

Chapter 11

Dementia



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1 Worldwide Trend of Dementia

The number of people living with dementia worldwide is rising rapidly. Dementia is considered to be one of the greatest global challenges for health and social care in the twenty-first century. The condition is associated with physical, psychosocial, and economic burdens on individuals and society [1, 2], and is one of the principal causes of disability and dependency among older populations. It is a significant public health issue not only in Japan but all over the world, given the growing incidence and high prevalence rate, primarily due to global aging. It is reported that about 47.5 million people were living with dementia in 2015, and the number is projected to reach 65.7 million in 2030 and 115.4 million by 2050 worldwide [3]. Another estimate speculates that dementia patients will increase to 75.6 million by 2030 and reach 135.5 million by 2050 [4]. Furthermore, following the World Alzheimer Report 2018, the projection was revised upwardly and reached 50 million in 2018, 82 million in 2030, and 152 million in 2050 [5]. The total estimated global cost of dementia was US\$818 billion in 2015, which is an increase of 35.4% over the estimates of previous years, and the global cost of dementia is expected to continue to increase [4]. About 85% of dementia costs are related to family and social care rather than medical costs. Dementia affects not only an individual but also the wider range of family, the community, and society in general; people

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affected by the disease lose potential opportunities to participate socially and economically and require health and social care.¹

1.1 *Dementia in Japan*

Japan is one of the most rapidly graying societies in the world. Based on national statistics, the Ministry of Health, Labour and Welfare (MHLW) estimated the number of older people (those aged 65 years and over) living with dementia as 4.62 million in 2012 and another four million were estimated to have symptoms of mild cognitive impairment (MCI). However, the estimated prevalence rate varies depending on the data sources. A public long-term care insurance database estimates the prevalence of dementia patients among the over 65s as, 9.5% in 2010 and 12.8% in 2025. Those included in the estimated were people with a clinical diagnosis of Grade II-a or higher according to the national standardized long-term care insurance evaluation system. This number is 2.80 million in 2010 and predicted to be 3.45 million by 2015 and 4.70 million by 2025. The evaluation method of the long-term care insurance system uses information on physical, cognitive and social conditions including the availability of care resources for the patient. Details of the system are reported in a validation study examining identification of dementia diagnosis and evaluation in the public long-term care insurance system [6]. A synthesis for the findings from Japanese population-based studies suggested an increasing trend for dementia prevalence [7–13]. Among them, the Hisayama study only reported the long-term trends for age-standardized dementia prevalence of 6.8% in 1985, 4.6% in 1992, 5.3% in 1998, 8.4% in 2005 and 11.3% in 2012 in a rural community with a population size of around 8000 [7]. The trend for dementia in representative samples of Japanese, however, remains to be clarified.

Among global figures, it has been reported that age-specific new dementia incidences have declined in the past few decades in some high-income western countries, including the USA, France, Denmark, the Netherlands, Sweden, and the UK [14–20]. In 2013, the Framingham Heart Study [17] reported that age-specific incidence rates of dementia had decreased by almost 20% in the past three decades. These days, a limited number of countries have reported a sharp increment in the age-specific incidence rate among high-income countries. Japan, however, has not reported a decreasing trend of age-specific incident cases. Moreover, a review on 14 studies that investigated trends in dementia prevalence (nine studies) and incidences (five studies) from high-income countries suggested that except for the Japanese study, most of the studies indicated stable or declining trend of new incidences of dementia [15]. This may be due to different trends in dementia occurrence, or it may relate to

¹In this chapter, we used the term ‘dementia’, which derives from the Latin words ‘De’ (= out of) and ‘Meus’ (= mind). In DSM-5 (Diagnostic and statistical manual of mental disorders, version 5) the term ‘dementia’ has been replaced by ‘Major neurocognitive disorders’. However, in this chapter, we used ‘dementia’ based on its familiarity and its frequent use in the literature we reviewed.

different sources of data, diagnostic methods and changing criteria of dementia evaluation, which requires further examination.

