within CHANCES also touch on the socioeconomic inequalities and consequent implications for society regarding the continuously increasing aging populations.

This evidence provides valuable information necessary for the development of health strategies that can contribute to the prevention and better treatment of major diseases affecting the older people, hence also improving their quality of life. In addition, CHANCES has provided a brief, validated, and standardized instrument to assess health and aging-related outcomes (Health Module) in a comparable fashion across European aging populations. Taken together, these results can be used to shape the agenda of European public health policy in order to help society to meet one of its greatest challenges: to treat older people as equal, active partners yet, at the same time, recognize their special needs and offer them a good quality of life.

In addition, the CHANCES project produced a platform of a well-established network of aging cohorts which can be used for further collaborative projects investigating the role of various health determinants and outcomes in the older people.

Summary

The challenges associated with the global aging of populations are among the major concerns of modern-day societies. Mortality, morbidity, and disability increase steeply with age. These burdens, which are associated with the aging of communities, necessitate actions that counteract the negative aspects of demographic aging by adding meaningful years to life, limit ill health, and increase opportunities of social involvement of older people. Good quality data on diverse health outcomes and determinants are fundamental to any such effort and should be valid (based on accurate measurements), precise (based on large populations), and repeatedly measured over time.

Toward this direction, CHANCES brings together 17 partners and 14 cohorts from Europe and North America in a consortium whose efforts are channeled through 11 Work Packages (WPs). The ultimate goal is to provide new evidence on the health of aging populations.

CHANCES focuses on four major groups of chronic conditions and disabilities, typical in the aging populations: cancer; diabetes, and cardiovascular diseases; fractures and osteoporosis; and cognitive function and dementia disorders. Harmonization of the available data across the diverse participating cohorts on outcomes and exposures of interest is successfully undertaken by the THL (National Institute for Health and Welfare, Finland) CHANCES partner and a

flexible and dynamic tool for the documentation and update of this procedure has been established.

The project develops an efficient and flexible infrastructure for conducting joint (pooled) analyses to estimate the prevalence, incidence, mortality, and economic implications (where appropriate) of the indicated conditions, as well as to identify/explore socioeconomic, environmental, lifestyle, and nutritional determinants.

Genetic profiles and biomarkers associated with aging are also investigated, identified, and estimated. In addition, a feasibility study for an intervention trial against progression of prostate cancer, based on a low-fat, plant-based, low-meat, and high-fish diet and regular exercise, is undertaken in Denmark.

Moreover, an Alzheimer's Disease (AD) registry with 372 validated cases of Alzheimer's disease and a set of suitable controls are created in Umeå, Sweden. Each had at least one blood sample available on which certain biomarkers are measured and their role in AD is further explored. In parallel, a brief, reliable instrument to assess health and aging-related outcomes (Health Module) in a comparable fashion in European aging populations is created within CHANCES.

Cross-References

- ▶ Alzheimer's Disease
- ▶ Big Data
- ▶ Cardiovascular Response
- ▶ Disability Measurement
- ▶ Frailty and Social Vulnerability
- ▶ Healthy Aging
- ▶ Telomeres

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Consortium on Interplay of Genes and Environment Across Multiple Studies

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Overview

The Interplay of Genes and Environment across Multiple Studies (IGEMS) group is a consortium of longitudinal twin studies of adult development and aging established a decade ago to explore the nature of social context effects and gene-environment interplay in late-life functioning. The combined data contains information from over 50,000 individual participants aged 25–102 at baseline (including nearly 20,000 complete twin pairs) with median follow-up of 9.5 years. Studies include measures of aging-relevant outcomes in three broad domains: physical health and functional ability, psychological well-being (emotional stability/depression), and cognitive health. Studies also include multiple indicators of the social environment, spanning early childhood through late adulthood, and, by virtue of different nationalities and birth years, encompass different environmental contexts with respect to healthcare, retirement systems, and other social policies.

Research has firmly established the association of social context with late-life health and functioning. Yet this research unambiguously explicates neither the basis for these associations nor how social context relates to the biological and genetic factors known to contribute to later life functioning. The advantage of twin studies is the strengthening of causal inference through co-twin control methods (McGue et al. 2010) and use of biometric models to quantify the extent to which associations between risk and outcome are driven by the same genetic or the same environmental influences (van der Sluis et al. 2012).

Several longitudinal twin samples, located in different countries and employing somewhat different measures, have individually accumulated substantial data. However, large sample sizes are needed to test gene-environment interactions, and collaborating across studies enriches environmental variation. Consequently, a collaboration among existing longitudinal twin studies was initiated, with a central focus on determining how social context is related to physical functioning (health, functional ability) and psychological functioning (well-being, cognition) in mid-life and older ages. Through this, a foundation has been laid for future studies of gene-environment interplay in late-life functioning.

The heuristic model that guides the investigation of gene-environment interplay in late-life functioning emphasizes the importance of two gene-environment processes, built on Schmalhausen (1946), Shanahan and Hofer (2005), Boardman et al. (2013), and Reiss et al. (2013). First, it is hypothesized that environmental exposures and social contexts do not occur at random but rather reflect an individual's genetically influenced behavior and choices (i.e., gene-environment correlation). It is known, for example, that there are heritable influences on social factors including social support, social engagement, and social isolation. It is further hypothesized that gene-environment correlations are a major contributor to late-life phenotypic stability. Data in the IGEMS consortium allow researchers to chart the contributions of changes in social context to behavioral discontinuities; the twin study design allows researchers to further explore the nature of gene-environment interplay in these transitions.

Second, it is hypothesized that experiential factors can either diminish or amplify the influences of genetic effects on late-life outcomes (genotype by environment interaction, G $\times$ E). Two alternative models of G $\times$ E are directly relevant. Evolutionary models predict that the G $\times$ E form recognized most broadly as the *diathesis-stress model* will be more pronounced in late life. Specifically, during most of life, the typical human lives in an environment that is low in stress relative to the environments in which their species evolved. In old age, biological, psychological, and social stresses are considered to be higher due to more negative change or declines. Thus, at times of relatively increased stress – such as old age – an organism's response to an unfavorable environment will depend on a unique combination of genes, so that deleterious genetic effects on physical manifestations of health will be maximized. This pattern of findings is supported by earlier work by IGEMS investigators, showing that the heritability of physical health in mid-life is maximized when current income (Johnson and Krueger 2005) is low.

Alternatively, environmental factors can suppress genetic effects. This model is particularly relevant to extreme forms of physical disability or disease, which diminish the impact of genetic factors by reducing the opportunity for self-selection of activities that maintain stable functioning.

Study Design and Features

IGEMS has grown from 5 studies to, now, 16 studies or cohorts, encompassing 5 countries: Sweden, Denmark, Finland, the United States, and Australia. The total sample size is 52,456 individuals including both members of 7064 monozygotic pairs and 12,686 dizygotic pairs, of which 3997 pairs are opposite sex. (Total Ns include members of incomplete pairs.) Brief descriptions for each participating study are provided below. Links to further information about each study can be found at https://dornsife.usc.edu/labs/igems/. Several studies have also made their data publicly available, for example, via the National Archive of Computerized Data on Aging.

Sweden

Swedish studies are independent samples each drawn from the population-based Swedish Twin Registry. The Swedish Adoption/Twin Study of Aging (**SATSA**) began in 1984. The base population comprises all pairs of twins from the registry who indicated that they had been separated before the age of 10 and reared apart, and a sample of twins reared together matched on the basis of gender, date, and county of birth. The **OCTO-Twin** Study (Origins of Variance in the Old-Old) included twin pairs who were over the age of 80 at baseline in 1991. **GENDER** is a study of unlike-sex twin pairs born between 1906 and 1925. The Twin and Offspring Study in Sweden (**TOSS**) includes 909 pairs of same-sex twins who were parents of adolescents.

Denmark

The Longitudinal Study of Aging Danish Twins (**LSADT**) began in 1995 with the assessment of members of like-sex twin pairs born in Denmark prior to 1920. The study of Middle-Aged Danish Twins (**MADT**) includes twins ranging in age from 46 to 68 years at the original assessment. The Mid-aged Danish Twin (**MIDT**) study includes 10,487 twins representing all members of the Danish Twin Registry for the birth years 1931 through 1969 not already participating in MADT.

Finland

The older Finnish Twin Cohort (**FTC**) study started in 1975 by contacting all same-sex Finnish twin pairs born before 1958 with both co-twins alive in 1975 (N = 13,888 pairs). From this cohort, female pairs aged 63–76 in 2000–2001 participated in the Finnish Twin Study on Aging (FITSA). Follow-up examinations were in 2003–2004 and a survey in 2011. FinnTwin16 (**FT16**) is a cohort of younger twins born between 1975 and 1979. Waves 4 and 5 are included in IGEMS.

United States

Each US study consists of an independent sample. The Minnesota Twin Study of Adult Development and Aging (**MTSADA**) is a population-based sample drawn from state birth records. Two-thirds of the sample was age 60 years or older at intake. The Vietnam Era Twin Study of Aging (**VETSA**) is a community-dwelling sample of male-male twin pairs, all of whom served in some branch of US military service sometime between 1965 and 1975. Wave 1 testing took place between 2003 and 2007; wave 3 is now underway. Mid-life in the United States (**MIDUS**) is a national telephone/mail survey originally carried out in 1995–1996 that included specific recruitment methods for twins. The Carolina African-American Twin Study of Aging (**CAATSA**) used public records including census, vital statistics, social security death records, a credit reporting service, and voter registration records to identify all living African-American twins in the State of North Carolina born between 1920 and 1970. Project Talent is a longitudinal study begun in 1960, with a nationally representative sample of 377,000 US high school students born 1942–1946. Follow-up surveys were conducted at ages 19, 24, and 29. The Project Talent Twin and Sibling Study (**PTTS**) tracked 96.4% of the original PT twins and siblings of twins in the PT sample, including 21.0% identified as deceased. A survey was mailed in 2014 to this sample, now aged 69–73, and cognitive assessments are underway.

Australia

Both Australian cohorts were recruited from the Australian Twin Registry. The Australian Over 1950s study (**A50**) is based on a questionnaire mailed between 1993 and 1995 to twins age 50–95. **OATS** incorporates in-person assessments every 2 years for twins aged 65 and older, and it is currently completing its fourth wave.

The range in study years and intake ages across the 16 IGEMS studies results in unique coverage of cohorts and historical periods. As shown in Table 1, the IGEMS sample permits sequential comparisons across six cohorts. This feature is an enormous advantage in sorting out age and cohort effects.

IGEMS Measures

Measures used in IGEMS analyses include aging-relevant outcomes in three broad domains: physical health and functional ability (e.g., self-reported diseases, subjective health, BMI, grip strength, motor function, activities of daily living), psychological well-being (e.g., depressive symptoms, anxiety symptoms, subjective well-being, loneliness), and cognitive health (i.e., scores on cognitive tests; survey assessments of dementia). Predictors and covariates include health behaviors (e.g., smoking, alcohol, physical

Consortium on Interplay of Genes and Environment Across Multiple Studies, Table 1 Number of individuals by birth cohort in IGEMS studies. Columns indicate birth years, while rows indicate age at first assessment. The number of cohorts shows the number of IGEMS studies contributing data to each row

	BIRTHYEAR (% Women)							
INTAKE AGE	<1914	1915-1929	1930-1944	1945-1959	1960-1974	1975+	TOTAL	# cohorts
<35			2540 (54%)	2279 (52%)	503 (60%)	5382 (54%)	10704 (54%)	4
35-49			319 (50%)	2817 (59%)	3471 (60%)	2 (0%)	6609 (59%)	3
50-64		764 (55%)	5602 (59%)	14323 (49%)	352 (56%)	1 (100%)	21042 (52%)	4
65-79	504 (65%)	5754 (58%)	3641 (51%)	1444 (53%)			11343 (55%)	4
80-94	2484 (65%)	241 (63%)	1 (100%)				2726 (65%)	2
95+	32 (66%)						32 (66%)	1
TOTAL	3020 (65%)	6759 (58%)	12103 (55%)	20863 (51%)	4326 (59%)	5385 (54%)	52456 (55%)	

activity, cognitively engaging leisure activity), social resources, and indicators of socioeconomic status.

Given differences across studies in how similar constructs were assessed, strong emphasis is placed on harmonization of relevant phenotypes and outcomes to enable the combined analysis of the multiple sets of data. Because integrative data analysis (IDA), where data are pooled across samples to increase power and finely consider between-study heterogeneity, is the preferred method, scale scores were created that are common across studies. This requires overlapping item content across the studies as well as across time for longitudinal hypotheses. For some measures, it was possible to identify a common metric, e.g., body mass index (BMI), lung function, and blood pressure. For harmonizing education and occupation, all studies were recoded to ISCED and ISCO, as an international standard. Where a common metric was not already available, item response theory (IRT) techniques were implemented to create harmonized scores across studies. Recoding was accomplished by identifying overlapping item content and response formats and then applying psychometric analysis to establish measurement invariance via IRT and factor analytic approaches. Multiple common items should be available to test that item functioning is similar across samples. Where there were no common items across studies, a separate sample was collected to whom was administered the different measures used in different IGEMS studies to measure a given construct, with those results used to establish "crosswalks" between the different scales (Gatz et al. 2015).

Major Findings

Co-twin Control or Within Pair Methods

Co-twin control methods test whether associations between early life exposures and late life outcomes are mediated by genetic influences. Associations between exposure and outcome for individuals to twin analyses that ask whether pairs who differ on exposure also differ on outcome were compared. For example, Mosing et al. (2018) found that reduced fetal growth was associated with dementia and cognitive impairment in adulthood. As these associations were somewhat attenuated in a co-twin control analysis, there is evidence that the association is in part due to a shared etiology, which could be either genetic influences that relate to both birth characteristics and cognition or to the environment shared within families.

Other within-pair work with monozygotic pairs used MZ within-pair differences to test for the presence of gene x environment interaction without having a specific measured early environment. With this approach, established evidence of GxE for BMI, depressive symptoms, a physical illness index, and cognition (verbal, spatial, attention, working memory, perceptual speed) was established (Reynolds et al. 2016), as well as for longitudinal grip strength trajectories (Petersen et al. 2016). Results also suggested that apolipoprotein (*APOE*) may represent a "variability gene" for depressive symptoms and spatial reasoning but not for BMI or other cognitive measures, with greater intrapair differences for noncarriers of the *APOE* ε4 allele. For grip strength trajectories, a buffering effect for *APOE* ε2 carriers emerged, with lower sensitivity to environments and better-maintained performance.

Biometric Methods for Testing Gene-Environment Interplay

GxE interactions in relation to cognitive performance (Pahlen et al. 2018; Zavala et al. 2018), depression (Petkus et al. 2017), subjective health (Franz et al. 2016), BMI (Johnson et al. 2012), and grip strength (Petersen et al. 2016) were examined. For most phenotypes, unique environmental variance was greater at older ages, presumably reflecting the accumulating importance of individual differences in environmental context with age. However, there was a nonuniform pattern for genetic factors over age, in combination with SES or sex moderation. In SES moderation analyses of cognition, for verbal ability and for perceptual speed (Zavala et al. 2018), genetic variance was diminished in those with higher SES, perhaps reflective of a buffering effect on normative aging processes particularly for speed, whereas for short-term/working memory and spatial performance, genetic variance was amplified with higher SES, suggesting enriched (high SES) environments may support genetic variation. For BMI (Johnson et al. 2012), there was also SES moderation with diminished genetic influences with high education. The extent and type of moderation differed by gender, country, and age group.

Using a harmonized measure of financial strain, it was found that financial strain moderated genetic and environmental influences on subjective health, such that greater financial strain dampened the expression of genetic variance for subjective health in men, only. Lower levels of financial strain were associated with greater heritability for men (Finkel et al. 2016).

Future Plans

Two features are being added to the next phase of IGEMS work. First, analyses are capitalizing on the availability of polygenic risk scores to analyze as a complement to and in combination with twin methods. Second, measures of the macroeconomic environment are being added which we will be used to characterize the influences from growing up and growing older in different countries and at different historical times. The two main themes driving current and future work are testing models of G-E interplay to better understand the SES-health gradient and applying twin designs to study possible etiological mechanisms in Alzheimer's disease and related disorders (ADRD).

IGEMS SES Project Summary

While most research on health disparities focuses on individual-level socioeconomic status – defined as social status that accrues to occupational classification, education, and income – new research has begun to focus on the macroeconomic environment. Further, although both genetic and environmental factors are known to contribute to the SES-health gradient, the mechanisms by which the two sets of factors combine to influence health outcomes (i.e., GE interplay) are poorly understood. Models of GE interplay differ in their environmental focus (disease-triggering effects of toxic environments vs. health-promoting benefits of favorable environments) and the expected genetic contribution to disease (maximized in adverse environments, in favorable environments, or at both extremes). Understanding whether high SES preferentially promotes good health among a genetically selected subset of individuals (i.e., social enhancement), whether low SES triggers poor health among a genetically vulnerable subset of individuals (i.e., diathesis-stress), or both is essential for translating research in this area into effective prevention strategies.

Dementia Project Summary

While it is well-recognized that ADRD occurrence reflects the influences of multiple genes and multiple environmental and lifestyle risk and protective factors, designs to elucidate potentially informative gene-environment interplay have been rarer. IGEMS studies offer measures of lifestyle, health, and psychosocial risk and protective factors across different life stages. Co-twin control methods strengthen causal inferences from observational studies. Other twin designs test the extent to which the association between risk or protective factor and ADRD reflects shared genetic or shared environmental explanations. In addition, PRS are being used as indicators of individual genetic risk for ADRD to test whether genetic risk for ADRD alters susceptibility to other risk and protective factors and PRS for specific risk and protective factors to test whether genetic risk for these factors alter their association with ADRD. A new focus reflects clarifying the nature of the relationship between education and ADRD; mid-life obesity, vascular risk, depression, and physical activity; and sex or gender differences in genetic risk, exposure to specific risk factors, susceptibility to specific risk factors, and sex differences in genetic interactions with specific risk factors. These questions importantly inform the design of interventions to prevent or slow occurrence of dementia.

Summary

The social stratification of health is well documented, pervasive, and of growing concern because it appears to be increasing over time. Reducing these social class disparities will require greater understanding of how social class impacts health than we currently have. The IGEMS consortium harnesses a combination of twin design and multiple studies representing different cohorts and contexts. The consortium demonstrates the feasibility of this type of collaboration in addressing gene-environment interplay with respect to important age-related outcomes.

Cross-Reference

► Genetics: Gene Expression

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Constancy of the Internal Environment

► Homeostasis in the History of Aging Research

Consumer Health Informatics

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Synonyms

Consumer informatics

Definition

Consumer health informatics (CHI) is the branch of medical informatics that analyzes consumers' needs for health information, studies and implements methods of making health information accessible to consumers, and models and integrates consumers' preferences into health information systems. Consumer health informatics stands at the crossroads of several disciplines, including nursing informatics, public health, health promotion, health education, library science, and communication science; and is perhaps the most challenging and rapidly expanding field in medical informatics (Eysenbach 2000). Consumer health informatics is applicable to all consumers, regardless of age, ethnicity, gender, and socioeconomic status.

Overview

In 1995, Ferguson introduced the term consumer health informatics as a new generation of medical information systems that serve both the doctors and the patients (Ferguson 1995). The traditional means for consumers to obtain health and medical information is from their medical doctors (Hesse et al. 2005). Although this source of information is most safe and reliable, access to it is limited by access to medical doctors. This limitation often makes consumers feel inadequate in medical and health knowledge, particularly when facing situations of decision-making about their own health (Ali and Muhammad 2014). The digital age has brought in substantial changes in the landscape of health information. The Internet provides a practical and cost-efficient health information source. By the virtue of its ubiquity, the Internet is anticipated to provide consumers and caregivers access to information that is otherwise inaccessible (Massey 2016), in addition to information available from the traditional means. Technologies such as the Internet and mobile phone, which consumers can directly interact with on a daily basis, have become the popular information sources for consumers.

Key Research Findings

Consumer health informatics has grown rapidly over the past 25 years, with a variety of technologies be developed to encourage consumers to take an active role in participating in their treatment processes to achieve better outcomes. For example, online health information published by trustworthy sources has improved consumers' health knowledge and has reduced their level of anxiety about their own health conditions. It has also improved their capability in making decisions about self-management of diseases, as well as reducing the pressure on healthcare professionals in educating consumers (Bath 2008; Eysenbach 2000). Mobile health applications can enable consumers to self-collect and record blood pressure and then send the data to their healthcare providers. This has facilitated both healthcare providers and patients to manage hypertension when patients are staying at their homes (Dou et al. 2017). Online patient appointment system provides convenience for patients to make the booking for an appointment with their medical doctor after work hours (Zhang et al. 2015). Increasing use of electronic health records in hospitals and other medical and health services has also made it more convenient for the health professionals to discuss disease management with patients. Meanwhile healthcare providers are also increasingly transitioning to Internet for disseminating cutting-edge health information (Jacobs et al. 2017).

In general consumers welcome the opportunity to access increased amount of health and medical information on the Internet, despite recognition of the inevitable drawback of overwhelming amount of information and false information. It was found in 2005 that consumers of all ages, including the older people, go online to find information that relate to their symptoms or diagnosis for self-assessment, diagnosis, or treatments (Lewis et al. 2005). The Internet has also provided the opportunity for health professionals and managers to reach out to patients electronically or by telephone (Uei et al. 2017).

Examples of Applications

Online Health Information

The major application of consumer health informatics is online health information for consumers. For example, since 1997, the US National Library of Medicine has started to publish and maintain MedlinePlus (medlineplus.gov), a website that provides free, reliable, consumer-oriented health information for the general public, i.e., patients and their families and friends (Zhang and Yu 2019). Over the years, billions of people worldwide have turned to the Web to find answers for their health concerns.

A major research interest in this area is the influence of consumer online health information seeking on the doctor-patient relationship. A cross-sectional online questionnaire survey was conducted with 562 consumers in Austria in 2015 (Haluza et al. 2017). The study found that both digital natives (age under 35 years) and digital immigrants (age above 35 years) refer to online health information as their major source of information, more than information from their doctors. For the regular Internet users in Austria, the age gap was not obvious for health-related information seeking. The study also found that although the majority of consumers (79%) desired to be more involved in health decisions and 82% of them felt comfortable to discuss online health information with doctors, only 25% thought that online information had facilitated their communication with doctors as an equal. Despite 40% of the consumers were willing for their doctors to recommend health websites, only 8% of consumers reported that their doctors actually did this. More than half of the consumers stated that they usually consult the Internet for additional health information after visiting their doctors; 28% of them stated that they did this because they received too little health information from their doctor. A Canadian study further found that there were four barriers for consumers to communicate with doctors about online health information: (1) concerns about embarrassment, (2) concerns that the doctor does not like to hear about it, (3) belief there is no need to bring it up, and (4) forgetting to bring it up (Silver 2015).

Electronic Health Information Exchange (EHI) Between Healthcare Providers and Patients

By 2015, 84% of hospitals in the USA had basic EHR systems, and 75% of physicians in primary care had a certified EHR system (Kim et al. 2017). This significant achievement in digital transformation of record keeping has made EHI feasible between healthcare providers and patients in the USA. The question is whether the older patients are interested in EHI with their healthcare providers. To address this question, Bluethmann et al. (2018) analyzed the results of a national, cross-sectional survey of US adults for the older adult population with and without cancer history. Bluethmann et al. (2018) found that 89% of adults aged above 55 years ($n = 7129$, including 1586 cancer survivors) perceived EHI to be important. However, those aged above 65 years were less likely than those aged between 55 and 64 years to think so. The participants with college education were more positive than the less educated people. Participants without experience using the Internet or Internet-based e-mail were significantly less likely to perceive EHI access as important as the Internet users. Only less than half of cancer survivors (42%, $n = 1586$) and all adults without cancer history (38%, $n = 5543$) were interested in using EHI with providers for lifestyle advice. Similarly, roughly half of survivors (46%) and other adults (42%) were interested in sharing information about symptoms with their providers electronically. In summary, the study observed a "digital divide" for perceived importance of EHI access and EHI exchange interests. It highlighted the importance of improving comfort/experience with technologies to support EHI use in self-management for older adults aged above 75 years. The study also found that cancer survivors may often have distinct EHI needs/preferences than otherwise and the information needs for the cancer patients can change at different stages of cancer. Overall, the study demonstrates the complexity of consumer expectations for EHI.

Virtual Healthcare Team for Geriatric Depression Management

Nearly 30% of older adults at primary care in the USA suffer from depression (Alexopoulos et al. 2000). Because of inadequate training or lack of time for many primary care physicians, very often these older people's mental health problems are not properly assessed or treated (Emery et al. 2012). The effectiveness of the models of collaborative depression intervention in primary care for treating mental health problems has been demonstrated through widespread screening and intervention for depression among older adults. The challenge for their implementation is the high resources required for the multidisciplinary care team, which are not always available. Therefore, a virtual healthcare team was established, which included primary care physician, psychology, social work, psychiatry, physical therapy, occupational therapy, dietetics, chaplain, and pharmacy (Emery et al. 2012). An intervention entitled BRIGHTEN (Bridging Resources of an Interdisciplinary Geriatric Health Team via Electronic Networking) Program was thus implemented. This included screening, assessment, virtual team communication, participant-centered treatment plan development, and connection to recommended evidence-based services.

The virtual team provided the 150 older people who were selected to enter the program with unique and comprehensive treatment recommendations. By utilizing team member resources effectively and efficiently, this team approach served to decrease stigma around mental health for older adults and physicians. Primary care physicians reported that their patients found it more palatable to go to a "program" rather than a psychiatrist in the same primary care clinic or outside mental health referral. From baseline to 6 months, significant improvement was found in depression symptoms and general mental health for these older people.

Challenges for Consumer Health Informatics

The Ability of the Traditional Healthcare Systems to Embrace New Consumer eHealth Innovation

Bloom et al. (2017) suggested that the forces driving consumer health informatics include new types of organization and new kinds of relationship between organizations and consumers.

They suggested that the factors that impede the rapid diffusion of consumer eHealth innovation include (1) government's lack of knowledge and experience to drive the digital health innovation at scale; (2) a lack of supportive regulatory environment; (3) the limited capacity of innovations to meet health service needs; (4) the time it takes to build new types of partnership between public and private actors; and (5) the acceptance of participants in the health and communications sectors.

Five key macro level challenges were identified in the UK government's implementation of a large-scale, national technology program that aims to deliver a broad range of digital services and products to the public to promote health and well-being, which is entitled Delivering Assisted Living Lifestyles at Scale (dallas) program (Devlin et al. 2016). They are (1) the challenge of establishing and maintaining large heterogeneous, multiagency partnerships to deliver new models of healthcare; (2) the need for resilience when facing barriers and setbacks, such as continually changing external environments; (3) the inherent tension between embracing innovative co-design and achieving delivery at pace and at scale; (4) the effects of branding and marketing in consumer healthcare market; and (5) the challenge of interoperability and information governance, when commercial proprietary models are dominant.

Negative Outcomes of Online Consumer Health Information

A qualitative study conducted in Canada with 56 adults aged 50 years and over elicited top six general concerns consumers have about online health information (Silver 2015). These include (1) credibility/limitations of online information, (2) limitations in one's own ability, (3) anxiety, (4) time consumption, (5) conflict, and (6) harm to privacy and security. The top concern is credibility/limitations of online information; the same result was found in an Austrian study (Haluza et al. 2017).

Another qualitative study also conducted by Canadian researchers examined the negative outcomes associated with using consumer health information from five complementary perspectives: consumers, family physicians, pharmacists, nurses, and health librarians (El Sherif et al. 2018). The negative outcomes were found at three levels: (1) internal, i.e., increase worrying; (2) interpersonal, i.e., a tension in the patient-doctor relationship; and (3) service-related, i.e., postponing a clinical encounter. The consumers also proposed three types of strategies to reduce the occurrence of these negative outcomes. These include providing consumers with reliable online health information, educating them on how to assess the quality of online health information websites, and helping consumers to present and discuss the information they acquired online with a health professional, in their social network or a librarian for confirmation.

Age Disparity in Online Health Information Access and Use

Age disparity in online health information access and use has been confirmed by various studies. One study investigated the use of a web portal by adult patients with prediabetes and type 2 diabetes mellitus (T2DM) seen in a family medicine outpatient clinic (Coughlin et al. 2018). It found that the population group aged between 41 and 45 years had the highest registration rate for the web portal. Patients who were aged 18–25 and more than 65 years had lower registration for the web portal than those 26–65 years.

Another study investigated the effect of age on digital health literacy in Taiwan (Hsu 2019). It validated the age disparity on digital health literacy between the older age group (between 55 and 72 years) and the younger adults (aged between 18 and 22 years). The former group had much lower digital health literacy than the latter. The two groups' health needs were also quite different. The older people's health needs included "diet and nutrition," "health and wellness," and "exercise and fitness," whereas the younger adults were more concerned with "beauty," "weight loss," and "fitness."

eHealth Literacy of Older People

Inadequate eHealth literacy has been a common barrier for older people to access and use the valuable online health information effectively. eHealth literacy is a multifactorial concept that includes health literacy, computer skills, and skills to use mobile phone when mobile intervention is increasingly used to improve consumer health. Barriers to access to and use of online health information can be caused by usability of eHealth services and consumer skills to access information and use eHealth services (Kim and Xie 2017). Older people's knowledge of what health resources are available and confidence in the ability to distinguish high- from low-quality need to be improved (Park et al. 2016). To date, there is a significant gap in the literature for improving digital health literacy for older people that targets at improving their health outcomes as the outcome of interaction, as well as a lack of theory-based interventions. The research design also needs to be improved (Watkins and Xie 2014).

Future Directions of Research

Internet sources have remained as the focus of research on consumer online health information seeking behavior (Sbaffi and Rowley 2017). Further research in this space includes clarity of the interaction between the variables associated with consumer health information seeking, increased consistency on the measurement of trust and credibility, an increased focus on specific Web-based health information sources, and enhanced understanding of the impact of demographic variables on trust and credibility evaluation (Sbaffi and Rowley 2017).

There is a lack of knowledge on what technologies should be invented for older people (Goldberg et al. 2011) and for improving their care (Demiris 2016). There is also the need for effective social networking strategies, improvement in the usability of web and mobile technologies and capabilities of search engines, and pervasive healthcare and intelligent transport systems (Demiris 2016).

There is also a need for conceptual development of health literacy and eHealth literacy in the Web context to enable better measurement of these concepts, as well as a pressing need for eHealth education and support for older people, i.e., how to access and evaluate the quality of health information (Park et al. 2016). These require understanding about how older people access the appropriate online health information and how they use the information in self-care and medical decision-making.

Summary

Consumer health informatics is a branch of medical informatics that focuses on providing consumers with better access to reliable health information. This is achieved through understanding consumer's health information needs and designing, implementing, and evaluating methods and tools to facilitate consumer access to health information. It has been adopted worldwide by millions of consumers and has brought changes to the traditional doctor-patient interactions and relationships. With fast development of digital technology into the mobile and wireless era, many consumer health informatics technologies are continuously developing, such as telemedicine, telehealth, mobile health, smart home, and wearable technology. The challenges for consumer health informatics are not just for consumers but also government regulatory bodies, policy-makers, healthcare providers, and insurance companies alike. Future research on consumer health informatics needs to develop innovative solutions to overcome obstacles and really deliver benefits for improving consumer health outcomes, lifestyle, and well-being.

Cross-References

▶ Health 2.0
▶ Health 3.0
▶ MedLinePlus
▶ Mobile Health
▶ Patient Portal
▶ Telehealth
▶ Telemedicine
▶ Wearable Technology

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Consumer Informatics

▶ Consumer Health Informatics

Contemplative Aging

▶ Aging: An Islamic Perspective

Continued Social Engagement

▶ Continuity Theory

Continuing Care Community

▶ Retirement Villages

Continuing Education for Older Adults

▶ Senior Learning

Continuing Learning at Old Age

▶ Senior Learning

Continuity of Care

▶ Post-acute Care

Continuity Theory

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Synonyms

Adaptation at old age; Continued social engagement

Definition

The continuity theory is based on the central assumption that there is a basic structure that remains over time and which guarantees considerable consistency of the thinking patterns, behavior, activity profiles, and social relationships particularly in middle-aged and older adults. In these life stages, adults profit from the weight of the past experience to use continuity as a primary adaptive strategy in order to face normal aging-associated changes (Atchley 1989). Notwithstanding those widespread changes which take place mainly in the health, the functional capacity, and the circumstances and conditions of life itself, a large share of adults tend to maintain similar behavior patterns and related to lifestyles, assuring a high consistency between the past and the present. This thought supports the definition proposed by Atchley, in his book on the reflection and preparation of the continuity theory as being "a theory of continuous adult development, including adaptation to changing situations" (Atchley 1999, p. 1). Continuity allows the anticipation of the individual path in aging and accentuates several aspects of the adult's development, mainly the role of resilience in life transitions associated to health changes, transition to retirement, or suffered losses.

Overview

The continuity theory assumes that middle-aged and older adults, by making adaptive choices which preserve their internal and external structures, use strategies associated to past personal experiences lived in their social world to face change. So, it is understood as part of the continuity, coherence, and consistency of the lifelong adopted patterns, without disruption or imbalance to the individuals. It occurs in connection with a person's perceived past, producing continuity in the internal psychological features of individuals, as well as in the social behaviors and circumstances (Atchley 1989).

However, Atchley's continuity vision doesn't tolerate the idea that everything remains unchanged in people's lives, in a monotonous and unchanging way. Contrarily, it alludes to a dynamic concept of continuity, admitting that a variety of changes may occur within the context delivered by the basic structure (Atchley 1989, 1999). Even significant, evolutionary and dynamic changes can be incorporated without causing special disruptions in the course of life or taking individuals to experiment crisis. In other words, this approach provides us with a framework for analysis or with a lens through which it is possible to explore the processes people use to create the sense of continuity when facing change (Cuskelly and O'Brien 2013).

As structural basis of the continuity theory, it is important to point out and explain the four main constructs that characterize it (Atchley 2006): internal structure, external structure, goals' setting, and maintenance of the adaptive capacity.

Internal structure – is formed by the relatively stable mental schemes created by thoughts, mental skills, and memory, which help individuals to understand the environment and interpret information of the surrounding world, conducting them in the definition of their personal goals, life philosophy, world vision, knowledge, preferences, moral structures, values, and coping strategies (Cooper and Beehr 2015). For individuals to keep those individual traits, attitudes, and dispositions as they get older, they use memory, and that is the reason why people with amnesia or dementia are not able to present identity and self-continuity. The lack of internal continuity can not only be a source of suffering for the individual who can neither envisage nor lead decisions taking or actions but also for those who usually interact with the individual and expect a certain degree of predictability (Atchley 1989). These general structures represent different dimensions, which, in a combined manner, form a unique whole, distinguishing a person from another. The continuous maintenance of these internal structures is sensed as a fundamental condition for the psychological safety (Atchley 2006).

External structure – refers to the physical and social environment in which people move, the social relationships they establish, the activities they develop, and the social roles they play, as a result of priority setting and of the selective investment made through adult life. In fact, the perceptions of an external continuity result from the fact that subjects move around in family environments, undertaking family activities and interacting with familiar people, maintaining the relationship structure and behaviors (Atchley 1989, 1999). These continuity perceptions are in the individuals' personal constructions and interpretations of his surrounding world, being based on a personal repertoire of concepts which may include social constructions of reality (Berger and Luckman 1966). The personal constructions define how each individual, on the basis of his external patterns, evaluates his continuity perception, articulating the present with the past and anticipating the future, doing it most of the times unconsciously. The continuity of activities and environments concentrates people's energy in familiar spheres, with the result that practice and familiarity contribute to inhibit or diminish possible losses and perpetuate ways of being and of relating. Thus, for example, if people in young ages are interested in participating in a volunteer project or in a certain type of social or sports events, it can be expected that they will be interested in those same activities in old age, with the result that the constancy of those external patterns raises personal safety, more satisfaction, and well-being, mainly in older individuals (Cooper and Beehr 2015). In fact, these unique and well-defined external structures are the ones that contribute to the definition of specific life patterns distinguishing each person from the others.

Goals' definition – the continuity theory advocates that adults have developmental goals which lead them to an idea of themselves and of their activities, relationships, and environments to which they wish to evolve. These developmental goals are simultaneously influenced by socialization and position in the social structure (e.g., social class, gender, environment, family ties) and by life experience (Atchley 2006). Life experiences influence decisions to be taken on the selective investments to be made in the course of life, linked either to the individual's features or to options to be made in various spheres (e.g., professional career to be made, groups and communities to get involved with, or activities to be performed).

Maintenance of the adaptive capacity – the adjustment to life arises from the accumulation of subsequent learning processes, adaptations, personal developments, and selective investments, based on the continuous improvement of an external structure which, complemented by an internal structure, allows individuals to attain the maximum possible satisfaction with life (Atchley 2006). According to the circumstances of life and the interaction with the social external environments, adults continue evolving and adapting to changes, maximizing internal and external patterns they have been building through life.

For Atchley, internal continuity worked as a facilitation basis of the daily activities, providing a feeling of ego integrity, contributing to self-esteem and was the means to meet each one's needs. External continuity was used to face pressure associated to distinct roles, provided social support, gave feedback from other individuals to anticipate the subject's self-concept, allowed old people to deal with aging's cognitive and physical challenges, and, finally, reduced the personal goal-related uncertainty. In conclusion, older adults would adjust to the aging process in the same way they adjusted to all other life changes (von Humboldt 2016).

Continuity over time does not inevitably mean a successful aging, and/or the continuity results are necessarily positive. Individuals with low self-esteem, abusive relationships, and a hard social adjustment resist the idea of abandoning their internal and external structures. For some people, it is preferably a miserable future to an unknown one. Likewise, the continuity theory can help us understand why people develop in a certain way, searching for organization and coherence in the dynamics of their life stories. However, it doesn't define which are the right or well-succeeded stories (Atchley 2006). It should also be noted that the continuity theory focuses on adaptation processes to normal aging and doesn't concern people who live incapacitating and pathological aging processes, since, not being able to meet their own needs, they put at risk the external continuity in their aging adaptation strategies (Atchley 1989).

The theoretical approach in analysis has thus expanded the activity theory (Havighurst 1963) that claimed that individuals will be in good health if they stay active in different vital spheres, namely, physically, mentally, and socially. On the contrary, it jeopardizes the disengagement theory (Cumming and Henry 1961) which considers naturally and desirably the withdrawal of individuals from the activities they usually perform and from the social systems where they are inserted. A certain tranquility is restored to the older people, until they prepare themselves for death, enhancing the generational replacement. Instead of promoting continuity, this approach claims that individuals, once they have withdrawn from the previous activities and roles, perform an abrupt change in the more advanced ages. Either based on an interactionist paradigm, to which the activity theory is linked, or through a structural-functionalism approach, in the case of the disengagement theory, we are facing a set of theories framed in the first generation of social gerontology theories. The continuity theory emerges on a second period/generation of the theoretical development in social gerontology (Bengtson et al. 1997). The triangle of the disengagement, activity, and continuity theories is best known and present in the first approaches in gerontology, having a decisive influence in the aging research modelling (von Humboldt 2016). These perspectives offered different points of view on old age, highlighting that activity and disengagement may generate life enjoyment and that older people look for continuity as they adapt themselves to the challenges of old age. The continuity theory presents a conceptual basis, which can be used for the analysis of activities general patterns, relationships, and mental constructions, being more influent over time than the disengagement and activity theories (Marshall 1994).

Often referred, and with some proximity to disengagement theory, arises the role theory (Biddle 1979) which claims that individuals may experience the loss of certain roles as they get older, making the old age adaptation process difficult. In fact, this theory does not consider the possibility that individuals may take up new roles based on their learning and previous experience. The relationship dynamics between internal and external structure shows how individuals deal with the loss of roles and how changes or variations are incorporated in the adaptation process. As highlighted by the continuity theory assumptions, the individuals' features, the ways of being and behaving in a role, may be transferred to the assumption of new roles. For example, if the individual takes on a leadership role in his job, he may continue having it in friendship or leisure relational contexts.

The life course perspective fits in a third generation of theoretical production in the field of social gerontology and tries to link the micro and macro levels of analysis of individuals and populations over time (Bengtson et al. 1997). This life course perspective (Elder 1992) focuses on the study of the contextual dynamics associated with the aging process, including the age-related transitions or critical incidents which led to life changes, the cultural meanings associated with different social spheres, and how the position in the social structure, time, and the effects of cohort events may shape the adult's development. Notwithstanding its contextual vision, this theory receives some criticism since by focusing on the environmental influences and on the impact of contextual effects, it doesn't emphasize so much the roles' loss or the individual differences, which may lead to distinctive aging adaptation forms. Thus, it is often used together with the role theory or the continuity theory to help explain the individual aging, particularly in the retirement adaptation (Wang and Shultz 2010; Cooper and Beehr 2015).

Key Research Findings: Main Conclusions of the Research

This theory had its first draft of what would become the theory of continuity, on the pioneer chapter of George L. Maddox: "Persistence of life style among the elderly: A longitudinal study of patterns of social activity in relation to life satisfaction," but it was Robert Atchley who, as from 1968, started the construction of an initial basis for the continuity theory, developing it between 1971 and 1999, with reference to the collected data in the Ohio Longitudinal Study of Ageing and Adaptation (OLSAA), which became, to a large extent, the empirical support for the construction of this theory. The study started with 1200 subjects, interviewed each 2 years. In 1981 Atchley obtained data from 700 initial participants, and in 1995 the cohort participants' number dropped to 273 (Cooper and Beehr 2015). Still in the beginning of the 1970s, while studying the transition to retirement, Atchley started claiming that this event had little or no effect on the individuals' capacity of preserving satisfaction with their activities and their lives, strengthening this idea with the result of various studies which advocated that the continuity theory was more widely applicable than the crisis theory in the explanation of the relationship between retirement and leisure participation. He testified that older individuals were not in crisis, as other theories claimed, stating that most of them were adapting themselves favorably to retirement.