At the same time, these findings of decreasing trend of age-specific incidence rate in some countries may suggest that dementia among the population can be preventable by targeting a number of modifiable risk factors. Some of the significant individual levels of behavioral and psychosocial changes and/or societal improvements in living conditions, including education, occupation, and healthcare conditions might be related to reduced risks of dementia incidence.

1.2 The Cost of Dementia

The transition phase during which a society from ‘aging’ ($7\% \geq 65+$) to ‘aged society’ ($14\% \geq 65+$) is considered to be a period in which preparation can be made for the infrastructure and social security systems to support an older population. Japan only took 24 years to become an aged society, while other European countries took a longer period; for example, 115 years in France or 45 years in the UK. However, other East Asian countries will take an even shorter time than Japan: 18 years in Korea and 20 years in Singapore to reach an aged society. Achieving preparedness for a dementia-friendly society is more difficult in those rapidly aging countries and the role of prevention is becoming increasingly important.

The World Alzheimer Report [21] pointed out that two-thirds of dementia patients currently live in low- or medium-income nations (Fig. 11.1), and these countries are expected to see a sharp increase in the number of such patients. In 2010, the total global societal costs of dementia were estimated to be US\$ 604 billion, 818 billion in 2015, 1 trillion in 2018 and 2 trillion by 2030 [22]. This

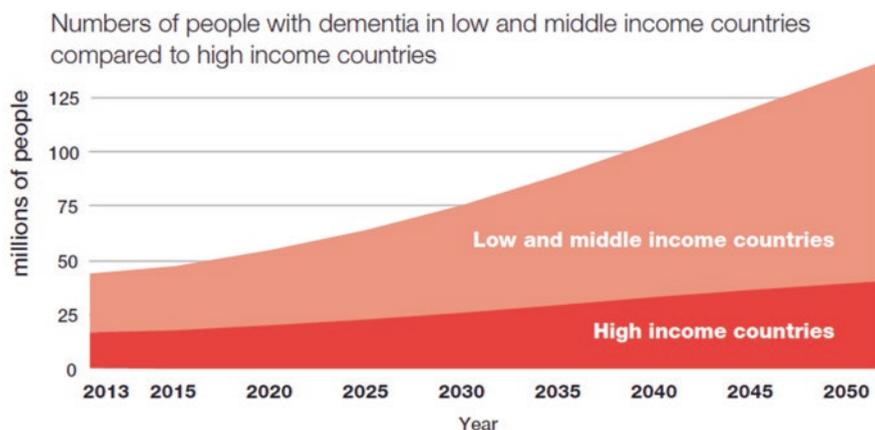


Fig. 11.1 Increasing numbers of dementia patients in high-income, and medium- to low-income countries. (Source: World Alzheimer report, ‘The Global Impact of Dementia 2013–2050’, *Alzheimer’s Disease International*)

corresponds to 1.0% of worldwide gross domestic product (GDP) in 2010, or 0.6% if only direct costs are considered. The Japanese government reported the annual cost for medical and social care for dementia in 2014 to be 14.3 trillion Japanese yen which is 3% of Japanese GDP. Of these, the costs for healthcare, long-term care, and informal care are 1.91 trillion (se 4.91 billion), 6.44 trillion (se 63.2 billion), and 6.16 trillion (se 12.5 billion) Japanese yen, respectively. It is expected to increase to 24.3 trillion in 2060. The cost per person with dementia appeared to be 5.95 million (se 27 thousand) yen in 2015 [23]. If these estimates are accurate and 60% of dementia patients worldwide require care in developing countries, serious problems will emerge because the medical and social security systems in such countries are not yet able to support this number of advanced dementia patients.

It is important to understand the determinants of dementia from the perspectives of social determinants of health (SDH) to prevent the onset of disease and to minimize disparities in healthy aging among the older population in societies facing an era of worldwide aging.