While recognizing the importance and necessity of studies that covered a wide social and psychological diversity of the old population, allowing the strengthening of that result, the continuity theory and the obtained results suggested that leisure may constitute a high positive impact in the transition between the pre- and post-retirement periods (Atchley 1971). Leisure activities may use the time released from work and provide continuity in the identity. Each person assumes various roles which grant identity and not only the role resulting from work. Many people may depend on leisure activities for the preservation of self-respect, mainly the ones who had unsatisfactory jobs (Atchley 1971). The article "Retirement and Leisure Participation: Continuity or Crisis?" (Atchley 1971) proved to be the starting point for the continuity theory approach.

In the subsequent decades, the OLSAA results have made it possible to support both the internal and external continuity. In the first case, it was apparent that most participants showed moderate to high continuity levels concerning their personality, the ideas constructed about themselves, self-confidence, personal goals, and emotional resilience. Even the retirement representations persisted. In the second case, concerning external continuity, the study assessed lifestyle dimensions, such as household composition, living conditions, marital status, means of transport, and income, having been possible to conclude that most dimensions remained stable and consistent over time. Physical activity stood out as a fringe discontinuity dimension. However, it was possible to understand that that result was due to the vicissitudes and losses related to physical aging rather than the preferences of the studied people.

The theory expansion to the concepts of internal and external structures of continuity is also registered in the journal *The Gerontologist*, with the famous article "A Continuity Theory of Normal Aging" (1989). At last he strengthens and consolidates his theory in the book *Continuity and Adaptation in Aging: Creating Positive Experiences* (1999). As time went on, Atchley refined even further the theory, as understood today, basing it on feedback systems. Adults follow internal structures, reinforced by years of feedback and experience, to lead them in the decision taking and preservation of lifelong satisfaction (Cooper and Beehr 2015). Continuity is present in the systematic repetition of those schemes or internal and external structures, highlighting stability.

According to this theory, older people should continue to live in their own homes as long as possible. If this is not possible, the family should attempt to locate housing for their older relatives in the same general area to maintain friendships and familiar environments. Continuity of roles and activities is effective in maintaining the capacity to meet social and emotional needs for interaction and social support and helps the individual concentrate energies in familiar areas of activity. Continuity does not mean that nothing changes, it means that new life experiences occur, and older people must adapt to them with familiar and persistent processes and attributes (Payson and Aitken 2019). Continuity theory claims that people do not change dramatically with regard to their behavioral preferences as they age but rather substitute new roles for those they may have lost, adapting to age-related changes as they occur. On the other hand, advocates that our personalities and core values become more pronounced: people who have always been outgoing and engaged in their communities are likely to continue to do so into old age, and those who are more reserved or withdrawn are not likely to suddenly become involved in organizations or new activities (Hasworth and Cannon 2015).

The continuity theory might be useful, thus, to identify aspects which contribute to the resilience when facing the aging challenges and the sense of self-identity at the end of life, by exploring the narrative of life, which may allow insights on the best methods to cope with the significant life and aging experiences and events, namely, the adaptation to the physical challenges; the changes of social networks; the continuity toward identity in order to maintain unity and life's purpose, particularly rooted in beliefs and lasting values; or the redemptive capacity to cope positively with life challenges (Browne-Yung et al. 2017).

Examples of Application

There are various studies' examples based on the continuity theory, as well as various fields where this approach is used. More specifically, concerning the retirement transition, the continuity theory does not see it as an abrupt disruption, but as an opportunity to keep a certain lifestyle and relationships (Atchley 1989), a possible strategy of favorable adaptation may be the involvement increase in leisure activities (Atchley 1971). Aiming at analyzing the patterns, meanings, and perceived benefits of a variety of innovative activities and their role in the aging process, with an intentional sample of retired people involved in the program "Learning and Retirement," it was possible to suggest that innovation may be growth producing and liberating, even in advanced age and, at the same time, in general protective of a certain internal continuity sense (Nimrod and Kleiber 2007). Researching the relationship between activity patterns (high, medium, low, passive leisure, work) in older age and health, testing the mediation role of the nature of the activity involvement (complete, partial, minimum), authors conclude that the groups which show high activity and work patterns, when compared to the passive leisure group, demonstrate better health and cognition results, especially those who are totally or partially involved. With regard to health, the fullest involvement (physical, cognitive, and social) may perform a more important role than the activity itself. This work allows us to highlight the vulnerability of the lower activity groups and of older people whose activities imply a minimum involvement. The development of programs should entail the design of intervention activities more focused on the involvement quality, both in the physical and cognitive fields as in the social one (Yu-Chih et al. 2018).

Emphasizing a longitudinal approach and analyzing age-related changes in 9 different leisure activities, through a representative sample of individuals who were followed 34 years long in Sweden, it was possible to observe as the most common pattern the decline in the participation rates over time. However, the engagement in activities in the earlier stages of life predicted the leisure participation in old age (Agahi et al. 2006). In general, the results seem to support the continuity theory. Other longitudinal studies which research the participation levels of older populations found out that the ones who remain in the follow-up phases of the study are usually the ones who were more active in the initial phase of the study (Bukov et al. 2002). Likewise, the participation in leisure activities in pre-retirement promotes the adaptation to retirement. Trying to test this relationship, Earl et al. (2015) pointed out that only one quarter of their study's participants adopted new activities in post-retirement.

Researching leisure and professional activities of retired professors, as well as the anticipated leisure activities of older employed professors, it was possible to find a few similarities in the current and planned activities of both groups, such as travel, sports or exercise, hobbies or learning new things, and also some differences such as a higher tendency for the involvement of retirees in volunteer activities. These findings may have implications in the education for retirement and in the planning of leisure policy. Considering the value of volunteer activities for themselves, it may be worth favoring the knowledge of volunteer opportunities within the communities. On the other hand, the planning of the leisure policy may emphasize travel arrangements, recreational and sports activities, or activities to foster intellectual growth and contribute to the health and well-being of retirees (Dorfman and Kolarik 2005). In future research, it would be valuable to perform similar studies with other occupational groups, identifying activity patterns of the retired professionals to support the development of suitable programs and activities for their interests and needs.

As we have already stated, another way of reacting to the retirement transition challenges may be performing volunteer work. Some authors seem to show that retirement increases the probability of starting volunteer work and the organizational engagement (Mutchler et al. 2003; Van den Bogaard et al. 2014). Analyzing factors that contributed to the fact that a set of ex-players switched to a sports practice-related volunteer work, based on the continuity theory, it was possible to verify that volunteers wished to keep their bond and involvement with sports and to continue the previously built relationships, contributing to the strengthening of the belonging sense. The competence feelings expressed through the external environment feedback also proved to be a motivating factor for the practice of volunteer work (Cuskelly and O'Brien 2013). The active life restructuring after retirement, by means of the increase of leisure or volunteering activities, may be associated to the well-being improvement after retirement or can at least be necessary to keep stability (Henning et al. 2016). Accordingly, employment in post-retirement, volunteer work, and leisure activity showed a positive impact in the adaptation to retirement, sense of continuity, and general satisfaction toward life (Kim and Feldman 2000). Particularly noteworthy is the importance of the encouragement for the creation of active intervention programs for young or middle-aged people in order to increase the future participation in leisure, especially in physical activities (Minhat et al. 2013). In this regard, Tong et al. (2019) sought to identify the needs in terms of physical activity of foreign-born older adults, since their self-reported health is not as good as of those nonimmigrants. They found that besides the fact that physical activity and mobility of foreign older people living in Canada benefit from the desire of well-being and socialization, gender and personal biography, including the work history and the desire for independence and the access to culturally familiar and linguistically accessible goods and services, also promote the participants' physical activity and mobility. Since foreign older adults and other minority older populations keep growing in several communities, the future planning of physical and social activities promoting the older adults' health should be culturally familiar and linguistically accessible, supporting the continuity sense of the individuals. Works of this nature should be object of future research, testing to which extent cultural norms and habits make the rules in what physical activity is concerned, aiming at the promotion of the older people's health improvement (Tong et al. 2019).

Another way of building the feeling of life continuity may be the extension of the labor force participation, in the so-called bridge employment. Trying to highlight transition predictors to the bridge employment, studies concluded that the main motivations were the search for financial security and the wish of continuity (Burkert and Hochfellneer 2017) also because employment guarantees the continuity of patterns, lifestyles, and daily routines necessary for the well-being (Wang and Shultz 2010). For example, for a significant group of retired teachers, the continuous work activity takes on the meaning and compensation of leisure, reinforcing the consistency of involvement and of the lifelong activity significance (Dorfman and Kolarik 2005).

A relevant aspect of the continuity theory is the assumption of the personality's and identity's adaptive potential as people get old. Breheny and Griffiths (2017) tried to interpret continuity descriptions of an old people's group, who described practices that supported the internal and external continuity and, particularly, the identity's continuity. Research data also confirm personality continuity through life, reinforcing the cumulative continuity model on the personality's development. Over time and with age, people interact in a more skillful way with the environment, promoting the consistency of personality, which reaches a peak in the fifth or sixth decade of life, so that with the time and the experience, the battle between change and consistency is won by the forces of continuity (Caspi and Roberts 2001). Following the same line, studies that assess differences in self-continuity show a positive association between chronological age and implicit and explicit aspects of self-continuity (Löckenhoff and Rutt 2017). This knowledge may benefit older people with intervention models using positive coping strategies, recognizing the importance of social ties and the involvement in activities which bring meaning and purpose to life, especially at times of loss or grief, influencing the way people adapt themselves in adversity moments, favoring the resilience buildup in old age (Browne-Yung et al. 2017).

Even when old people live in a nursing home, testimonies express consensus when it comes to appeal to the biographic continuity of the residents, by means of a personalized treatment, based on the needs, preferences, and habits, as opposed to the adaptation to the home as a total institution (Harnett and Jönson 2017). Thinking about the professional practice of the certified occupational therapy assistants, Payson and Aitken (2019) highlight the importance of reminisce about past activities that may have meaning to old people. The information gleaned from the individual could give more insight into a selection of activities that are most appropriate, and the performance of meaningful activities promotes competence, independence, and well-being. Likewise, families look for ways to keep their roles as family members and caregivers consistent, particularly in the first year after sending the relative to a nursing home (Gladstone et al. 2006). Still in the field of social relationships, widowed people show higher levels of informal social participation and prefer to keep relationships and activities which were relevant throughout life, to keep continuity in the mourning and loss period (Utz et al. 2002).

In conclusion, in the various examples given, old people tend to value family environments, social relationships, and routines kept throughout life, and continuity is used as the main adaptation strategy resulting in the maintenance of satisfaction with life at the end of adult life, according to what the continuity theory features (Atchley 1989).

Future Directions of Research

Since continuity may be considered as total stability or lack of change, or as evolution linked to gradual development over time, its use in gerontology has been ambiguous (Atchley 2006). For this reason Atchley claims that the best word to represent the evolutive concept of continuity would be consistency, admitting that it is unlikely that the name will change. Internal or external, the continuity extension is determined by an assessment here and now, made by the individual and based on his memory; therefore, existence and effects of continuity can only be studied retrospectively (Atchley 1989). One of the main criticisms about this theory concerns the limited empirical tests, focused on transversal or short-term data, making difficulty in the understanding of observed patterns. However, aging adaptation can only be tested through data collection on the same people over a long period of time. Although these longitudinal approaches are expensive and slow, they present a high potential for the stability study in the aging adaptation and the changes that occur with age; in the behavior; in life circumstances, such as mourning, death, or retirement transition; or in the personality traits (von Humboldt 2016). The continuity theory offers a conceptual framework that can be used to analyze general patterns of activities, relationships, and mental constructions and to distinguish operationally continuity and discontinuity, as long researchers have longitudinal data (Atchley 1989, 1999).

In a review study on the retirement effects on well-being, based on longitudinal researches, it could be perceived that generically retirement doesn't seem to affect negatively the well-being (Henning et al. 2016). However, most studies do not consider the difference between the transition period and the subsequent developments, concerning the analysis of the real changes and alterations of well-being. Thus, authors point out the need of future studies based on Atchley's approach in order to understand better the change and continuity patterns, which accompany the different stages and the adaptive processes that individuals activate during transition to retirement or in other events of their lives. Current research doesn't help to understand completely how individuals decide to retire or what kind of retirement should be chosen (full-time or part-time). On the other hand, organizations should be able to adjust the work environment so that older workers may stay there successfully. Continuous research on retirement background, processes, and results will have to mobilize the continuity theory as a decisive theoretical constructor in the conduction of these works (Cooper and Beehr 2015). Likewise, the relevance of the continuity theory is suggested for a better understanding of the continuous involvement of volunteers in civil society organizations (Cuskelly and O'Brien 2013), namely, in the explanation of the influencing factors of the continuous involvement in volunteering activities, whether in sports context or other environments, mainly through longitudinal approaches.

In a more recent reflection on the continuity theory, Atchley (2006) points out the importance of researchers to take fuller account of the subjective perceptions of continuity/discontinuity that stem from participants and not so much of the stable and objective definitions of continuity made by researchers, with the result that data underestimate the perceived continuity prevalence. The difficulty in incorporating change as part of identity continuity has concentrated the research focus more in the behavioral patterns adopted over time than in the construction of identity. It is suggested that the continuity theory should be more explored to understand the meaning people built on their lives, namely, through the role of narrative (Breheny and Griffiths 2017). Other theoretical perspectives, such as identity theory, may offer complementary insights in the research on the complex identity notions in the context of transition and extension to another role (Cuskelly and O'Brian 2013).

Apart from the fact that theory focuses on the normal aging processes, relegating the vulnerable and pathological aging, a common criticism derives from the fact that it doesn't demonstrate how the contexts, institutions, and social pressure impact individuals and the way they adapt to aging. Thus, complementarity with the life course perspective would allow a crossover of approaches at the micro and macro level (Duberley et al. 2014) and an impact analysis that culture operates over the continuity desire. Like the criticism directed to other theories, feminist approaches understand that the gender focus is neglected and must be considered at the micro context of social meanings (Bengtson et al. 1997).

Regardless some methodological-theoretical notes which may contribute for the improvement of continuity theory-centered approaches, it has offered a conceptual basis which can be used to analyze general patterns of activities, relationships, and mental constructions and has been used, since the end of the 1990s, to restructure research on a wide range of subjects, such as adaptation to retirement, sports participation in advanced age, identity stability, adaptation to disabilities, mental health, social support systems, recollection, and leisure activities, suggesting that this theory has proved to be useful as the basis for a research on adaptation (Atchley 2006), being this purpose still valid.

Summary

The continuity theory, being one of the most prominent approaches in the field of social gerontology, has focused on the way individuals develop and adapt themselves to change situations throughout life. It assumes that adults and old people, oriented by internal mental structures, use continuity as an adaptation strategy, replicating similar behavioral patterns, lifestyles, and relationships kept over years. However, evolutionary and dynamic changes are expected in the course of life and are incorporated in the continuity concept, so that continuity and change occur simultaneously. Atchley, the mentor of this theory, contributed to its expansion and strengthening using, as an empirical support, recollected data over various decades in the Ohio Longitudinal Study of Ageing and Adaptation (OLSAA). The consolidation of the continuity theory expresses itself in his work *Continuity and Adaptation in Aging: Creating Positive Experiences* (Atchley 1999). It explores, as the theory core, the concepts of internal continuity (mental structures which define personal goals, values, life philosophy, and the construction of an image of oneself) and external continuity (physical and social environment, social relationships, activities, and social roles). Continuity is present through the systematic repetition of these structures, ensuring psychological safety and predictability in the ways of being and of relating to others. The improvement of the theory, as known today, allows it to be a

conceptual basis of high importance for multiple researches targeted for the adaptation processes and for the analysis of general patterns of activities, relationships, and lifestyles.

Cross-References

- ▶ Activity Theory
- ▶ Adjustment to Aging
- ▶ Delaying Retirement
- ▶ Healthy Aging
- ▶ Leisure Activities and Healthy Aging
- ▶ Life Course Perspective
- ▶ Self-Continuity
- ▶ Successful Aging

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Continuous Identity

► Self-Continuity

Continuum of Care

► Self, Informal, and Formal Long-Term Care: The Interface

Control Beliefs

► Locus of Control
► Perceived Control

Convoys of Care

► Self, Informal, and Formal Long-Term Care: The Interface

Coping Assistance

► Social Support

Copy Skills

► Adjustment to Aging

Co-residence

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Synonyms

Extended family structure; Intergenerational co-residence; Intergenerational living arrangements; Multigenerational families; Sandwich-generation families; Skipped-generation families

Definition

Co-residents are people in the same household (sharing a dwelling and with some common housekeeping or shared living space) and co-residence simply refers to living together. Co-residents are generally, but not necessarily, members of a family or kin group linked by blood or marriage. In the gerontological literature, the term "co-residence" is often used as shorthand to refer to *intergenerational* co-residence when adults of two generations live together, or *multigenerational* co-residence involving three or more generations.

Overview

Intergenerational co-residence is one of the main "currencies" of exchanges of support between older parents and adult children. This support may primarily flow downward from the older to the younger generation, upward from the younger to the older, or be of mutual benefit. In some societies over 80% of older people live with a child, in others fewer than 10%.

In general co-residence is more usual in less developed regions of the world, least common in modern advanced economies and negatively associated with per capita income. However, large variations in co-residence between and within countries with similar levels of economic development, and close examination of historical trends, indicate that it is an oversimplification to regard economic factors as the sole drivers of levels of co-residence; demographic and cultural influences are also important. In North America, Europe, and parts of East Asia, levels of co-residence declined substantially in the second half of the twentieth century. However, in some countries, such as the USA, co-residence rates have recently increased slightly, a trend attributed to the greater challenges young people are experiencing in establishing and maintaining separate households. In other regions of the world, there are also indications of declines in co-residence, although evidence is less clear. As recognized in the Madrid International Plan of Action on Ageing (UN 2002), living with younger generations is not necessarily the preferred or best option for older people and the implications of co-residence for their well-being vary according to both societal and personal factors.

Key Research Findings

Pathways to Co-residence

There are three main pathways to intergenerational co-residence between older parents and adult children (Grundy 2000). An adult child may have never left the parental home, may have returned to the parental home after a period away, or the older parent(s) may have moved to a child's household. In all these situations, co-residence may be a means of meeting the needs of the adult child, those of the older parent, or be of mutual benefit. For example, an adult child may remain in the parental home in order to work on a family farm or shared enterprise, perhaps in the expectation of inheritance (mutual benefit); because he or she is unable to live independently for economic or health reasons (benefit to child); or in order to provide care or economic support to an older parent or parents (benefit to parent). Similarly, adult children may return to the parental home because unemployment, divorce, health problems, or other adversities mean they are unable to maintain a separate residence, or to meet parental needs for assistance. Parents, especially widowed parents, may move to a child's home to help care for grandchildren, perhaps enabling a daughter or daughter-in-law to participate in the labor market, or because of their own needs for economic support, company, or personal assistance. In long-term intergenerational households, the balance of flows may shift over time, for example, initially favoring the adult child and later the older parent (Chen 2005).

Direct information on support flows within households is generally not available in censuses or survey series such as the Demographic and Health Surveys (DHS). However, some inferences about the direction of flows may be drawn from indicators such as household headship (or household reference person), gender and marital status of the parent and child, and other characteristics of one or both generations, such as health or employment status (Grundy 2000; Ruggles and Heggeness 2008). Information on the gender of a co-resident married child also provides an indicator of the extent of patriarchal norms, most prevalent in parts of Asia and Africa, favoring co-residence with a married son rather than a daughter (Bongaarts and Zimmer 2002).

Choices, and constraints, depend on the broader economic, social, cultural, and policy context, as well as individual preferences. Trends in fertility and mortality determine the size and composition of kin groups so the demographic context is also important and demographic constraints on co-residence have been emphasized in much of the literature (Glaser et al. 2006).

Demographic Influences on Co-residence

A prerequisite for intergenerational co-residence is, for older people, availability of an adult child and for adult children availability of a surviving parent. Availability of children is predominantly determined by fertility rates and to some extent by mortality patterns as these influence the probability of a child pre-deceasing parents. Availability of an older parent is determined by levels of mortality and ages at parenthood which determine age gaps between parents and children (Murphy and Grundy 2003). Changes in these demographic parameters have different effects on the likelihood of co-residence for parents and children. Having fewer children reduces co-residence opportunities for older parents, but having fewer or no siblings increases the chance of co-residence for a child.

Both fertility and mortality rates have declined substantially over the past half century, although in much of Europe the transition to lower fertility started earlier than this and there have been some fluctuations in trends. These include the post-World War II marriage and fertility boom. Reduced fertility implies fewer opportunities for co-residence with children, but it is important to consider distributions by family size, as well as average levels of fertility. For example, the impact of having four rather than five children on co-residence opportunities in later life is much less than the impact of having two versus one or no children. In many European countries the proportion of women remaining childless was lower among cohorts born from the 1930s to the mid-1950s – the parents of the baby boom – than in either preceding or succeeding cohorts (Murphy et al. 2006). Transitions to lower fertility in Asia and Latin America in the second half of the twentieth century, now largely completed, also largely reflected decreases in the proportions of women having large families. Concerns have been raised that these trends will restrict opportunities for intergenerational co-residence in the future (Glaser et al. 2006), but simulation studies tend to show relatively small effects from the parental viewpoint (Knodel et al. 2000). However, more recent changes in some European and East Asian societies have included increases in the proportions never having children or having only one. This will have greater implications for future co-residence opportunities, especially in societies with cultural preferences for co-residence with a child of a particular gender.

Reduced mortality has increased the proportion of mid-life adults with an older parent still alive, reduced the proportion of older adults pre-deceased by their children, and led to increases in the proportion of families including three or four living generations. This implies increased potential for intergenerational co-residence for adult children. However, in societies in which co-residence is associated with widowhood, lower mortality rates, and changes in the differential mortality of older men and women, may have a slight countervailing effect as the proportions of widows will be lower.

Global Variations in Co-residence

Globally co-residence with children is the predominant living arrangement for older people, but there are huge differences in co-residence around the world. A recent United Nations overview (UN 2017), largely based on censuses conducted in 2010–2011 or Demographic and Health Surveys (DHS) conducted in a similar time period, reported that in Asia 67% of women aged 65 and over lived with a child, as did half of older women in Africa and in Latin America and the Caribbean (LAC). Among men the proportions living with a child were slightly lower than those for women in Asia and LAC, but higher than for women in Africa. By contrast in Europe and the USA fewer than 20% of persons aged 65 and over lived with a child. These estimates may include some cases of older men living with minor children (and this may account for the higher rate of co-residence for men than women in Africa), but comparisons for those aged 80 and over show only slight differences in levels of co-residence and a similar variation by world region.

This UN study also found a negative association between co-residence with children (by people aged 60 and over) and a country's gross national income per capita, especially in middle- and high-income countries.

These variations are consistent to some extent with a substantial body of literature, particularly dominant in the mid-twentieth century, which attributed differences in household and family structures to variations in economic systems, living standards, the extent of urbanization, and "modernity" or "Westernization" (Goode 1963). Following functionalist sociologists, Goode (1963), for example, proposed that nuclear rather than extended household structures were best adapted to meet the needs of an industrial economy implying that co-residence would decrease as industrialization spread. Such broad generalizations have been challenged by a range of studies noting mismatches between the timing of economic change and change in households (Cherlin 2012) and very wide variations in the extent of intergenerational co-residence in societies with similar levels of economic development.

More recent studies have also called this interpretation into question. One comparative study of 43 less developed countries based on DHS data from around 2000 found that the proportions living with children tended to be lower in areas with higher levels of education. However, there were no associations with GNP per capita, percentage rural or life expectancy (Bongaarts and Zimmer 2002). Another analysis of census microdata for 15 less developed countries, eight of them from Latin America, examined trends in co-residence for periods from the 1970s to 2001/02. Results showed no clear trend in the overall proportion of older people living in intergenerational households, and some indication of an increase in intergenerational households headed by an older person. Moreover, older-head intergenerational co-residence was positively associated with GDP per capita leading the authors to conclude that where intergenerational co-residence is strongly valued, increases in living standards allow more people to achieve it (Ruggles and Heggeness 2008). However, the 2017 UN report, which is based on more recent data, indicates a decline in intergenerational co-residence between 1990 and 2010 in most of the countries, including those in less developed regions, for which data were available (UN 2017).

In Europe, North America, and East Asia, rising living standards in the second half of the twentieth century have also been advanced as an explanation for changes in intergenerational co-residence, but here, it is argued, the effect has been to allow more older people to maintain residential independence and realize preferences for privacy. Declines in intergenerational co-residence of older people in these regions in the second half of the twentieth century were so great that they have been described as "a quiet demographic revolution" (Elman and Uhlenberg 1995).

In the 1950s and 1960s, it was quite common for older widowed people to live with a child, in Scandinavia, other North West European countries and North America, whereas now this is unusual (Tomassini et al. 2004; UN 2017). Recent analyses of European Social Survey data for the period 2002–2014, for example, found that in Northwest Europe only 10% of widows aged 65 and over co-resided with a child (Grundy and Murphy 2017). Trends in other parts of Europe, and other industrialized countries, are similar although the extent of co-residence continues to vary, and is generally higher in Southern, Central, and Eastern Europe (and Ireland) and in Japan and South Korea than in Northwest Europe or North America, being lowest of all in the Nordic countries. In Japan, the proportion of older people living with a child fell from 87% in 1960 to 47% in 2005 (WHO 2011). This decrease appears consistent with hypotheses linking co-residence to levels of economic development or "modernization"; however, these conceptualizations cannot explain why the level of co-residence in Japan is still considerably higher than in Western countries with similar levels of income and urbanization. The sizeable variations between countries, and between groups of differing heritages within countries, point to the continuing importance of cultural factors (Reher 1998).

Recently, there have been some indications of a slowdown, or even a reversal of the shift away from intergenerational co-residence in some advanced industrial societies, a change interpreted as a family response to high unemployment rates, poor job prospects, and financial hardship among young adults. In the USA, for example, the proportion of 25–34-year-olds living with a parent increased from 11% in 1980 to 24% in 2012 (Fry and Passel 2014). In many cases, the parents of these young adults would be aged under 65, but the declining ability of some groups to afford independent housing may underlie the 5% increase between 1990 and 2010 in the proportion of older women in the USA living with a child (UN 2017).

Implications of Co-residence for Older People's Well-Being

Potential benefits of co-residence (for both older and younger generations) include availability of intra-household emotional and practical support and economic benefits from economies of scale (Rendall and Speare 1995). Potential disadvantages are reduced autonomy and associated possible reductions in self-esteem, stress attendant on any intra-household conflict and, in some cases, overcrowding.

The balance of positive and negative effects of a particular living arrangement is likely to vary according to individual circumstances, such as health and socioeconomic status, the availability of familial or state provided extra-household supports, and dominant values and norms. Several recent studies suggest beneficial effects of co-residence with children for the mental health and happiness of older parents in some settings, but not others. For example, a recent European study found that older widows in Europe reported higher levels of life satisfaction and happiness if they lived with a daughter and this positive impact was greater in Southern and Eastern than in Northwestern Europe (Grundy and Murphy 2017). Similarly, Aranda (2015) found that "doubling up" was associated with better mental health for older people in European countries with a Catholic tradition but not for those in countries with a Protestant tradition. Another study of parents aged 55–75 found that in Northern, but not Southern, Europe those who had an adult child return to an "empty nest" experienced a decline in their quality of life (Tosi and Grundy 2018).

Results from other parts of the world also find mixed effects of co-residence on older people's well-being; in some being positive (Do and Malhotra 2012), in others negative (Lowenstein and Katz 2005). A three-generational perspective may sometimes be needed. Research on China, where there is a pattern of migration to urban areas by adult children who sometimes leave their own children with their parents in rural areas, has found that older people who lived with an adult child, or with a grandchild without the middle generation, were happier than those in single generation households, with an important mediating influence in skipped generation households being the receipt of remittances from adult children (Silverstein et al. 2006).

These, and other, studies suggest that the implications of intergenerational co-residence for parental well-being may depend on the cultural and institutional context, as well as personal factors. As recognized in the Madrid International Plan of Action on Ageing (UN 2002), living with younger generations is not necessarily the preferred or best option for older people and the implications of co-residence for their well-being vary according to both societal and personal factors.

Future Directions of Research

Much of the research on co-residence is based on cross-sectional sources, and there is a need for more studies which use longitudinal data to analyze transitions to and from co-residence, preferably for all household members. This would enable better assessment of the benefits and disadvantages of co-residence as the prior characteristics of co-residents could be taken into account. More evaluation of the impacts of policy changes, such as the introduction of social pensions, on co-residence is also needed, together with further modeling of the impacts of demographic change on opportunities for co-residence. In some settings, the most pressing need is for the collection of good quality data on co-residence so that trends and differentials in this living arrangement can be assessed.

Cross-References

▶ Aging Households
▶ Crowded Nest
▶ Empty Nest
▶ Family Demography

► Kin Availability
► Living Arrangements in Later Life
► Multigenerational Families

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Coronary Artery Disease (CAD)

► Ischemic Heart Disease

Coronary Atherosclerotic Heart Disease

► Ischemic Heart Disease

Coronary Heart Disease

▶ Ischemic Attack

Coronary Heart Disease (CHD)

▶ Ischemic Heart Disease

Corporate Social Responsibility and Creating Shared Value

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Synonyms

Conscious capitalism; Sustainable capitalism; Value creation

Definition

Corporate social responsibility (CSR) is a concept describing the responsibility of businesses to act in accordance with legal, ethical, economic, and social standards in a way that does not cause environmental or societal harm. While an attempt to be a good citizen lies in the core of the CSR concept, the principle of creating shared value (CSV) emphasizes that apart from being a good citizen, the corporation also needs to be a good capitalist. Making an economic profit while solving social issues and thus contributing the interconnectedness between societal and economic progress present the most significant contribution of the CSV principle within the modern understanding of capitalism.

Overview

During the last two centuries, the capitalist system has changed from being predominantly profit-oriented toward being more conscious and responsible not only for the consequences of its actions but also for the environmental and societal issues connected to their production or philosophy (Friedman 1970; Porter and Kramer 2006). Currently, population aging is one of the crucial socioeconomic issues affecting corporate sustainability. Endeavors to solve it are being guided by the concepts of corporate social responsibility (CSR) and the creation of shared value (CSV). Porter and Kramer are one of the most prominent authors in this field, addressing the higher form of capitalism within which business and society are mutually dependent actors. They stress that the creation of shared value is an essential factor contributing to corporate sustainability, due to the fact that an investment into the creation of societal value also brings economic value and contributes to corporation's competitive advantage (Porter and Kramer 2011: 4).

Key Research Findings

Although the concept of CSR is ubiquitous in business and economic field, throughout the history, numerous meanings were assigned to it. While some scholars emphasized CSR as a mean to mitigate harm and maintain good reputation (Bowen 1953; Davis 1960), others emphasized that business has to address the needs of the society (Committee for Economic Development 1971). In 1979, a four-part definition of CSR was developed by Archie B. Carroll, a business ethics scholar. He emphasized that socially responsible businesses embrace an economic, legal, ethical, and philanthropic level of social responsibility at all times (Carroll 1991: 282–283). In practice, it means that socially responsible business "*makes profit obeys the law, is ethical and is a good corporate citizen*" (Carroll 1991: 289). In 1999, Porter and Kramer emphasized

CSR as an essential element of corporate philanthropy. They stressed that strategic donations, contributing society, create more value, and bring competitive advantage to the corporation. Later, in 2006, they elaborated on the concept of CSR, defining it as "*a source of opportunity, innovation, and competitive advantage*" (Porter and Kramer 2006: 2). In addition to that, they differed between responsive and strategic CSR and used the latter as a prerequisite for shared value creation, which is according to the authors, the main and the most crucial objective of the "modern capitalism" (Porter and Kramer 2006). While responsive CSR is more fragmented and defensive (e.g., damage control and public relations campaigns), strategic CSR, on the other hand, is characterized by a more integrated approach, emphasizing CSR as a strategy to improve corporation's competitive advantage and a prerequisite for shared value creation (Porter and Kramer 2011).

Porter and Kramer defined CSV as "*policies and operating practices that enhance the competitiveness of a company while simultaneously advancing the economic and social conditions in the communities in which it operates*" (Porter and Kramer 2011: 6). Addressing particular societal issues (related to the productivity in the corporation's value chain) benefits the corporation – not in a philanthropic way but in a purely economic way of making a profit. The concept of CSV acknowledges that redistribution, typical for CSR approach, is not the solution anymore; rather it is the application of the business model to address social issues that represents the new way of thinking about capitalism, and it brings competitive advantage to the corporation. The importance of making an economic profit while simultaneously benefiting the society with corporation's actions represent an essential contribution of CSV concept for the studies of the relationship between business and society. According to Porter and Kramer (2011: 7–13), there are three ways companies can create shared value opportunities. The first is by addressing costumers through (innovative) product and market development. The second is by changing practices in the value chain, and the third by enabling local cluster development (Porter and Kramer 2011: 12–13). Creation of shared value is a prerequisite for corporate sustainability; and in order for corporations to achieve it, they need a strategic plan, thorough investigation, and careful selection of the social problem they decide to address. The creation of shared value has the most potential if the addressed social problem is in relation to the productivity in the corporation's value chain (Porter and Kramer 2011).

Even though it may seem that CSR and CSV are similar regarding the legal and ethical component as well as in easing and reducing harmful corporate effects, there are important differences between them. Moczadlo (2015: 251) emphasized that the most crucial difference between the concepts of CSR and CSV is in their emphasis on profit maximization – it represents an integral part of the CSV while it is absent in the concept of CSR. There were many critiques of Porter and Kramer's concept of CSV (Beschorner 2013; Reyes et al. 2017; Moon and Parc 2019). However, the most public attention was given to the critique, written by Crane, Palazzo, Spence, and Matten, published in *Harvard Business Review* as well. They criticized CSV's supposed unoriginality: ignorance of the tensions between economy and society and Porter and Kramer's assumption that businesses (are pleased to) comply with legal and moral standards at all times (Crane et al. 2014: 140).

Since Porter and Kramer's (2011) introduction of strategic CSR and CSV as the most important mean for the achievement of corporate sustainability in 2011, other authors developed theories that originate and further develop concepts of CSR and/or CSV, with an objective to achieve corporate sustainability. In 2013, Osburg (2013) stressed that social innovations are the most crucial element for corporate sustainability, while Grayson and Hodges (2017) emphasized the creation of corporate social opportunities as the crucial factor for corporation's sustainability. Even though the means needed to reach corporate sustainability differ among authors, what they have in common is their acknowledgment of the interconnection between economic and societal progress.

Addressing Population Aging Through the Concepts of CSR and CSV

Taking into account the demographic and welfare crisis resulting from the imbalance between generations and growing number of people in need of constant help and care, as well as the threat of depleted natural resources and decayed human cultures, the utmost critical conditions to be met by corporations is to make a leap from using external motivational factors (such as profit and traditional understanding of capitalism) to internal motivational factors (such as solidarity, cooperation, and sensitiveness). According to Leichsenring et al. (2013), the process of solving the age-related demographic crisis depends on three factors that have to be dealt with creatively in order to make further development possible. These factors are: (1) successful economy – investing into and supporting active and healthy aging of their workforce and society respectively; (2) development of humane and sustainable long-term care for a significantly bigger pool of people in need of care; and (3) empowerment of every member of society to willingly participate in new solidarity between the generations (e.g., educating and sensitizing) (Leichsenring et al. 2013: 107–109). Population aging represents a unique opportunity for corporations to address all three abovementioned factors and gain competitive advantage through addressing healthy and active aging, supporting and developing innovative products and services contributing to the development of sustainable LTC solutions, and strengthening of intergenerational solidarity. However, it is crucial that a thorough investigation of the corporation's value chain is done before the corporation addresses a specific (social) issue or adopts a strategy. Either for CSR or CSV, it is essential that both sides (society and corporation) benefit in the process; however, only application of CSV assumes profit maximization as one of the main objectives for the corporation (Porter and Kramer 2011).

Aging of the Workforce as an Opportunity for Socially Responsible Companies to Evolve and Create Shared Value in the Community

Demographic statistics and research show that the labor force is aging rapidly (Eurofound 2018; United Nations 2017). There are companies in which the part of 50+ employees is predicted to increase dramatically, and for some indispensable jobs which are being performed by older workers, it is becoming increasingly challenging to find younger successors. Aging of the workforce presents an opportunity for corporations to address the issue of unsustainable balance between younger and older generations of workers and thus create shared value. For the corporation and the society, respectively, shared value can be created by offering and retaining jobs for older workers (Zacher et al. 2018), adopting innovative employment schemes, implementing pro–age policies, flexible work arrangements, application of innovative mentorship or internship programs, and through the development of activities and practices, addressing healthy and active aging, strengthening of the intergenerational solidarity, mutual respect and positive communication (Barnes et al. 2009; Hassard et al. 2011; Cortijo et al. 2019: 204). In addition, Naegele and Walker (2006: 27–28) emphasized seven essential preconditions for maintaining or developing corporate sustainability in times of aging of the workforce: (1) age awareness among managers; (2) careful planning and implementation of pro-age policies and practices; (3) improvement of working conditions and implementation of practices supporting healthy and active aging; (4) promotion of cooperation and intergenerational solidarity within the corporation; (5) open and continuous communication;

(6) internal and external monitoring; and (7) conscientious evaluation and assessment of applied measures.

Above mentioned (innovative) work schemes create value and opportunities for older adults to pass their knowledge to a younger successor, to age more actively and healthily and to expand their working years well into the retirement if they wish to. On the other hand, retention and investment in older workers also addresses the labor shortage, because if older workers feel valued and have good working conditions, there is an increased possibility that they will continue to work past their retirement age (Heisler and Bandow 2018: 423). Furthermore, Heisler and Bandow (2018: 428) emphasized that working conditions and rewards, along with human resource practices, addressing older workers and opportunities for knowledge sharing, are among the most important element contributing to the retention and productivity of older workers.

The Silver Economy as an Opportunity for Value Creation

One of the deciding factors in the corporation's sustainability is its market successfulness. The development of silver economy and silver markets serves as a good example of how the creation of shared value, embedded into the core organization of businesses, brings with it new opportunities and thus contributes to the corporation's competitive advantage. Population aging prompted the development of a cross-economy known as the silver economy, within which older adults play a crucial role as producers, consumers, entrepreneurs, and investors (Klimczuk 2015: 78). To improve living conditions and environment of older adults and to contribute to their successful aging, a network of age-friendly cities and communities was developed and spread in the last decade. The common feature connecting age-friendly cities and communities is a set of "*policies, services, settings, and structures, supporting and enabling active ageing*" (WHO 2007: 10). In practice, it means that in such cities or communities, infrastructure, services, and products are adapted to the various needs of older people, enabling older adults to age successfully in a familiar environment (WHO 2007: 1) (See ► "Age-friendly Cities and Communities").

Among various others, an essential element contributing to the sustainability and development of age-friendly cities and communities is smart technology (Hoof et al. 2018: 6–7). Gerontechnology – an emerging field combining the science of aging with the development of smart and supportive technology for grey consumers; supports healthy and active aging to improve wellbeing, primarily of older adults, but also of their relatives/carers (Fukuda 2011; Özsungur 2019). Demiris and Hensel (2008) developed six categories of technology, addressing older people's needs used in contemporary society. These categories are: physiological monitoring (measuring vital signs, such as heart rate and blood pressure); functional monitoring (measuring activity level); safety monitoring and assistance (preventing environmental risks) (e.g., fire or a gas leak); security monitoring and assistance (human threats); social interaction monitoring (measures social activity of the individual); and cognitive and sensory assistance (such as automatic reminders to take medications) (Demiris and Hensel 2008: 34). Even though smart technology developers presuppose that older adults are experienced users of information-communication technology (ICT), that is not always the case; it is true that generations of older adults are increasingly ICT literate; however, there are cohorts, especially the oldest old (80+) still lacking knowledge and experiences with it. Because younger generations have advanced knowledge of ICT, transferring it to older adults presents an opportunity for the utilization of intergenerational solidarity which is, according to Leichsenring et al. (2013), among the three crucial solutions for the demographic crisis. The development of gerontechnology creates shared value for corporations as well as for older adults – while it improves older adult's wellbeing and health status; selling and developing (innovative) gerontechnological products (such as active bracelets and home sensors) brings profit to the corporation and contributes to its successful and sustainable development (See ► "Sustainable Development Goals and Population Aging", ► "Gerontechnology").

Future Directions of Research

Demographic and welfare crisis brings with it issues that influence a corporation's sustainability. In the future, corporations will inevitably have to adapt their internal processes to the aging of the workforce, and external processes to aging consumers as well as to other societal issues relevant for corporation's value chain productivity; therefore, research on corporate sustainability will be of extreme importance. In gerontology, the concepts of CSR and CSV are still underrepresented, even though there are numerous opportunities for their application. Further research should focus on the effect smart technologies have on the wellbeing of older people and their caregivers, and vice versa the effect that expansion of smart technology use among older adults and their caregivers has on competitive advantage and sustainability of companies, developing products for silver consumers. Furthermore, in connection to the aging workforce, there is a growing need for the development of innovative workplaces adjusted to the growing number of older people, longing to stay actively involved in the labor market, even after they meet the retirement criteria.