2 Health Disparities in the Onset of Dementia Based on Socioeconomic Factors

Livingston et al. [3, 24] suggested that around 35% of dementia cases are preventable and attributable to a combination of modifiable lifestyle-related factors. These include early determination of education (at age 11 or 12 years), mid-life hypertension, obesity, hearing loss and later-life depression, diabetes, physical inactivity, smoking, and social isolation. On the other hand, unmodifiable factor, a well-known major genetic risk factor, including Apolipoprotein E (ApoE) $\epsilon 4$ allele [25, 26] is calculated to be related to a 7% of dementia cases based on a weighted population attributable fraction calculation [3, 27].

In 2018, the World Health Organization issued lifestyle guidelines to reduce the risk of dementia. It emphasized the basics of regular exercise, eating a balanced diet, stopping smoking, drinking in moderation, and staying socially and intellectually active. Furthermore, control of body weight, maintaining healthy blood pressure, cholesterol and blood sugar levels are suggested to be important factors related to dementia incidence.

Among the risk factors regarding social determinants of healthy aging, it is important to understand the socioeconomic background and its association with the incidence and prevalence of dementia, as it is strongly connected with lifestyles and elevated biomarkers. In this chapter, we review the relationship between onset of dementia and socioeconomic status (SES), which includes educational attainment, length of education, occupation, income, parents' educational history, and income level during childhood. Although some studies [28, 29] have found no association between SES and dementia onset, most have concluded that a disadvantaged SES is associated with increased risk of the onset of dementia including both Vascular dementia (VaD) and Alzheimer's dementia (AD) [30–36].

2.1 *Education and Risk of Dementia*

Researchers have long discussed the relationship between shorter education and higher risks of incidence and prevalence of dementia including its mechanism of occurrence. Meta-analysis of 13 cohort and 6 case-controlled studies concluded that a shorter period of education is associated with higher risks of developing dementia [37]. Those with a shorter education had a 1.59-fold greater relative risk of developing dementia than those with a longer education. This relative risk came from a 1.80-fold higher risk of Alzheimer's dementia (AD), and a 1.32-fold higher risk of non-Alzheimer's dementia. A pooled analysis of four European countries in the EURODEM Study (16,334 subjects) showed that a shorter education (8–11 years and less than 7 years) indicated a higher risk of developing dementia than those with 12 years or more education [38]. However, the results showed gender differences. For women, the findings suggested that compared with a longer education (12+ years), those with a middle-level (8–11 years) have a 2.5-fold greater risk, and those with a shorter education (up to 7 years) have a 3.8 times greater risk of developing all types of dementia. Considering the risk of developing AD in women, those with a middle-level education showed a 2.6-fold greater risk relative to longer education, while women with shorter education showed a 4.3-fold greater risk. However, no such association was observed in men [38]. Reports from the studies included in this research, such as the PAQUID project [39] and the Rotterdam Study [40], and the findings of previous studies in various countries, including Canada [41], Sweden [42, 43], USA [44, 45], and Italy [46], indicated that although the results on gender differences were inconsistent, most cohort studies showed that a shorter education indicated higher risk of dementia. A follow-up survey that targeted 3623 older people living in Massachusetts, USA, reported that for every 1-year increment in length of education, the risk of developing AD decreased by approximately 17% [44]. Recent studies also showed an association between duration of education and incidence of dementia after considering competing risks of death and onset of other diseases [47].

The association between length of education and the risk of dementia onset has also been reported in Japan. For example, both the Adult Health Study conducted by the Radiation Effects Research Foundation [13], and the Hisayama Study [48], have shown an association between shorter education and elevated risks of dementia incidence and prevalence. The results from the Hisayama study were introduced as a government report on the prevalence of dementia, and risk factors for dementia incidence in Japan. The Osaki-Tajiri Cohort Project [10] and the Japan Gerontological Evaluation Study (JAGES study) [49–51] showed that shorter education was associated with a higher risk of dementia. A number of other studies from Asian countries [52–54], have also reported on the relationship between length of education and incidence of dementia.