Summary

In the modern capitalist system, making a profit is not enough for corporation's success anymore, because environmental and social consciousness, as well as responsibility for the wellbeing of their workforce and cooperation with the (local) communities, becomes increasingly important elements, contributing to corporation's successfulness and sustainable development. The concept of CSR emphasizes that socially responsible corporations comply, among other things, with social regulations and serve the needs of the society, while the concept of CSV stresses that investment into societal issues brings economic value and profit to the corporation and contributes to their competitive advantage. On the one hand, social changes, consequent to population aging, stimulate the development of innovative products and services, bringing profit to the corporations. On the other hand, these products and services improve everyday life and wellbeing of older adults (and their relatives), thus profiting society.

Cross-References

► Age-Friendly Cities and Communities
► Digital Health
► Social Entrepreneurship and Social Innovation in Aging
► Sustainable Development Goals and Population Aging

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Cortical Cataract

► Cataract

Cost Sharing

► User Fees (Coinsurance, Copayment, and Deductibles)

Costa Rican Longevity and Healthy Aging Study

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Overview

The Costa Rican Longevity and Healthy Aging Study (CRELES, or *Costa Rica Estudio de Longevidad y Envejecimiento Saludable*) is a set of nationally representative longitudinal surveys of health and life-course experiences of older Costa Ricans, conducted by the University of Costa Rica's *Centro Centroamericano de Población* in collaboration with the University of California at Berkeley. CRELES is part of the growing set of Health and Retirement Surveys being conducted around the world (See ► "Health and Retirement Study"). Costa Rica is of particular interest to study given its high longevity: life expectancy is greater than that of the United States, despite being a middle-income country.

CRELES comprises five waves of data from two birth cohort panels (See ► "Cross-Sectional and Longitudinal Studies"). The original **CRELES Pre-1945** cohort is a sample of more than 2,800 Costa Rica residents born in 1945 or before. There are three waves of interviews for this panel conducted mainly in 2005, 2007, and 2009. Wellcome Trust funded this panel (Grant N. 072406). The **CRELES 1945–1955 Retirement Cohort (RC)** is a sample of about 2800 Costa Rica residents born in 1945–1955 plus 1400 of their spouses, interviewed mainly in 2011 and 2013 (waves 4 and 5). The US National Institute on Aging (grant R01AG031716) funded this panel through the University of California, Berkeley.

CRELES data are well-suited for studying longevity and health determinants, relationships between socioeconomic status and health, stress and health, patterns of health behaviors, and prospective mortality.

Study Design

The Samples

The samples for the two panels are probabilistic, following complex, multistage designs. The populations represented in the samples are residents in Costa Rica at baseline dates, born in the years specified for each panel. The CRELES pre-1945 was randomly drawn from a larger probabilistic sample of 9600 individuals systematically selected from the 2000 census database. Sampling was stratified by age with oversampling of older individuals (details in Rosero-Bixby et al. 2004). Individuals were linked to birth, death, and voting national registries to conduct survival-time analyses by 2000 census characteristics (see, for example, Rosero-Bixby 2018). The sample for in-depth interviews was obtained in a second stage, consisting of the systematic selection of 60 "health areas" (out of 102 for the whole country). All individuals from the larger sample living in these 60 areas were eligible; the final sample excluded those who had died between 2000 and 2005, those severely impaired, and individuals who couldn't be found (details at http://www.creles.berkeley.edu/pdf/Methods_w1.pdf).

The CRELES RC sample followed a four-stage probabilistic design. The first stage was the aforementioned systematic selection of a sample of 60 Health Areas for the pre-1945 panel. The second stage selected 222 clusters, each composed of two or more census enumeration areas (*segmentos censales*) contiguous to each other in order to have at least 15 households with age-eligible individuals in each cluster. In the third stage, all households with at least one age-eligible individual were selected with complete certainty (probability one). In the fourth stage, among all people born between 1945 and 1955 in each household, one person was randomly selected as the main, or "target," informant. The spouse of the target respondent, if any, was also interviewed.

C

Interviewing

Data (and biological specimens) were gathered through face to face interviews in the homes of the participants by means of structured questionnaires programmed in handheld computers (Hidalgo-Céspedes et al. 2007). The computer drove the flow of the interview executing skips and filters and checking for inconsistencies and out of range responses, as well as automatically generating variables such as date and time. The device also contained preloaded data on the location and identification of each sampled participant. Daily uploaded data allowed real-time quality monitoring during fieldwork.

The main questionnaires took about 90 min to administer at baseline and less than 60 min in follow-up waves and in spouse's interviews. Questionnaires in follow-up waves were shorter since characteristics that do not change over time (such as education attainment or childhood conditions) were not reasked.

A cognitive evaluation at the beginning of the main interview helped to determine whether or not a "proxy" informant was needed to help respond to the survey. In the pre-1945 panel, 24% of baseline participants required a proxy, compared to only 2% in the RC panel. There was also an "exit questionnaire" in waves 2, 3, and 5 for participants who died between visits. A proxy respondent (next-of-kin) provided information about the subject's final days.

During baseline visits, the field team gathered data on the geographical coordinates of the place of each participant's residence, using GPS devices. They also filled out a community questionnaire with information about the neighborhood, including physical infrastructure, services, and access to health providers.

Two teams of three interviewers, a phlebotomist, and a supervisor conducted the fieldwork. The teams worked year-around. Completing the interviews for the entire sample took nearly 2 years, after which the teams started a new wave of visits. During the first contact, participants granted their informed consent by means of their signature using a consent form approved by the Bio-ethics Committee of the University of Costa Rica.

Response and Attrition Rates

Table 1 shows the number of participants in the five waves of CRELES and the response rates: 93% in the pre-1945 baseline and 66% in the retirement cohort. From those interviewed, more than 90% agreed to provide blood by venipuncture and to allow anthropometric measurement and other

Costa Rican Longevity and Healthy Aging Study, Table 1 Response and attrition rates

	Pre-1945 cohort			Retirement cohort	
	Wave 1	Wave 2	Wave 3	Wave 4	Wave 5
Eligible	3,024[a]	2558	2067	4,254[b]	2749
Interviewed	2827	2364	1855	2798	2430
Response rate	93%	92%	90%	66%	88%
Years	2004–6	2006–8	2009–10	2010–11	2012–14
Deaths	–	269	297	–	49
Blood specimen	95%	95%	–	94%	–
Anthropometry	90%	88%	89%	98%	97%
Short interview				491	
Spouse interview					
Eligible				1768	1512
Interviewed				1338	1109
Response rate				76%	73%

[a]Not counting individuals in the 2000 census who couldn't be found (N = 806), or had died (601), or were severely impaired (291)
[b]Not counting closed homes with no information

physical examinations. Attrition rates between waves, after excluding deaths, were approximately 10% in each two-year interval. Because of the high level of nonresponse in the RC panel, a short interview was conducted with 500 participants to assess key characteristics of nonrespondents.

Content

The main topics of the study are: socioeconomic and demographic characteristics; Mini-mental cognitive evaluation (See ▶ "Mini-Mental State Examination (MMSE)"); basic characteristics of household members, spouses, resident and nonresident children, parents, and in-laws; fertility; insurance and pensions; health (chronic diseases, symptoms, use of health care and expenditures, geriatric depression, stress); lifestyles (smoking, alcohol consumption, physical activity); childhood conditions; functional status (ADLs and IADLs); medications (inventory of items in participant's medicine chest); family and social support; employment history and income; house amenities; diet (consumption frequency and quantity of selected foods); anthropometry and physical tests (flexibility, strength, blood pressure); neighborhood characteristics; and death (cause of death, hospital and assisted-facility stays, bequests).

The interview for spouses (RC panel only) used a shorter version of the questionnaire, centered mainly on health and social support.

Biomarkers and Physical Measures

Table 2 summarizes the biomarkers and physical measures available from each CRELES wave (See ▶ "The Social Environment and Biomarkers of Aging Study (SEBAS)"). The 2005 wave of the CRELES Pre-1945 cohort included fasting blood and overnight urine collection, with blood collection repeated in wave 2. The baseline CRELES-RC (wave 4) drew nonfasting venous blood. DNA has been extracted from blood cells in both cohorts. Other biomarkers measured are blood pressure, anthropometrics, frailty, and mobility. Details on collection procedures and assay techniques are in Rosero-Bixby et al. (2010).

Auxiliary Data

CRELES participants were linked to the birth, death, and voting registries using the number on their ID-card (the *cédula*) that all Costa Ricans have. Foreigners (2% of the sample) are left out of this linkage. Ages are computed with the exact dates of interview and birth. Daily local weather conditions (rain, surface temperature, and humidity) in each sample cluster during the entire fieldwork period have been linked from remote sensing and local stations. A complementary sample of 91 centenarians from the Nicoya region has been studied with the same protocols of the three waves in the pre-1945 panel. This sample, however, is not part of the public databases (Rosero-Bixby et al. 2013).

Key Findings

The analysis of CRELES data has introduced new evidence about a nonexistent or reverse socioeconomic gradient in mortality, health, and utilization of health services in developing countries, like Costa Rica, Taiwan, and Mexico (Goldman et al. 2011; Rosero-Bixby and Dow 2009; Rosero-Bixby 2018). This pattern is observed in a context where Costa Rican nonagenarians have a life expectancy as high as their peers in industrialized countries, and the Nicoya Peninsula – a rural region in the Pacific coast – is considered a global hot-spot of high longevity. Older Costa Ricans have an advantage in cardiovascular health compared to other countries, and Nicoyans have an even greater advantage, as well as longer telomere length and higher DHEAS levels (See ▶ "Telomeres"), which are markers of healthy aging (Rosero-Bixby 2008; Rosero-Bixby et al. 2013).

Future Plans and Innovations

Data collection in the households ended in 2010 for the pre-1945 panel and in 2014 for the RC panel. Computerized follow-up of the two panels for

Costa Rican Longevity and Healthy Aging Study, Table 2 Biomarkers in CRELES waves

Biomarkers	W1	W2	W3	W4	W5
Main year	2005	2007	2009	2011	2013
Anthropometry (weight, height, knee height; abdominal, hip, calf, and arm circumference; tricipital and sub-scapular skin folds)	X	X	X	X	X
Blood pressure	X	X	X	X	X
Hand grip strength	X	X	X	X	X
Peak breathing flow	X				
Flexibility and mobility (standing, sitting, bending, and walking)	X	X	X	X	X
Agility	X	X	X	X	X
Walking speed	X	X	X	X	X
Overnight urine	X				
Creatinine clearance	X				
Epinephrine	X				
Norepinephrine	X				
Cortisol	X				
Fasting[a] blood (venipuncture)	X	X			
Glucose	X	X			
Glycosylated hemoglobin	X	X		X	
Total cholesterol	X	X		X	
HDL-cholesterol	X	X		X	
Triglycerides	X	X			
Serum creatinine	X	X			
C-reactive protein	X	X		X	
DHEAS	X	X			
Genetic markers from leukocytes	X	X		X	
DNA extraction and storage	X	X		X	
Telomere length	1200	1000		2800	
Methylation	1000				

[a]Nonfasting blood in wave 4

survival-time analyses continue to be updated annually. Further DNA analyses are also in development.

Among the innovations and unique features of CRELES are: (1) oversampling of oldest old: 279 participants are 90 years or older at baseline; (2) data from year round that allow studies of seasonal variation; and (3) use of a small number of interviewers, which allows analysis and corrections of interviewer bias.

Data Access

CRELES data (excluding identification variables) and documentation are downloadable from:

The National Archive of Computerized Data on Aging of the University of Michigan (ICPSR 2015).

The CRELES web site at the University of California (http://www.creles.berkeley.edu) (Berkeley Population Center 2012).

The Gateway to Global Aging Data at the University of Southern California (CESR 2018). This is a harmonized data file across waves and with HRS-type surveys in other countries.

Cross-References

► Cross-Sectional and Longitudinal Studies
► Health and Retirement Study

▶ Mini-Mental State Examination (MMSE)
▶ Telomeres
▶ The Social Environment and Biomarkers of Aging Study (SEBAS)

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Cost-Based Payment

▶ Fee-for-Service

Cougars and Silver Foxes in Film and TV

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Synonyms

Gender and age in film; Sexuality in old age

Definition

The terms “cougar” and “silver fox” are related to the representation of older men and women in cinema. “Cougar” refers to older female characters who develop relationships with younger men, whereas “silver fox” refers to grey- or white-haired male actors in their 50s and older who are considered to be attractive.

Overview/Key Research Findings

The term “cougar” started to be used in 2001 with the publication of Gibson’s *Cougar: A guide for older people dating younger men*. In her book, Gibson intends to empower women who would not usually be considered sexually attractive because of their age and encourage them to not only embrace their aging processes but to overcome sexual taboos in relation to women and aging by developing relationships with younger men. “Cougar” was quickly adopted by the cinema and TV industry to refer to those women in their middle years who were sexually attractive and showed an interest in having an active sexual life. Authors such as Montmerruno and Siefken (2014), Wohlman and Reichenpfader (2016), and Ames and Burcon (2016) agree on the fact that the figure of the cougar, as well as its popularization through cinema and TV, is an ambivalent one when considering female aging. Whereas cougars clearly break with the image of the older woman as described in Sontag’s double standard of aging (1978), since they are actually presented as sexually attractive and willing to experience desire, this trait may also be considered a way of “denying aging” (Montmerruno and Siefken 37). As Montmerruno and Siefken (2014) argue, cougars may contribute to the promotion of superficial images of aging femininities. Ames and Burcon similarly point out that the term is problematic because it focuses “on a woman’s appearance as being the most important aspect to consider on the sexual desirability scale” (175). On the other hand, they also recognize that this new label is applied to women who are “more likely to resist societal expectations thrust upon them” (201). The first film in which the term cougar was prominent was *The Cougar Club* (2005), followed by the sitcom *Cougar Town* (2009–2015). Wohlman and Reichenpfader (2016) and Ames and Burcon (2016) agree that the early years of the twenty-first century were the time when the figure of the cougar became prominent in visual culture, especially in television. Series such as *Sex and the City* (1998–2004), *How I Met Your Mother* (2005–2014), and *Desperate Housewives* (2004–2012) introduce storylines around cougars, and these are often used for comic relief.

The term “silver fox” has been mainly used in the press to refer to actors in their 50s and older who are considered attractive. The adjective “silver” refers to their white hair, an attribute that despite having been considered a sign of aging and, to some extent, decay takes on a new meaning through the performances of actors who are not only active, energetic, and attractive but who are also involved in romantic plots. Although, following Sontag’s double standard of aging, Woodward (1999), Chivers (2011), Dolan and Tincknell (2012), and Whelehan and Gwynne (2014), among others, agree on the fact that the physical signs of aging are more penalized in women than in men, agism does affect both men and women. As Gravagne (2013) states, despite the existence of “multiple masculinities” (59), hegemonic masculinity, in which traits such as youth, physical strength, self-control, and aggression are favored, is still the dominant model in film and television. Thus, the image of the silver fox embodied in reputed actors such as Richard Gere, George Clooney, and Daniel Day Lewis offers a depiction of masculinity into old age which moves away from stereotypes based on loss and decay. *The Second Best Exotic Marigold Hotel* (2015) and *Phantom Thread* (2017) with Richard Gere and Daniel Day Lewis starring, respectively, are recent examples of films in which two men close to retirement not only retain their creativity and savoir faire in their jobs but also become involved in romantic and passionate plots.

Summary

Despite the fact that both terms, cougars and silver foxes, focus on appearance rather than on the relevance of the person within his/her society or on the possible advantages of experience and even wisdom, both contribute to questioning the binary youth/attractiveness and old age/unattractiveness. In other words, these terms open up the possibility of considering aging bodily characteristics such as wrinkles, white hair, and sagging skin as attractive and sexually appealing, thus also pointing out to the fact that human beings are sexual beings throughout all their lives, not just during their youth.

Cross-References

- ▶ Age Stereotypes
- ▶ Gendered Aging and Sexuality in Audiovisual Culture
- ▶ Silvering Screen
- ▶ Stereotype Embodiment Theory
- ▶ Television Series on Aging: Aging and Serial Narration
- ▶ The Performativity of Age

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Council Housing

- ▶ Social Housing

COVID-19 Pandemic and Geriatric Oncology

Treatment Decision-Making, Healthcare Organizations, and Research

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Synonyms

SARS-CoV-2

Definition

The outbreak of COVID-19 is now a worldwide coronavirus pandemic. The severity of the virus can range from mild symptoms such as fever, cough, tiredness, and loss of taste and smell to symptoms such as acute shortness of breath and can lead to severe pneumopathy with the need for resuscitation. In addition, COVID-19 has dramatically impacted the lives of human beings in every respect. Health care practitioners have also implemented major essential changes in their daily organization patterns and decision-making processes.

Overview

At the end of July 2020, the World Health Organization reported 16,262,481 cases of COVID-19 worldwide and 648,913 deaths (WHO 2020a).

In a recent publication, Kuderer et al. observed that 56% of patients with concurrent COVID-19 and cancer were over 65 years of age (Kuderer et al. 2020). In this study, 279 patients were aged 75 years or older. The most prevalent cancers were breast (21%) and prostate cancers (16%). 45% were reported to be in remission and 43% to have an active cancer.

Importantly, the impact of the virus seems to differ between groups of patients, and a higher mortality rate is observed among older patients with cancer (Livingston and Bucher 2020; Kuderer et al. 2020). Moreover, older adults probably did not benefit to the same extent from resuscitation. In this context, decisions in geriatric oncology are more complex than among younger patients regarding both competing risk factors (cancer, comorbidities, and COVID-19) and the heterogeneity of cancers and treatments as well as the heterogeneity of frailty levels among cancer patients (Falandry et al. 2020).

The COVID-19 pandemic has raised new challenges in geriatric oncology, especially in the treatment decision-making process, in healthcare organizations, and in graduation of care.

The first challenge faced by practitioners, especially in geriatric oncology, has been the emergence of new major ethical dilemmas. In this latter setting, it is vital to determine the benefit-risk balance. To this end, it is useful to predict possible outcomes among elderly patients in order to establish the respective weights of unreasonable obstinacy and the principle of beneficence (Boulahssass et al. 2020). In critical situations, medical teams should propose innovative treatment plans but also take their decisions taking into account the levels of risk, which differ from one country to another but also between cities within a given country. Consequently, standardized clinical care recommendations should be graduated to fit the context. A second challenge involves developing specific e-health tools for the monitoring and assessment of this specific population. Finally, a third challenge entails avoiding loss of follow-up regarding concomitant comorbidities which could lead to bad conditions and overmortality.

Key Research Findings

Recommendations for Intervention

The International Society of Geriatric Oncology (SIOG) recently formed a panel of experts to propose consensus recommendations for adapting care of older patients with cancer during the COVID-19 pandemic. These recommendations stressed the importance of the geriatric assessment as a means to drive the decision-making process by assessing the risk-benefit balance and the need for efficient monitoring of patients via tele-health development (Battisti et al. 2020). The SIOG recommendations for general interventions include: (i) Maintain physical distancing; (ii) Implement strict infection-control policies in residential care facilities and hospitals, and minimize or discourage all nonessential visits; (iii) Deploy telehealth care; (iv) Encourage provide access to technologies to maintain social network; (v) Implement a coordinated and pragmatic treatment journey to rationalize patients' appointments; (vi) Evaluate clearly the goals of care; and (vii) Consider advance care planning discussions where appropriate (Battisti et al. 2020).

The SIOG recommendations for care domains include: (i) Select older patients requiring a complete comprehensive geriatric assessment using tools screening such as G8 or VES13; and (ii) Use e-health tools to implement GA and tumors boards, Self-administered screening tools: G8, VES-13, SOCARE team telehealth-geriatric assessment. For surgery, recommendations include: (i) Prioritize surgical management based on patients' evaluations, care organizations, cancer prognosis, and symptoms evaluations; (ii) Defer noncritical surgery if possible; (iii) Use local anesthetics if appropriate; (iv) Consider neoadjuvant endocrine therapy to defer breast cancer surgery for HR-positive, HER2-negative breast cancer; and (v) Consider primary endocrine therapy instead of surgery for HR-positive, HER2-negative breast cancer. For radiotherapy, recommendations include: (i) Prioritize radiation therapy approaches based on patients' evaluations, care organizations, cancer prognosis, and symptoms evaluations; (ii) Delay noncritical radiotherapy if possible; (iii) Omit radiotherapy if no clear survival or symptom controls benefit; and (iv) Use adapted therapies when possible (Hypofractionation for breast cancer, Short-course neoadjuvant radiotherapy for rectal cancer, Single-fraction radiotherapy for palliative care, and Intraoperative radiotherapy for breast cancer, for example). For systemic therapies, recommendations include: (i) Prioritize systemic treatments based on patients' evaluations, care organizations and cancer, and symptoms evaluations; (ii) Implement the use of chemotherapy toxicity prediction tools (CARG or CRASH); (iii) Prescribe primary G-CSF prophylaxis; (iv) Delay noncritical systemic treatments if possible; (v) Omit systemic therapy if the ratio benefit/risk is not good; (vi) Maintain physical activities; (vii) Practice nonmedical approaches (meditation, mindfulness, or deep breathing exercise); and (viii) Use a care plan for nutrition comorbidities provide with the primary care (Battisti et al. 2020).

Meanwhile, the French Society of Geriatric Oncology also proposed some general guidelines according to this health crisis (Mourey et al. 2020), which include: (i) The priorities remain containment and barrier measures as for the rest of the population; (ii) Consultation between the oncologist and the geriatrician remains fundamental for difficult decisions; (iii) Explorations of the diagnosis including geriatric assessment and additional examinations should be weighted according to the evaluated prognosis of the tumor pathology; (iv)Tele-consultations are preferred for follow-up if there is sufficient understanding and noncritical physical clinical examinations; (v) The recommendations of the other societies published on the occasion of this crisis and taking into account the stage of the disease and the expected risk benefit ratio for the treatments are to be applied without a priori age limit and taking into account the local epidemic context; (vi) Deferral of cancer surgery should be discussed collegially if it does not obviate the cancer prognosis; and (vii) Using treatments to delay the surgery or the chemotherapy should be preferred when possible (such as hormonotherapy in breast cancer, for example). In case of acute respiratory distress syndrome related to SARS-Cov-2, it is important to note that the management in resuscitation is prolonged and difficult with an uncertain outcome.

Treatment Decision-Making

The main risk during the COVID-19 pandemic is the reduced accessibility of older patients to treatment for cancer and other ailments. Even if a section of this older population should be considered at high risk of complications, alternative strategies could be proposed.

In a recent paper, Falandry et al. advanced a number of proposals regarding such alternatives, e.g., patients with hormone-sensitive cancers should be offered endocrine therapies as a waiting treatment, possible therapeutic breaks for stabilized cancers, or a 4-week regimen for check-point inhibitors (Falandry et al. 2020). Other strategies are also possible as advised by the SIOG recommendations, e.g., postponement of noncritical surgery and delaying noncritical radiation. However, the panel of experts also focused on prioritizing standard treatment when necessary following an analysis based on global states status (geriatric assessment) and the patient's wishes (Battisti et al. 2020).

The treatment decision should give rise to an appropriate care plan and avoid both undertreatment and overtreatment of critical situations by adjusting treatment schedules, dose reductions, or radiotherapy fractionation, whenever possible. The treatment decision should take into account cancer type, cancer extent, and the global prognosis. However, clinicians also need to assess the potential additional risk of viral infection due to treatment-induced neutropenia as well as to previous general conditions. In addition, medical teams must educate patients and caregivers in safety precautions and social distancing. Whenever possible, collective decisions shared with the geriatric team remain the optimal strategy in the analyses of the benefit/risk ratio (Mourey et al. 2020).

Healthcare Organizations

Geriatric and oncologic assessments help to prioritize both oncologic treatments and geriatric interventions.

Geriatric Assessment

The first major question to arise at the onset of the COVID-19 pandemic is to determine which patients could benefit from a geriatric assessment (GA) and how to conduct it in clinical practice. The first step recommended by the SIOG is to use screening tools (G8, VES 13) by patients (or caregivers) before deciding whether to perform geriatric assessment (Soubeyran et al. 2014; Saliba et al. 2001).

The SIOG panel group recommends encouraging practitioners to promote and enhance telehealth consultations in their institutions. In our experience, this type of consultation needs to be prepared in advance by phone with the patient and/or the caregiver. Other teams proposed a pre-consultation by telephone before the teleconsultation so as to screen for potential deficits in the GA (Di Giovanni et al. 2020). It should be stressed that not all patients can benefit from this type of consultation on account of the prevalence of isolation and cognitive impairment in this population. New strategies must be proposed during the coronavirus crisis. For instance, 1-day hospitalization could be initiated to perform all the necessary investigations (geriatric assessment and oncologic workup). Alternatively, evaluations at home could be introduced involving a mobile geriatric team. In addition, complex cases should undergo a classic geriatric assessment at the hospital. In this case, the best strategy is to discuss this option during committees regarding the prognosis, the type of treatment, and the patient's condition. The discussion should include all the health-partners (geriatricians, surgeons, radiotherapists, and oncologists). The increased use of e-tools during the crisis has created new opportunities to undertake kinds of communication and discussion.

For example, digital platforms, which facilitate connection between health partners, provide the possibility of tumor boards and collegiality. For patients, these technologies could support the provision and coordination of health services, the monitoring with telemedicine, and the communication with their families.

What Are the Key Features of GA that Should Be Focused on During the Current Pandemic?

First, it needs to highlight assessments of the risk of an early death (Soubeyran et al. 2012; Boulahssass et al. 2018; Angeli et al. 2020; Boulahssass et al. 2020) as well as the chemotoxicity risk (Extermann et al. 2012; Hurria et al. 2011). The balance benefit-risk is crucial in the decision to treat, to delay, or to omit an oncologic treatment. If the patient is likely to die during the next weeks, it is probably necessary to provide him with best supportive care alone. Especially during the COVID-19 crisis, the assessment of the chemotoxicity is important using the CRASH or the CARG score and recommended by the SIOG. This prediction of this toxicity could lead oncologist to delay or adapt the treatment.

Social support for the patients is crucial in this context, and a complete assessment should be made of the patient's ability to implement the care plan without difficulty with the support of appropriate monitoring (Battisti et al. 2020). To this end, it is crucial to determine whether the patient is fully capable of conducting the monitoring, when necessary, using e-health tools based on the use of smartphone or tablets (Battisti et al. 2020).

During the lockdown following the spread of COVID-19, it is vital to evaluate patients' mood disorders and cognitive functions (Padala et al. 2020). Indeed, the COVID-19 crisis has generated a significant increase in anxiety among patients, sometimes culminating in bouts of delirium or depression (Chevance et al. 2020; Hamm et al. 2020; Sher 2020). In such cases, preventive measures are required to eliminate such complications. During the current pandemic, oral therapies have frequently been delivered to patients in place of systemic treatments. Cognitive function evaluations would help avoid unnecessary difficulties in the management of such therapies.

Another major issue concerns the management of concomitant comorbidities. When faced with COVID-19 and other concurrent conditions, older cancer patients are frequently afraid to consult several different practitioners and, consequently, do not receive necessary follow-ups for critical diseases and are thus open to major complications (Crispo et al. 2020). The geriatric assessment could help in this context by checking on competing risks and the possible need to adapt the medications prescribed. Furthermore, the geriatric assessment could provide relevant information about patients' global frailty level, their physiological reserve, and their treatment preferences.

Finally, one useful feature of the geriatric assessment lies in the establishment of geriatric interventions. Some aspects of GA can be handled by other healthcare partners, such as dieticians, nutritionists, psychologists, or psychiatrists, even if there is no geriatrician on the team. A nurse could coordinate and educate patients and could refer them to practitioners able to provide them with simple measures such as nutritional support, advice or physiotherapy. The COVID 19 pandemic underlines the necessity of a call for comanagement involving several health-networking offering smooth lines of communication and shorter referral times. Future developments in geriatric oncology will further the integration of innovative case-management professionals and the development of specific e-health tools.

What Are the Key Points to Focus on Regarding the Oncologic Assessment?

Oncologic team assessment will need to highlight treatment aims (curative, palliative, or symptomatic). It is crucial to determine the type and stage of the cancer, patient sensitivity to the therapies available, and the possibility of introducing new therapies to establish a prognosis. Evaluation of the impact of side effects on the immune system calls for an appropriate analysis in order to calculate the benefit/risk balance. Moreover, practitioners need to keep in mind that even if the goal of the care plan is palliation, appropriate treatment must be implemented in order to control symptoms using home-based medical services, if available.

Ethical Dilemmas

The main dilemma arising in the field of oncologic care for the elderly during this unexpected coronavirus health crisis has been to balance the risk of progression of the cancer with the risk of exposure to COVID-19. The best strategy is still to perform an individual benefit-risk balance assessment including screening, an adapted geriatric assessment using tele-health tools, or a complete assessment, if required. However, whenever possible, it is important to reach a consensus decision within a geriatrics team. Whenever possible again, medical teams should obtain institutional support from their ethics committees to assist them in achieving a balance between unreasonable obstinacy and the principle of beneficence. Inevitably, in critical situations involving a high incidence of the COVID-19 virus, practitioners will need to rely on their own judgment.

With regard to resuscitation, several ethical issues are open to debate. There is no rational consensus on the provision of health care in the event of a shortage of ventilators combined with a major influx of patients. Should age limits be established for admission to intensive care units? In clinical routine, it has been observed that the resuscitation process is lengthy and survival rates in the elderly would seem to be low, with the additional risk of irreversible posttreatment loss of autonomy. Resuscitation should probably be offered only to fit patients. More than ever, advanced care planning is imperative in this population.

Issues Surrounding Translational and Clinical Research Developments in Oncology in Older Adults During the COVID-19 Pandemic

The scientific and medical communities have actively developed COVID-19-related clinical and translational research programs designed to develop vaccines, curative and preventive treatments, and diagnostic tests (Berkley 2020; Graham 2020). The immediate consequence has been an amazing number of publications in the COVID-19 field (featured on the PubMed website (https://www.ncbi.nlm.nih.gov/pubmed)) over a very short period of time, as of early 2020. This has enabled rapid dissemination of pivotal information toward the scientific community. It is noteworthy that most of these research programs have been based on the use of biological samples (cells, tissues, and biofluids) from positive COVID-19 patients that were associated with clinical and epidemiological data. Epidemiologic studies, however, rapidly reported that the mortality and the morbidity rates of the disease were much higher among the elderly, and even more so in older patients suffering from a malignancy (Du et al. 2020; Liang et al. 2020; Xia et al. 2020). Thus, a number of studies were performed in aged patients infected with SARS-CoV-2 displaying, for example, several characteristic tissue lesions, mainly in the lung parenchyma, as well as in other organs such as the gastrointestinal tract, the kidneys, and the central nervous system (Wang et al. 2020; Xu et al. 2020).

A direct consequence of the COVID-19 pandemic in elderly cancer patients has been a dramatic decrease in their healthcare routines due to fewer hospital visits and opportunities for cancer treatment. This is undoubtedly one of the more obvious and visible negative impacts of the pandemic. However, another repercussion in the oncogeriatric field is the sudden discontinuation of most of the translational and clinical research programs, notably those using biological specimens. These specimens were previously collected prospectively or stored in biobanks and used retrospectively for various purposes. For reasons related to biosafety during the COVID-19 crisis, many biobanks decided to discontinue collecting tissues and biofluids (Centers for Disease Control and Prevention 2020; Hofman et al. 2020; Iwen et al. 2020; World Health Organization 2020b). Furthermore, some biobank employees were rapidly redirected to clinical departments to help deal with the sudden influx of positive COVID-19 patients. In this context, we need to be aware that future translational oncogeriatric research programs could be severely handicapped by the reduced availability of samples in general, and specifically of samples from older patients (Hofman et al. 2020). Moreover, during the COVID-19 pandemic, the lockdown on experimental laboratories and clinical trial platforms has had a massive impact for the future of cancer science, and most crucially in the field of oncogeriatrics (Colbert et al. 2020; Editorial 2020; Ledford 2020a). Nonetheless, it is crucial to continue developing research in oncogeriatrics, notably among positive COVID-19 patients, on account of the many remaining unknowns and uncertainties associated with the SARS-CoV-2 infection (Ledford 2020b; Weston and Frieman 2020). COVID-19 has raised some specific issues in the biobanking world. In this area, the vast scope of the pandemic, with almost 3 million cases globally as of mid-May, means that laboratories and biobanks are likely to be handling many samples involved in the establishment of diagnoses and the development of vaccines. It is imperative that elderly patients, and notably those with cancer, should participate actively in these developments.

Future Directions of Research

The current COVID-19 health crisis highlights a need to anticipate and study organizational models of care. Management models, protocols, and health procedures need to be assessed and enhanced. In the near future, a global strategy aimed at slowing down transmission of the virus, and thus reducing mortality and morbidity should also incorporate a set of robust guidelines. Such a strategy should be based on population risks and levels of frailty as revealed by geriatric oncology. The COVID-19 pandemic has generated a call for new professional positions such as case-manager, and these actions need to be developed and evaluated such as the development of the monitoring of interventions with the tele-medicine and tele-consultations (see ▶ "Telemedicine", and ▶ "Telehealth").

The COVID-19 pandemic has given rise to massive technological breakthroughs worldwide in the development of dedicated e-tools, and the adaptation of these tools to older patients.

In this population, it is crucial to investigate the risks related to undertreatment of diseases concomitant with cancer in order to maintain essential health services and prioritize a strategic planning heath system.

The new challenges are also to use the COVID-19 experiences to develop new approaches for treatment and ethical issues in order to help practitioners in further health crisis by developing new guidelines and innovative organizations to fight against viral diseases.

Summary

The COVID-19 pandemic has brought about major changes in treatment decision-making, in health establishment, and in the research field. The International Society of Geriatric Oncology (SIOG) recently formed a panel of experts to propose consensus recommendations to guide future changes to the care delivered to elderly cancer patients during the coronavirus pandemic. These recommendations stress the importance of the geriatric assessment in driving the decision-making process by calculating the risk-benefit balance and the need to devise an efficient patient-monitoring system through the development and implementation of telehealth technologies. The main risk for older patients during the COVID-19 pandemic is the reduced accessibility for these patients to cancer treatment, as well as to other therapies. Practitioners are facing new major ethical dilemmas, notably in geriatric oncology. Analysis of the benefit-risk balance is crucial in this situation while outcome prediction among older patients could help in the analysis of the opposition and balance between unreasonable obstinacy and the beneficence principle. The first challenge facing medical teams is not only to propose innovative treatment plans in critical situations but also to rethink their decision-making processes in the context of risk levels which differ from one part of the world to another as well as within a given country. The second challenge still consists of devising specific e-health tools to monitor and assess the population of older patients with cancer. The third challenge is to prevent the loss of follow-up for comorbidities, a situation which could lead to severe medical conditions and overmortality. Wherever possible, it is important to pursue the access to clinical and translational research.

Cross-References

- ▶ Cancer Diagnosis
- ▶ Cancer Screening
- ▶ Chemotherapy Toxicity
- ▶ Clinical Trial Design for Older Cancer Patients
- ▶ COVID-19 Pandemic and Healthy Aging
- ▶ Frailty Screening
- ▶ Geriatric Assessment for Older Adults with Cancer
- ▶ Mini Datasets for Research in Geriatric Oncology
- ▶ Monitoring and Clinical Research in Oncogeriatrics
- ▶ Prediction of Outcomes Among Cancer Patients

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COVID-19 Pandemic and Healthy Aging

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Synonyms

SAR-CoV-2

Definition

Coronavirus disease 2019 (COVID-19) is a novel coronavirus disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that was first reported in December 2019 (WHO 2020a). On March 11, The World Health Organization (WHO) declared the outbreak of COVID-19 as a pandemic (WHO 2020b), and as of June 2021, the pandemic is still ongoing.

Overview

Since the first confirmed case of COVID-19 in December 2019, the pandemic has spread rapidly around the world. As of mid-May 2021, there have been more than 160 million cases of COVID-19 confirmed in over 220 countries/territories, with an estimated death toll amounting to over 3.3 million (WHO 2021). As declared by the United Nation Secretary-General, the COVID-19 pandemic has been the single most severe international public health crisis since World War II (United Nations 2020). Although the pandemic is still ongoing in much of the world, COVID-19 has profoundly changed the world, not only as a public health crisis but also as a historical event of major significance. Older adults have been one of the most vulnerable populations in this pandemic (Sands et al. 2020). One of the most pressing challenges of the COVID-19 pandemic has been to decrease rates of infection and fatality among older adults and safeguard their well-being and care during the outbreak (Miller 2020).

Outbreak of COVID-19

According to current reported records, the first known case of COVID-19 was diagnosed by Chinese doctors in Wuhan, China, on December 8, 2019. Although the origins of SARS-CoV-2 remain unknown, the spread of COVID-19 across the world was rapid. On January 30, 2020, WHO declared the COVID-19 outbreak to be a Public Health Emergency of International Concern, WHO's highest level of alarm, and on March 11, WHO declared the outbreak as a pandemic (WHO 2020b). Since March 2020, infections increased from 100,000 per 2 weeks in mid-February, to 100,000 per week in early March 2020, and to more than five million per week from mid-April 2021 to mid-May 2021, although there were several ups and downs in between (WHO 2021).

Responding to the initial outbreak of COVID-19, China took a series of actions since January 2020. After approximately 3 months, COVID-19 transmission was effectively contained in mainland China. Wuhan, the epicenter of the outbreak, officially reopened on April 8, 2020 after a lockdown of 76 days. During this period, however, the active transmission of COVID-19 moved to European countries in mid-March 2020 and soon thereafter to the United States as of March 2020 (ECDC 2020). As of mid-May 2021, the United States reported over 3033 million confirmed cases of COVID-19 with nearly 600,000 attributable deaths. Following the large outbreak in the United States, India and Brazil have reported the second and third largest numbers of confirmed cases, respectively, as of mid-May 2021. The number of reported cases exceeded 24 million with a death toll over 260,000 in India, and the corresponding figures for Brazil were 15 million and 430,000. In Africa, since the first case was detected in mid-February 2020, over 3.4 million cases have been reported as of mid-May 2021. And now more recently, several new variants of the virus have been detected in various countries around the world – some of which are reported to be more infectious and/or contagious than earlier strains (Center for Disease Control and Prevention 2021).

Based on statistics provided by WHO (see the CVOID dashboard of WHO at https://covid19.who.int/), although most countries have implemented lockdown policies, many even with several periods of lockdown, and with vaccines being developed and distributed, many regions of the world have been witnessing increases in new cases since March 2021.

Etiology, Transmission, and Clinical Characteristics

It has been reported that SARS-CoV-2, the virus that causes COVID-19, is under the subgenus Sarbecovirus of β-CoV in the Orthocoronavirinae subfamily, the family Coronaviridae, order Nidovirales. It is enveloped in a shape of round or elliptical particles with a diameter of about 60~140 nm (China National Health Commission 2020; Zhu et al. 2020). Natural and intermediate hosts of SARS-Cov-2 have not yet been identified, but it is shown to be highly related to bat-derived severe acute respiratory syndrome (SARS)-like coronaviruses (Lau et al. 2020; Lu et al. 2020b; Zhou et al. 2020).

In pathogenesis, viral entry is through binding the viral trimeric spike protein to the human receptor angiotensin-converting enzyme 2 (ACE2), a receptor protein with the primary physiological role to control blood pressure and body fluid homeostasis (Chen et al. 2020; Lu et al. 2020a; Yan et al. 2020). ACE2 expression is thus associated with susceptibility to SARS-CoV-2 (Chen et al. 2020). The spread of SARS-CoV-2 is mainly through: (1) respiratory droplet transmission, in which droplets emit when a person with COVID-19 coughs, sneezes, or speaks; (2) direct contact transmission, in which individuals touch objects or surfaces with droplets containing virus particles and then touch their eyes, nose, or mouth; and (3) aerosol transmission, in which aerosols generated by infected persons are inhaled by others (Chan et al. 2020; Li et al. 2020a, b; WHO 2020c; Zhu et al. 2020). Some scientists have argued that aerosol transmission is only possible in certain enclosed environments with high concentration of the viruses (Lu et al. 2020b). To date, there has been no reported cases of fecal-oral transmission (digestive tract) – although some researchers have detected SARS-CoV-2 in feces and effluent (Guan et al. 2020a; Guo et al. 2021; Mallapaty 2020).

The initial reproductive number of COVID-19, R0, as the average number of infected individuals from one infected individual without any intervention, varies depending on the development/stage of the outbreak. The R0 was between 2 and 2.5 based on data from China (WHO 2020d). In European countries, the averaged R0 from February to June 2020 was estimated to be around 3.87 (Flaxman et al. 2020). In New York City, the initial R0 was 4.6 before March 17, 2020 (Li et al. 2020b). It was also reported that the newly identified variant detected in the United Kingdom could increase transmissibility by 40–70%, producing an R0 of 1.5–1.7 (WHO 2020e). A review further suggests that the global R0 was approximately 2.87, with a high degree of variance across nations (Billah et al. 2020). Nevertheless, there are some shortcomings of R0, and it is a challenge to get an accurate value of R0 because of availability and accuracy of data at the beginning, modeling strategy, and other obstacles (Bauch 2021).

Studies show that biochemical indicators of COVID-19 infection are featured by a declined count of leukocytes, and lymphocytopenia, and increased count of monocytes (Zhu et al. 2020). Elevated C-reactive protein levels and erythrocyte sedimentation rates are also observed in most patients. Some patients may also exhibit high aminotransferase, lactate dehydrogenase, creatine kinase, and myohemoglobin. For severe cases of COVID-19, increased D-dimer and decreased peripheral blood lymphocytes are observed (Zhu et al. 2020). In terms of CT characteristics, local patchy shadowing and interstitial abnormality are typical in the early stage of disease, which can develop into bilateral ground-glass opacity and infiltration shadowing, and eventually lung consolidation for severe cases (Zhu et al. 2020). Fever, dry cough, and fatigue are common clinical manifestations of COVID-19 in patients. Another symptom such as pharyngeal discomfort is sometimes observed as well. Approximately half of patients have dyspnea 1 week after infection, among whom the severe cases develop acute respiratory distress syndrome (ARDS), septic shock, irreclaimable metabolic acidosis, and coagulation dysfunction (China National Health Commission 2020). Some COVID-19 patients are reported to lose the sense of smell and/or taste (Menni et al. 2020).

COVID-19, SARS, MERS, and Influenza

SARS-CoV-2, the severe acute respiratory syndrome coronavirus (SAR-CoV), and the Middle East respiratory syndrome coronavirus (MERS-CoV) are all β-CoV. SARS-CoV-2 has approximately 79% genetic similarity to SARS-CoV and around 50% similarity to MERS-CoV (Zhu et al. 2020; Xu et al. 2020). In comparison with SARS patients, the RNA concentration peak of COVID-19 patients arrives earlier with higher volumes. It usually takes 7–10 days for SARS to reach the RNA concentration peak after onset, whereas for COVID-19, it is within 5 days. Moreover, the peak volume of COVID-19 is more than 1000 times higher than that of SARS (Wolfel et al. 2020). SARS-CoV-2 is thus more infectious than SARS-CoV (Wolfel et al. 2020; Yang et al. 2020a; Zhu et al. 2020). The case fatality rate (CFR), i.e., the percentage of deaths among those with a given disease, is estimated at around 3–4% for COVID-19 (Duan 2020; WHO 2020d, f), lower than that of SARS (approximately 10%) and MERS (approximately 35%) (EWG for NCIP Epidemic Response 2020; Wang and Wang 2021; Wilson et al. 2020; Xie and Chen 2020). However, the CFR of COVID-19 varies temporally and spatially (Sorci et al. 2020) and can be influenced by many confounding factors, such as how to define COVID-19-related deaths, the quality of the death-reporting system in place, and other issues of mortality counting and reliability across systems (Sorci et al. 2020).

SARS-CoV-2 and influenza viruses are similar in that they are both transmitted by contacts, droplets, and fomites (WHO 2020c). However, the spread of COVID-19 is slower than influenza. For influenza, the median incubation period, i.e., the time from infection to symptom appearance, is usually 3 days, in which transmission is possible. For COVID-19, the median incubation period is approximately 1 week, and the transmission in this period, though possible, is not the primary pathway. In addition, the proportion of severe cases is higher in COVID-19 (15–20%) than influenza (about 2%), and the fatality rate of COVID-19 (3%) is much higher than seasonal influenza (<0.1%) (Duan 2020; WHO 2020d, g; Wilson et al. 2020).

COVID-19 and Underlying Health Condition

COVID-19 patients often have underlying health conditions. According to 19 studies on COVID-19 published between January 1, 2020, and February 21, 2020, approximately 36.8% of confirmed cases had underlying health conditions – with the most prevalent conditions including diabetes (11.9%), hypertension (18.6%), and other cardiovascular diseases (14.4%) (Rodriguez-Morales et al. 2020). COVID-19 patients with underlying health conditions have significantly higher risks of severe illness and death compared with otherwise healthier patients (Guan et al. 2020b). Based on more than 44,000 confirmed cases in China, one report showed that patients with underlying health conditions, such as diabetes, hypertension, cardiovascular disease, chronic respiratory disease, and cancer, had a mortality risk that was about 6–10 times greater than those without these conditions (EWG for NCIP Epidemic Response 2020). The US CDC COVID-19 Emergency Response also reported that the risk of ICU admission was significantly higher among COVID-19 patients with underlying health conditions (approximately 8.5%) compared with those without underlying conditions (about 1.5%) based on 1.3 million confirmed cases from January 22 to May 30, 2020; in the same period, the risk of death among the former was 19.5% in comparison with 1.6% among the latter (Stokes et al. 2020).

Older Adults and the COVID-19 Outbreak

Older adults have been the most vulnerable population during the COVID-19 outbreak, with higher risks of infection and higher CFR than younger adults (EWG for NCIP Epidemic Response 2020; CDC COVID-19 Response Team 2020a, b). Table 1, which is based on the data available as of April 23, 2020, shows that adults aged 60 years and older had much higher rates of COVID-19 infection compared with younger people. Note that the older adult

COVID-19 Pandemic and Healthy Aging, Table 1 Distributions of confirmed COVID-19 cases and deaths among older adults in selected countries

Country/areas	Confirmed cases	% of adults aged 60+	% of adults aged 80+	Deaths	% of adults aged 60+	% of adults aged 80+
Global[a]	825,457	34.8	9.7	—	—	—
China	44,672	31.1	3.2	1023	90.0	20.3
United States	607,590	24.2[b]	12.5[c]	23,358	78.9[b]	29.6[c]
New York City	141,467	24.1[b]	11.5[c]	10,288	73.1[b]	48.3[c]
Spain	152,587	52.8	20.7	13,078	95.2	58.3
Italy	158,624	54.3	23.0	21,550	95.2	53.7
Germany	—	—	—	5094	95.6	63.0
France	—	—	—	13,464	93.6	58.9
Belgium	38,496	51.0	28.3	5683	93.3	47.6
Nederland	34,134	52.3	23.4	3916	97.0	58.8
Canada	18,468	36.5	13.8	607	93.6	62.8
Portugal	22,353	36.1	15.3	820	96.3	67.2
Japan	11,630	29.3	8.0	210	93.3	52.9
South Korea	10,669	23.7	4.5	234	91.5	47.9

Note: Infection and death statistics in the table may be incomplete due to reporting lags, and in some countries, cases of unknown age are not included. Data for China are from the Chinese Center for Disease Prevention and Control (CCDC), and the Epidemiology Working Group for NCIP Epidemic Response (2020). Data for the United States are from the CDC (2020), with infection data dated as of April 22, 2020, and death data dated as of April 23, 2020, excluding 10,492 cases with 2 causes of death (as general pneumonia and COVID-19). Data for New York City are from the New York City Department of Health and Mental Hygiene (2020), dated as of April 23, 2020. Data for Italy are from the Italian National Institute of Health (https://www.epicentro.iss.it/), and only in-hospital deaths are included, with infection data dated as of April 16, 2020, and death data, dated as of April 22, 2020. Data for Canada are from Wikipedia, dated as of April 17, 2020. Data for Spain, Germany, France, Belgium, Netherland, Portugal, South Korea, and Japan are from the Ministry of Health in each country, respectively, dated as of April 22, 2020

[a]Global data are based on the incomplete records of 113 countries in the WHO global monitoring system (WHO 2020g), excluding China, as of April 17, 2020

[b]Proportion of adults aged 65 years and older

[c]Proportion of adults over age 75 years

populations in these countries, except for Japan, accounted for less than 30% of the total populations (United Nations 2019). As shown in Table 1, with the exception of the United States, almost 90% of deaths in other countries in the table were among people aged 60 years or older in these countries; whereas with one exception for China, nearly half of the deaths were people aged 80 years or older. The most recent data as of mid-May 2021 (not shown), more than one-year later than those in Table 1, have similar distributions. Although the estimations may vary by stage of the outbreak, testing level, and reporting criterion, the vulnerability of older adults during the COVID-19 pandemic is unquestionable.

Biomedical Perspective

The vulnerability of older adults to COVID-19 is both biomedically and psychosocially based. From a biomedical perspective, there are at least five major factors at play. First, immune function declines at older ages. Immune function is especially crucial against SARS-CoV-2, particularly in the absence of widespread vaccinations to date. For older adults, the quantity and quality of immunocytes such as T lymphocyte (T cell), B lymphocytes (B cell), and natural killer cells (NK cell) all decline significantly, impacting the immune system's capacities for immunological host defense, phagocytosis, and elimination of pathogens (Li and Yin 2013). Research shows that the number of functioning B cells in older adults is only 1/50–1/10 of that in people in their 20s when exposed to the same pathogens (Imai et al. 2000).

Second, older adults generally have poorer lung function than their younger counterparts. For SARS-CoV-2, the lungs are the primary organ of infection. The lung's vital capacity, its expansion, and contraction functions decline with age. Consequently, older adults often have a slower response to the viral infection, higher risks of severe illness and fatality, and more difficulty in recovery. Moreover, both the ACE2 expression and the Interleukin-6 (IL-6) expression increase in older ages, which may also add to vulnerabilities among older individuals (Chen et al. 2020; Herold et al. 2020; Rosa et al. 2019).

Third, chronic diseases are more prevalent in older adults. For example, according to the Chinese Longitudinal Healthy Longevity Survey (CLHLS), more than 60% of Chinese adults aged 65 years and older had at least one chronic disease, and approximately 40% had two or more comorbid chronic conditions. The rates of disease in most OECD countries were similar or even higher (OECD 2019). As detailed above, underlying health conditions increase risks of COVID-19 infection and fatality in older adults. In particular, older adults suffer disproportionately more from chronic obstructive pulmonary disease (COPD) and other diseases of the extrapulmonary organ system than younger adults and, in turn, escalate risks of severe infection from compromised respiratory tracts.

Fourth, older adults are more likely to have malnutrition than the general population. Nutrition is foundational to immune function in human beings (Chandra 2002). Malnutrition can also affect pulmonary function – with some research showing that malnutrition is highly prevalent in pneumonia patients (Shi et al. 2019). Approximately 30–40% of older adults globally are estimated to be at high risk of malnutrition, with even higher risks among those who have chronic diseases (Cereda et al. 2016). Malnutrition in older adults is often more prevalent in low- and medium-income countries, compared with high-income countries (Alliance for Aging Research 2016; Michel 2014).

Finally, older adults can have higher rates of missed diagnoses and misdiagnoses during the COVID-19 outbreak. Due to multimorbidities, cognitive impairment, and/or perception difficulties, older adults may not be able to accurately report their medical histories, which may complicate or postpone new (or exiting) disease diagnoses. Furthermore, because physiological responses diminish with age – i.e., cough reflexes may weaken, and body temperature of infected individuals may not reach diagnostic criteria – the timely detection and diagnosis of COVID-19 may be hindered.

Psychosocial Perspective

A series of psychosocial factors may also contribute to the higher risks of infection and fatality among older adults. First, the risk of infection among older adults may increase due to the daily care and/or medical services they receive. During the COVID-19 pandemic, particularly in the early stages of the outbreak, there was a high rate of transmission among medical professionals and social workers. Indeed, prior studies have shown that the likelihood of older adults contracting infectious diseases through medical institutions is roughly three times higher than that of younger adults (Han and Zheng 2014). During the COVID-19 outbreak, older adults in nursing homes have had extraordinarily high rates of infection and fatality – mainly attributed to the high probability of cross-transmission and mass infections from the crowding of older adults in confined locations (Brown et al. 2021). To date, around 5% of older adults in developed countries live in nursing homes (and upward of 10% in some nations), compared with around 1–2% in developing countries (United Nations 2017). Such disparities in institutional care made these sources of COVID-19 infection much more striking in the United States and other Western countries (Grabowski and Mor 2020).

Second, the likelihood of a COVID-19 infection may also increase among older adults due to their living arrangements, neighborhood characteristics, and social networking. In developed countries, especially Nordic countries, a large portion of older adults live alone or with their spouse (United Nations 2017). Thus, the absence of children, social support, and limited social services in community during the lockdown may (in) directly impact well-being, health behaviors, and other aspects of life that may leave older adults more vulnerable to sickness. Older adults in developing countries, on the other hand, who often live with their children or extended family members, may encounter different challenges. As family members often assume caregiving duties, the risks of becoming infected by family members cannot be underestimated. Indeed, a report from Tianjin, China, revealed that around 60% of confirmed cases of COVID-19 were acquired through relatives, and about 20% came from family gathering (Dong et al. 2020). Similarly, community interactions can also play a role. Being less likely to use social media compared to young populations (Schumacher and Kent 2020), people of older ages tend to socially interact more with their peers (face-to-face) for daily interactions and thus expose themselves to increased risks of infection.

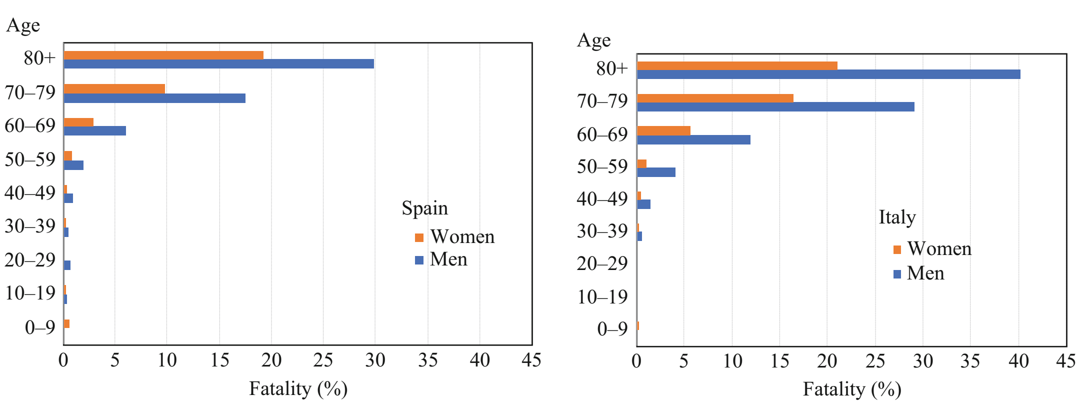
Third, poverty may exacerbate the impact of COVID-19 on older adults. Poverty is one of the main global threats to the health and well-being of older populations (UNFPA & HelpAge International 2012). Health inequalities rooted in socioeconomic inequalities can further impact the COVID-19 crisis (Khalidi 2020). Even in Western societies, many older adults have insufficient financial resources in later life, live in crowded conditions, and reside in poor community environments. Some may even lack access to adequate medical insurance and/or healthcare. During the outbreak, therefore, these individuals may fail to receive timely treatment or care after becoming infected.

Fourth, and relatedly, low socioeconomic status (i.e., education level) is another important factor contributing to vulnerabilities of older adults during the COVID-19 outbreak, especially among racial/ethnic minorities, and among those in developing countries (Stokes et al. 2020). Socioeconomic factors are highly associated with health literacy (Heidi et al. 2013), health behaviors, and a wide range of health resources and health outcomes (see ► "Socioeconomic Differentials in Health: Divergence, Convergence, and Persistent Inequality Theories"). In older adults, lower levels of education may contribute to poor mastery of knowledge about COVID-19 and less ability (and resources) to effectively reduce exposure to disease. More strikingly, the socioeconomic disparities among older adults from diverse racial and ethnic backgrounds revealed the deep and pervasive inequalities in vulnerability to disease within many societies, particularly the United States (Stokes et al. 2020). For example, data from New York City, Chicago, and the State of Louisiana revealed that African Americans accounted for approximately two-thirds of all deceased COVID-19 patients, whereas this group accounted for only one-third of the total local populations.

Fifth, the psychological status of older adults may also play a role in the COVID-19 outbreak. Older adults are often faced with declines in physical functioning, diagnosed chronic illnesses, widowhood, and reduced social ties in later life. Consequently, many older adults may suffer from psychological issues such as fear, anxiety, depression, tension, loneliness, and feelings of uselessness (Yan et al. 2011; Zhao et al. 2017). During a public health crisis, psychological issues can become more pronounced, as fear and anxiety about uncertainties in the world, and may lead to elevated stress and the exacerbation of existing conditions (Fofana et al. 2020). It has been shown that older adults reported greater levels of depression during the SARS outbreak, compared with periods before and after the outbreak (Lai 2008; Lee et al. 2006) as well as during the COVID-19 pandemic (Robb et al. 2020). Additionally, lockdown measures during the COVID-19 outbreak may further reduce the availability of psychiatric or other medical resources needed for older adults with mental health issues (Yang et al. 2020b).

Sixth, discrimination against older adults (or ageism) in some countries may make older adults more vulnerable to infection or complications. According to the World Values Survey that is conducted in 57 countries, 60% of participants agreed that older adults are not well respected (see ▶ "Ageism Around the World"). In the context of such perspectives, there is a large body of evidence showing that older adults who experience age discrimination tend to have poorer psychological well-being, poorer physical and cognitive function, and a shorter overall life span (see ▶ "Stereotype Embodiment Theory"). There is evidence to show that discrimination toward older adults further intensified during the pandemic (Aronson 2020; Soto-Perez-de-Celis 2020; Xi et al. 2021; see ▶ "Ageism in Media and Visual Arts", ▶ "Critical Gerontology"). In addition to its immediate effects on health and well-being, such discrimination may prevent older adults from seeking care, maintaining/obtaining timely medications, receiving adequate treatments, and/or procuring other important social services during the pandemic (Cesari and Proietti 2020).

Finally, there is a notable and significant gender disparity among older adults in the rates of COVID-19 infection and fatality. Figure 1 presents CFR of COVID-19 in Spain and Italy by gender and age group as of April 23, 2020. Aside from the significant increase in mortality at older ages, the case-fatality rate of men far exceeds that of women in each age group. The most recent data as of mid-May 2021 (not shown), more than one year later, shows similar gender difference with mildly to moderately reduced CFR at older ages. These gender differences are not entirely understood but could be potentially due to a combination of biomedical and psychosocial factors, including immunological differences between



COVID-19 Pandemic and Healthy Aging, Figure. 1 Case fatality rate of COVID-19 in Spain and Italy by gender and age group as of April 23, 2020. Sources: see Table 1 men and women (Cai 2020; Wenham et al. 2020), as well as differences in health behaviors, such as diet, fitness, and hygiene, etc. (Moran and Del Valle 2016). Smoking, for example, could provide a partial explanation – with its association with the incidence of chronic lung diseases, increased finger contacts with the mouth and nose, and promoting ACE2 activities (Cai 2020; Patanavanich and Glantz 2020; Sharstri et al. 2021). China has one of the highest rates of smoking in the world (WHO 2019) – among smokers who developed COVID-19, 21% were severe cases and 12% were critical cases or death; whereas, the corresponding numbers for nonsmokers were only 14% and 5%, respectively (Guan et al. 2020a). Moreover, according to the CLHLS, 40% of Chinese men aged 65 years or older are currently smokers, in contrast to only 5% of smokers in older Chinese women. These patterns are also consistent with other Western nations, although the disparities are often smaller (Creamer et al. 2019; Lugo et al. 2013).

Prevention and Protection Strategies for COVID-19 in Older Adults

Comprehensive strategies for the prevention and mitigation of COVID-19 are necessary for older adults at local, national, or even global levels. The most effective measures and policies against the COVID-19 pandemic require vigilant personal action, strict community management, strong national governance, and close international coordination.

Older Adults and Their Families Are at First Line of Defense

Older adults are primary stakeholders in the prevention and control of COVID-19. Maintenance of a healthy and hygienic lifestyle greatly reduces the likelihood of infection from contiguous diseases (Moran and Del Valle 2016) and COVID-19 (Gao et al. 2020). During the outbreak, older adults are encouraged to engage in physical exercise, maintain a healthy diet, ensure adequate sleep, and avoid smoking and excessive drinking. They should also wash hands frequently, keep indoor environments clean, and minimize participation in social gatherings. If going out is necessary, older adults should wear protective masks, adhere to social distancing, and avoid crowded public areas such as shopping malls and train stations. It is also important for older people to obtain timely and accurate information on COVID-19, particularly in their community. For those with underlying health conditions, they should be vigilant in maintaining medication adherence, and when possible, avoid unnecessary hospital visits (by seeking alternative approaches when available [e.g., telemedicine] see ► "Tele-"Telehealth", ► "Telemedicine"). In the event that a friend or family member has a suspected/confirmed case of COVID-19, older adults should adhere to appropriate physical distance (quarantined), seek testing, and have a vaccine if available from a local health agency.

Family members can facilitate and reinforce the importance of healthy behaviors and health maintenance (Tucker 2002). During the COVID-19 outbreak, family support is of great significance for prevention (and overall well-being) among older adults. Family members can also be more attentive to their older relatives, talking with them to reduce stress, educating them to follow public regulations, encouraging them in implementing preventive measures, and helping them to make personal care emergency plans. For older COVID-19 patients who are quarantined or hospitalized, family members can provide valuable emotional support – during their isolation and after they are released (Banskota et al. 2020).

Community and Society Play a Crucial Role

Local communities are central to the communication, implementation, and enforcement of public regulations to mitigate the spread of the virus. In China, for example, community leaders played a key role in effectively controlling the spread of COVID-19 within 3 months. In doing so, community leaders and grassroots stakeholders delineated regulatory zones of individual responsibility, monitored the entry and exit of community members (with registration), arranged the delivery of groceries and medicine to households, and coordinated the testing, diagnoses, and hospital transfers of its residents. It is worth noting that many Chinese communities leveraged smartphone apps (e.g., WeChat) to facilitate communication and action among community members. At the state level, the Chinese Central Government prioritized the prevention of COVID-19 among community older adults. These state-issued guidelines played a major role in protecting older people during the early stages of the outbreak and underscored the cultural norms that recognize the status of older adults in the community. Such actions also required community members to collect information about older adults with disabilities and/or chronic diseases to offer necessary assistance during the outbreak. The state also recognized the need for mental health services among older adults – with an official guideline requesting hotlines for providing psychological assistance and consultation for seniors. Finally, there was an early and heightened concern from the government about the transmission of COVID-19 in nursing homes and other medical facilities, and strategic efforts were made to protect older adults in these institutions throughout the outbreak in China. All these measures have well protected older adults in China. Most other countries have provided similar guidelines as well in prioritizing the protections for older adults, and likewise prioritizing treatments for older patients to help minimize severe illness and death. Most countries have also prioritized the vaccination of older adults, in addition to frontline and essential workers. Overall, communities and societies have played an important role in protecting older people during the pandemic in most countries.

International Community Needs Solidarity

The fight against COVID-19 will not be successful unless every nation eliminates the threat of this pandemic. Ideally, world powers should be united to build a global response system for health emergencies that helps to unify detection, prevention, and control, share all relevant knowledge, experience, and data, collaborate on the development of vaccines and therapeutic drugs, and provide guidance and assistance to developing countries. In distributing vaccines, as only a limited number of countries possess the capacity to produce vaccines on their own, a global effort is warranted to ensure equity, fairness, and effectiveness, and to ensure that priority is given to older adults, in addition to frontline and essential workers, and other vulnerable populations (Jecker et al. 2021). To this end, there are calls for continued (and expanded) leadership from WHO – the key platform for the United Nations' global public health mechanism of multilateral cooperation. Respecting and enhancing the role of WHO is necessary to promote better global health governance. As our experiences with COVID-19 have shown to date, the world needs WHO to facilitate early detection and warning of future outbreaks, to disseminate valuable knowledge and lessons learned in each country, to coordinate prevention and control strategies across countries, to deploy and distribute medical resources, and to organize international cooperation and aid. The role of other UN agencies, such as the Food and Agriculture Organization (FAO), the UN Children Fund (UNICEF), and so forth, are also essential during this and future pandemics.

Supporting older adults throughout this pandemic has been a major test to achieving the recent global initiative targeting a "Decade of Healthy Aging." In 2020, the World Health Assembly and the United Nations General Assembly both endorsed a proposal to use the forthcoming decade to 2030 to promote healthy ageing in older adults, a term defined as "the process of developing and maintaining the functional ability that enables wellbeing in older age" (WHO 2020h). Four major actions areas are highlighted as follows: (1) Change how we think, feel, and act toward age and ageing; (2) ensure that communities foster older people's abilities; (3) deliver person-centered care and services that respond to older adult's needs; and (4) provide access to long-term care for older people who need it (WHO 2020h). Although the inception of this initiative has faced a devastating setback due to the COVID-19 pandemic, such public health crises can also provide an unexpected catalyst for the world to be reminded of the importance of promoting health and wellbeing of older adults. Through a sustained global commitment, a decade of healthy aging may still be within reach.

Summary

The COVID-19 pandemic has revealed daunting challenges to protecting human health and well-being on this planet. As of May 2021, the pandemic continues to rise globally. Due to a wide array of biomedical and psychosocial factors, older adults have been the most vulnerable population during this health crisis. As a result, older adults have suffered with the highest risks of infection, severe illness, and excess mortality. Effective strategies at individual, family, community, government, and global levels are needed to end the COVID-19 pandemic, as well as future possible public health emergencies that threaten our oldest and most vulnerable populations.

Cross-References

▶ Active Aging and Active Aging Index
▶ Healthy Aging

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Cozymase

► Nicotinamide Adenine Dinucleotide (NAD+) in Aging

Cozymase I

► Nicotinamide Adenine Dinucleotide (NAD+) in Aging

Creative Arts

▶ Expressive Arts Therapy

Creative Engagement of Older People

▶ Late-Life Creativity

Creativity Across the Life Span

▶ Late-Life Creativity

Creativity and Aging

▶ Late-Life Creativity

Critical Approaches in Gerontology

▶ Critical Gerontology

Critical Assessment of Health Technology

▶ Health Technology Assessment of Aging Therapies

Critical Care

▶ Emergency Care

Critical Care Nursing

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Synonyms

Emergency care nursing; High-acuity care nursing; Intensive care nursing

Definition

Critical care is defined by the US Department of Health and Human Services as the direct delivery of care for people who are critically ill, which means that an illness or injury has acutely impaired one or more vital organ system to a degree that there is a high probability of life-threatening deterioration (Duke 2006). According to the Association of American Critical Care Nurses, critical care nursing is a specialty that deals specifically with human responses to life-threatening problems; a critical care nurse is a licensed professional nurse who is responsible for ensuring that critically ill patients and their families receive optimal care (Burns 2014).

Overview

Critical care nursing emerged from the early 1950s. At that time, the use of mechanical ventilation and cardiopulmonary resuscitation began, and there was a great demand for providing efficient care to gravely ill patients (Perrin and MacLeod 2012). Dr. William McClenahan recommended that critically ill patients should be cared in a separate unit (Fairman et al. 2000). However, at that time, there was a lack of highly competent nurses to work in the new units who were familiar with the latest developed monitors, resuscitation procedures, and rapid decision-making. Since the 1950s, there were a rapidly increasing number of critical care nurses in the United States. They started to provide care for patients in a 1:1 ratio to manage complex and multiple critical conditions of the patients. These nurses collectively organized a national group, namely the American Association of Critical Care Nurses (AACN), to develop standards of care, a core curriculum to educate new nurses on critical care, and a national examination to certify nurses' knowledge and competency in critical care (Fairman et al. 2000). Gradually, a body of knowledge was accumulated to guide nurses to provide care for the people with a critical illness.

Population aging is a global phenomenon. Patients are also older in the hospital. The aging population impacts on the role of critical care nurses (Biel et al. 1999). In the last decades, people admitted to the hospital are sicker and older than before. In the past, they would not have survived long enough to be in the hospital. However, because of the recent development of medical technology, these patients live longer after major surgery and often suffer from coexisting conditions like diabetes, hypertension, and kidney failure which are treated with more advanced therapies (e.g., use of advanced medications and devices) that require more intense vigilance and monitoring (Nurses and Corporation 2003). This imposes challenges to critical care nursing.

In contemporary critical care nursing, nurses' role is more than implementing procedures directly related to care for critically ill patients. According to the AACN Synergy Model for Patient Care, critical care nurses play five major roles: clinical inquiry, clinical judgment, caring practices, advocacy and moral agency, and systems thinking (Hardin 2005). For the clinical inquiry, critical care nurse should be engaged in the "ongoing process of questioning and evaluation practice and providing informed practice" (Hardin 2005, p. 98). For the clinical judgment, a nurse should engage in "clinical reasoning which includes clinical decision-making, critical thinking, and a global grasp of the situation, coupled with nursing skills acquired through a process of integrating formal and experiential knowledge" (Hardin 2005, p. 59). For the caring practice, "nursing activities should create a compassionate, supportive, and therapeutic environment for patients and staff, with the aim of promoting comfort and preventing unnecessary suffering" (Hardin 2005, p. 227). For the advocacy and moral agency, "the nurse promotes, advocates for, and protects the rights, health, and safety of the patient" (Hardin 2005, p. 63). For systems thinking, nurses manage the existing environmental and system resources for the benefit of patients and their family.

Key Research Findings

Medical research has demonstrated that the care provided by critical care nurses and intensivists in intensive care unit (ICU) produces better outcomes for critically ill patients (Kelly et al. 2014; Levy et al. 2008) and is more cost-effective (Levy et al. 2008). There have been increasing trends of acuity (Lilly et al. 2017) and patients with acute respiratory infections (ARI) in ICU (Laporte et al. 2018). Furthermore, like the aging of population in many developed countries, ICUs have experienced increased elderly admissions over the past decade (Laporte et al. 2018; Lilly et al. 2017). Research and the maneuvers in evidence-based practice are essential dimensions for the best quality of care for patients and their families in ICU. Research findings can inform and drive healthcare professionals and administrators in their approaches to practice and policy development concerning ICU care and organization (Laporte et al. 2018). From a nursing perspective, in additional to the physical and physiological needs of patients, issues about family engagement, end-of-life care, shared decision-making process, ICU outreach services, and care bundles in ICU are key examples of contemporary focuses of research.

Family engagement is increasingly gaining impetus to the work of healthcare professionals and outcomes in ICU and is becoming a popular topic for research funding (KE Burns et al. 2018). Clinicians and researchers are encouraged to work actively with patients and their families to advance critical care and research. This perspective of care is in line with the AACN Synergy Model for Patient Care in which family is an integral dimension and partner of care that contributes essentially to the holism and synergy of critical care and its outcomes (Hardin 2005). A recent report, from the task force of the World Federation of Societies of Intensive and Critical Care Medicine regarding the results of a cross-sectional survey on patient and family engagement in the ICU, provided insights on how the engagement played an important role in intensive care (Kleinpell et al. 2018). The report introduced successful strategies, tactics, and implementation techniques, which could help ICU clinicians to address the challenges and practice of patient and family engagement. More development in this area of research is anticipated in the coming years in substantiating the ways, based on evidence, of engaging families in ICU care for better outcomes.

Higher risk of mortality and related care of dying patients are common encounters of the healthcare professionals in ICU. Critical care nurses are expected to have foundational skills in palliative care integrated into their routine practice (Akgun et al. 2015). In particular, the window of care provided to dying patients in ICU is relatively short and closer to end of life (EOL). There are studies on the evidence of various aspects of EOL care, for instances, regarding the caring processes and the related ethical considerations, as well as the EOL decisions in ICU. Results highlighted the importance of self-care and peer support groups of clinicians to minimize burnout risk for themselves in providing EOL care (Akgun et al. 2015); and there were differences in the EOL collaboration of care and decision-making process between doctors and critical care nurses (usually according to doctor's preference and seniority of the nurses, with overall accountability assigned to the doctors) (Flannery et al. 2016). The main challenges were initiation of EOL discussion, role ambiguity, and communication issues among the parties involved. There were also challenges on how to ensure patients who clearly benefit from the critical care receiving it at the end of life (Chaudhuri et al. 2017) and balancing technology with compassion for the shared decision of when to stop (Montgomery et al. 2017). Ongoing research is needed for a more standardized, comprehensive approach to support medical and nursing staff in EOL care decision-making and patient screening for ICU, which constitutes a far more humanistic dimension than the conventional technological focus of critical care.

Other directions of critical care research include ICU outreach services/"intensive care without walls," follow-up services and longer-term outcomes, and care bundles for specific patient conditions in ICU (e.g., care bundles for patients with sepsis, ventilation-acquired pneumonia/VAP, etc.). The ICU outreach services involve collaboration of medical and nursing professionals for patient care during the hospitalization out of ICU setting and technological support for early detection of patients at risk of critical deterioration in the hospital for swift responses (Gordo and Abella 2014), e.g., rapid respond team (RRT), medical emergency team (MET), and high-acuity response team (HART). These services aim to improve patient safety during the hospitalization process. Early detection for actions was found to be beneficial and can contribute to reduce hospital cardiopulmonary arrests (Abella Alvarez et al. 2013). On the other hand, critical care follow-up was introduced as early in the 1980s in the United Kingdom, where it has been the center of research for such service in the past decades. Results of a systematic review suggested that follow-up services were the only variable between study groups by which the current studies did not include additional resources that might have confounded the data. Additional research with a robust study design in lower income countries would provide better assessment of effectiveness from ICU follow-up services in a wider variety of resource settings (Schofield-Robinson et al. 2018). Finally, from a systematic review of 6 randomized trials and 31 before-after controlled studies about the effects of care bundles on patient outcomes (Lavallee et al. 2017), very low quality evidence from the controlled studies was found in reducing risk of negative outcomes when compared with usual care.

Better quality evidence from the six randomized trials was even more uncertain. Future research should focus on explicit, transparent, and higher-quality control and reporting of the fidelity of care bundle implementation.

Examples of Application

Critical care nurses work collaboratively within the interprofessional team to meet the overwhelming needs of patients and their families having life-threatening health crises. They offer best-specialized care with meticulous judgment, advanced knowledge, maintaining evidence-based practices to problem-solve, and the proficiencies in using forefront medical technological support. Being culturally and ethnically sensitive, care that is age-appropriate is vital.

Standards of care and standards of practice pertinent to critical care nurses have been established with measurement criteria in various professional bodies (Bell 2015; Critical care services Ontario 2012; The Canadian Association of Critical Care Nurses 2009). In addition to the AACN Synergy Model for Patient Care (Hardin 2005), AACN recommends the use of nursing process as the framework to guide and evaluate practice standards (Bell 2015). This includes assessment, diagnosis, outcome identification, planning, implementation, and evaluation. The framework is adopted in gerontological and critical care nursing (Foreman et al. 2010) with the below highlights of its application to the older adults.

Assessment and Diagnosis

With greater longevity, older adults, especially the old-old, post unique challenges. For example, apart from multiple comorbid conditions, these older patients may have vague atypical signs and symptoms (Mick and Ackerman 2004). They are less likely to complain of chest pain, thereby missing the diagnosis of myocardial infarction. Decreased chest wall and alveoli compliance, lower ventilation-perfusion ratio, and increased work of breathing make older adults prone to hypoxemia and susceptible to chronic ventilator dependence.

Outcome Identification

Helping and navigating the patients and their families to endure the uncertainties or the burden of prolonged journey of critical illness are essential (Minton et al. 2019). Skilled communication and true collaboration with patients' families in decision-making play a unique role in the care of older adults having critical care illnesses. While aggressive treatment and cure are the core ICU care, promoting comfort in a technological environment, fostering partnership and dignity, and the transition from active treatment to a peaceful death are all significant aspects of care. Facilitation of decision-making when shifting from curative to palliative or end-of-life care demands seamless and meticulous communication for such transition. Many older adults with declining health may still prefer aggressive treatment and should not be underestimated. Advance care planning and living wills should be well documented and followed (Murphy et al. 2000). Meanwhile, changes in their decision should be respected.

Planning and Implementation

Critical care nurses endeavor to promote collaborative practice and provide leadership that foster professional growth and resources utilization. For example, extracorporeal membrane oxygenation used for both cardiac and pulmonary failure (Calhoun 2018) is effective to elderly patients, resulting in hospital survival similar to that of younger patients (Saito et al. 2007). These practice standards centered on professional knowledge and skills, critical thinking, and competence. Time management, demonstration of expert skills, and bedside teaching are imperative to enable less experienced nurses to gain experiences with sophisticated and unfamiliar interventions.

Delirium and safety issues such as nosocomial infection will lead to serious injuries and prolonged hospital stay. Delirium is a common disorder in ICU having sensory overload, heavy sedations, and restricted visitations in the ICU environment. Such condition is often exacerbated in patients with advance age. Frequent assessment of delirium and proactive actions such as frequent orientation to the patient and daily interruption of continuous sedations may minimize onset of confusion (Foreman et al. 2010). It was suggested that improving resources and involvement of ICU nurses had less reported central catheter-associated bloodstream infections (catheter-associated BSIs), urinary tract infections (UTIs), and ventilator-associated pneumonias (VAPs) (Kelly et al. 2013). Clinical guidelines and resources have been developed and shared in different online platforms (e.g., World Federation of Critical Care Nurses 2017). Critical care nurses should be aware of available resources and evidence to guide their practice.

Evaluation

Systematic and ongoing evaluation of patient outcomes, reflection, and audit on the nursing actions may ensure competence and best possible care for the older patients. It is noteworthy that the expansion of ICU care and grow in complex technologies implementation posed the controversies of resources utilization (Ward and Chong 2015). To optimize resource allocation for the stakeholders, risk-adjusted mortality and health outcomes are considered. Severe comorbidities and short life expectancies may post ethical dilemmas to rule-driven policies and even deny the autonomous right of older adults to access to the scarce resources in ICU care. Critical care nurses must be assertive and advocate the best interest of these older adults with sensitivity, sensible judgment, motivation, and asserting collaborative actions (Foreman et al. 2010). Older adults should engage in the development, evaluation, and revision of policies to assure quality, ethical, and effective practices.

Recognizing the value and contribution of critical care nurses, role modeling, and pursuing a healthy work environment are imperative to transform the care of the aging population. Workforce standards are developed based on systematic and evidence review from both consumers and professional perspectives and appraisal by independent assessors, to ensure effective nurse staffing and quality of care (Chamberlain et al. 2018).

Summary

Critical care nursing is a specialty to provide care for patients with critical illnesses and their family. Since the 1950s, critical nursing has been evolving to have developed its own body of knowledge and training curriculum to prepare critical care nurses to manage complex clinical conditions. Population aging increases the care challenge that more knowledge is needed to handle aging-related problems and comorbidities. Contemporary roles of critical care nursing focus on clinical inquiry, clinical judgment, caring practices, advocacy and moral agency, and systems thinking. Critical care nursing research focuses on patients' physical and physiological health, family engagement, end-of-life care, shared decision-making process, outreach services, and care bundle development. Critical care nurses are also part of an interprofessional team. Care application at the clinical level includes providing precise assessments, diagnosing problems, identifying outcomes, planning appropriate care, and evaluating the care provided.

Cross-References

▶ Personalized Medicine and Decision-Making
▶ Special Care Units

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Critical Feminist Gerontology

► Feminist Theories and Later Life

Critical Gerontology

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Synonyms

Critical approaches in gerontology; Critical perspectives on aging; Critical research of gerontology; Critical studies on aging; Critical theories of aging; Critical thinking about aging issues; Ideology critiques in aging research; Macrostructural perspective of aging; Political economy of aging; Social phenomenology of aging

Definition

There is no consensus about the definition of critical gerontology in the existing literature (Baars et al. 2013; Doheny and Jones 2020; Katz 2019; Minkler and Estes 1999; Phillipson 2003). Broadly defined, critical gerontology refers to applications of critical theories or thinking into gerontology (Lynott and Lynott 2002). Specifically, the term "critical gerontology" is used to describe a myriad of theoretical perspectives, including, but not limited to, neo-Marxist political economy, political gerontology, phenomenology, moral economy, cultural gerontology, humanistic gerontology, feminist gerontology, and postmodern gerontology to counter the conventional construction of old age, aging, and related policies that often overlook the social, economic, political, and environmental factors at play (Estes and Grossman 2007; Katz 2019; Lynott and Lynott 2002; Moody 2008; Phillipson 2003). It can also be understood as a combinative way of questioning and criticizing the assumptions and theories of mainstream or conventional gerontology, or "a collection of questions, problems and analyses that have been excluded by the established mainstream" (Baars 1991, p. 220).

The core elements of critical gerontology include the following: (1) the recognition of the ideological and socially constructive conceptualization of aging at societal, community, and individual levels, as well as subjective dimensions of reflexivity and narratives in historical and cultural contexts; (2) the understanding of aging as a dynamic process; and (3) the rejection of aging as a biomedical construct, with instead emphasis on the political, social, economic, and cultural contextual forces that shape the process of aging (Baars et al. 2013; Dalmer 2017; Katz 2015, 2019; Minkler and Estes 1999; Polivka 1999; Wellin 2018).

Critical gerontology offers a rich and multi-perspective framework that broadens the scope of aging studies beyond the views of conventional biomedical models of aging – often emphasized in biogerontology and geropsychology. It also enriches and widens the scope of social gerontology, cultural gerontology, environmental gerontology, political gerontology, economic gerontology, gerontechnology, feminist gerontology, humanistic gerontology, and postmodern gerontology from which it was derived and oriented in its early stages (Katz 2015). It aims to change the ways in which aging is constructed and the ways that shape the lives of older people. It also aims to improve the quality of life, empowerment, and social equality in health and aging of older adults (Baars et al. 2013; Katz 2019; Phillipson and Walker 1987; Ziegler and Scharf 2013).

Overview

Originating from several disciplines – in particular critical theory, political economy, and social phenomenology – critical gerontology has rapidly developed since the early 1980s as a vibrant and hybridized subfield within gerontology that integrates ideas in humanities and social sciences to broaden aging studies beyond biomedical models and ageist social policies and practice (Katz 2019).

Evolution

In 1969, Horkheimer and Adorno (1969) proposed *critical theory* which emphasizes the interplay between science and philosophy, explains issues with the current reality, identifies agents of change, and provides clear goals to transform society. Critical theory gave rise to *critical psychology* and *critical sociology*, and eventually *critical gerontology*, which emerged in the late 1970s in the United Kingdom and the United States (Baars 1991). The emergence of *critical gerontology* is rooted in the political and economic crisis in Western societies in the 1970s and 1980s and subsequent ideological changes about the roles of older people and impacts of population aging on socioeconomic development (Bernard and Scharf 2007). Such crises caused budgetary and expenditure cuts in various social welfare programs, reductions in the scope and quality of healthcare and social services, and ideological critiques of older people as a "burden" to society, which brought profound consequences on the quality of life of older people (Bernard and Scharf 2007).

People gradually become socially disconnected and disempowered after retiring from the labor force. The 1970s and 1980s crisis worsened the disadvantages of older adults and made many researchers in fields of critical theory, political economy, and humanistic gerontology that have a root with Marxism or theories of the state become aware of its consequences on older adults' daily lives (Katz 2015). These researchers started to criticize society's shift of its old-age care responsibility onto private individuals (Ranzijn 2016). They rejected the biomedical model of aging and sought to understand aging as a social construct.

In the early years, the critiques covered a broad range of issues faced by older adults, from insufficient income (social security) and poor housing, to inaccessible healthcare (medical programs) and ageism (Estes and Grossman 2007; Minkler and Estes 1991, 1999; Polivka 1998). The critiques emphasized disparities by social class, gender, and race/ethnicity (Estes 2001), and the transformation of old-age care systems (Phillipson 2003), which led to the emergence and development of critical gerontology in the early years (Baars et al. 2013).

Concurrently, the development of other branches and theories in gerontology in the late twentieth century has expedited critical gerontology's theoretical boom (Minkler 1996). These branches and theoretical orientations include life-course theory (Elder 1974), life-span development (Baars et al. 2006), person-environmental theories, women's empowerment, biopsychosocial framework of health, person-centered service norm, quality of life, active and productive aging, and lifelong learning. Collectively, these areas have directly and indirectly contributed to the theoretical development of critical gerontology.

By the turn of the twenty-first century, socioeconomic pressures on welfare states had reached a global pitch (Dannefer 2003). Individual states found themselves unable to cope with the complexity of providing for older people (Phillipson 2006). The challenges facing traditional welfare systems facilitated an international consensus on prioritizing and addressing aging-related issues. Unfortunately, such globalization also exposed individual countries to transnational threats in areas such as economy and public health, as can be seen in the last two decades (Awdel et al. 2020).

Although the initial themes focusing on social security and medical programs that constituted older adults' "structured dependency" of aging are still vibrant today (Townsend 2007), new themes have emerged and have been driving forces for a rapid expansion of research, theory, and practice in critical gerontology. New fields include climate variability, environmental degradation, globalization, digital aging and telemedicine, older people in conflicts or crises, age-friendly cities/communities, resilience, healthy aging, and so forth.

Scopes, Approaches, and Popular Areas

Critical gerontology comprises an assortment of issues and foci that are often omitted by mainstream branches in the field. Driving principles in this field are based on initial work in closely linked fields: sociology of aging, demography, political economy of aging, and anthropology (Baars et al. 2006), which understands aging as a social construct. In conceptualizing age and aging, critical gerontologists mainly draw from three core theories: critical theory, political economy, and social phenomenology (Lynott and Lynott 2002).

Originating from the Frankfurt School with roots in Marxism (Moody 2006), critical theory queries the purpose of knowledge and suggests the answers to be cognitive interests in control, understanding, and emancipation (Habermas 1971). Moody (1988), in his attempt to apply critical theory to aging studies, adopted the Frankfurt school of thought and argued that critical theorists should be concerned about "how they represent a language serving to reify experience as something separate from those doing the experiencing" (Moody 1988, p. 26). Critical theorists argue that treating concepts in age as indicative of things unconnected with their human origins facilitates their use in social control. However, even Moody (1988) has acknowledged that his emancipation ideal was still nowhere to be found. Nevertheless, with critical theory integrated into mainstream gerontology, critical awareness in the field has expanded. This expansion has furthered the epistemological and ideological concerns of social phenomenologists and political economists.

Political economy scholars who recognize new-Marxist perspectives understand the personal struggles of older adults, such as depression and loneliness, as being rooted in the relations between a capitalist economy and the state (e.g., Estes et al. 1996). Political economists from mostly European nations and North America reject both the individualist activity theory and the structural-functionalist disengagement theory and focus on age as a public issue, and to the association of public issues with private problems. They criticize the view that classifies older people as a burden and passive consumers. They hold the view that "older persons individually are powerless to alter their social status and condition" (Estes 1979, p. 15), arguing that it is social, economic, and political factors and institutional arrangements that have generated the struggles of old age, and shaped the aging process and the experience of aging (Minkler and Estes 1999). They further posit that these macrofactors create social-structural dependence of older adults and that such dependence should be minimized by good governance and health and social services (Minkler 1996). In addition to highlighting the influence of the macrolevel socio-structural factors on individual aging processes, political economists focus on the ways microlevel factors such as race, socioeconomic status, social roles, and gender collectively influence aging (Estes and Grossman 2007; Minkler and Estes 1999).

Social phenomenology scholars (e.g., Gubrium and Lynott 1983, 1985) argue that mainstream theories of aging take for granted the day-to-day lived experiences of people as they age. Although these theories examine alternatives in the conceptualizations of age and aging behavior, the alternatives are predominantly understood as contextual or extraneous factors operating upon older people. Accordingly, the interpretation and subsequent reinterpretation of these daily living factors are, therefore, often lost. By contrast, social phenomenologists pay attention to processes by which age and age-related phenomena are generated and regenerated most initially. They are concerned with the way ideas about, and objects of, aging being comprehended by those who encounter them, and the role these encounters play in generating and regenerating themselves. Alzheimer's Disease has been widely used to demonstrate the social construction of age and age-related phenomena. Nevertheless, critics argue that social phenomenology is unable to comprehensively address the issue of disempowerment faced by older people because its analysis ignores the structure of social production, despite paying attention to the process (Klimczuk and Tomczyk 2020).

Various areas and approaches within critical gerontology have evolved over time, informing on the field's formation, growth, and achievements (Wellin 2018). Estes and Grossman (2007, pp. 129–130) summarize the following five basic features of critical gerontology: (1) criticizing the biomedical model of aging, emphasizing the role of social and behavioral processes; (2) highlighting economic, political, and sociocultural factors and forces in shaping individual process of aging; (3) methodologically, applying multiple levels of analysis (micro, meso, and macro) in analysis of aging; (4) recognizing the importance of social constructions of old age and aging and the role of the family, the media in establishing such norm; and (5) linking aging issues with the development and organization of social and political action. They also highlight four major areas of critical gerontology concerns, including (1) how public policy is framed and resources are allocated for old-age care; (2) how social media presents images of older adults; (3) how caregiving work (both formal and informal) provided by women is credited; and (4) how social ideologies value the lives and earlier contributions of older people, and how such social norms are practiced within their families, in the workplace, and by the state and the market.

These five features and four research dimensions reflect the core approaches of critical gerontology such as human rights, biopsychosocial processes, and life-course perspectives. Popular areas of inquiry include health disparities, ageism, vulnerable older adults, successful aging, age-friendly communities/cities, and environmental health. This broad coverage reflects its likewise broad definition. Regardless of its scope and approach(es), critical gerontology should "span both micro and macro levels of analysis as well as subjective dimensions of reflexivity and narrative" (Katz 2019, p. 396).

The International Network for Critical Gerontology (INCG) was established at McMaster University in Canada in 2008 to bring together international scholars and graduate students who are interested in critical approaches to the study of aging and later life. Its initial meeting was held at Keele University, United Kingdom, and the original network was essentially comprised of European and North American researchers. Today, INCG is growing with scholars and students from other regions of the world. It is expected that this network will further promote a critical gerontology boom worldwide in the foreseeable future.

In sum, critical gerontology has evolved from challenging the manner in which Western societies construct aging and shape the lives of older people (Phillipson and Walker 1987), to establishing its own approach in the systematic study of aging-related issues. Critical gerontology has become an important branch of gerontology.

Key Research Findings

With the wide scope, approaches, and popular areas discussed above, critical gerontology arguably covers almost every theme related to age and aging. One objective of critical gerontology is not "just to understand the social construction of ageing but to change it" (Phillipson and Walker 1987, p. 12). The development of critical gerontology over the past few decades has enhanced our understanding of the social construct of aging, promoted the empowerment and parities in the health and well-being of older people, and much more. The following themes are worthy of attention.

Health Disparities by Socioeconomic Status

Critical gerontologists emphasize that views and experiences on aging are socially constructed through economic and social processes that eventually cause imbalances of power and inequalities between social groups (Baars et al. 2006; Estes and Grossman 2007; Minkler and Estes 1991). Critical gerontology considers gender, race/ethnicity, and social class as key variables that predetermine older adults' position in the social structure and analyzes the extent to which political and socioeconomic forces interact to shape the individual experience of aging (Freixas et al. 2012). Accordingly, health disparities by socioeconomic status (SES) are one of the core areas in which critical gerontologists began their work (Baars et al. 2006, 2013; Estes et al. 1996; Estes and Grossman 2007; Minkler and Estes 1991). Older adults' SES influences their financial affordability of health services, accessibility to supportive health technologies, and their biopsychosocial well-being (Marmot 2004; Berkman et al. 2014; Cockerham 2013). Older adults with higher SES tend to be able to manage economic stress and have better life satisfaction, self-confidence, and other forms of well-being (Jang et al. 2009; Pinquart and Sörensen 2000); they are also more optimistic about life circumstances, have greater means to access healthcare, and are more likely to experience successful aging (Yeung and Xu 2011). By contrast, older adults with lower SES often experience discrimination and prejudice, which place additional burdens on their physical well-being (Kim and Fredriksen-Goldsen 2017). Health risk factors such as smoking, obesity, and depression, coupled with inadequate knowledge on screening, diagnoses, and treatment, are more often found in older adults with lower SES (Byng-Maddick and Noursadeghi 2016). Lower-SES older adults are also susceptible to chronic illnesses related to cognitive, mental, physical, self-rated, and functional health (McEniry et al. 2018). As the provision of health care increasingly relies on Internet access, older adults who could not access technological advances, such as telemedicine or healthcare portals due to age or lower SES, would be disadvantaged. Overall, socioeconomic characteristics such as race, class, and gender are the major determinants governing access to resources. These social determinants contribute to greater exposure to diseases, health disparities, and premature death for people with lower resources (Berkman et al. 2014; Duran et al. 2019).

However, in addition to studying individual microlevel socioeconomic resources, critical gerontologists posit that health disparities by SES at older ages are mostly caused by structural problems in society. They focus on policy solutions to address aging issues and posit that local or state policies could influence the economic and health security of older adults regardless of race, ethnicity, class, and gender (Estes and Grossman 2007). They argue that improvements in social status of the community and individuals (Schoeni et al. 2018) through education, and providing affordable health care, improving effective communication between the healthcare sector and older adults, could reduce health disparities by SES (Wong et al. 2019).

Ageism

Ageism is another frequently studied theme by critical gerontologists. Ageism refers to people's negative attitudes and views toward people because of their age, including negative stereotypes, prejudice, and discrimination (see ▶ "History of Ageism"). Ageism is one of three major forms of discrimination against people (The other two are sexism and racism). Research has shown that about 30% of adults aged 50 or older in the United States and 35% people in 28 European countries reported experiencing some sort of age discrimination in everyday life (see ▶ "Ageism Around the World"). A report using the World Values Survey data from 57 countries suggested that 60% of the participants agreed that older adults are not well respected (Officer et al. 2016). Ageism has become a global issue (WHO 2021). The United Nations has persistently worked on fighting ageism through its network and formulating international action plans. Ageism can have significant consequences for various health-related outcomes. Research has consistently shown that older adults with experiences of ageism tended to have poorer psychological well-being, more impaired memories, delayed physical recoveries, reduced hearing functions, and a shorter lifespan (see ▶ "Stereotype Embodiment Theory"). With associations to such a wide array of negative health outcomes, research shows that ageism can occur from within the family, workplace, as well as public places.

Ageism in the Family

Due to ageism, abuse and neglect of older adults is not uncommon within the family (see ► "Older Adults Abuse and Neglect"). Ageist attitudes are often shaped when older relatives are viewed by family members as a burden (see ► "Ageism in the Family"). For example, the tradition of filial piety has led many older Chinese adults to expect support and care from their grown-up children who may not share the tradition. This expectation has arguably led to a greater intrafamilial conflict and an increase in psychological abuse among older adults with Chinese descent (Chang and Dong 2014). To promote mutually beneficial familial relationships, older relatives, such as grandparents, may provide childcare for their families to postpone the realization of an older self-image, and develop positive thoughts and feelings about their own aging (see ► "Intergenerational Programs on Anti-ageism"). While this arrangement benefits both children and grandparents and decreases childcare costs, the benefits would be outweighed by additional and elevated stress if children are left to grandparents for prolonged periods of time (Noriega et al. 2016). Ageism-reducing familial relationships could also be enhanced by encouraging intergenerational exchanges, which foster intergenerational solidarity. This measure appears promising, especially in the period of lockdowns implemented during the COVID-19 pandemic (Ayalon et al. 2021).

Ageism in the Workplace

Ageism in the workplace is possibly a more studied theme than other ageism themes by critical gerontologists. In the workplace, older workers may experience unfair treatment in job selection, promotions, and personal and professional development (Griffin et al. 2017; see ► "Age Discrimination in the Workplace"). They could experience discrimination through social isolation, contemptuous language, and ageist attitudes (Giles and Gasiorek 2011). Ageism in the workplace arises from negative age stereotypes and perceptions held by workers or superiors, which leads to discriminatory behaviors against older colleagues or employees (Rupp et al. 2006). Older employees are often stereotypically described as inefficient, change-resistant, slow-to-learn, job-hopping, and costly, but trustworthy (Posthuma and Campion 2009; see ► "Age Discrimination in the Workplace").

In the workplace, ageism leads to insufficient interpersonal cohesion and ineffective interpersonal communication, which are detrimental to organizational performance (see ► "Age Discrimination in the Workplace"), person-environment fit (Bayl-Smith and Griffin 2017), employee retention (Griffin et al. 2016), and job attitudes and well-being (Griffin et al. 2017). Organizations with increased age diversity tend to allow stereotypes to develop against older workers (Kunze et al. 2011), when employees protect their own self-esteem by making ominous assessments against those from a different age group. The Positive Education about Aging and Contact Experiences (PEACE) model recommends having older workers instruct their younger colleagues to facilitate diversity education and intergenerational contact (Levy 2018). Organizations that enforce inclusive age-diversity policies are key to setting the normative standards of inclusive behaviors (Boehm et al. 2014).

In other public venues, such as healthcare places or old-age care centers, ageism is also frequently reported among older patients or services users in terms of manners of medical staff interacting with older patients and in the access to specialized therapies and services (see ► "Ageism in Healthcare"). Supporting and educating older formal and informal caregivers is vital to improving quality of life and battling abuse against older adults. Future studies should assess both feasibility and efficacy of such measures.

Aging Among Older Vulnerable Adults

Race, gender, and class are the most studied domains by critical gerontologists, especially in its early stages. Accordingly, older minorities and older women are the most frequent study subjects for critical gerontology.

Older Minorities

The interaction between racism and ageism has become important as the proportion of ethnic minority older people rises globally. The changing perception of older minority adults and their traditions (Fortune 2005) reflects the challenges faced by minorities and prevents them from accessing resources (Swift et al. 2017). Older African American adults were often denied entry at or segregated in nursing homes (Woody 2015). Jones et al. (2017) reported that discrimination beyond ageism and misogyny was predicted by racism. A workplace disparity analysis showed that older African American adults are more likely to face demotion and gain less income and obtain fewer benefits relative to their same-age peers (Wilson and Roscigno 2018; see ▶ "Racism and Ageism"). The discrimination older minorities faced earlier in life also contributed to later-life disadvantages, such as unstable housing and limited health insurance (Angel and Angel 2006; Kum 2017). At work, older ethnic minorities were further discriminated against because of their age. Older African Americans experience a pay gap and are at greater risk of demotion than their peers (Wilson and Roscigno 2018).

Even with family support, minority older adults, because of their comparatively unstable work histories, are less likely than white older adults to have savings, private pensions, or draw social security benefits and are likely to rely more heavily than white older adults on SSI benefits, Medicaid, and Medicare (Minkler and Estes 1999). Large segments of future generations of minority older adults are likely to be even more reliant on these federal programs given the declining employment and wages of many younger minority cohorts over the last 25 years. The Black Lives Matter Movement (Gottbrath 2020) has recently underscored the lasting and deep-rooted racism that exists in some Western countries.

Older Women

Like other branches of gerontology, critical gerontology values the close relationship between physical and psychological well-being and underlines the importance of health as a basic predictive element of well-being in older adults (Freixas et al. 2012). In the contemporary world, the process of aging is not the same for women as for men in that numerous personal, social, and other contextual factors have made the lives of women and men significantly distinctive. Women tend to live longer than men. However, the greater longevity of women does not mean that they enjoy better states of health and well-being in old age. On the contrary, their health, especially physical health, and well-being are poorer than those of men of the same age (see ▶ "Gender Disparities in Health in Later Life"; ▶ "Gender Equality in Later Life"; ▶ "The Male-Female Health-Mortality Paradox"). Furthermore, women usually have a lower SES and thus are more likely to live in poverty (▶ "Gender Inequity"). Women have far less economic security in retirement than men, and many women have no retirement system (Minkler and Estes 1999). For example, in the UK, two-thirds of low-income pensioners are women (Holstein and Minkler 2007; see ▶ "Poverty and Gender Issues in Later Life in the UK"). In the United States today, older women are significantly more likely than older men to live in poverty (Li and Dalaker 2021), and this may be more dramatic among minorities as older women from ethnic minorities are more likely to be victims of ageism and racism. Consequently, older minority women may face triple forms of discrimination (Angel and Angel 2006; Kum 2017).

Although women typically have poorer physical health and lower SES, they are likely more advantageous in psychosocial capacity. For example, women are more likely to engage in physical exercise, pay more attention to their diet, and create powerful networks of friendship, neighborliness, and community that provide invaluable intimate support when needed (Freixas et al. 2012). One of the objectives of critical gerontology is to empower women, seek out, and showcase affirmative images of older women, without denying their weaknesses, vulnerability, and dependency that accompany their aging process. Feminist gerontological research aims to document how older women experience aging and to promote new interpretations of female aging. However, one important issue to critical gerontologists is the role of women in caregiving due to the gendered nature of that role. Much caregiving work in most countries is done by women (Sharma et al. 2016). In the United States, for example, 60% of caregiving work is done by women (NAC and AARP PPI 2015). Yet, caregiving activities have not been legitimized in most countries; they are not linked with social security and other welfare programs. Female informal caregivers do not receive their deserved credit for providing such massive investments in caregiving (Minkler and Estes 1999), depleting their social security that is meant to support later life. This is also a challenging issue in most developing countries (Shahly et al. 2013).

Older Migrants

Older migrants usually refer to older adults who are foreign-born and are growing old in a country of destination other than those native-born counterparts (see ► "Aging Migrants"). In many cases, older migrants have been neutralized as citizens in their destination countries. Although some studies showed that the health of new migrants could be better than that of natives, such advantages in health diminished with time in destinations, especially among minorities (► "Aging Migrants").

Older migrants consist of two subgroups, those who arrived at old age and those who arrived at younger ages and became older. Regardless of these two types, older migrants on average occupy disadvantaged socioeconomic positions in destination countries with less social security benefits (or receive lower benefits), healthcare, and other social welfare benefits in these countries (see ► "Aging Migrants"). Many face language barriers and culture shock and need to reestablish social connections. They are also more likely to live in poorer neighborhoods (Bonvalet and Ogg 2008), in substandard housing, and fewer own homes compared to their native counterparts (Green et al. 2009). Consequently, they suffer more from chronic social stressors (see ► "Aging Migrants"). Without their family social capital, aging migrants can suffer poorer health outcomes, especially in mental health (Bécares et al. 2018; Sabater and Graham 2016). They are less likely to be "aging well" in destination countries (Martineau and Plard 2019) where discrimination against older migrants is common. Minority older migrants and female minority older migrants may also suffer from racism and sexism in addition to ageism.

Due to increased international migration, there is a growing need to understand both the nature of the migratory experience of older migrants and the policies that adequately address barriers and discriminations encountered by older migrants when they seek a better life and for aging well in their foreign countries (Baars et al. 2006). Fortunately, critical research on this theme is growing (Karl and Torres 2016; Lawrence and Torres 2016).

Successful Aging

Successful aging has been defined in various ways over the years. Tesch-Römer classified different definitions into five categories (see ► "Successful Aging 2.0"). The pragmatic perspective focuses on the functional health of the aged, with success measured by a low rate of illness, high functioning, and active participation in life events. It calls on policies to focus on health prevention and promotions (Rowe and Kahn 1997). The hedonic model, following Havighurst (1963), acknowledges diversity in individuals, deeming successful aging as the balance between life satisfaction and dissatisfaction. Associated health policies focus on improving the subjective satisfaction of older people. A eudemonic model considers successful aging from the human development perspective by examining experiences throughout an individual's life span. It perceives negative experiences as opportunities for growth, nudging policies toward foci on counseling and educational support to aid older adults in achieving life stage-appropriate milestones. The capability-related perspective values subjectivity and recognizes human diversity. It centers successful aging on the diverse pathways that relate a person's values to their functioning (goals), commodities (resources), and capability (opportunity structures) in life (Sen 1993). This perspective emphasizes policies that enable successful aging through boosting environmental needs and opportunity structures of individuals (Beard and Petitot

2010). The care-related definition understands successful aging as the joint efforts of care recipients and caregiver in maintaining care recipients' quality of life (Baltes et al. 1991) rather than dismissing older adults with impairments as unsuccessful agers. It encouraged policies to ensure caregivers, and care institutions maintain quality care that addresses the long-term care needs of older people (Tesch-Römer and Wahl 2016).

The most popular framework of successful aging is Rowe and Kahn's pragmatic model. Their first version of successful aging and most of the five models of successful aging are biomedically or biopolitically oriented. Critical gerontologists criticized the inherent problems of the biomedical model built on the assumption of equal opportunity to achieve good physical and mental functioning. They argue that people in different cultural contexts have different experiences of aging with distinctive levels of importance attached to good health, independence, support, and social connectedness. They contend that the biomedicalization of aging fails to account for particular life trajectories and environmental realities of different individuals (Holstein and Minkler 2007) and that emphasis on independence, productivity, and self-maintenance could lead successful aging to a biopolitical and ageist model and limits older adults' own subjective experience and definition. Furthermore, some critical gerontologists also have challenged the term "successful aging," especially when it focuses on the biomedical or biopolitical model of health. This is because the term "successful" excludes "failed" older adults and thus possibly devalues nonsuccessful aging adults and introduces ageism and negative stereotype (Holstein and Minkler 2007; Martinson and Berridge 2015). In response to various critiques, Rowe and Kahn more recently extended the framework as a biopsychosocial model to include socioeconomic, biological, environmental, and psychological components and stressed the role of society or state in achieving individual and societal levels' successful aging (Rowe and Kahn 2015; see ▶ "Layperson-Defined Successful Aging"; ▶ "Objectively Rated Successful Aging"; ▶ "Subjectively Rated Successful Aging"; ▶ "Successful Aging 2.0"). Critical gerontologists are keen on the way policymakers take comprehensive steps to help different individuals achieve their own successful aging goals under social justice and equity across the life course (Baars et al. 2013).

C

Healthy/Active/Productive Aging

Along with the term successful aging, there are other similarly popular terms in the literature, such as healthy aging (see ▶ "Healthy Aging"), active aging (see ▶ "Active Aging and Active Aging Index"), and productive aging (see ▶ "Productive Aging"). These are not merely economic or medical terms conceptually but are defined as strategies to maximize older adults' potential and quality of life, which is good for society as a whole (Wellin 2018). These concepts reflect positive views on aging, which is a radical or even reversal of understanding about aging over the negative views prevalent several decades ago (Moody 2007). However, much like in the case when critical gerontologists criticize the biomedical model of successful aging, some critical gerontologists deny the attempt to using achievements and outcomes to revalue older adults if outcome measures of these terms are mainly bodily functional ability. Instead, critical gerontologists assert that older adults are valuable and deserve respect because of their early contribution to the society (van Dyk 2014). They contend that healthy aging (or active aging/productive aging) is an outcome of interaction between an individualized aging process and external social, economic, and political contexts (van Dyk 2014). Thus, to reduce individual health and well-being disparities or inequalities among older adults, critical gerontologists posit that efforts should be focused on social structural factors at the community, national, regional, and global levels, and that there is a need to restructure nations' welfare system and make healthcare services as a social good for all individuals (Estes and Grossman 2007).

While these indicators can be defined as outcomes, they can also be measured as processes. For example, WHO recently defined healthy aging as a "process of developing and maintaining the functional ability that enables well-being in older age" (WHO 2015, p. 28). The functional ability in the definition is "determined by the intrinsic capacity of individuals, the environments they inhabit and between them" (WHO 2015, p. 28). This definition of healthy aging highlights a life-span process and personal adaptations and fulfillment for everyone regardless of whom is currently free of disease or disability (WHO 2015). The framework of WHO healthy aging aims to challenge ageism, create inclusive environments that embrace age diversity and listen to diverse voices, abolish mandatory retirement ages, reform pension systems to allow older adults to stay in labor force based on their willingness, support gradual retirement options and flexible work arrangements, and so forth. This definition made a shift from considering healthy aging as the absence of disease to fostering the functional ability that enables older adults to be able to fulfill their goals. More recently, WHO and the United Nations General Assembly (UNGA) endorsed a declaration on "Decade of Healthy Aging: 2021–2030" (WHO 2020; UNGA 2020). What concerns critical gerontologists is how to implement such new global strategy in addressing population.

Age-Friendly Cities and Communities

Most people live and will age in cities in many countries (see ▶ "Age-Friendly Cities and Communities: New Directions for Research and Policy"). Economic austerity and sustainability, exclusion of disadvantaged groups, rapid urban development, and local program implementation issues have been barriers to building age-friendly cities. The World Health Organization (WHO) identified eight areas in a Global Age-Friendly Cities project to address these barriers, "housing, transportation, respect and social inclusion, social participation, social and civic engagement, outdoor spaces and buildings, community support and health services, and communication and information" (WHO 2007, p. 9; see ▶ "Age-Friendly Cities and Communities: New Directions for Research and Policy"). The WHO's Global Age-Friendly Cities project aims to advocate and to provide guidelines for countries to build livable communities to enable older people to live in safe, adequate, supportive, barrier-free environments (WHO 2007). The purpose and guidelines of this project coincide with the principles of critical gerontology that underscore the roles of external factors, both social and physical, in influencing individual's health and well-being (Plouffe et al. 2015). Unfortunately, in the global climate of austerity, many cities are cutting budgets meant to provide infrastructure and services for older people (Toynbee and Walker 2017). To reap economies of scale, the UN-Habitat (2016) suggested that projects that focus on age-friendly cities and sustainable cities – both WHO-sponsored initiatives – could be linked.

Critical gerontologists argue that building and rebuilding infrastructure to create age-friendly communities and cities would help to reduce the aging problem (Ranzijn 2016). To improve the age-friendliness of cities, older adults with disadvantaged backgrounds must be involved in decision-making processes that affect them (see ▶ "Age-Friendly Cities and Communities: New Directions for Research and Policy"). This includes running programs for older adults who are not "healthy," such as the frail and cognitively impaired older persons (Grenier 2007).

Urban development should consider age-friendliness issues, including poverty dynamics on older city-dwellers, and the impact of modern renewal on their lives (see ▶ "Age-Friendly Cities and Communities: New Directions for Research and Policy"). Implementation issues of WHO's recommendations at the neighborhood-level should be addressed. An example is the naturally occurring retirement community (NORC), a community-based program in which local service providers, with partner organizations, assist older adults in maintaining and expanding social networks by linking them to supportive services such as therapy and home repair (WHO 2015). However, critical gerontologists argue that older adults can be isolated while staying in their homes if there are no walkable neighborhoods with grocery stores, restaurants, or other places that supply services and social interaction and allow for healthy aging in place (Bernard and Scharf 2007;

see ▶ "Age-Friendly Cities and Communities: New Directions for Research and Policy").

Cultural Gerontology

Compared to other conventional branches of gerontology, cultural gerontology addresses the nature and experience of old age in a wider sense (Twigg and Martin 2015). Critical gerontologists argue that each culture has its distinctive definitions for constructs of health, illness, aging, and so forth (Luborsky and Sankar 1993), and that cultural values, beliefs, customs, and contexts are crucial in shaping the understanding of aging. Culture has significant influence on an individual's perception of older people and one's aging journey (Samanta 2017). Accordingly, older adults from different cultures may perceive the aging process differently and prioritize things of importance related to aging in a distinctive way (Luborsky and Sankar 1993). For example, more than 60% of Singapore's older adults rated filial piety as important in determining their understanding of aging (Feng and Straughan 2017), which may not be the case in the United States (Phelan et al. 2004). Additionally, Japanese Americans and white Americans have different constructs for successful aging (Phelan et al. 2004). In ageism, the cultural context has exerted its strong influence as well (WHO 2021). For example, the Confucian concept of filial piety in the Eastern Asian countries contributed to the positive view of aging while the importance of autonomy and independence in the West rendered a negative opinion of aging (Chow 2009; Vauclair et al. 2017). As a result, ageism may be less prevalent in Eastern countries than in Western societies (WHO 2021). Recent findings have shown that older adults in Eastern cultures during the COVID-19 pandemic period are more respected than their Western counterparts. Recent findings show that older adults in Eastern cultures are more respected than their Western counterparts during the COVID-19 pandemic (Xi et al. 2021; see ▶ "Ageism in Media and Visual Arts"; ▶ "COVID-19 Pandemic and Healthy Aging").

Nevertheless, in the existing literature of critical gerontology, the majority of research has focused on comparisons between Western and Eastern Asian cultures (Swift et al. 2019) due mainly to the opposing nature of individualistic and collectivist traditions (Chow 2009; Swift et al. 2019). Furthermore, most theories in the field are based on Western cultures, which is inadequate to understand the complexity and the shifting cultural context of the global south. Research on transcultural, multicultural, or culturally informed critical gerontology, especially from less developed regions, is needed (Luborsky and Sankar 1993).

Globalization and Aging

Globalization has accelerated since the beginning of the twenty-first century with the advent of the digital era. Globalization has brought a growing awareness about the challenges of global environmental problems and population aging in almost all countries. As a transnational process in socioeconomic, cultural, institutional technological fields, globalization has created new conditions, environments, challenges, and opportunities for every older adult and every society (Townsend 2007). Globalization has influenced ideology about the social construction of aging. Aging is no longer "viewed as a 'national' problem or issue but one that affects trans-national agencies and communities" (Phillipson 2003, p. 144). Both age and aging are being transformed because of globalization (Baars et al. 2006). Because of the influence of multinational, international, or even global contextual factors, the experience of old age by an individual could be different under the context of globalization compared with the past. For example, an economic crisis or an epidemic that occurred in some country could spread rapidly to other countries (e.g., global pandemic such as the COVID-19 pandemic, the 2008 global economic crisis), which will eventually directly and/or indirectly influence socioeconomic conditions, health, and well-being of older adults in all countries.

Recently, critical gerontologists have paid particular attention to globalization and its effects on health and aging (Estes and Grossman 2007; Walker 2005). Critical gerontologists argue that globalization has brought a shift in the welfare system from local and national arenas to global ones. On the one hand, this shift has reduced the number of persons with adequate pensions, especially among women, because employers need to seek cost reduction in the highly globalized competition (Minkler and Estes 1999). On the other hand, it may increase deficits in the social security fund in some countries because of possible increases in pension benefits under competitive systems across countries. Critical gerontologists also argue that the increasing penetration of multinational corporations into the health and social care systems due to globalization has weakened the service provision capacity of community-based service programs, which has brought the hardest hit for the poorest older adults in the community (Baars et al. 2013). Accordingly, critical gerontologists argue that globalization deepens the inequalities across countries (Phillipson 2006). Critical gerontologists further argue that globalization creates tensions or conflicts between policies made by a country in response to its demographic change and those formulated by international organizations (Baars et al. 2006). They point out that aging has become constructed as a global problem, rather than a local issue (Ziegler and Scharf 2013).

An understudied field in the existing critical gerontology literature is the advantages of globalization in addressing population aging issues. There are many advantages of globalization. First, globalization promotes economic growth in terms of increased international and global trade, foreign direct investments, global migration, and so forth. All these could boost travel/tourism, transportation/aviation, commerce and related industry sectors. Consequently, these will help build friendly communities and cities. Second, globalization increases the spread of new knowledge and technology, which improves education and skills of the labor force, especially in less developed countries, and promotes lifelong learning. Third, globalization promotes cultural exchanges and helps people to access new cultures, and understand the human civilization of different countries. Fourth, globalization facilitates global unified action to tackle local, national, regional, and global issues, including climate changes, pandemics, degradation of ecosystem, economic crises, and so forth. All these advantages likely overweigh the disadvantages that globalization may have induced. Critical gerontology should aim to disentangle how socioeconomic and political factors at local, national, regional, and global levels have intertwined each other in determining individualized aging and how to build uniformed international frameworks to address aging and inequalities based on its fundamental approaches. Cross-national critical studies are needed to underpin how power, ideology, and social stratification are linked to global forces that influence the lives of older people across diverse social contexts, and to examine how forces of globalization are increasing inequality among older populations both within and between countries (Arber 2007).

Human Rights-Based Approach

The human rights-based approach (HRBA) aims to actualize three core human rights principles – inclusivity, informed participation, and accountability – regarding the health of individuals, including older adults (WHO and OHCHR 2008; Kalache and Blewit 2012). What critical gerontology underscores is that each right is "universal," nonfulfillment is a "violation," and rights are "human" and not only civil or political (Bernard and Minkler 2007; Townsend 2007). This means that legislative and other institutions should ensure the effective exercise of the rights of older persons for a decent life without discrimination and inequality, including their rights to social security, healthcare, access to social services and facilities, respect, adequate housing, social inclusion, and independent living (Townsend 2007). As such, HRBA provides a rigorous analytical framework for a sound basis of antidiscriminatory research (Townsend 2007).

More generally, HRBA could benefit aging and health by (i) stimulating multisectoral interventions to address aging issues beyond healthcare, (ii) placing older adults at the forefront of the health response, thus ensuring care standards, (iii) ensuring accessibility, and (iv) empowering older adults with knowledge on their health-related rights (WHO Regional Office for Europe 2012; WHO Regional Office for the

Eastern Mediterranean 2006; WHO Regional Office for the Western Pacific 2014).

One possible pitfall in promoting equality and human rights in public life is that legislation could overly stress employment and overlook education, housing, citizenship, and social services that are more relevant to older adults. To ensure the implementation of equality and human rights, critical gerontologists argue that monitoring the state and progress of some key human rights indicators locally, nationally, regionally, or internationally would bring about accountability and, ultimately, effectiveness (Baars et al. 2006).

Life-Course Approach

Critical gerontology has long recognized that aging is a lifelong process and a comprehensive understanding of aging requires a life-course approach. The life-course (biographical) approach – that earlier life events influence later life events and outcomes – offers a perspective to understand long-term patterns of socioeconomic conditions, health, and well-being at older ages. The overarching principle of a life-course approach is that a better understanding of human development and aging, which are lifelong processes, requires a long-term perspective that fully recognizes how health and well-being at older ages are influenced by socioeconomic conditions and health from childhood to late life (Zeng et al. 2007). Specifically, adverse childhood conditions can have long-term negative effects on late-life health, independent of achieved status in adulthood; whereas favorable environments (e.g., better access to education and health care) in early life usually result in a higher socioeconomic status, better health, and well-being in later life (Zeng et al. 2007; Wen and Gu 2011). This argument is consistent with cumulative advantage/disadvantage theory (see ▶ "Socioeconomic Differentials in Health: Divergence, Convergence, and Persistent Inequality Theories"). Evidence also shows that the negative effects of adverse conditions experienced in childhood on old-age conditions can be offset by achieved status in adulthood. Similarly, positive effects of favorable conditions in early life stages on later-life conditions can be undermined by adverse conditions in adulthood (Gu et al. 2017; Zhang et al. 2010). The life-course approach understands aging as a process rather than a state throughout the life course. Critical scholars underscore the examination of health and well-being in the context of inequalities over the life course (Estes and Grossman 2007).

Methodologically, in addition to a life-course approach, critical gerontology lays the foundation for multilevel analysis, although all levels of analysis are essential to understanding the meaning of experiencing aging, its dynamics, and consequences of inequality within the nation and the world. The multilevel analysis of aging includes microlevel, macrolevel, as well as intermediate/meso-level institutions and their interactions that contribute to shaping experiences of aging (Wellin 2018).

Future Directions of Research

Critical gerontology has witnessed a boom in the last few decades in terms of expansions of its scope and in developing itself as a multidisciplinary branch of gerontology. However, critical gerontology is now facing an even enlarging scope of work that involves more complicated social problems arising from rapid changes in technology and modernity (Estes and Grossman 2007). Among its numerous emerging themes, the following subfields may deserve additional attention.

Aging Among the Most Vulnerable Groups

Older LGBT Adults

Older LGBT, LGBTI, LGBTIQ, and LGBTIQA adults refer to older adults who self-identify as lesbian, gay, bisexual or transsexual, intersexual, queer/questioning sexual, or asexual and engage in same-sex behavior and romantic relationships or engage no sexual attraction or no romantic relationships (Fredriksen-Goldsen 2016; see ▶ "LGBT in Old Age"). These populations are relatively newly defined and are mostly observed in Western societies with more open and tolerant cultures. A Gallup poll in 2017 showed that around 4.5% of American adults identified themselves as LGBT, a 1% increase from 2012 (Newport 2018). Research has shown that older LGBT adults are more likely to have chronic conditions, higher risks of obesity, depression, and substance abuse disorders. LGBT older adults in communities are more likely to be marginalized, discriminated against, and feel alienated (Ramirez-Valles et al. 2014). They also face challenges and discriminations in receiving long-term care services (see ▶ "LGBT in Old Age"). To adequately address discrimination toward the LGBT population and improve their human rights, more research from a critical gerontological perspective is clearly needed (Katz 2019).

Older Adults in Conflict and Crisis Situations

Due to increased outbreaks of domestic and international conflicts, wars, and human rights violations, the global number of forcibly displaced populations (i.e., refugees, asylum seekers, and internally displaced persons) is increasing, reaching 80 million in 2019, and doubled since 2010 (UNCHR 2019; see ▶ "Older Adults in Conflicts and Crises"). Older refugees and older displaced persons are often disadvantaged, facing barriers in access to care facilities, food, and clean water, and age discrimination. Some critical gerontologists have found significant disadvantages and vulnerabilities among refugees in Europe (Warnes et al. 2004). In response, there have been calls for appropriate actions, policies, and interventions to address the well-being of this population, and calls for more research on this population. More recently, refugees' situation has likely worsened during the COVID-19 pandemic (Elisabeth et al. 2020). The longer-term social consequences of the pandemic may also disproportionately influence refugees.

Furthermore, with the increased frequency of extreme weather events and associated disasters, older adults are disproportionately affected in such events, and the consequences are more devastating. For example, 55–75% of victims in Hurricane Katrina in New Orleans in 2005 and in the Great East Japan Earthquake in 2011 were people aged 60 or older (Help Age International 2015). During the COVID-19 pandemic period, more than 90% of COVID-19-related deaths in many countries are adults aged 60 or older (see ▶ "COVID-19 Pandemic and Healthy Aging"). Collectively, this evidence shows that older adults during conflict and crisis situations are particularly vulnerable.

Future studies should also focus on approaches to inform relevant stakeholders about the vulnerability of older adults in natural disasters (Gamble et al. 2013; see ▶ "Climate Change, Vulnerability, and Older People"), and propose strategies to reduce these vulnerabilities and improve the capacity of older adults to plan, adapt, and respond to emerging climate changes. Studies on how environmental, economic, and social factors influence older people's ability to respond and recuperate from extreme weather incidents should also be encouraged. Furthermore, critical gerontology should also pay more attention to other vulnerable populations whose aging processes are understudied, such as older persons in prisons (see ▶ "Older Prisoners"), kinless children (see ▶ ""Three-No" and "Five-Guarantee" Older Adults"), and nursing home residents (Hedman et al. 2019), especially nursing home residents during the COVID-19 crisis (Leibing 2020).

Aging and Intergenerational Equity/Justice

Since World War II, intergenerational justice has become prominent because of the environmental crisis and economic stagnation coupled with rapid population aging in the 1960s and 1970s (Moody 2007). It is natural to think of the rights of the currently young and future generations when the world faces a prospect of diminishing natural resources, degrading environment, and more frequent extreme climates. It is also appropriate to ask questions about equity and justice between generations when society faces a deficit in social security and medical insurance funds. Would future generations have a less comparable life than the present generation because of depleting resources? Could future generations receive comparable amounts of social security as the present generation when there are budget deficits? Would the quality of life of future generations be compromised due to unsustainable lifestyles in production and consumption of present generations? Will existing environmental policies harm future generations? These questions are relevant to intergenerational justice that is either directly or indirectly linked with population aging and should be prioritized in critical gerontology.

Policies should be made to improve the lives and livelihoods of the current generation, without compromising those of future generations. The present generation should share responsibility and obligation for future generations. This philosophy has been a consensus and is well reflected in the United Nations' 2030 agenda for Sustainable Development Goals where sustainable development is defined as development that meets the needs of the present without compromising the ability of future generations to meet their own needs (United Nations 2017). Some critical gerontologists have argued that critiques on aging issues have been extended from welfare policies oriented older populations to ageism between generations (Bernard and Scharf 2007). One possible area for critical gerontologists is to develop strategic policies and/or intervention programs, and to evaluate the effectiveness of these policies and programs in enhancing intergenerational solidarity and in reducing tensions and conflicts between generations.

International Actions on Aging Issues

Critical gerontologists have paid special attention to the growing role of intergovernmental agencies in addressing aging issues from a perspective of the social construction of old age in an era of globalization (e.g., Estes et al. 2003). Given rapid internationalization, globalization, and worldwide population aging, it seems that aging issues can only be adequately addressed at the international or global level. Critical gerontologists argue that contemporary societies require greater commitment to long-term planning to address aging issues than ever before (Heller 2003).

In addressing global population aging and improving the well-being of older adults, various national, regional, international, and global organizations have been working together for years. For example, in working on Member States, other international organizations, and nongovernmental organizations (NGO), the UN has been a leader on the forefront in addressing global aging issues since the late 1960s and has formulated numerous action plans. These action plans include the "Vienna International Plan of Action on Aging" in 1982, the "Madrid International Plan of Action on Aging" in 2002; as well as from endorsing Agenda 21 in 1994, to Millennium Development Goals in 2000, to Sustainable Development Goals in 2015, and to the Decade of Healthy Aging in 2020; from designing the International Day of Older Persons (October 1) in 1991 to the International Years of Older Persons (1999); from formulating plan actions on antiageism, to healthy aging, lifelong learning, the age-friendly cities, and to constructing concrete schemes and guidelines for fighting against pandemics (such as COVID-19); from developing strategies to address population aging to conceiving global blueprint of addressing aging-related issues such as climate variability; and from coordinating inter-governmental multilateral cooperation to cooperation between all stakeholders and global uniformed actions. All of these international efforts have advanced our understanding of aging and have improved the quality of life of older adults in all countries in one way or another. Notably lacking is how to monitor the implementation of these plans, how to evaluate their achievements and effectiveness, and how to share successful experiences in improving the well-being of older adults between countries or communities.

Older Adults in the Digital World

The advent of gerontechnology will bring about delayed, mitigated, and fewer age-related health and functional declines (Graafmans 2016; Millán-Calenti and Maseda 2014; see ► "Gerontechnology"). In the future, older adults are likely to interact more frequently with robots and mobile devices in daily living and for health reasons. Digital health and smart care allow for greater independence and individual self-care (Hall et al. 2012; Martin 2012). It also facilitates access to health and social care. When integrated within the healthcare system, digital health resources have been effective at improving health outcomes of patients suffering from a variety of conditions such as diabetes (Frias et al. 2017) and obesity (Bennett et al. 2018). Nevertheless, while the number of older people worldwide using digital technology is increasing, various barriers to digital health utilization remain due to lower IT literacy (see ▶ "Gerontechnology"). In response, future research should address the fit of digital health resources to appropriate levels of digital health literacy of older adults. Future research should also develop evidence-based interventions and rigorous research designs in enhancing electronic health literacy for older adults (Watkins and Xie 2014) and enhance lifelong learning (see ▶ "Senior Learning"). The prevalence of mental illness and dementia among older adults provides opportunities to develop and to increase the evidence base for digital interventions as well (Hatch et al. 2018; WHO 2017).

Research Participation

One recent development in Western society is to engage older adults in academic gerontological research process (stakeholder engagement), in the production and dissemination of gerontological knowledge, and include them in the development process of policy and practice (Ziegler and Scharf 2013). This follows the approach of "give voice to the experiences of older people" started in the 1990s (Bernard and Scharf 2007). Older adults' direct participation in research presents a new paradigm of engagement, recognizing older adults not as objects of study but as partners. Such approaches can improve their empowerment, lead to social change in ways that are more meaningful for aging adults, and alter the public's stereotypic view of them. However, in disadvantaged communities, these approaches often face challenges as they require substantial investments of time, resources, and commitment. Digitalization may facilitate older adults' participation in research and policymaking. Nevertheless, whether this approach is applicable to less developed communities or countries is largely unknown. More research on this is clearly warranted.

Summary

Critical gerontology hybridizes a broad spectrum of theoretical perspectives in the humanities and social sciences and extends the scope of aging research beyond biomedical models of aging and ageist social policies and practices. In the past half century since its formation, critical gerontology has complemented biomedical gerontology, psychological gerontology, and other branches of gerontology. It has facilitated a more comprehensive understanding of aging and has become an indispensable theoretical perspective that allows the imagination of a different future for aging. With emergent and culture-influenced dimensions becoming embraced in its scope, critical gerontology requires creative methodologies and new perspectives to more effectively address the challenges of rapid population aging, globalization, digitalization, and climate variability. Critical gerontology is expected to continue to play a critical role in offering a fuller conceptualization of age and aging in an increasingly diverse older adult populations.

Cross-References

- ▶ Active Aging
- ▶ Age Discrimination in the Workplace
- ▶ Ageism in Media and Visual Arts
- ▶ Age-Friendly Cities and Communities: New Directions for Research and Policy
- ▶ Age Discrimination in the Workplace
- ▶ Ageism Around the World
- ▶ Aging Migrants
- ▶ Biogerontology
- ▶ Climate Change, Vulnerability, and Older People
- ▶ COVID-19 Pandemic and Healthy Aging
- ▶ Gender Disparities in Health in Later Life
- ▶ Gender Equality in Later Life
- ▶ Gender Inequity
- ▶ Healthy Aging
- ▶ Layperson-Defined Successful Aging
- ▶ LGBT in Old Age
- ▶ Life Course Perspective
- ▶ Objectively Rated Successful Aging

- ▶ Older Adults in Conflicts and Crises
- ▶ Poverty and Gender Issues in Later Life in the UK
- ▶ Productive Aging
- ▶ Racism and Ageism
- ▶ Socioeconomic Differentials in Health: Divergence, Convergence, and Persistent Inequality Theories
- ▶ Subjectively Rated Successful Aging
- ▶ Successful Aging 2.0
- ▶ The Male-Female Health-Mortality Paradox
- ▶ "Three-No" and "Five-Guarantee" Older Adults

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Critical Perspectives on Aging

► Critical Gerontology

Critical Research of Gerontology

► Critical Gerontology

Critical Studies on Aging

► Critical Gerontology

Critical Theories of Aging

► Critical Gerontology

Critical Thinking About Aging Issues

► Critical Gerontology

Cross-Cultural Geropsychology

► Cross-Cultural Psychogerontology

Cross-Cultural Psychogerontology

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Synonyms

Cross-cultural geropsychology; Cross-cultural psychology of aging; Psychological aging across cultures

Definition

Cross-cultural psychogerontology deals with universals and differences in psychological aspects of aging across cultures.

Overview

Population aging is a phenomenon that affects most parts of the world. According to recent data from the World Population Prospects (United Nations 2017), the number of older persons – those aged 60+ – has reached 962 million worldwide and is expected to climb to 2.1 billion in 2050. In spite of these general world trends, life expectancies differ still largely, and aging remains a highly diverse experience across the world. While universal developmental tasks are markers for older age in all societies (e.g., becoming a grandparent), expectations with regard to typical life trajectories and the timing of transitions vary. This "social clock" (Neugarten et al.

1965) or “cultural chrononormativity of aging” (Brinkmann and Musaeus 2018) is also expressed in legal regulations and policies (e.g., availability and timing of retirement schemes). Normative and nonnormative life events and their interpretation as on time or off-time might thus be defined very differently depending on the cultural (and historical) context (see also Baltes et al. 1980; Wrosch and Heckhausen 2005).

This leads to one of the central questions of cross-cultural aging research: Are aging processes universals across cultures and societies in the Western, Eastern, Northern, and Southern parts of the world – or do aging processes differ between cultures and societies? If culture-specific differences are found, age seems to be at least partly a social construction and social age might hence be a more appropriate indicator than chronological age here (Albert and Trommsdorff 2014). Given cultural and societal differences, an important task of cross-cultural psychogerontology is the identification of underlying cultural and societal factors (e.g., Bleidorn et al. 2016). The knowledge of these factors might give insight into age as social construction – and possibly also indications for potential societal interventions (Kemper et al. 2016).

Early life-course theories defined specific developmental tasks based on biological factors and social expectations (see Erikson 1968), and the consideration of historical and sociocultural context is a principle of life-span psychology (Baltes et al. 1980) (See ► “Life-Span Development”). It is therefore astounding that only recent research has systematically addressed cross-cultural differences in aging, whereas most theories stem from a Western perspective.

Cross-cultural psychogerontology (See ► “Geropsychology”) starts from the theoretical assumption that individual development over the life span takes place in social contexts that differ in their emphasis of individuals’ embeddedness into social groups and societal context, often operationalized as collectivist versus individualist cultures (Kanagawa et al. 2001; Mayer et al. 2012; Triandis 2001). In individualist, mostly Western cultures, developmental pathways of independence are emphasized, stressing autonomy, personal choice, and self-fulfillment, whereas in collectivist, mostly Eastern cultures, interdependence is emphasized, highlighting obligations toward others and social harmony (Greenfield et al. 2003; Rothbaum et al. 2000). Thus, culture assumes the role of a “canalizer” that provides constraints which guide human development in a certain direction, however without exactly determining development (Valsiner 1996). Hence, both universals and differences in psychological aspects of aging might be observed across cultures.

Key Research Findings

Views on Aging

Views on aging have a double impact on individual development over the life span: they might bias behavior toward older people through stereotypes, prejudice, or ageism (Chasteen et al. 2015), and they can influence older adults’ self-concepts through internalization and self-stereotyping (Kornadt and Rothermund 2015) (See ► “Self-Perceptions of Aging”). It has been argued that in traditional and Eastern societies, more favorable views toward older adults and aging might be prevalent, for instance, due to Confucian values of filial piety, a concept that refers to lifelong mutual obligations and respect toward elder family members, typical for East Asian cultures such as China, Korea, and Japan (Hwang 1999). A meta-analysis by North and Fiske (2015) including 37 papers and 23 countries, however, challenges this assumption: contrary to expectations, participants in Northern American and Anglophone countries were found to show generally less negative attitudes toward older adults, whereas most negative views were documented for East Asians. Europeans were the most negative among the Western countries and East Asians more negative than Southeast Asians. The speed of population aging was related with ageism on aggregate level. Nonetheless, it might be important to look at different areas of development here. For instance, Löckenhoff et al. (2009) found in their college student sample from 26 countries more negative ratings with regard to age-related changes in attractiveness, everyday tasks, and new learning – all related to biologically based processes – whereas expectations of increases with age were found for general knowledge, wisdom, and respect, hence more culturally based aspects. Culture-level indicators and perceptions of aging were weakly linked in physical and cognitive areas, but more strongly related regarding socioemotional aspects and societal views.

Cognitive Processes

It has been argued that – in line with the distinction between mechanics and pragmatics (Baltes 1993) of cognitive functioning – the lifelong accumulation of cultural knowledge would lead to larger cross-cultural differences in the pragmatics of cognition with age. Park et al. (1999) have developed a framework model suggesting that different age trajectories might also be task-specific. Whereas effortful and controlled tasks that are highly resource demanding would show smaller cultural differences in older age due to universal biologically based decline, older adults would profit from their lifelong cultural experiences in tasks that involve automatically activated processes which reduce the cognitive effort needed to carry out a specific task. Accordingly, older adults from Eastern versus Western contexts differed more strongly compared to younger individuals with regard to recall of material that belongs to taxonomic categories (e.g., grouping animals with similar characteristics). The use of such categories is more common in Western compared to Eastern contexts, and as categorical information can help to recall information, Westerners who employ this strategy automatically might need less cognitive resources compared to Easterners who are less experienced in the use of categorical information (see Fang et al. 2017). Culture-specifics of neurocognitive aging have also been demonstrated in cross-cultural neuroimaging studies where, for instance, East-West differences in older adults' activation of object processing areas were found (Park and Gutchess 2006).

Social Relations

Socioemotional selectivity theory (Carstensen et al. 2003) posits that the size of social networks diminishes with age, whereas existing relations with close social partners are strengthened – a pattern that has been typically found in Western contexts. In the collectivist context of China, these associations between number of network partners (peripheral and close) and age were only found for participants who were low in interdependence, whereas larger social networks were found for older participants with medium or high levels of interdependence (see also Ajrouch et al. 2018 for Japan, Lebanon, Mexico, USA). Different meanings of social relations could be at the core of such differences: Westerhof et al. (2000) report that US older adults described social relations more in their function for emotional regulation, whereas for Congolese elders, the meaning of social relations was more instrumental. Social relations might thus serve diverse goals (e.g., emotional vs. old-age security value of children, Kağıtçıbaşı 1982), and these could be satisfied by different strategies regarding social networks across age.

Subjective Well-Being

Regarding cross-cultural differences in subjective well-being, Karasawa et al. (2011) expected more positive age trajectories for Japanese compared to US elders in particular regarding eudaimonic aspects due to cultural values attributed to aging in line with Confucianism. They found that Japanese older adults scored higher on personal growth compared to younger counterparts, whereas the opposite age pattern was found in the USA. Interestingly, purpose in life showed decrease in both samples which the authors interpreted as difficulties to provide meaningful involvement opportunities for elders in technologically highly advanced societies. Hedonic aspects of well-being were reported to increase (positive emotions) and decrease (negative emotions), respectively, in both samples, whereas Fang et al. (2017) have referred to a decrease of negative affect in particular for US elder adults. This latter finding was again explained according to independent and interdependent orientations: whereas for Westerners positive emotions might be important in enhancing their self-esteem in line with cultural values of independence and autonomy, for the more interdependently oriented Easterners, it could be important to attend to both positive and negative information in order to establish harmonious social relations (See ▶ "Successful Aging 2.0").

Preparing for Old Age

Preparing for anticipated changes in older age might help to tackle challenges related to aging and thus be beneficial for well-being later on. Kornadt et al. (2018) found differences in preparation for older age between adults in the USA, Germany, and China (Hong Kong). Participants from the USA and Germany reported generally more preparation compared to participants from Hong Kong, but cross-cultural variation was also found depending on domains of preparation (such as healthcare, work, finances, social relations, end-of-life concerns). Apart from diverging welfare policies, these East-West differences were also in line with culture-specific expectations of passive versus active age in Eastern compared to Western elders.

Informal Care

In light of population aging, the issue of care is highly prominent as old age is still associated with a high probability of physical and functional impairments (Ferring 2010). Although family remains an important pillar in old age support provision all over the world, cultural norms and expectations about responsibilities for care differ largely, and even among European countries policies and practices vary (See ▶ "Intergenerational Family Caregiving in Welfare Policy Context"), with higher public care provisions in the North and more intense family care in the South (Dykstra 2017). Different care preferences and expectations for mutual support are related to cultural values and norms (for a summary see Albert et al. in press). According to the Confucian value of filial piety (See ▶ "Filial piety and responsibilities among the Chinese"), the eldest son and his wife are responsible for care of elder parents (Hwang 1999), and a high familism goes along with a preference for informal care also in Southern and middle America (Crist et al. 2009; Hwang 1999). However, due to social change, traditional patterns can be adapted, as has been shown for urban contexts in China where daughters might take over care responsibilities as the traditionally rather preferred sons and their wives might not be available (for a summary see Pinquart et al. 2018).

Future Directions for Research

In this final section, directions for further research will be discussed, emphasizing both new theoretical perspectives and methodological tools for enhancing cross-cultural psychogerontological research.

Theoretical Perspectives

A simple transfer of Western-based theories and concepts such as future time perspective might not hold in other contexts as cultural beliefs (such as spirituality or religion) might bias goals and behavior. For instance, cultures differ in how they structure the life course, how they see afterlife and their relations with ancestors (Arnett 2016). In addition, aspects of acculturation and multiculturalism should also be taken into account. For instance, one could ask how social networks and psychological aspects of aging are affected by migration from a more collectivist to a more individualistic context (see also Burholt et al. 2018) or how biculturals deal with challenges of aging.

Methodological Challenges

Studies on cross-cultural differences and culture-specifics in aging are often based on cross-sectional design of most studies. Differences between cultures could indicate cohort rather than age effects in light of societal change. As a consequence, more longitudinal and cohort-sequential studies might be conducted in cross-cultural psychogerontological research. Also, whereas most studies have focused on East-West comparisons – often US and European versus East Asian samples – inclusion of further countries seems highly needed to gain a deeper insight into culture-specifics. At the same time, clustering countries as Eastern or Western seems too simplifying, as within these broad categories cultural contexts vary largely; thus a thorough description of cultural contexts is needed beyond dichotomies such as individualist-collectivist. Finally, culture-specific aging experiences might not be fully grasped by quantitative survey data, and caution is needed when using Western-based questionnaires without cultural adaptation.

Summary

The present entry focused on cultural similarities and differences with regard to aging. After describing typical developmental pathways of independence and interdependence that guide human development, selected research findings regarding views on aging, cognitive development, social relations, well-being, preparation for old age, and care arrangements were described. Finally, new approaches and suggestions for future research were outlined such as a closer look at the culture-specific meaning of Western concepts that cannot be transferred into other cultural contexts without any changes.

Cross-References

▶ Filial Piety and Responsibilities Among the Chinese
▶ Geropsychology
▶ Intergenerational Family Caregiving in Welfare Policy Context
▶ Life-Span Development
▶ Self-Perceptions of Aging
▶ Successful Aging 2.0

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Cross-Cultural Psychology of Aging

▶ Cross-Cultural Psychogerontology

Cross-Generational Relationships

▶ Intergenerational Relationships

Cross-Generational Support

▶ Intergenerational Exchange and Support

Cross-National Differences in Adult Child-Parent Relationships

▶ Intergenerational Family Caregiving in Welfare Policy Context

Cross-Sectional and Longitudinal Studies

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Synonyms

Cohort study; Observational study; Panel study; Prevalence study; Prospective study; Retrospective study; Transverse study

Definition

Cross-sectional study refers to a study where researchers observe and analyze data from a sample at a single point in time. In a longitudinal study, researchers conduct multiple observations over a period of time, ranging from weeks to many years.

Overview

Time is an important dimension in social scientific research. In other words, researchers are interested in both the *prevalence* and *dynamic changes* over time regarding a topic of interest. Cross-sectional studies measure the prevalence of social phenomena in a population at one point in time. Information derived from cross-sectional data is used to examine an association – for example, a relationship between physical activity and psychological well-being. However, cross-sectional studies cannot establish what is cause and what is effect, as several biases may arise due to the selection effect. A longitudinal study alleviates the problem since it involves multiple observations of the same population over a longer period of time. A major benefit of a longitudinal study is that researchers can examine changes within individuals and groups in the target population. To return to the previous example, longitudinal data can demonstrate whether physical activity increases the psychological well-being or if better psychological well-being leads individuals to be more physically active. In general, researchers begin with a more time- and resource-effective cross-sectional study to study the link between certain variables and then suggest a cause-and-effect relationship with a longitudinal study.

Key Research Findings

Both cross-sectional and longitudinal studies are observational in nature, meaning that researchers measure variables of interest without manipulating them. Cross-sectional studies gather information and compare multiple population groups at a single point in time. They offer snapshots of the important current social phenomena. For instance, nationally representative studies such as the Health and Retirement Study, Americans' Changing Lives study, and National Social Life, Health, and Aging Project show the prevalence of several age-related diseases, including diabetes, cardiovascular diseases, cancer, and dementia. Another major strength of cross-sectional data is the relative ease of collecting data for a wide array of variables at the same time without additional cost. However, cross-sectional studies pose at least three important limitations. First, the findings from a single time point are associative rather than causal, in that the direction between independent and dependent variables are unclear (i.e., reverse causality). Second, parameter estimates may be biased due to cohort-specific effects and selection bias. When a cross-sectional study compares multiple age groups in terms of health, two mechanisms may be operant. While a social benefit mechanism exists when a social factor enhances health outcomes, a social selection mechanism is present when healthier people are more likely to participate in study. Previous research suggests that social benefits and selection processes operate simultaneously and should be investigated as such. Finally, cross-sectional data are not suitable to investigate the process, change, or trajectory. Singer and Willett (2003) illustrates that individual differences at one time do not represent change, since the variability in one construct at any given time is different from the change over time. Thus, it is quite common that the focal independent variables associated with an outcome in a cross-sectional analysis are not predictive of the same outcome in a longitudinal analysis (Maxwell et al. 2011).

In longitudinal studies, time itself becomes a focal variable of interest. Thus, the understanding of longitudinal research design begins with an understanding of the methodological role of time in predicting changes (George and Jones 2000). Time here is not considered a theoretical "cause" of changes. For instance, age-related chronic conditions are not caused by time, per se; rather, time is a metric in order to reflect the change process. Longitudinal data analyses reveal how much individuals change over time (within-individual variation, intra-individual) and how individual changes vary across people (between-individual variation, inter-individual). Since measurement of independent, dependent, and control variables occur multiple times, researchers can examine the baseline levels as well as the changes in their core concepts, both within and between individuals (Ployhart and Vandenberg 2010; Singer and Willet 2003). By its temporal scope, longitudinal studies tend to better indicate temporal sequences compared to cross-sectional studies. Yet longitudinal studies are not without limitations, and the most serious concern is respondents' attrition between multiple waves due to refusal, serious illnesses, and mortality. Health selection effect is present when healthier and more resourceful individuals are likely to continue participating in studies and remain healthy and not vice versa. In fact, studies show that participants in longitudinal studies are physically healthier, highly educated, and less depressed compared to nonparticipants (Lindenberger et al. 2002). The key consideration here is that the individuals who participate in the study are systematically different from nonparticipants. Data not missing at random will lead to biased parameter estimates. Should the longitudinal data require adjustments for nonrandom missing values, there are analytical strategies to deal with this issue (e.g., Allison 2001; Byrk and Raudenbush 1992; Heckman 1979). Recent developments in multilevel models (MLM) substantially reduce parameter biases. Byrk and Raudenbush (1992) point to several advantages of MLM. First of all, by modeling varying intercepts and regression coefficients, researchers can allow individuals to vary at baseline and subsequent waves (i.e., growth curves). Second, the error correlations among the repeated measures can be modeled at both inter- and intra-individual levels. Third, MLM still produces unbiased parameter estimates with different temporal spacing between persons. Fourth, it is possible to model time-invariant and time-varying coefficients in the same model. Finally, MLM has a capacity to handle missing values at varying time points since it does not assume identical number of observations or fixed time points (Hox et al. 2017).

An example of cognitive performance highlights the differences between cross-sectional and longitudinal studies. Cognitive performance is affected by a myriad of social factors, such as physical activity, social activity, psychological well-being, and physical functioning (Baltes et al. 1998). Cross-sectional and longitudinal studies show different patterns of relationships (Fabrigoule et al. 1995). For instance, in an 18-year longitudinal study of Canadian older adults, Brown et al. (2016) show that an increase in social activities predicted better cognitive performance 12–18 years later. Moreover, they showed that within-person change in social activities (i.e., an increase in social activity) was a consistent predictor of better memory, fluency, and reasoning performance even after controlling for other relevant covariates and between-individual changes (i.e., being more socially active than the average older adults). The findings indicate the significance of individual opportunities and motivation for participation in social activities, which in turn benefits cognitive performance. Using Baltimore Longitudinal Study of Aging, Gunstad et al. (2010) showed that though there was no cross-sectional association between obesity and executive cognitive functioning, higher body mass index was linked with a *faster* decline in global functioning, executive function, and memory. This finding illustrates that obesity maybe a predictor of the rate of cognitive decline rather than the baseline level. Further, Gunstad et al. (2010) noted that the sample is consisted of well-educated and healthier older adults, which is in line with Lindenberger et al. (2002) showing that data on cognitive performance is affected by two major types of bias including mortality and participation biases. In fact, Lindenberger et al. (2002) showed that mortality/participation bias is prevalent and substantial since individuals with higher mortality or morbidity are more likely to drop out of the study at subsequent waves. The analysis revealed that the total selectivity effects accounted for a medium-size effect.

Future Directions for Research

Despite the advances in more sophisticated and scientifically rigorous longitudinal modeling, there are issues to be addressed. First of all, it is important to study discontinuous and nonlinear growth curve models. Many concepts in aging, such as activity engagement, cognitive aging, and disease development, are likely to change in a nonlinear fashion; there have been few applications of such models in the literature, such as Generalized Latent Growth Curve Models (GLCM) (Singer and Willet 2003). Second, study of mediation requires longitudinal data. Mediation implies an intermediary process by which an independent variable affects an outcome variable (Kenny 1979; Maxwell et al. 2011; Preacher 2015). Cross-sectional and even some longitudinal studies create biased estimates due to the failure to account for changes in mediator and the outcome variable. Kraemer et al. (2008) elucidated that it is crucial to "use longitudinal studies with at least two and usually three time points to establish moderators and mediators" (p. 106). Third, longitudinal studies can benefit from appropriate spacing between time (e.g., age, years, months, and days). Though there is no one appropriate "lag" at which to examine an effect, certain traits change more rapidly over time and should be measured more frequently than others. A more comprehensive understanding between variables can be achieved from assessing them at reasonable temporal intervals.

Summary

Both cross-sectional studies and longitudinal studies reveal different population processes, and the decision to pursue one type of study ultimately depends on the research question. Whereas cross-sectional study may be confounded by selection process, temporal autocorrelation, and cohort-specific effects, longitudinal studies may lead to biased parameter estimates due to selection effects and attrition. Combining both types of investigations and adjusting for the selection effects are probably the most preferred approach.

Cross-References

► Age-Period-Cohort Models
► Hierarchical Models
► Latent Class Analysis
► Selective Bias in Longitudinal Studies

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Crowded Nest

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Synonyms

Cluttered nest; Mature coresidency; Parent-adult child coresidence; Refilled nest

Definition

Crowded nest refers to the phenomenon of adult children living in the parental home. It has become synonymous with the household structure that is created when adult children return home after a period of time when middle-aged parents lived without children in the household (i.e., home returning) or when adult children experience delayed residential independence (i.e., delayed home leaving).

Overview

Parents and their adult children may live together for a variety of reasons related to children's needs, parents' needs, or both, and their experiences with this living arrangement may depend on those reasons. Aging parents may benefit from or require social support (e.g., companionship) or instrumental support (e.g., in managing illness or household chores). However, as more young adults live in the parental home, attention has shifted to their motivations for staying or returning to the nest. Despite common reference to "crowded nest syndrome" in popular culture, crowded nest need not connote something pathological, problematic offspring, or negative experiences or feelings on the part of aging parents (Mitchell 2000). Indeed, a host of social, economic, demographic, and cultural factors undergird the development and increase of crowded nest households. That is, many demonstrated predictors of crowded nest living arrangements are structural with some mixed evidence for psychological reasons (Aquilino 1990; Mitchell 2000; Sandberg-Thoma et al. 2015). Aging parents may have negative experiences with crowded nest living arrangements when adult children are highly dependent on parents for basic needs, when there are frequent disagreements with adult children, or when adult children return multiple times (Aquilino and Supple 1991; Mitchell and Gee 1996). However, research suggests that parents tend to report satisfaction with their living arrangements and return to the parental home may enrich young adults' life course trajectories and the lives of both generations (Aquilino and Supple 1991; Mitchell 2000; Roberts et al. 2015).

Key Research Findings

Causes and Consequences

At older ages, parents may coreside with children because of their health or economic needs. However, middle-aged parents of young adults are more likely to temporarily share their home with an adult child for the benefit of the child (Wiemers et al. 2017). Thus, considerable attention to the causes of crowded nests focuses on the motivations of young adults for staying in the parental or returning. This attention is warranted according to studies that have found children's needs to be the driving force (Sassler et al. 2008; Ward and Spitze 2007). Adult children may be motivated to coreside with their parents for socioeconomic advancement (to pursue higher education, save money), personal hardships (unemployment, divorce), psychosocial reasons (comfort to explore and plan for the next stage of life), mental health, and combinations of these reasons (Mencarini et al. 2017; Merten et al. 2018; Mitchell 2000; Roberts et al. 2015). Moreover, these motivations are undergirded by macro level, cultural, social, economic, and demographic factors that influence acceptability of and need for coresidence.

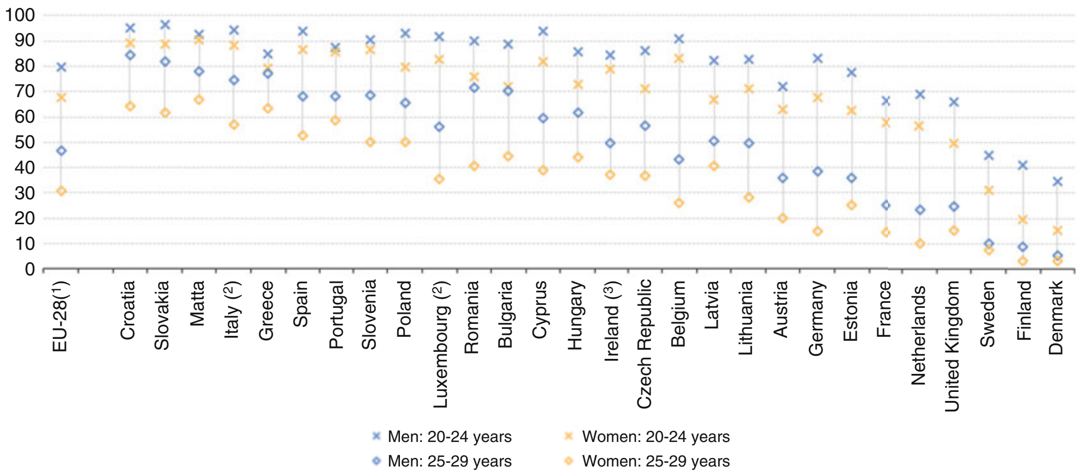
Demographic trends such as delayed or foregone marriage and childbearing make adult children more likely to live with their own parents into older ages (White 1994). Moreover, increases in the age of childbearing, longevity, and divorce rates among older adults ("gray divorce"; Brown and Lin 2012) place aging parents in circumstances that are more conducive to having a coresident adult child. In the context of demographic changes, economic opportunity structures determine adult children's abilities to be fully independent from their parents, especially in times of economic crisis or recession (Donat Lopez and Berngruber 2019). Culturally, some groups expect young adults to live with their parents until marriage (Roberts et al. 2015), and unmarried adult children are significantly more likely to live in the parental home than their married counterparts (White 1994). Social expectations for achieving adult status have shifted over recent decades leading to a period of life referred to as "emerging adulthood" in which young people who may have been residentially and financially independent from their parents in earlier times receive substantial and important forms of support from their parents (Fingerman and Yahirun 2015). Taken together, these macro level factors influence the acceptability and need for parent-adult child coresidence while also shaping the consequences that aging parents experience in crowded nest living arrangements.

The consequences of crowded nest living arrangements for adult children dominate the literature; however, parent-child relationships and the consequences for aging parents have garnered significant attention. Parents may benefit from receiving various sources of support from their adult children, such as emotional support and companionship or help with domestic work (Craig et al. 2015; Grundy and Murphy 2018; Mitchell 2000). Parental satisfaction with crowded nest arrangements is more likely when adult children provide help and support to parents, are more independent, and are engaged in less conflict with parents (Aquilino 1999; Aquilino and Supple 1991; Mitchell 2000). These factors that can lead to greater parental satisfaction vary by gender of the child and whether the adult child is not employed nor seeking education/training (Craig et al. 2015; Sassler et al. 2008). Widows may be happier when coresiding with daughters (Grundy and Murphy 2018). Parents' marital satisfaction may suffer as a consequence of having coresident adult children but perhaps only so under certain circumstances such as when children leave and return multiple times (Mitchell and Gee 1996). Despite some evidence of negative experiences with crowded nest living arrangements, aging parents generally have positive experiences while the needs of their adult children are met.

Current Trends

Recent data from the European Union demonstrate the scope of crowded nests across the region. Fig. 1 displays the percent of young adults living with their parents in 2016 by nation, gender, and age group. This graph shows significant variation in the percentage of young people living with parents across EU countries with the lowest in Scandinavian nations. It is the most common for men aged 20–24 and least common for women aged 25–29 to be living with parents. At least 90% of 20–24 young men were living with parents across 11 out of 28 EU countries in 2016, whereas fewer than half of these men lived with parents in only 3 countries (Sweden, Finland, and Denmark). Nearly half of all men and 30% of all women aged 25–29 in EU lived with their parents.

On average across the EU, there is a wider age gap for women than men and a narrower gender gap among the younger age group. Gender and age group differences are less pronounced in Malta and Greece though highly differentiated in Germany, Belgium, and the Netherlands. For example, in Germany approximately 15% of 30–34-year-old women lived with parents compared to more than 80% of 20–24-year-old men.



Crowded Nest, Fig. 1 Percentage of young adults living with parents, European Union 2016. Note: Ranked on the average proportion for young men and women aged 20–29 years (1) Estimate, (2) Provisional, (3) 2015. (Source: Eurostat (online data code: ilc_lvps 08))

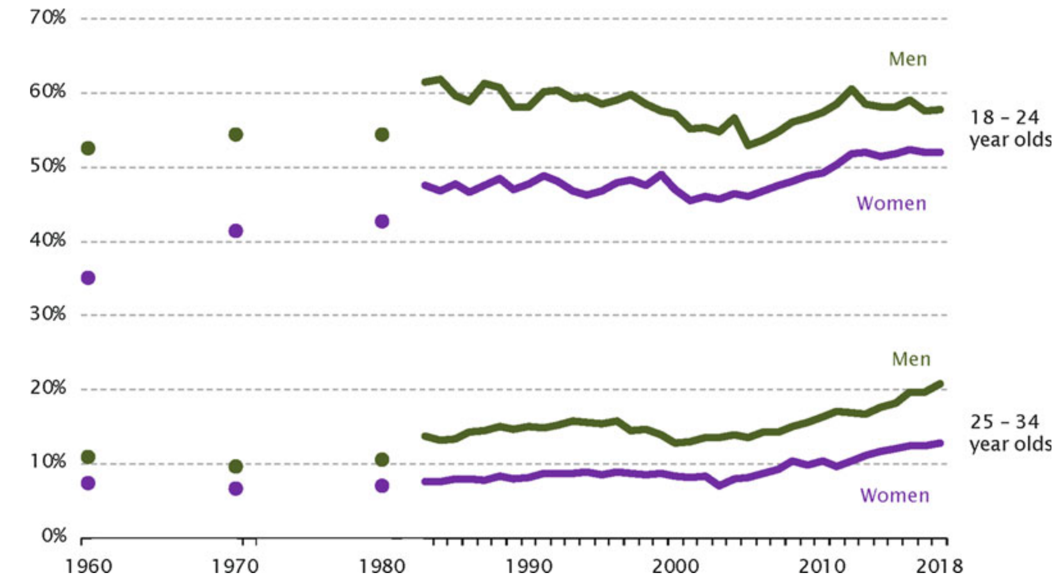
In Greece, using the same groups, there is a difference of 61% compared to 85%.

Overall, these patterns implicate cultural differences across Europe in adult children residing with their parents. Among British young adults graduating from university, motivations for returning to the parental home are diverse, and experiences may be positive for their adult trajectories (Roberts et al. 2015). In research comparing France and Italy, Mencarini et al. (2017) find that young Italians benefit from coresiding with parents more because of cultural differences in the division of domestic labor wherein young adults (especially men) spend less time on domestic labor. French families tend to incentivize living with parents less (Mencarini et al. 2017). Donat Lopez and Berngruber (2019) compare Spain and Germany citing important differences in determinants of residential autonomy in Southern and Western European countries that remain influential during economic crises that depress young adults' ability to be independent from their parents. Thus, differences within and across countries implicate a confluence of demographic, social, and economic factors shaping parent-adult child coresidence across the region and beyond.

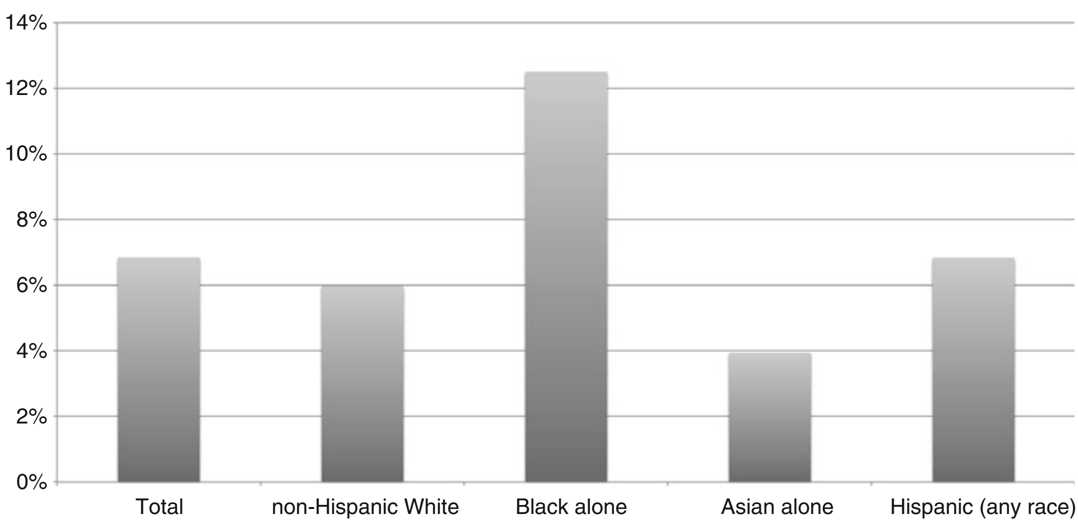
In the United States, the crowded nest phenomenon is less pronounced than in many EU nations, although men and college-aged adults also reside with their parents at higher rates than women and those 25–34 years old, respectively (see Fig. 2). These gender and age differences reflect a longstanding tendency of women to leave earlier and be less likely to return, while young adult men are more likely to return home (White 1994). In 2016, between 50 and 60% of 18–24-year-old Americans lived with their parents. At the same time, approximately 20% of men aged 25–34 lived with their parents, compared to about 12% of women in the same age group.

Figure 2 displays US Census data on the trend over time in young adults living in the parental home. In the United States, the number of 25–34-year-olds coresiding with their parents has been trending upward since the turn of the millennium. Among 18–24-year-olds in the United States, the overall trend has been less clear. However, gender differences have narrowed among this younger age group with about a 3% difference separating men and women in the latest data compared with an almost 20% gap in 1960. The narrowing of the gender gap mirrors trends in increased college enrollment among American women, as well as a range of other moves toward gender equity in the United States.

Figure 3 displays racial and ethnic variation in families in which the head of household lives with a(n)adult child(ren) in 2016. This graph



Crowded Nest, Fig. 2 Percentage of young adults living in parental homes, Unites States 1960–2018. Note: Unmarried college students living in dormitories are counted as living in group quarters in decimal data but as living in their parental home in CPS data. (Source: U.S. Census Bureau, Decennial Censuses, 1960–1980, and Current Population Survey, Annual Social and Economic Supplements, 1983–2018)



Crowded Nest, Fig. 3 Percent of families comprised of householder with adult child(ren) by race/ethnicity. (Source: U. S. Census Bureau, Current Population Survey, 2016 Annual Social and Economic Supplement)

demonstrates significant subgroup differences in crowded nest households in the United States. This household type is most common among Black and Hispanic Americans. The tendency for these groups to live in extended family arrangements has been well documented (White 1994). These patterns of crowded nest living arrangements for ethnic minorities may reflect cultural biases toward the family unit or economic necessity to pool resources in a shared household. Research by Merten and colleagues (2018) may shed light on the life course processes leading to these racial and ethnic group patterns. Circumstances of disadvantage may set off a process in which young adult roles are achieved relatively early in life (e.g., early childbearing or school completion), which may negatively affect socioeconomic prospects, mental health, and relationships with parents (Merten et al. 2018). These factors may then lead to an increased likelihood of the young adult returning to the parental home under circumstances that are most likely to yield negative consequences for both adult child and aging parent(s). Thus, the option to live with parents can be a comforting "safety net" for more privileged young adults but a culmination of accumulated disadvantages for others.

The crowded nest phenomenon, born of myriad demographic, social, and economic trends, will likely persist. Research on this phenomenon should supplant pop culture depictions that overgeneralize and pathologize parent-adult child coresidence to inform expectations and quell the negative stereotypes that can shape perceptions of crowded nest arrangements. This may be particularly important in light of evidence that parents' expectations about adult children leaving/returning affect how they experience coresidence with adult children (Mitchell and Gee 1996).

Future Directions of Research

Decades of scholarship on the crowded nest phenomenon in Europe and North America highlights a complex set of circumstances that lead to parent-adult child coresidence in a sociocultural context that generally favors the nuclear family structure. Additional research is needed to better understand the impacts of parent-adult child coresidence on aging parents and the correlation between crowded nest living arrangements and other changes in aging households. For example, how do adult children in the parental household influence the likelihood of divorce and/or cohabitation among older adults? Also, Merten et al. (2018) demonstrate a correlation between precocious childbearing and/or marriage and later coresidence in the parental home. However, questions remain about the extent to which the "domestic comfort" experienced by some young adults may be exacerbating trends toward delayed marriage and childbearing.

Although the crowded nest phenomenon has been well studied in Europe and North America, multi-generation households are a mainstay in many less developed countries around the world. A disaggregation of multi-generational households would further research on the household type characterized as the crowded nest in such countries to better understand cross-cultural differences in the causes and consequences of crowded nests, as well as parental expectations for adult children's household contributions. The contexts of developing countries may importantly shed light on the psychosocial consequences of parent-adult child coresidence when necessity outweighs comfort as the primary reason for this type of living arrangement.

Finally, future research should consider the societal level consequences of crowded nest living arrangements. Factors such as the economic burdens of higher education, diminished returns to education in the labor market, and stagnant wages intersect with social trends such as helicopter parenting in a way that may promote crowded nest living arrangements while concurrently enhancing the social acceptability of young adults living in the parental home. The result may benefit families with positive intergenerational relationships and economic resources, in particular pooling resources to protect inheritance. This may serve to further socioeconomic divisions in societies wherein more disadvantaged groups will fall further down the class ladder.

Summary

Crowded nest refers to the phenomenon of adult children living in the parental home.

Adult children may experience delayed residential independence or return home after a period of residential independence. Parent-adult child coresidence commonly serves the needs of young adults within the context of social, cultural, demographic, and economic circumstances that make residential independence from parents impractical or unsustainable. Aging parents also reap some benefits from coresidence and generally report being satisfied with these living arrangements. Still, popular culture tends to focus on negative possibilities such as “crowded nest syndrome” (negative mental health consequence) or “failure to launch” (problematic or immature adult child). Negative consequences are demonstrated under particular conditions, though these may align poorly with popular media depictions of the crowded nest. This type of living arrangement for middle-aged and older adults is likely to persist into the foreseeable future as young adults are faced with socioeconomic and psychosocial needs stemming from a confluence of demographic, social, and economic factors.

Cross-References

▶ Co-Residence
▶ Empty Nest
▶ Living Arrangements
▶ Sandwich Generation
▶ Stem Family

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Crowdsourcing and Crowdfunding in Aging Research

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Synonyms

Citizen science; Geroscience funding frameworks

Definition

Activities in which a large group of individuals contribute financial support, data, and/or work in a collaborative manner toward the purpose of increased healthy human longevity.

Overview

Crowdsourcing, a portmanteau of the words crowd and outsourcing coined in 2005 (Estellés-Arolas and González-Ladrón-de-Guevara 2012), describes a method of distributed effort by which a goal is accomplished by a large group of people, typically initiated by a public call-to-action. Crowdfunding is the practice of a project or venture being funded via crowdsourced financial contributions (Merriam-Webster Dictionary 2019).

While both crowdsourcing and crowdfunding have been utilized throughout history, such as the British government offering a public monetary prize for the best way to measure a ship's longitudinal position in 1714 (Dawson and Bynghall 2012), the advent of the Internet and the mainstream adoption of related connective technologies have made these paradigms of work and funding increasingly prominent in the twenty-first century. This shift has the capability of creating new and unique opportunities for driving advancement in the field of gerontology, just as with any other field.

The Path to Crowdsourcing and Crowdfunding Aging Research

Historical Context

The applicability of Internet-based crowdsourcing to assist in scientific endeavors first truly sparked in the public consciousness with the launch of projects such as SETI@home in 1999 (UC Berkeley 1999), which allowed owners of personal computers to volunteer otherwise unused computing power to aid in the search for extraterrestrial frequency emissions, and later with regard to biology specifically with projects such as FoldIt in 2008 (University of Washington Center for Game Science 2010), which involved over 57,000 participants helping to discover the topology of native protein structures through playing an online protein-folding puzzle game (Markoff 2010).

This type of crowdsourcing, in which every individual participant involved contributes to the final work, was different from earlier examples of crowdsourcing, in which a reward is offered to any individual or group that can accomplish a stated goal – so-called inducement prizes. This is not to say that inducement prizes are not still utilized. One such prize notable in the field of aging research is the Methuselah Mouse Prize or Mprize, which was created in 2003 and directly inspired by the 1714 Longitude Prize (Dawson and Bynghall 2012) and which rewards breakthroughs in the increase of maximal life span in mice as well as successful mouse rejuvenation (Bailey 2004).

Crowdfunding in the modern sense of the word truly became mainstream with the launch of online platforms specifically dedicated to the distributed collection of funds, such as Indiegogo in 2008 (Indiegogo 2019) and Kickstarter in 2009 (Kickstarter 2019a). While general solicitation of donations via a standard website, such as that currently employed by many longevity-focused organizations such as the SENS Research Foundation (2019) and International Longevity Alliance (2019), can rightly be considered a form of crowdfunding, the term typically denotes the use of dedicated platforms such as Kickstarter and Indiegogo when used in common parlance without further qualification.

Use of Crowdfunding Platforms for Science and Aging Research

Dedicated crowdfunding platforms typically employ a campaign-style structure, where users contribute funds via various payment methods, such as credit card processors and PayPal, toward a specific goal amount that is intended to be reached by a specified date. In some campaigns the specified goal amount must be reached by the deadline for any funds to be transferred, so-called "all-or-nothing" campaigns, while some platforms allow the transfer of funds regardless of whether the specified goal amount has been reached, so-called "flexible funding" campaigns. Campaign contributions can be in the form of donations with no additional reward or can be rewarded by the campaign creators with specified items or experiences commensurate with the amount contributed, typically demarcated into discrete reward levels. In exchange for hosting campaigns, crowdfunding platforms typically take a small percentage of raised funds as a fee.

Crowdfunding platforms are inherently social in nature, allowing contributors to easily share a campaign with friends via social media or email, as well as news of their specific campaign contributions in order to incentivize others to do likewise. This ability to easily enlist supporters can be of great use to various scientific endeavors, longevity-focused projects included, but when it comes to the largest crowdfunding platforms such as Kickstarter and Indiegogo, scientific projects tend to underperform.

One reason for this is because crowdfunding platforms showcase high-performing campaigns, featuring them on the platform's homepage, email newsletters, etc., and this special treatment in turn drives additional attention and traffic to these specific campaigns. Such a process inherently favors campaigns which have a strong dedicated marketing team behind them, and which involve a goal within popular categories such as gaming, tech, and fashion (Wikipedia 2019d). The team composition and goal of scientific projects rarely fit these criteria, and, as such, even promising campaigns are typically underfunded on these platforms (Rider 2016). Furthermore, such platforms have implemented policies that limit the allowed scope of biotechnology-focused campaigns specifically, such as Kickstarter restricting the involvement of genetically engineered organisms (Geere 2013) and prohibiting "any item claiming to diagnose, cure, treat, or prevent an illness or condition (whether via a device, app, book, nutritional supplement, or other means)" (Kickstarter 2019b).

Possibly as an answer to some of these issues, the year of 2012 saw the launch of multiple crowdfunding platforms dedicated specifically to the support of scientific projects, such as Microryza, later rebranded as Experiment (2019a); Walacea, later rebranded as Crowd.Science (2019a); and Petridish (2019). Each platform further differentiated itself with respect to feature set: Experiment focusing on donation-based campaigns without contributor rewards and showcasing updates for completed campaigns in the style of lab notes, Crowd.Science and Petridish choosing to allow rewards for campaign contributors, etc. The most successful of these platforms has proven to be Microryza/Experiment, raising over eight million dollars for scientific projects (Experiment 2019b), while, in contrast, Crowd.Science has raised a fraction of this total, and Petridish is currently no longer in operation. MedStartr (2019), another platform launching in a similar timeframe, has since pivoted away from crowdfunding to pursue the facilitation of traditional investment arrangements.

While science-focused platforms such as Experiment and Crowd.Science have been successful in raising funds for various projects, the amounts raised on a per-project basis have been insufficient as compared to that typically required for biotechnology projects involved in aging research – the average amount raised by a project on Experiment being approximately $4,000 (Experiment 2019b) and the average amount raised by a project in the health campaign category on Crowd.Science being less than $10,000 (Crowd.Science 2019b). These amounts are significantly below other sources of funding open to credible biology research projects, such as SBIR grants in the United States (Small Business Innovation Research 2019), for example. Additionally, projects have a success rate of less than 50% in reaching their goal amounts, and this may serve as a further disincentive toward researchers launching a project requiring a larger budget. Whatever the determining factors may be, the circumstance has been that projects in the field of aging research have appeared with negligible frequency on these platforms.

Crowdfunding Specifically for Aging Research

In 2015, the Life Extension Advocacy Foundation (LEAF) (Life Extension Advocacy Foundation 2019a) launched the crowdfunding platform Lifespan.io (2019b), which was dedicated specifically to funding aging research projects and expressly focused on addressing factors that may hamper projects of this type from being successfully crowdfunded. Unlike pre-existing platforms, Lifespan.io only accepts a few projects each year, each project passing a thorough evaluation process by the board and scientific advisory board of LEAF. Furthermore, LEAF provides each project direct support in terms of graphics and video creation, campaign text editing, and PR support in the form of various social media, marketing, and outreach initiatives. This strategy has proven successful, with 100% of the campaigns hosted on Lifespan.io successfully raising their goal amounts, and the average amount raised per project being greater than $47,000. Projects funded on Lifespan.io include research projects from teams such as those at Harvard Medical School and the SENS Research Foundation, as well as projects focused on developing biomarkers of aging (Lifespan.io 2019c).

Beyond focusing exclusively on aging research projects, another distinguishing characteristic of Lifespan.io is its ability to raise funds for for-profit initiatives in a manner that is potentially tax-deductible for United States citizens. This is because LEAF is a registered 501(c)(3) nonprofit organization in the United States, unlike other platforms such as Kickstarter and Experiment which are for-profit, and, as such, it can serve as a Fiscal Sponsor (Wikipedia 2019c) for initiatives concordant with its nonprofit mission.

While it is unclear which of Lifespan.io's unique features have been responsible for its success in raising funds for aging research projects as compared to other platforms, the existence of this success proves that crowdfunding can be a viable alternative to traditional funding mechanisms for suitable projects in the field of aging research. This is especially important given that lack of funding for early-stage research projects in gerontology is one of the main bottlenecks needed to be overcome (McCaslin 2018; National Institutes of Health 2018a) to hasten the progress of the field and crowdfunding has been demonstrated to raise the amount of funds sufficient for this purpose.

Crowdfunding as Compared to Traditional Funding Approaches

Bridging the Biotechnology "Valley of Death"

One of the primary reasons crowdfunding is particularly attractive to both researchers and entrepreneurs working on longevity promoting and rejuvenation biotechnology projects is that it has the ability to circumvent specific challenges in attaining funding unique to the field of aging research.

Beyond the usual difficulties in acquiring grant funding, due to high competition for limited resources (Alberts et al. 2014; National Institutes of Health 2018b), receiving grants for early-stage studies into the mechanisms of aging is especially challenging, given that traditional funding bodies such as the NIH are not yet well-equipped to support projects of this type. Directly addressing the root causes of the aging process is a paradigm-shifting idea, and, as such, government allocations for such research are far below that of various end-stage diseases, such as cancer and Alzheimer's (National Institutes of Health 2018a), and there is a related lack of subject matter experts within the system of grant distribution to evaluate aging research projects efficiently.

Crowdfunding provides a viable alternative to this funding approach, because, while fully bringing a potential therapy to market can take many years and millions of dollars, completing early-stage basic research which lays the groundwork for such a path can often be accomplished with amounts which crowdfunding can raise. There is also an additional benefit in crowdfunding in that it presents a lower barrier-to-entry in terms of paperwork as compared to the traditional grant application process, which can often be arduous. All that is required with most crowdfunding platforms is that the campaign creators comply with the platform's stated terms of service and privacy policy, just as with many other websites. Even in cases where more rigor is required due to project evaluation and/or fiscal sponsorship relationships, as with projects hosted on Lifespan.io, such processes are straightforward and do not require significant time to complete.

Aging research projects have unique difficulties to overcome in terms of acquiring investment capital as well. Investors want to maximize Return on Investment (ROI) as quickly as possible, and the longtime horizons involved in aging research therapies – due to longevity being the endpoint for success, as well as the length of clinical trials in general – have historically made traditional investment in such projects difficult (McCaslin 2018).

Generally, investors will want to see a strong proof-of-concept before putting money into such a venture and are unlikely to fund the creation of said proof-of-concept itself. This is where crowdfunding can be of great use, as the funds typically required to conduct the basic research necessary for creating a proof-of-concept are small enough to be successfully raised in this manner. The process of creating a successful crowdfunding campaign also helps prepare the start-up and/or research team to convey the details of their work in a compelling manner, which will be useful throughout the ongoing process of bringing a successful therapy to market.

Another benefit of crowdfunding is that donation-based platforms such as Experiment and Lifespan.io provide non-dilutive capital, and thus allow young biotech companies to preserve more control at the early stage of development in terms of equity. This, in turn, allows a company to have a more favorable position with respect to later potential investment, by keeping the company's capitalization table clean and allowing more room for future equity negotiations.

It is important to note that crowdfunding is not actually a competing source of funding in terms of grants and investment capital, but rather a potentially synergistic one. With grants, for example, it is often a requirement that the applying team has secured additional sources of funding in order to be eligible for grant approval, and crowdfunded capital can be one such source. With regard to investment, a successful crowdfunding campaign serves to not only raise capital to create a proof-of-concept that investors will want to see but also further de-risks the investment prospect by demonstrating that the crowdfunded project can gather public support and that the research team is capable in conveying the details of their work.

Crowdfunding platforms can also serve as a hub for the investment community, with the platform administrators actively working to handshake successful project teams with interested investors for potential follow-on funding, helping to take the crowdfunded project beyond the basic research phase. As an example specific to aging research, LEAF has assisted teams that have run successful campaigns on Lifespan.io acquire additional investment capital for their projects, by matchmaking them with a network of investors coordinated by LEAF and specifically interested in longevity and rejuvenation biotechnology projects (Lifespan.io 2019d).

In this way, crowdfunding can serve as a novel and vital piece of building a bridge across the so-called investment valley of death (Wikipedia 2019g) and help therapies that can overcome the diseases of aging to reach the public as fast as possible.

Synergy with Advocacy and Catalyst for Increased Public Funding

When evaluating the impact of crowdfunding in terms of hastening the progress of aging research, it is important to consider the effect of raising public awareness and support regarding the feasibility and social benefits of increased healthy lifespans, in addition to the direct funding raised on the platforms themselves. The public nature of crowdfunding campaigns, and the ease with which news of their success can be shared on social media and news outlets, makes them a powerful source for informing an increasing percentage of the population on the scientific realities of the field, which in turn can build societal pressure and catalyze increased funding from governments and international organizations for related research.

An instructive precursor of modern crowdfunding to examine in this regard is the work of The Jimmy Fund (2019), a charity created by early cancer research advocates to raise awareness and funds from the public. Using the story of one particular boy as a fulcrum point, The Jimmy Fund conducted various initiatives, such as radio broadcast solicitations, marathons, and telethons – all of which can rightly be considered forms of crowdfunding – to raise millions of dollars during a time when financial support was otherwise scarce. This public support was then capitalized upon to launch further initiatives such as letter-writing campaigns to members of the US congress, urging them to support increased funding for cancer research, and bold tactics such as commissioning full-page advertising spreads in popular newspapers beseeching the Nixon administration to act. These tactics were successful, and in 1971, the National Cancer Act (Wikipedia 2019h), also known as the "War on Cancer," was passed, eventually leading to billions of dollars being allocated by the US government, far beyond the amount that was raised directly by The Jimmy Fund itself.

This example of The Jimmy Fund has been explicitly referenced by the founders of LEAF (Comito 2016) as a model to follow regarding raising direct funds for research as a catalyst to vastly increase government funding and public support, in addition to being a goal in and of itself, noting in particular three specific steps: (1) create a clear and consistent call-to-action behind which the public can rally; (2) build a strong grassroots movement in support of this call-to-action, through the implementation of highly visible initiatives focused on engaging mainstream attention; and (3) leverage the power of this movement to effect change at the national and international levels.

In the case of LEAF's activities, the first step was the creation of the Lifespan.io, a crowdfunding platform dedicated specifically to aging research projects. To implement the second step of the strategy, LEAF has launched numerous initiatives to gather widespread support for increased healthy human life span, including building a significant following on social media platforms such as Facebook (120,000+), producing the most highly trafficked online news outlet (Life Extension Advocacy Foundation 2019c) on the subject of aging research, orchestrating interviews and appearances on mainstream news outlets like Fox News and The Young Turks (Life Extension Advocacy Foundation 2019b), and collaborating with YouTube celebrities to create videos that have informed and engaged millions of viewers (Life Extension Advocacy Foundation 2019d).

In addition to related outreach initiatives, the hosting of various aging research projects on a single platform allows for organizations in the field to demonstrate unification of purpose in a publicly visible way, which can in turn serve to boost positive perception among the public and confidence in the progress of the field. To see a project from Harvard and a project from the SENS Research Foundation listed side by side, for example, is an occurrence that would not have been seen even 10 years ago, and is itself a powerful signal that the field is maturing around a shared scientific framework and common goal.

Furthermore, the transparent nature of crowdfunding promotes an understanding of, and sense of direct agency in, the scientific process and realities of aging research among the public. This can have a powerful effect to preemptively address common concerns the layperson might have regarding the work of the field. For example, one of the most prominent misconceptions (Bagalà 2017a) about aging research is that the result of successful breakthroughs will be a protracted period of frailty, rather than a prolonged period of health. Well-crafted crowdfunding campaigns can counter this perception by accurately explaining the expected and desired results of the projects, and having this information being widely dispersed in related PR and social media initiatives. Another example is that the layperson may expect that, even if rejuvenation biotechnology projects are successful, the benefits of this work will only apply to the rich (Bagalà 2017b). This concern is directly mitigated by the public dissemination of information inherent to crowdfunding campaigns, especially if the project creators are obligated to make the results of their project Open Access (Wikipedia 2019f), and thus freely available to the public, as is the case for all projects on Lifespan.io.

Crowdfunding has also begun to play a role in creating pressure for societal change at the government and international levels, the third step of the aforementioned strategy. The clearest example of this involves the World Health Organization's 2019–2023 "General Programme of Work" (World Health Organization 2018), a 5-year action plan on global health and of which the original draft included no specific prioritization dedicated to aging or age-related disease. In response to this, the Lifespan.io community, along with a coalition of other organizations and advocates, launched a letter-writing campaign to the World Health Organization (Milova 2017) which was successful in bringing about the addition of these priorities to the forthcoming Programme of Work (Milova 2018).

To build upon this work, LEAF is currently creating new campaign types for Lifespan.io that will facilitate crowdsourced advocacy initiatives, similar in functionality to online petition services such as Change.org (2019), which is itself a form of crowdsourcing. This could be used to, for example, allow members of the biological research community, as well as members of the public, to sign onto an open letter which highlights how current government healthcare spending is failing to promote healthy lifespans for citizens and thereby create pressure for change. Such a letter could, being presented on a richly featured crowdsourcing platform, include compelling interactive infographics and links to related statistics and papers (Goldman et al. 2013) that make clear the societal and economic benefits to be gained from overcoming age-related disease. This, in turn, will allow other organizations which focus specifically on healthcare policy issues, such as the Global Healthspan Policy Institute (Global Healthspan Policy Institute 2019) in the United States, to use this information and show of support from the research community and the public to advocate in their respective countries for policy and budgetary changes that prioritize the increase of healthy human lifespan.

In this way, crowdsourcing and crowdfunding can be a vital driving force in accelerating the development of aging research, both by directly supporting individual research projects and by engendering societal conditions that will bring increased positive attention and funding into the field in general.

Examples of Application

Crowdsourcing and crowdfunding have been effectively utilized by organizations focused on aging research since at least the early 2000s. In particular the Methuselah Foundation has been crowdsourcing advancements in robust mouse rejuvenation through inducement prizes, such as the Methuselah Mouse Prize, or Mprize (Wikipedia 2019e), as well as crowdfunding philanthropic support in a semi-limited manner through initiatives such as the Methuselah 300, a community of philanthropic donors pledging $25,000 over 25 years, at a minimum of $1,000 annually.

Subsequently, other aging-focused organizations, such as the SENS Research Foundation and the Immortality Institute, have raised funds via donation pages on their respective websites. The fundraising efforts of the Immortality Institute, which later adopted the additional name of LongeCity, have approximated some features of dedicated crowdfunding platforms, in that the LongeCity website incorporates an active member-based forum, the users of which participate in specific goal-based fundraising initiatives (LongeCity 2019).

With respect to dedicated crowdfunding platforms, platforms which host a wide range of project types, such as Kickstarter and Indiegogo, are technologically capable of hosting campaigns relating to aging research, but few such projects have been launched on these platforms. Of over 400,000 projects launched, Kickstarter's project search function returns zero aging research projects for relevant search terms such as "longevity," "life extension," "biology," "gerontology," and other related phrases. This absence may be partially accounted for by Kickstarter policies which prohibit the involvement of genetically engineered organisms in projects (Geere 2013), as well as any projects aimed at producing disease diagnostics and/or cures (Kickstarter 2019b). While Indiegogo does not share these same explicit restrictions regarding biotechnology projects, only two campaigns hosted on the service involve aging research: a 2013 project aiming to test a combination of geroprotective drugs in mice (Wuttke 2013) and a 2015 project to create a longevity-focused cookbook (Konovalenko 2015).

The crowdfunding platform Experiment is more thematically suited to aging research projects, being explicitly science-focused, but thus far only one such project is listed on the platform, namely, a 2015 campaign aimed at developing various physiological biomarkers for age (reaction times, sense of touch, etc.) and determining which testing techniques provide the most useful results (Small and Hoekstra 2016).

The Lifespan.io crowdfunding platform, launched in 2015 and specifically dedicated to supporting aging research projects, has successfully raised funding for seven such projects. Supported projects include those from research teams at nonprofit organizations such as Harvard Medical School and the SENS Research Foundation, as well as for-profit entities such as with the AgeMeter project, a direct follow-up to the physiological biomarker project launched previously on Experiment. In 2017 Lifespan.io also began to host campaigns designed to collect recurring monthly donations, similar in functionality to the art patronage crowdfunding platform Patreon (2019). It has thus far utilized this functionality to raise funds for its own continued operations, as well as other operations of LEAF (Lifespan.io 2019a).

In addition to donation-based crowdfunding platforms such as Kickstarter, Indiegogo, Experiment, and Lifespan.io, there also exist equity-based investment platforms, such as WeFunder (2019), StartEngine (2019), and Republic (2019), as well as start-up investment listing websites such as AngelList (2019). While such platforms and websites can rightly be considered a form of crowdsourced investment, which could be used to support aging research-focused companies, thus far there have been no examples of their use for this purpose. This may be due in part to the newness of equity-based crowdfunding, and the related regulatory landscape surrounding this type of investment having yet to fully settle (Wikipedia 2019b).

Summary and Future Directions

While crowdsourcing has thus far been used to raise funding for aging research projects, current advances in technology with regard to decentralized work, coupled with the increasing ubiquity of the Internet, are creating opportunities for new paradigms in the field. Crowdsourced data collection through the use of mobile applications and wearable diagnostic technologies, for example, can be of a great use in research projects where physiological biomarker data can serve as a reliable proxy for age-related damage, as with Parkinson's or Alzheimer's disease. Large-scale technology companies are also beginning to build in systems that facilitate this data collection into their products. One such example of this is Apple's ResearchKit SDK (Apple Inc. 2019), which streamlines the integration of physiological biomarker data from a patient's iPhone, as well as assisting with bureaucratic elements of clinical trial administration such as the management of patient informed consent forms.

This ability to acquire diagnostic data from many participants in an easy and uniform manner can also serve to overcome common hurdles in structuring traditional clinical trials, such as competition over limited patient pools and difficulty enrolling appropriately sized cohorts which ensure studies' results have sufficient statistical power. Furthermore, such systems also have a unique ability to drive research into therapies without traditional profit motive, due to lack of patentability for example, as patients themselves can provide incentive via crowdfunding and/or data sharing. Properly structured crowdsourcing systems can also allow those who are already self-experimenting with potential longevity therapies to create meaningful data, as part of a cohort, instead of such data being lost in isolation.

Accordingly, this opens pathways for organizations to begin structuring new types of clinical trials, those where therapy administration and data collection are crowdsourced by the patients themselves. Indeed, several organizations have already begun moving in this direction, such as Open Longevity (2019) in Russia, and OpenCures (2019) in the United States. There are still challenges which need to be overcome in order to structure such initiatives in ways that will result in credible and publishable data, such as ensuring proper compliance with data privacy regulations such as HIPAA (US Health Insurance Portability and Accountability Act 1996) and the UK Data Protection Act (2018), and it remains to be seen how quickly such crowdsourced clinical trials will become common practice.

It is important to note that the emerging technology of Blockchain (Wikipedia 2019a), most commonly known as the core of Bitcoin and other virtual currencies, will likely play an important role in future crowdsourced medical endeavors, including those relating to aging research. This is because its ability to create a distributed and cryptographically secure data ledger – which can enable health data transactions in an efficient, verifiable, and permanent manner – allows for not only crowdsourced collection of data but also various transactions to be performed upon this data with regard to access and/or financial compensation for its sharing with companies or clinical trial organizers. Although there are no fully realized blockchain initiatives focused specifically on longevity, several related initiatives are currently in progress, such as the eHealth First (2019), an in-development platform for personalized health management, and Nebula Genomics (2019), a service which allows users to store and be compensated for the sharing of their DNA sequence data.

While the precise effects of emerging crowdsourcing-based systems for the collection, analysis, and sharing of health data cannot be predicted, there is great potential for such technologies to improve the quality and pace of aging research.

Cross-References

▶ Clinical Translation Acceleration
▶ Longevity Activism
▶ Longevity Advocacy

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Cultural Aging

▶ Representations of Older Women and White Hegemony

Cultural Differences in Caregiving

▶ Caregiving and Ethnicity

Cultural Representations

▶ Feminism and Aging in Literature

Cumulative Advantage/ Disadvantage Theory

▶ Socioeconomic Differentials in Health: Divergence, Convergence, and Persistent Inequality Theories

Cumulative Inequality

▶ Theory of Cumulative Disadvantage/ Advantage

Curatorship

▶ Guardianship

Custodial Care

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Synonyms

Board and care; Nonmedical care; Residential care and non-skilled care

Definition

Custodial care refers to nonmedical care that helps individuals with their daily basic needs, such as dressing, eating, and bathing (Kagan 2017). Custodial care is provided by family members and nonmedical professionals such as personal care aides and nursing assistants.

Overview

Due to disease, mental illness, and frailty, older adults will lose the capacity to perform activities of daily living (ADL) such as eating, using the toilet, bathing, getting dressed or out of bed, and moving around on their own (Amerigroup Real Solutions in Healthcare 2018). The needed help with ADL typically does not require skilled care (See ▶ "Skilled Care") and can be provided by caregivers with no medical or nursing training, who can be family members or paid care aides (See ▶ "Formal and Informal Care"). Recipients of such assistance are said to be in custodial care. Differing from skilled care, custodial care is not provided by or under the supervision of licensed and trained medical professionals.

Key Research Findings

Custodial care can be provided within a nursing care facility or at home in the community. Most needs associated with custodial care tasks can be met by either in-home caregivers or facility care aides. Cost for custodial care, which can be prohibitive, is often covered with private funds and savings. Other forms of coverage for the cost of custodial care in the USA may include Medicare, Medicaid, or private insurance. Medicare typically only pays for skilled care in a nursing facility, and does not cover custodial care if that is the only type of care the older person needs. Medicare will only cover on the conditions that the care is medically necessary and prescribed by a licensed physician or authorized medical personnel and that the care is provided by Medicare-contracted healthcare providers.

Medicaid, a public assistance program, covers custodial care in a nursing facility. The requirements and services for Medicaid coverage vary across states. To be eligible for Medicaid, beneficiaries would have to pay for custodial care out of pocket until their assets have been depleted. Custodial care at home is typically covered under long-term care (LTC) insurance or Medicaid Waiver programs.

Individuals could purchase private LTC insurance to cover long-term custodial care (See ▶ "Personal Care"). While such policies vary greatly, many provide coverage for nursing home and in-home care for a fixed period of time: 3, 4, or 5 years (See ▶ "Care Home Stories"). Annual premiums on LTC insurance are fixed for the life of the coverage, and policyholders are reimbursed a specified amount for each day of custodial care received during the period of coverage. Medicaid Waiver programs have similar income and physical function eligibility to Medicaid-covered nursing home care, except that an individual receives care at home and in the community.

Research has focused on impact of provision of long-term custodial care on family caregivers, particularly for those who take care relatives with Alzheimer's disease and related dementias (Van der Lee et al. 2014) (See ▶ "Aged Care Homes"). Evidence-based interventions (e.g., psychosocial education) and service programs (e.g., respite care) are in place to assist family caregivers (Chen et al. 2015; Pendergrass et al. 2015), and yet, access to such support varies across regions and ethnical/cultural groups (Gilmore-Bykovskyi et al. 2018; Sun et al. 2007).

Research on custodial care in facilities have mainly focused on ensuring the safety and quality of life of residents, who are vulnerable to abuse and neglect by staff members or care aides. More training, education, and support are recommended for facility staff members to help them self-care as well as deliver quality care for residents (Senior Living).

Future Directions for Research

Custodial care for older adults can be short term right after an acute medical event but typically spans long term. The lack of financial support for long-term custodial care is a pressing issue for millions of low- and middle-class families who do not have long-term care insurance nor qualify for government-sponsored programs. Future research should focus on sustainable ways to support family caregivers in long-term custodial care.

Summary

Custodial care is essential to meeting the basic needs of a frail older person. The low entry level to a paid custodial care aide position contributes to low payment, high stress, and great turnover rates in this workforce. Similarly, family caregivers who volunteer to provide custodial care for their older relatives also experience stress, burden, and social restriction. Only when the society and policymakers place high values on the care of older citizens, we can expect an improvement in the quality of life across frail older adults as well as their caregivers (paid or unpaid).

Cross-References

- ▶ Aged Care Homes
- ▶ Care Home Stories
- ▶ Formal and Informal Care
- ▶ Personal Care
- ▶ Skilled Care

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Cybercounseling

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Synonyms

Computer-mediated counseling; Digital counseling; *E*-Counseling; Electronic therapy; E-Mail counseling; *E*-Psychotherapy; *E*-Therapy; *E*-Writing therapy; Internet counseling; Internet psychotherapy; M-Therapy; Online counseling; Technology-based counseling; Telehealth services; Telemental health; Virtual counseling; Web counseling

Definition

Cybercounseling is a component of counseling that is implemented in a virtual environment where the counselor and the counselee are not sharing the same physical space. They use distance information and knowledge communication technologies (IKCT) that may be computer-generated and/or Internet-based, to promote ease (health) literacy (Sorensen and Pleasant 2017; Saboga-Nunes et al. 2019), dis-ease literacy, or management of life-course events. Cybercounseling can be either formal or informal. Formal cybercounseling is delivered by counselors who present standards for licensure, acting individually or under the auspices of formal counseling organizations or associations. Informal cybercounseling is delivered by counselors who have an independent activity outside of formal counseling organizations or associations mostly favored by fragmentation with IKCT support environments and outside formal bodies of licensure supervision (see also Nystul 2016).

Overview

Cybercounseling development is rooted in the emergence of a new landscape characterized by the exponential growth of information and knowledge communication technologies (IKCT). This growth was made possible because of the computer revolution and the democratization of the Internet, from strictly military to public purposes. This establishes a new set of possibilities when questions regarding access to counselors are put under scrutiny in the context of older adults (Tsai et al. 2010).

Far before mobile tools were ubiquitous, Morrissey defined cybercounseling as "the practice of professional counseling and information delivery that occurs when client(s) and counselor (s) are in separate or remote locations and utilize electronic means to communicate over the Internet" (National Board of Certified Counsellors (NBCC) 1997, p. 1). Later NBCC proposed another definition where Cybercounseling "involves asynchronous & synchronous distance interactions among counselors & clients using e-mail, chat, & videoconferencing features of internet to communicate" (NBCC 2001, p. 1). Few years later, Mallen and Vogel defined cybercounseling as "any delivery of mental and behavioral health services, including but not limited to therapy, consultation, and psychoeducation, by a licensed practitioner to a client in a non-face-to-face setting through distance communication technologies such as the telephone, asynchronous e-mail, synchronous chat, and videoconferencing" (Mallen and Vogel 2005, p. 764). Mallen and Vogel's emphasis on the "non-face-to-face setting" needs to be revisited, since today, face-to-face communication is embedded in mobile technologies. High speed Internet communications have made face-to-face communication a commodity in the pocket of a person. Also, videoconferencing, once dependent of expensive technological paraphernalia, has become obsolete as new concepts such as "Skype," "WhatsApp," "Zoom," "Slack," or "Teams" have enabled many with a simple intelligent phone, to have free face-to-face communication with one or several persons in different locations at a same time.

While both definitions highlight the needed practitioner (or counselor), with the increase of self-made counselors (e.g., influencers, youTubers, instagrammers, bloggers, twitterers, snapchatters, and streamers) extensively using IKCT, a new landscape emerged out of the control of established *status quo* counseling services (from now on referred in this entry as informal cybercounseling). Concurrently with the rise of Artificial Intelligence (AI), new cybercounseling solutions, based in decisional algorithms, are becoming strong competitors to human interaction. AI is changing the way health promotion or disease management, public services, mobility, and many other domains of human activity and interaction are implemented today with new ethical and practical issues emerging.

Also, more and more user friendly and simpler applications, demanding very low digital literacy to be installed and used (e.g., a smart phone), responding to voice commands or simple gestures, are opening the way to new venues in cybercounseling. Realities of transmuted real lives into virtual worlds (e.g., Second Life) have introduced new options (e.g., to solve confidentially issues) with new paradigms of interaction in counseling. This has triggered a rapid decay of appropriateness of existing regulations, with ethical frameworks following quite behind the pace of innovation and change in cybercounseling. This pace of innovation has been embraced by the older adults. More and more senior citizens are engaging in tech adoption, as its use climbs steadily: In the USA, smartphone use has quadrupled among seniors in 5 years, showing the new competences and possibilities that are being established (in early 2000, just 14% of seniors were internet users, while in 2017, 67% of adults ages 65 and older go online) (Anderson and Perrin 2017). This shows that the basic competences and conditions for cybercounseling are being overwhelmingly established in the older population.

Key Research Findings

Older Population Increase and Cybercounseling Enhancement to Provide On-Time and Person-Centered Services: Dealing with Fragmentation by Multiple Players

Concurrently to the speedy and instant communication possibilities, societies are dealing with eroding conditions to provide on-time and person-centered services. The growth of older population has posed new issues, such as providing accurate immediate support to their needs. Cybercounseling is needed and worth it to study in gerontology. Nevertheless, the field of cybercounseling lacks a theoretical framework and elicitation of techniques to guide counselors (Suler 2000). Consequently, loss of control by centralized public services, transnational exchanges in the global village, and organizations and associations of traditional counseling services, adding the lack of guidance in the field of cybercounseling raise questions and limitations of Cybercounseling in the wired society. Also, characterizing who is entitled to be a cybercounseling professional, what legal or ethical issues are at stake, has become a fluid area where no specific developments have followed the IKCT increment. This fluidity has facilitated the emergence of informal cybercounseling that has an independent activity outside of formal counseling organizations or associations that compete with formal cybercounseling. The real dimension of informal cybercounseling is not known, and unless careful attention is given to frame cybercounseling, its fragmentation by multiple players, with IKCT help, may jeopardize cybercounseling potential.

Smart phones are at the center of this discussion: On one hand, they have paved the way to make distant processes of communication much easier and accessible to nonexperts in IKCT. On the other hand, smart phones have claimed an area of expertise that has been populated by the alliance between IKCT specialists and stakeholders of different origins and motivations, in the development of applications (usually called "apps"). Therefore, while informal cybercounseling can be based at different generic IKCT tools (such as Vlogs, Youtube, etc.), the built and delivery of apps are still a niche reserved for a few specialists, because of the financial costs that are implicated. Making this niche a promising place, where formal cybercounseling can thrive and implement an environment of trust and reliability, needs to be considered.

The Need for an Ethical Code of Conduct to Ensure Trust and Reliability in Cybercounseling

One question that is today an eroding place in cybercounseling is the public demand that counselors would need standards for licensure. Virtual communication has promoted a track record that relies much more on the "likes" than on the certificates or training courses of counselors that would ensure reliability (Khelifa 2007). A trend of popularity, replacing reliability and the negative consequences of embarking in self-exposure and big data utilization, has been the basis why, in sensitive fields of information, a normative has come into force in order to protect individual rights, such as the General Data Protection Regulation (GDPR 2018). Examples of ethical codes of conduct include the Guidelines of the British Psychological Society (BPS), HCPC (Health Care

Professionals Council), Information Commissioner's Office in the United Kingdom, and Council for Accreditation of Counseling and Related Educational Programs (CACREP).

Another reference in this area is NBCC which focuses on (i) a review of pertinent ethical and legal codes; (ii) Informing of encryption methods and how long data will be kept; (iii) verifying parental/guardian approval for services to minors; (iv) discussing procedures of how to contact a counselor in ways other than online; (v) obtaining a name of at least one counselor on call in the client's home area; and (vi) explaining the possibility of technological failure. The Center for Credentialing and Education (CCE) has a specialty credential in distance counselling (Distance Certified Counsellor (DCC) CCE 2011), a 15-hr distance counsellor training program. To get access to it, a counsellor must hold a master's degree in counselling, or in any related field, and have a valid license to practice counselling. General Data Protection Regulation (GDPR 2018) will be used here since it applies to individuals and organizations and can be set as a standard in the practice of Cybercounseling, following the strictest rules of compliance to ethics. GDPR is also a good example for establishing a base for Cybercounseling, since it is applied at a supranational level, where borders are a fluid frontier (when cybercounseling is in place). Verifying also the local regulations, where both counselee and counselor are based, would be mandatory in order to shield the nature of cybercounseling.

Although the application of the above referred GDPR is implemented within the borders of the European Union (EU), for the process (collect and use) of personal data, taking GDPR as a benchmark would help ensure counselors the appropriateness to deal with confidential information of cybercounseling, such as personal data. In this case, the following rights for individuals are considered: (i) the right to be informed; (ii) the right of access; (iii) the right to rectification; (iv) the right to erasure; (v) the right to restrict processing; (vi) the right to data portability; (vii) the right to object; and (viii) the right not to be subject to automated decision-making including profiling.

The GDPR ensures information record collection, confidentiality, and it's breach, taking into consideration situations of breach confidentiality in case of crisis team (harm to self), police (harm to others / an organization, e.g., in case of terrorism), child protection services, counsellor emergency, and need to be replaced by a trusted person or managing complaints and indemnity. GDPR includes insurance provisions, supervision sharing information, and management of informed consent. In this case, how consent is given by a counselee to a counselor for the cybercounseling process should verify that it is given freely in a specific informed and unambiguous way. A positive opt in – consent cannot be inferred from silence, preticked boxes, or inactivity but must be separated from other terms and conditions – is ensured. Also, an offer of simple ways to withdraw consent must be available.

GDPR endorses age-related issues. In cybercounseling, critical issues such as age verification – as special concern should be given to children – find for the first time GDPR appropriate consideration aiming at special protection for children's personal data (only at 16, a child can give their own consent). At young age, it is mandatory to get consent from a person holding "parental responsibility." GDPR can also be considered regarding appropriateness of electronic platforms to secure cybercounseling. It demands that data transmitted during meetings, webinars, and chat sessions are encrypted and secured in platforms and are compliant with Privacy Shield Agreements (e.g., Zoom, Skype, or WhatsApp video streams).

Protection by design could be a practice to follow to ensure that privacy and data protection compliance are always a high priority in cybercounseling. Therefore, in order to empower the counselee (Wallerstein and Bernstein 1988), a sequence of symbols should give him/her the tools to decide to trust the cybercounseling process. These symbols can be graphic information that is posted in the websites or mobile applications, which would state conformity to quality criteria (such as seals of quality). This can be done by cybercounseling adhering, for example, to seals of good conduct (e.g., HonCode, The

Health on the Net Foundation that aims for medical and health Web sites to stick to reliability and credibility of information) (e.g., www.parar.net HonCode certificate). Consequently, HonCode can be referred as one example (e.g., the eHealth Code of Ethics, by Internet Health Coalition) to help establish external verification processes of good practices in health and cybercounseling.

Examples of Application

In-line with the above, application of cybercounseling is today *ubiquitous in the Internet.* For example, during times of hindrances to access health support and services, or of particular social disturbances (e.g., the COVID-19 pandemic) (Calton et al. 2020), cybercounseling may play a crucial role together with telemedicine (DiGiovanni et al. 2020). The development of a telehealth geriatric assessment model in response to the COVID-19 pandemic (DiGiovanni et al. 2020) is one example that could be referred in such domain.

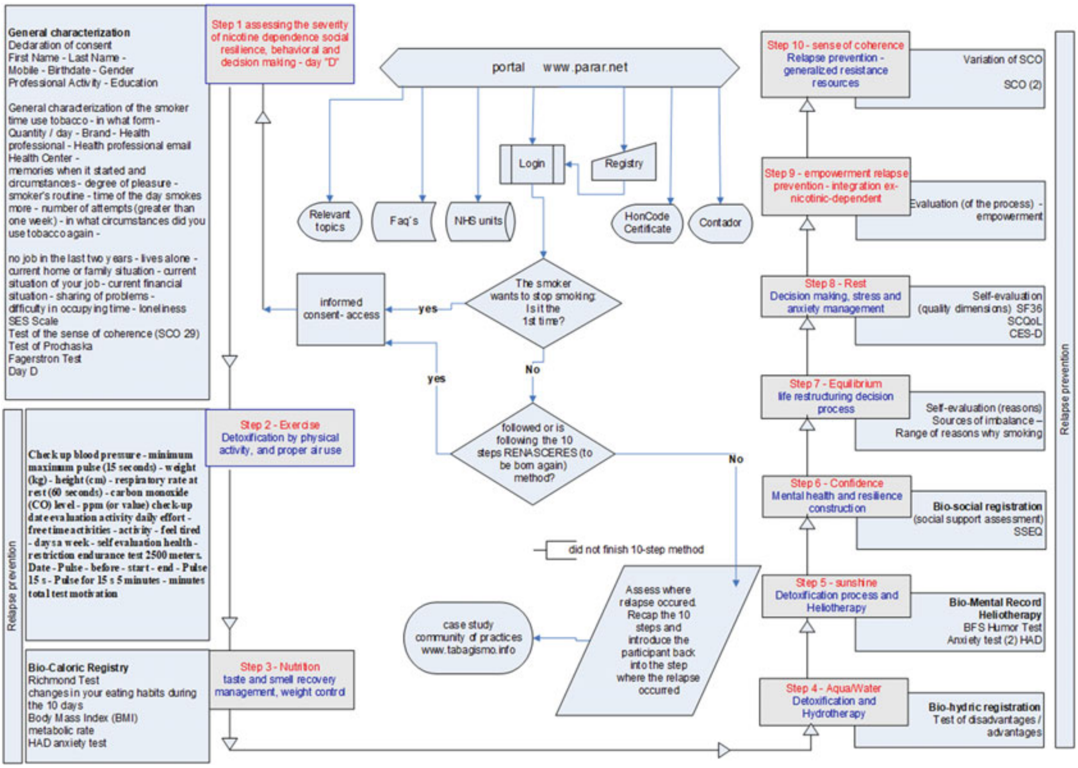
Therefore, one example of how Cybercounseling may answer needs, consequence of shortness of human and financial resources, will be introduced (i.e., cybercounseling in smoking cessation). Also, this example will be considered because of its use of Artificial Intelligence (AI) establishing a cybercounseling process routed in the sense of coherence theoretical framework.

Quitting smoking has been emphasized, but the uptake of cessation assistance has exceeded the capacity of services in several countries. This is a context to consider the potential of cybercounseling and of new theoretical and practical venues to offer alternative options to people willing to stop smoking (Mallen et al. 2006). The use of IKCT and health literacy, as a means of empowering people to make behavioral changes, can therefore be explored in the context of cybercounseling. Also, the trade-off on the use of the Internet as a tool for smoking cessation (it can reach a vast number of people for a small cost (efficiency) demonstrating to work in the domain of smoking cessation (efficacy)) is a study case of cybercounseling implementation.

From this standpoint, a cybercounseling process based in AI aiming to support smoking cessation was developed and installed in the Internet, at *parar.net* ("parar" means "stop"). It was structured according to the acronym "Renasceres" (from the *renaissance* perspective of a new birth), constructed in a ten-step process – in which each cybercounseling step carries the participant through different stages toward the goal. For example, before the stage at which the counselee would be able to decide on his/her Dday (of stop smoking), comes the stage to access the degree of nicotine dependence (Fig. 1) where cybercounseling plays a major role of actualization. Therefore, in this example, the cybercounseling is a permanent interactive and tailored process, where information computation is intended to promote knowledge creation, leading the person to decision-making, before becoming an active agent in his or her own life changes.

The core content of this cybercounseling strategy is organized around the mnemonic and acrostic *renasceres,* in ten letters that correspond to ten steps, with two major areas: 1) (step 1) where diagnostic tools establish the basis for the quit attempt, and 2) relapse prevention tools (step 2 to step 10). Once logged on, it is prompted to the counselee to go to the home page where she or he can have access to general information. In this case, cybercounseling process is composed of two sources of information. When combined, they allow information and knowledge management of a tailored smoking-cessation administration process, based on a user-centric approach (Bock 2004). It is aimed at leading the person to aim toward the ease pole of the dis-ease/ease continuum.

On the one hand, there is a source of information (the cybercounseling at parar.net) which includes advice on how to help and sustain intentions of behavior change in smoking cessation. This embodies a standing reserve favoring smoking cessation support. A second source of information – one that originates in the counselee interaction with the cybercounseling process – is developed through different stages. This enframing progression occurs as the counselee in the cybercounseling process takes various



Cybercounseling, Fig. 1 organigram of a cybercounseling strategy based in AI aiming at supporting smoking cessation (parar.net). (Source: organigram by the author)

decisions such as activating the next levels of knowledge management processes, answering questions, and participating in and complying with the personalized process of the AI in place.

Presented sequentially, the process is structural, with an ease *e*literacy approach (Fig. 1). Before login, information about demographics, smoking history, and cigarette load are inserted. Then, access to the cybercounseling program is open to register counselees who can enter the portal with a self-chosen login name and a password (first phase). If it is the first time the counselee is interacting with the platform, she or he is prompted to follow each of the stages that lead to establishing a Dday. In stage one step one, after registration at *parar.net*, the user is prompted to enter Step 1 of the cybercounseling. **Step 1** refers to the *resiliency* construct, assesses nicotine dependency (FTND), offers a smoking cessation personal journey (SCPJ), and evaluates the sense of coherence, stages of change, motivation, and self-efficacy. In order to self-monitor smoking habits before quit-date (Dday), the user can download a personalized journal. Awareness and *consciencientização* about the deconstruction of the habit is triggered. This is intended to promote self-efficacy. An interactive feature calculates the amount of money a user has spent since he or she started to smoke as well the number of cigarettes smoked (taking as a basis the average tobacco prices for the year). Step 1 is the central project of the cybercounseling mechanism, as it includes preparation for quitting and sets a quit date (Dday).

During these stages, the counselee loads the portal with information concerning smoking history (second phase), comprehensibility, manageability and the meaningful nature of life events, motivation, dependence on nicotine, or self-efficacy. The counselee is also invited to provide information that allows clarification of stages of change that together develop an interactive tailoring process based in the theoretical framework of the sense of coherence. Therefore, these ten steps are organized in two groups: *1) Stop smoking awareness facilitator and 2) Relapse prevention.* In this last group, once the decision to set a Dday has been defined, the cybercounseling prompts the user using *parar.net* with a tailored message to proceed to Step 2 where *exercise* and physical activity are promoted to implement a *Relapse Prevention Programme (RPP).* As a mechanism for facilitating nicotine excretion, weight control, and mental health promotion, with **Step 2**, the Relapse Prevention Programme (RPP), focusing on a bioregistry process and motivation evaluation, is initiated. Following Step 2, **Step 3** focuses on *nutrition.* A weight-management program is explained with biocaloric-registry, including variables such as motivation and anxiety and depression assessment (by means of the hospital and anxiety and depression scale. In **Step 4**, *Agua* (water), the cybercounseling continues to focus on nicotine excretion, bio-hidric-registry, and the advantages-disadvantages of smoking and stopping-smoking. **Step 5** spotlights the advantages of the use of *sun*light to promote nicotine excretion through the skin and to enhance mental health. Here, besides variables considering biomental-registry, humor, Benefit Finding Scale (BFS), and Hospital and Anxiety and Depression Scale (HAD) (b) are used to collect raw information for continuing the tailoring process of support. **Step 6** focuses on strengthening *confidence* and trust in the life decision to stop smoking. This step of *parar.net* aims at mental health promotion, and variables such as biosocial-registry, social support, and Smoking Self-Efficacy Questionnaire (SSEQ) are collected. With **Step 7,** the cybercounseling advises the user to reframe the basic assumption of *equilibrium* and positive health in a life free from tobacco. In order to help organize new habits, this RPP step is aimed at promoting self-knowledge and evaluation of the user's resources when continuing toward a life without tobacco. Tension and sleepless nights can be the consequence of smoking cessation, the focal point of **Step 8**: *Rest* is considered a key to life quality. Different variables are gathered with different instruments, such as Health Survey, SF-36 (SF-36), Smoking Cessation Quality of Life (SCQOL), and Center for Epidemiologic Studies Depression Scale (CES-D), in an effort to manage mood and contribute to reestablishing the circadian cycle of the ex-smoker facing withdrawal symptoms. This aims at increasing relapse prevention. In **Step 9**, a call to take control of life without the support of the cybercounseling is set out, and a shift is made between the *parar.net* platform-leading roles toward the user's ultimate self-control of life stressors. Indicators of *Empowerment* and life control, general resistance resources, are assessed. In the last step, **Step 10**, the termination of the program with an assessment of the *sense of coherence* aims at evaluating manageability, comprehensibility, and the meaningful dimensions of a life without tobacco. The cybercounseling *parar.net* program ends with an online certificate of achievement. These **10 steps** call the user **to be born again (*renasceres)*** to a life without tobacco. This word, constituted of ten letters, is both a mnemonic and an acrostic that is built with the starting letter of the basic concepts proposed for moving away from a life with tobacco to the new life experience without nicotine: *r*esiliency, *e*xercise, *n*utrition, *a*gua, *s*un, *c*onfidence, *e*quilibrium, *r*est, *e*mpowerment, and *sense* of coherence. These first letters constitute the word *renasceres,* which gives the program its identity. With this, not only specific support for common issues related to smoking cessation is obtained, but also a broader approach is suggested, focusing on lifestyles and health promotion.

If the counselee needs to halt the cybercounseling interaction temporarily, then after coming back to it and logging in, he or she will be prompted to go to the last registered stage, which means that it will be easy to continue, without loss of time. Each phase of the cybercounseling interaction is presented in an interactive format, and various tools assist smokers in (a) progressing from one phase to the other, (b) answering the questions online and receiving immediate tailored feedback, and (c) setting a Dday for smoking cessation.

A quitting guide provides counselees with evidence-based information about smoking cessation. The counselee can print every tailored phase of the cybercounseling interaction, and this could constitute, at the end, her or his story(telling) of the process toward a life without tobacco. This way, every cybercounseling interaction is allowed to be revisited at a later time.

The task of this cybercounseling process is to support self-efficacy while unveiling a set of conditions that can facilitate the counselee's willingness to change, by enabling a first small step: establishing a Dday. The responsibility for change lies with the counselee (motivation enhancement therapy, Miller WR and Rose GS 2009). Acceptance of small shifts in attitude as worthy of a first step in behavior change is in accordance with principles of motivational interviewing, a mechanism that is commonly used to address smoking cessation (Rollnick et al. 1999). An action plan is proposed within the context of a cybercounseling holistic lifestyle perspective (where various aspects of life are interrelated).

Future Directions for Research

While cybercounseling has become a ubiquitous reality in the information society, the real impact of its development, efficacy, and efficiency is not sufficiently established. More research needs to be done in what best practices will sustain the negentropic impact of cybercounseling. There is a need for a theoretical foundation and cybercounseling effectiveness. Specifically, the difference between informal cybercounseling and formal cybercounseling can be further improved – as an evidence-based practice – if cybercounseling is embodied in a theoretical sound approach (Yates 2013). Being embodied in a theoretical sound approach, will not only serve the purposes of efficacy, but also be the basis for cost-effectiveness of interventions. As an example, the theoretical Antonovsky's foundation of the sense of coherence needs to be further explored to frame a theoretical embodiment in cybercounseling (Saboga-Nunes 2016).

Taking this theoretical frame of reference, cybercounseling should avoid the dichotomous characterization of counselees (as either sick or healthy), and instead, look at every person in a continuum (on the dis-ease/ease continuum) where a counselee progresses or regresses in terms of negentropy (i.e., chaos decrease) (Saboga-Nunes et al. 2019).

If it is possible to express a negative variance of entropy, between time 1 and time 2 in the encounter between a counselor and a counselee, it could be argued that counseling has contributed to negentropy (Fuhriman & Burlingame 1994; Robinson et al. 2011; Wright 2002). Moving from information to decision/action is what ease (health) literacy implies. Not moving from information to decision/action is what dis-ease literacy means. Therefore, more than providing information, cybercounseling can play this role of assuring negentropy in periods of time when life seems to become more and more chaotic. The reasons for this perception of increasing entropic life experiences can be mitigated with videoconference cybercounseling while enhancing social support and mental health changes in depressive symptoms in older populations (Tsai et al. 2010).

A second domain of cybercounseling efficiency is related to IKCT supporting the stages of information interpretation, conversion and processing and managing overload, or the emergence of noise (Lindsay et al. 2008, p. 317), considered as the foundations of empowerment (that leads to information interpretation and conversion, which are the basis for cybercounseling processing (adapted from Choo 1996), hopefully moving the person in the direction of the ease pole of the continuum dis-ease/ease in cybercounseling).

To interpret information, the person needs to activate personal resources that establish a connection between information and his conscious self. This actualization contributes to negentropy. During the last 20 years, the Internet has become one of the most extensive and least expensive sources of actualization, a critical issue in cybercounseling (nearly 70% of those searching for health care information on the Internet do so before visiting a doctor's office (Brown 1998)). The counselor in cybercounseling that becomes a facilitator in this need fulfills a crucial "node" role (Internet of Things). This new form of organizing human existence "the *information age,"* the present state of human development (Alberts and Papp 1997), has led naturally to incremental growth of cybercounseling. Guided action, doing all that is possible to preserve energy and gain information, is then an attribute that can be considered as being the singularity of cybercounseling, along with knowledge creation.

In summary, the Salutogenic approach to cybercounseling could pursue negentropic features based on low levels of energy expenditure. The concept "salutogenesis" is the composite of two words: salus (Latin for "ease" or "health") and genesis (Greek for "origins"). Cybercounseling aims at health (ease) or deals with its menace consequences (dis-ease). This is done through a process of information and knowledge management, where counselor's enframing capabilities play a major role in the development process of improving the *generalized resistance resources* (Antonovsky 1987, p. 28) of counselees, to perceive the world as *comprehensible*, *manageable,* and *meaningful* (i.e., their sense of coherence, the center of life control (Antonovsky 1987)). By this process, a standing-reserve becomes a reservoir of resources for ease (health) literacy creation, a cybercounseling dynamic goal.

Very often counselees preload their interactions with counselors with information that is not of their expertise (e.g., mining on "Dr. online" search engines). This increases the strain of providing appropriate tailored cybercounseling by counselors – that very often need to deconstruct, in a first stage, what was "built" online. This is one example of the power shift between main actors in cybercounseling processes (the counselor and counselee) that today are set in a new environment where increased competences are acquired by counselees that can challenge counselor's flexibility and trustworthy role. Therefore, the balance of power has established a new environment that intensifies the need of strong foundations for the pursuit of cybercounseling. Making theoretical structural foundations explicit is one aspect that can be today a strong argument for a sound cybercounseling process, where qualified counselors will be recognized unquestionably for their role. This impromptu way which has no track record of sound professional proficiency can only help professional cybercounseling counselors to gain a better understanding of their activity.

Summary

Cybercounseling development is rooted in the emergence of a new landscape characterized by the exponential growth of information and knowledge communication technologies (IKCT). The "*information age"* became the natural environment for cybercounseling implementation since it has provided the tools and has also originated new challenges.

Although Cybercounseling may be recognized as a component of counseling, it is nevertheless specific, since it is implemented in a virtual environment where the counselor and counselee are not sharing the same physical space. Alternatively, the use of IKCT and their ubiquitous influence is felt also in the development of cybercounseling, may it be computer-generated and/or internet based. Considering a paradigm shift where the dichotomy sick/healthy is replaced by active strategies to promote ease (health) literacy, dis-ease literacy or management of life course events will help individuals to become managers of their own well-being, while in interaction with others (e.g., counselors).

There is sufficient evidence that a new set of codes of conduct are needed today for cybercounseling (that is quite distinct from other forms of counseling). The fluidity of the Internet landscape, where cybercounseling is naturally embedded, mandates that counselors involved in cybercounseling establish a strong hold of quality and reliability, based on sound theoretical foundations. Lifestyles are an area where counselors are most requested today. An example on smoking cessation in the cybercounseling domain was presented in order to explore the needed research to deepen the feasibility, efficacy, and efficiency of cybercounseling strategies.

Cross-References

- ▶ Digital Health
- ▶ Gerontechnology
- ▶ Home Health Technology
- ▶ Telehealth
- ▶ Telemedicine
- ▶ Telerehabilitation (Remote Therapy)

C

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Cyberpsychology and Older Adults

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Synonyms

E-psychology; Internet psychology; Virtual psychology; Web psychology

Definition

Cyber psychology is a subdiscipline of psychology that examines the interaction of humans with others via technology, the influence of technology on human behavior and psychological states, and the adaptation of technology as per human needs (Kirwan and Power 2014). Technology may include internet, mobile computing, mobile phones, games consoles, virtual reality, artificial intelligence, and any other technology that may modify the human behavior directly or indirectly (Kirwan 2010).

Overview

It is after the 1970s and 1980s that digital technology becomes earnestly penetrated in our lives. Before this era, it was possible to get retirement without interacting with the digital world. But after this digital revolution, technology is becoming more common and mobile phones, computer, and internet become an integral part of our lives. Digital literacy becomes inevitable for daily tasks like shopping, billing, banking activities, etc. and to get access to news, entertainment, and social life (Harley et al. 2018).

Aging comes with inevitable physical and cognitive degeneration which reduces the energy, physical dexterity, dulled senses, impaired memory and information processing and difficulty in multitasking. These inexorable signs of aging can make interaction with the digital world exasperating and impedes the competent use of cyber technology. This physical deterioration can make it difficult for older individuals to perform daily functions that involve technology operations. These daily functions range from socializing like getting in touch with the other family members to technical issues like processing bank-related information (Harley et al. 2018).

Nevertheless, simultaneously, digital literacy can help older adults in healthy aging by maintaining independence and wellbeing (Czaja et al. 2006). The online modes of socialization can replace the physical mobility and traveling thus providing better opportunities for communication. The cyber technology let the older adults maintain the social ties and help in establishing new connections thus facilitates the ongoing process of psychosocial and self-development (Harley et al. 2018).

Key Research Findings

Cyberpsychology is a least studied phenomenon in older adults but being part of nondigital age and then growing old in the cyber era may be stressful (Harley et al. 2018). Although older adults resist the adoption of digital technology, there is an increasing trend towards possession and use of emerging technology. The main reasons for their avoidance are the age-driven cognitive and physical impairments, like difficulty in processing and retaining new information, their unaccustomedness with the digital technology, and poor education (van Deursen and Helsper 2015).

For those who are coming online, the main reason is to stay connected with the long-distanced family and relatives (Hill et al. 2008), especially the grandchildren (Luijkx et al. 2015). The digital world let older adults adopt new social identities and roles (Harley et al. 2018), and this mainly comes through connecting digitally with existing family and friends, which helps them in getting rid of loneliness, and strengthens the overall family bonding, thus affirming the new generational identities (Siibak and Tamme 2013). The most common digital media used by the older individuals to communicate with the families are emails (Gatto and Tak 2008), video calls on Skype (Zamir et al. 2018), Facebook (Jung and Sundar 2016), and sharing of photos and videos on social networking sites (González et al. 2012).

The use of digital technology may provoke computer anxiety (Laguna and Babcock 1997), especially for older adults (Harley et al. 2018); however the use of digital technology like browsing the internet can have a positive effect on their cognition, cognitive flexibility, processing, selective attention, and short-term memory, that is, capabilities that may decline with age (Vance et al. 2007; Slegers et al. 2009). Digital technology also helps in a cognitive adaptation like the selective and socioemotional use of resources that can compensate their age-related impairments (e.g., using online shopping may overcome lack of mobility, using alarms and reminders to overcome memory issues). Digital technology also tends to optimize their existing cognitive functions, that is, playing games can improve reaction time (Goldstein et al. 1997), can enhance visual-spatial ability, and processing speed (Zhang and Kaufman 2016). Playing video games can also improve control, multitasking, and short-term memory and has an impact on cognitive processes in a broader sense like executive functions, memory, and reasoning (Anguera et al. 2013; Stern et al. 2011).

Applied Cyberpsychology

Research studies demonstrated a promising relationship between Internet use, mental health, and well-being. Cross-sectional as well as longitudinal studies reported statistically and clinically significant inverse correlation between Internet use and depression (Hunsaker and Hargittai 2018). Additionally, Cotten et al. (2012) suggested that the use of the internet decreased the likelihood of depression in older adults above 50 years of age. It also reduces the probability of depression in old older adults (Cotten et al. 2014). A significant relationship between Internet use, social support, decreased loneliness, increased life satisfaction and well-being, and improved mental health were reported by several studies (Hunsaker and Hargittai 2018). Particularly, the use of social media is linked with better psychological well-being because of the higher perceived social support and greater connectedness in old age (Yu et al. 2016).

The use of the Internet and social media may enhance the independence of older individuals as compared to their offline peer group (Henke 1999). Also, according to a survey conducted by Sum et al. (2008), the use of the Internet lowers the loneliness and enhances socialization among older adults. They further studied the importance of online communities for older adults and its impact on their lives. A highly positive relationship was revealed between a sense of belonging with online communities, a sense of community, and overall well-being. Also, it was demonstrated that Internet use promotes health satisfaction, healthy relationships, and happiness (Sum et al. 2009). Digital technology usage was associated with decreased chronic ailments and depressive symptoms and enhanced subjective well-being (Chopik 2016). Involvement in social media can give the health-related knowledge like the diagnosis, prevention, and treatment of different medical conditions and the availability of support groups on social media can also offer care in overcoming the loneliness (Leist 2013).

Intervention studies using Internet use and skills in their protocols reported a significant positive impact of the Internet use on mental health and well-being (Forsman et al. 2017). Technological interventions in older adults revealed improvement in depression (Laganá and García 2013), increased life satisfaction (Shapira et al. 2007), and higher perceived social support (Torp et al. 2008). The abovementioned studies encourage to investigate the further association between mental health outcomes due to technology usage among older adults.

Future Directions of Research

Cyberpsychology research has identified numerous implications and risks involved with engaging in cyberspace but mostly the focus is on younger generations, and older individuals are largely overlooked. There are positive and negative factors that are associated with going online like the boost of self-esteem and self-confidence (Karavidas et al. 2005). Also, the use of digital technology can significantly reduce social isolation and enhance the well-being and overall quality of life (Heo et al. 2015; Czaja et al. 2006). Negative factors that may be accompanied by the adoption of emerging technology are the abnormal pattern of digital usage, technology anxiety, and other cyberspace-related issues, such as bullying, cybercrimes, among others. The phenomena that are already studied in the younger generations are not yet thoroughly examined within the context of older age. These areas greatly needed to be explored, the possible benefits that the older population can get from the cyberspace and the potential negative impact of technology adoption in the older community.

Cross-References

▶ Adjustment to Aging
▶ Aging in Place
▶ Digital Participation
▶ Performance Anxiety
▶ Psychogeriatrics
▶ Psychopathology

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Cytomegalovirus and Human Immune System Aging

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Definition

Cytomegalovirus (CMV) is a persistent viral infection that is present in most older people. Effective control of infection depends on a strong and sustained virus-specific immune response, and there is concern that this can weaken the ability to control other infections and may lead to immunopathology. Epidemiological studies have shown that infection does increase mortality risk in some populations, but this has not been seen consistently. We now need to understand the biological basis of these conflicting findings and to develop treatment approaches for older people at risk.

Overview

Cytomegalovirus is a member of the herpesvirus family, and chronic infection is widely prevalent in the human population (Reddehase 2006). Infection can be a major clinical problem for the fetus or in patients who are immunosuppressed, and there is now concern that it may also cause health problems in apparently healthy older people. In particular, a strong and sustained immune response is required to suppress viral reactivation, and over many decades of life, this balance may become disturbed with increasing levels of virus and a reactive and "inflated" immune response (Moss 2019). Several epidemiological studies have shown that CMV infection is associated with an increased mortality rate in older people (Wikby et al. 2002), but this is not a universal finding. Indeed, other reports reveal a beneficial influence of infection on immune function and may point toward a positive influence from the CMV "virome." Endothelial cells are a major site of viral tropism, and an increased incidence of vascular disease in CMV-seropositive older people may therefore represent the consequence of immune-mediated tissue pathology. Efforts to limit the clinical consequences of chronic CMV infection are under investigation through the use of antiviral drugs and may represent an important intervention for populations at risk.

Key Research Findings

The Epidemiology of Cytomegalovirus Infection

Cytomegalovirus is one of the eight herpesviruses that can infect humans and is the largest virus within this family. Cytomegalovirus infection is widely prevalent across the world and thus the majority of older people are infected. An important principle of all herpesviruses is that they are never eradicated following primary infection but establish a “latent” or “persistent” infection for the rest of life. Control of infection is dependent on sustained immunological surveillance of viral replication, and this underlies the profound immunological consequences of CMV infection and the potential clinical importance of infection in older people.

CMV can be transmitted by a number of routes but by far the most important are through breast milk or contact with recently infected infants who continue to shed virus in the urine for up to 6 months (Reddehase 2006). The effectiveness of transmission by these two routes underlies the very high prevalence of infection in most populations. Indeed, infection rates typically exceed 80–90% even during childhood in the most parts of the world. However, in many developed countries, infection rates with CMV have fallen dramatically in recent decades. The reason for this is not entirely clear but may relate to a reduction in breastfeeding. In these settings infection rates around 30–40% are seen in younger adults but do increase slowly thereafter due to recurrent episodes of primary infection, typically approximating to 1% for each year of life. As such, older people who remain CMV-seronegative represent a minority group in almost all populations. The overt clinical consequences of CMV infection are subtle. The virus is very well adapted to *Homo sapiens*, and the vast majority of primary infections are silent. A “glandular fever” with CD8 T cell lymphocytosis is observed in a minority of people, but this is much less common than seen in association with primary EBV infection. Thereafter, in immunocompetent individuals there are very few established clinical sequelae associated with persistent infection. As discussed later, this balanced relationship between the virus and the immune system appears to break down in older people where several immunological studies have suggested a negative impact on health and longevity.

The Immunological Control of Cytomegalovirus Infection

At the time of primary infection, the virus infects a range of somatic tissues, and these are presumed to contain stem cell populations. To date, relatively little is known about the spectrum of tissues that acquire viral infection. However, hemopoietic stem cells, differentiated monocytic leukocytes, and endothelial cells are established sites of tropism. Herpesviruses typically undergo two major forms of transcriptional regulation following infection of a cell. *Lytic* infection is characterized by viral replication and subsequent destruction of the host cell at the time of viral release. In contrast, *latent* infection is associated with production of a very limited number of viral transcripts, minimal immunological “exposure” to the host immune system, and apparently minor impact on cell physiology. These two patterns are seen most clearly with Epstein-Barr virus infection, in which the B cell lineage is a site of latent infection while lytic infection may also occur in B cell or epithelial targets. For CMV the balance is less clear, and it is not entirely clear to what extent latent infection is involved in viral maintenance. In contrast, low level and intermittent viral release through lytic replication may be the physiological norm. As such, CMV poses a constant attritional challenge to the host immune system and as a consequence has perhaps the most profound impact on the profile of the immune repertoire of any infectious agent.

Primary infection with CMV is associated with a rapid and persistent adjustment in the profile of both the innate and adaptive immune response, and this is sustained throughout the life course (Gillespie et al. 2000). The most profound impact is on the cytotoxic component of the cellular immune response. In particular, infection triggers a large increase in the number and percentage of CD8+ T cells within peripheral blood which are typically 30–40% higher in CMV-seropositive people compared to uninfected individuals (Chidrawar et al. 2009). CMV-specific CD4+ T cells also express a predominant cytotoxic profile, and the presence of significant numbers of CD4+CD28− T cells within an individual is virtually synonymous of persistent CMV infection (Pachnio et al. 2016). This suggests that control of viral replication requires effective lysis of virally infected cells that express HLA Class II, potentially representing dendritic cells or activated endothelial cells. The magnitude of the CMV-specific CD8+ repertoire exceeds that of CD4+ and leads to a decrease in the CD4:CD8 ratio which tends to decrease further with advancing age (Jackson et al. 2017).

CMV-specific T cells have an unusual phenotype and display a profile of extreme differentiation with loss of co-stimulatory and anti-apoptotic molecules such as CD27 and CD28 and acquisition of proteins such as CD57 and CX3CR1. These changes are so profound that it is possible to predict, with reasonable confidence, whether a person is infected with CMV or not on the basis of the phenotypic distribution on their peripheral T cell repertoire (Weinberger et al. 2007). As discussed later, the relative magnitude of these changes has been associated with "immune risk phenotype" in some older people and may act as a correlate of associated health problems.

This T cell immune response against CMV is striking in its magnitude and reflects a huge metabolic investment by the host (Sylwester et al. 2005; Vescovini et al. 2007). The scale of the CMV-specific immune response varies within different individuals although the etiological factors underlying this are not entirely clear. Recent murine experiments have shown that the magnitude of the initial viral inoculum at the time of primary infection may be an important determinant of subsequent viral-host "set point" (Redeker et al. 2018). In particular, low viral doses trigger a relatively modest virus-specific immune response and a less differentiated phenotypic profile. In contrast, high doses of initial inoculum drive large and strongly differentiated virus-specific T cell compartments. It is currently unclear if these factors are also important in determining the magnitude of CMV-specific immunity in humans. The heterogeneity of peak viral load at the time of primary asymptomatic infection is largely unknown and certainly has not been correlated with subsequent immune response. Furthermore, a number of studies have shown that this cellular immune response can increase in age in a process termed "memory inflation." Inflation is driven by presentation of viral antigens on non-hemopoietic cells within secondary lymphoid tissues during intermittent episodes of viral replication.

The humoral immune response to CMV is also substantial and antibodies are made against a wide range of CMV proteins. The virus encodes over 160 proteins but many of these are immunodominant for antibody responses. The role of the humoral response in control of viral infection is uncertain, but it appears that antibodies against the pentameric complex glycoprotein H (gH)/gL/pUL128-131 play an important role in viral neutralization. The titer of CMV-specific antibodies increases with age and is also correlated with the magnitude of the cellular CMV-specific immune response.

In addition to an increase in the magnitude of the CMV-specific T cell response in association with aging, alterations in the phenotypic profile of the virus-specific immune response are also observed. In particular, T cells become further differentiated in older individuals and display a strongly cytotoxic phenotype with very high level expression of perforin and granzyme. In addition expression of PD-1, a negative regulator of T cell activation, decreases with advancing age. As such, the profile that emerges is of a gradual increase in both the magnitude and cytotoxic potential of CMV-specific T cells in older people, a pattern shared by both CD4+ and CD8+ T cells. Furthermore, although it has received considerably less attention, it is now clear that CMV infection impacts strongly on the "footprint" of the NK cell repertoire within infected donors. No major alterations are seen in relation to the total number of circulating NK cells, but infection is associated with the relative expansion of cells which express NKG2C, a subset which displays potent antibody-directed cellular cytotoxicity (ADCC) (Costa-Garcia et al. 2015). An emerging concept within cytomegalovirus infection is the extent to which infection with the virus may act to modulate the immune response to heterologous pathogens. Indeed, the expansion of NK cells with such ADDC activity could provide a beneficial effect in a range of infections, and potentially even during malignant disease.

The accumulation of this very substantial virus-specific cytotoxic immune response following infection might be expected to lead to an increase in the "inflammatory" profile of cytokines and chemokines within the vascular system. However, although aging is itself associated with relative increase in inflammation in serum markers, a process sometimes termed as "inflamm-aging," prospective studies have not demonstrated that CMV is a risk factor for this development (Bartlett et al. 2012). A more detailed analysis of how viral carriage impacts on the peripheral proteome will certainly emerge from the increased availability and usage of complex proteomic analysis.

The delicate balance that exists between CMV infection and immunological control in healthy donors breaks down in the setting of immune suppression. The most devastating example of this is seen during primary infection of the fetus in utero. This may occur when the pregnant mother acquires primary CMV infection herself during pregnancy or may reflect a maternal reactivation of persistent virus. The prevalence of fetal infection is typically around 0.4% of births in the developed world, and CMV is by far the most important infectious cause of neonatal morbidity. Indeed estimates have shown that up to 10% of children who acquire a primary infection in utero develop some degree of auditory impairment. In addition, the virus can reactivate in many clinical settings, most notably during therapeutic immune suppression for procedures such as transplantation or cancer chemotherapy. CMV has been an important infectious cause of death following allogeneic transplantation, particularly stem cell and lung allografts, but the improved availability of antiviral medication and early detection through PCR technology have helped limit this burden of viral-mediated disease to some degree.

CMV Infection and Health Outcomes in Older People

The importance of CMV as a risk factor for morbidity and mortality in elderly people first emerged in 2000 in epidemiological studies of octogenarians and nonagenarians in Sweden (Olsson et al. 2000). These investigations revealed that the relative risk of mortality was increased in CMV-seropositive individuals and was, at the time, a wholly unexpected finding. Moreover, the team went on to demonstrate that certain parameters within the immune system, most notably an inverted CD4:CD8 ratio and increased numbers of highly differentiated CD8+ T cells, could act as a correlative "immune risk phenotype" within populations at risk (Wikby et al. 2002). The size of the octogenarian and nonagenarian cohorts was relatively modest, and as such it was difficult to ascertain specific clinical phenotypes that were associated with CMV infection in this group. Nevertheless, the clear correlation with immune phenotype did suggest that this might be related to immunological function. This supposition was reinforced by the emerging studies at that time showing the remarkable magnitude of the CMV-specific immune response in healthy people. However, despite this association, it has been relatively difficult to demonstrate a major increased susceptibility to infectious disease within CMV-seropositive older people.

Not surprisingly, these provocative findings triggered interest in corroborative studies in a wide range of epidemiological cohorts (Wang et al. 2010; Vescovini et al. 2010). Many of these have been supportive of the initial hypothesis although the findings have been somewhat mixed (Table 1). Our own study utilized samples available from the Cognitive Function in Ageing Study (CFAS) cohort (Savva et al. 2013). Serum samples taken at recruitment, at an average age of 72 years, were used to determine CMV serology status and assess how this correlated with mortality over the subsequent 18 years. The findings demonstrated that CMV infection at this age was associated with a 42% increased risk of annual mortality. This was reflected in a 3.7-year reduction in overall survival. Interestingly, this excess mortality within CMV-seropositive donors was due to a near doubling of vascular disease, a category that included heart failure, stroke, and myocardial infarction. In contrast, there was no excess mortality from disorders such as cancer or respiratory disease.

In contrast, a number of studies have failed to demonstrate any significant impact of persistent CMV infection on the health of older people or indeed in murine models (Marandu et al. 2015; Derhovanessian et al. 2013; Matheï et al. 2015).

Cytomegalovirus and Human Immune System Aging, Table 1 Some major publications on the association of CMV infection with health outcomes in older people

Manuscript	Setting	Outcomes
Olsson et al. (2000)	80-year-old subjects in Sweden	CMV was associated with inversion of the CD4:CD8 ratio which had previously been correlated with increased 2-year mortality
Roberts et al. (2010)	1468 older Latinos aged 60–101 years in California	All-cause mortality 1.43 times higher over 9 years in the group with the highest quartile of CMV-specific antibody titer
Savva et al. (2013)	511 donors of mean age 74 years in UK Midlands	CMV infection increased the annual mortality rate by 42% with 3.7 year reduction in life span. Doubling of cardiovascular mortality
Adriaensen et al. (2017)	235 individuals aged 81 years or older in Belgium	All-cause mortality increased 1.5-fold among women with every increment in the CD4:8 ratio from <1 to $1 < 5$ and to >5. Mortality rate for CMV-seropositive women was reduced by 50%
Derhovanessian et al. (2013)	50 participants of the Leiden 85-plus study	Low frequency of CD8+ naïve T cells and a pro-inflammatory response to CMV correlated with longer 8-year survival

Indeed, there have even been suggestions that CMV may act to support immune function in selected populations. A striking finding was observed in the Belfrail cohort of people over the age of 81 years where CMV infection was seen to decrease mortality risk in women by 50% (Adriaensen et al. 2017). The story that emerges is one of a complex interplay of viral infection with clinical consequence, and this is likely to reflect the interaction of determinants such as the nature and timing of primary infection, viral sequence, host genotype, and environmental factors (Cudini et al. 2019; Goldeck et al. 2016; Misra et al. 2015). As such, any potential consideration of medical therapy directed against viral replication will need to address the population at risk.

CMV Infection May Potentially Confer Beneficial Effects to the Host

Given the clinical importance of CMV infection in patients with immunodeficiency, it is perhaps not surprising that consideration of its impact in healthy immunocompetent donors has focussed largely on negative associations. In contrast, there is now increasing evidence that CMV carriage can confer beneficial effects upon its host.

An interesting example is observed in the relationship of herpesvirus status on the immune response to childhood vaccination in sub-Saharan Africa (Holder et al. 2010). Here, CMV infection was not associated with any detrimental effect on the vaccine response to meningococcal polysaccharides or measles. In contrast, EBV-seropositive children demonstrated reduced antibody responses to both antigens, but those who were also co-infected with CMV infection recovered a robust immune response to measles. As such this suggests that the response to T cell-dependent antigens such as measles hemagglutinin may be restored by infection with CMV. In addition, the important work of Furman and colleagues revealed that persistent CMV infection had a clear positive influence on the titer of the humoral response to influenza vaccine challenge in younger people (Furman et al. 2015). This effect was most pronounced in those aged <44 years, within reproductive age, and as such the data suggest that this beneficial effect may act as an evolutionary mechanism of positive selection to support the maintenance of the virus within the population. Studies in older groups had revealed a potential impact of CMV infection on the response to influenza vaccination (Trzonkowski et al. 2003), but this has not been seen in all reports (den Elzen et al. 2011; van den Berg et al. 2018; Miles et al. 2019).

These encouraging associations with vaccine responsiveness have led to interest in a potential association of CMV carriage with the immunological control of cancer. This would certainly appear to be a credible concept as inflammatory Th1 immune responses appear critical in cancer control and are strongly matured following CMV infection. Potential mechanisms might include maintenance of the balance of M1 inflammatory macrophages within the tumor microenvironment, bystander activation of neoantigen-specific T cells, or maturation of NK cells with direct tumor-specific activity. Interrogation of this association will require large-scale epidemiological studies, but to date no such association has been confirmed.

The mechanisms that underlie this positive effect on immune function are not clear but are likely to be dominated by bystander effects, potentially due to systemic alterations in serum cytokines and inflammatory mediators (Pera et al. 2014). CMV carriage is associated with increased levels of IFNγ in younger people but it was noteworthy that this association was not observed in older people (Furman et al. 2015). As such this again suggests an age-related effect on the immunological consequence of CMV serostatus.

Examples of Application

CMV and the Development of Vascular Disease

The increased risk of vascular disease in association with CMV infection has driven investigators to interrogate the pathological basis for this association (Strandberg et al. 2009; Simanek et al. 2011). The vascular endothelium is a major site of viral tropism although the specific cellular targets for viral infection remain unclear. As indicated earlier, the vascular system is the most important anatomical site for CMV-specific T cells and as such it is conceivable that the clinical complication of vascular disease could reflect immunopathology resulting from immune-mediated control of virally infected cells (Smith et al. 2014).

Studies are now revealing a link between persistent CMV infection and stiffening of arteries and arterioles. This process, termed *arteriosclerosis*, is associated with decreased elasticity of blood vessels and consequently faster transmission of the pulse wave through the arterial tree. Increased pulse wave velocity (PWV) is a risk factor for cardiovascular disease and is likely to reflect decreased "buffering" of the systolic pulse wave and impaired perfusion of cardiac tissue during diastole. CMV infection is correlated with increased pulse wave velocity, a finding that is particularly pronounced in patients with impaired renal function, a group that is known to suffer quite markedly from arteriosclerotic pathology (Wall et al. 2013; Yu et al. 2017). Increased cellular immune responses to CMV have also been correlated with vascular stiffness. Of note, a study performed with the Lothian cohort indicated that CMV infection was associated with a 3 mmHg increase in systolic blood pressure in healthy volunteers aged over 70 years (Firth et al. 2016). This increment might appear relatively modest but in fact would be predicted to increase the risk of stroke by over 20%, and, as such, it is possible that CMV-induced hypertension may begin to explain some of the impact of the virus on impaired health in elderly populations (Bolovan-Fritts and Spector 2008; Cheng et al. 2009).

Attempts to Control the Impact of CMV Infection on the Health of Older People

A considerable body of data now indicates that CMV can act as an important environmental determinant of health problems in certain elderly populations. As such, there is interest in the development of therapeutic approaches that may help to overcome this. At the current time, it is impossible to eradicate CMV following initial infection, although the remarkable success of antiviral therapy targeting hepatitis C infection does bring confidence that this may become possible in the medium term. Vaccination against CMV is an important ambition, primarily to prevent primary infections within the fetus, but would also act to reduce the burden of viral infection within older donors over time. The importance of vaccination to boost endogenous immune responses in patients with established infection is less clear.

Antiviral therapy is certainly one consideration as a means to improve immune function. Experience from HIV infection has shown robustly that reduction of viral load does lead to a subsequent reduction in the magnitude of the antiviral cellular immune response, and this is likely to reflect diminished reactivation of established memory responses. Experience with murine models has shown that vaccination can markedly suppress CMV-specific immune responses, but treatment does need to be given for prolonged periods, possibly as a reflection of the longevity of CMV-specific T cells (Beswick et al. 2013). Our own experience with using antiviral drugs within healthy donors over the age of 65 years has shown that relatively high doses of medication over periods of 6 months are not associated with significant falls in virus-specific T cell responses. Potential explanations here may include relatively limited activity of such medication against CMV, or the very long half-life of survival for virus-specific populations. Nevertheless, in patients on immune suppression, in whom viral reactivation is more common and frequent, such antiviral treatment has been shown to reduce both the virus-specific cellular and humoral immune responses, with associated improvements in vaccine response and pulse wave velocity (Chanouzas et al. 2019).

Future Directions of Research

Although several studies have shown that CMV infection may represent an important risk factor for increased morbidity and mortality in older people, there remain many questions that need further investigation. The fundamental nature of the relationship between viral replication and the immune system is unclear, and it is important that we begin to understand the breadth of tissue sites of viral infection and also the specific role of the different arms of the CMV-specific immune response. The clinical consequences of persistent infection in older people appear to vary markedly in different populations, and large epidemiological studies are needed urgently in order to delineate the critical factors that may underlie this heterogeneity. These investigations should focus on viral and host genetic diversity, the nature and magnitude of the primary infection, and the importance of environmental determinants. The clinical phenotype of CMV-associated morbidity during aging requires further definition, and the nature and pathobiology of vascular disease remain uncertain. Finally the potential utility of antiviral drugs, and in particular the range of novel agents that are now becoming available, should be investigated in studies of older people who are at risk of CMV-associated health problems.

Summary

Cytomegalovirus is an extremely common and persistent infection, and although the virus is well tolerated in healthy people and can even boost immune function in early life, it may become a health concern in some populations of older people. Individuals with a particularly strong CMV-specific immune response, reflected in an inverted CD4:CD8 ratio and high antibody levels, appear to be at particular risk, and here approaches such as antiviral medication may represent a novel therapeutic approach to improve and extend life span.

Cross-References

▶ Aging and Cancer
▶ Human Immune System in Aging
▶ Hypertension
▶ Immunological Theory of Aging
▶ Influenza Vaccination in Older Adults
▶ Prevention of Age-Related Cognitive Impairment, Alzheimer's Disease, and Dementia
▶ Vascular Diseases of Ageing

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