2.2 *Occupation, Income, and Other SES with Risks of Dementia*

Sociodemographic background other than the length of education, such as occupation, subjective and objective income level and, childhood SES also showed an association between risk of cognitive function and onset of dementia in various countries [34, 35, 38, 42–44, 53–55]. Qiu et al. [42] reported that manual labour, such as working on a factory production line, increased the risk of developing dementia. Occupation comprises several aspects which affect cognitive function, for instance, social status, economic status, psychosocial stress related to autonomy and reward-demand balance, work-life balance, work-family conflicts, complexity of the work, mentally challenging activity as cognitive stimulation, and exposure to certain environments including hazardous substances. The PAQUID study conducted in France reported that the risk of developing dementia was higher in female agricultural workers than in female specialists and/or managerial workers [56, 57]. Research by Evans et al. [44] showed that individual SES components including short education, limited income and low-status occupations were associated with increased risks of developing AD. After mutually controlling for those three components, only length of education was independently associated with incidence of AD. Likewise, research by Karp et al. [43] reported that if mutual influence was taken into account, length of education showed an independent relationship after adjusting for occupation and income, but neither occupation nor income showed an independent association. As a part of socioeconomic status, length of education showed an independent association with onset of dementia and the association cannot be fully explained by occupation nor income. Occupation showed association with risk of dementia based on the psychosocial factor of works, including complexity, challenges, control possibilities, and social demands at work [58–60]. Moreover, Karp et al. [43] stated that the relationship between length of education and the onset of AD could be explained by occupation after reaching adulthood, and suggested that other factors during early childhood, middle life, or early old age may have different effects on the onset of dementia throughout the life-course. In 2017, the Health and Retirement Study (HRS) compared various SES indicators including length of education, parental education level and individual income and their association with late-life memory performance and decline. That study showed a significant association between cognitive decline and individual income levels [61]. In terms of other aspect of SES, the English Longitudinal Study of Ageing (ELSA) reported that the index of multiple deprivation was associated with cognitive performance in older age independently of individual levels of education and SES [47, 62]. However, findings from the Seoul Dementia Management Project suggested that individual SES level contributed more to the development of cognitive impairment than district-level SES [63]. Discussion of area-level socioeconomic condition and individual SES and their association with cognitive decline and the onset of cognitive impairment remains ongoing [64].

2.3 Hypothesis on the Influence of Social Factors on Dementia Onset

There are several hypotheses regarding the relationship between SES and dementia. One of these is the cognitive reserve theory, and another, the brain battery theory [65–67]. The cognitive reserve theory was advocated by Katzman [68] and expanded by Stern [65] and is related to the influence of social determinants at a relatively early life stage. One of the arguments on the hypothesis is that education determines a person's ability to acquire accurate information and knowledge, which helps enhance cognitive function and keep it at a relatively high level, even when it declines in the later stage of life. High education, occupational work complexity, as well as a mentally and socially integrated lifestyle in late life could work as cognitive reserve factors and postpone the onset of clinical dementia and Alzheimer's Disease [67]. Furthermore, a higher level of education encourages individuals to adopt a healthier lifestyle which helps maintain cognitive function. This process happens through individual behavior and decision making, rather than securing a lifestyle associated with living circumstances with social status and elevated income level. This hypothesis supported the results shown by Karp et al. [43] who indicated that educational attainment was associated with the risk of dementia independently of social status or income. In his brain battery theory, Del Ser [57], argues that better education is associated with high income and high social status, since individuals with a higher education level will work in occupations that have little or no exposure to hazardous substances and enjoy better access to medical resources and healthier lifestyles. Ultimately, this will have both long-term and short-term health benefits.

Although discussions on the mechanisms have yet to reach a conclusion, a review of previous research appears to show that socioeconomic conditions influence the onset of dementia as an undisputable risk. We will next examine the possible pathways and countermeasures that target dementia. Similar to the other non-communicable diseases, it is important to understand the accumulating effects of individual behaviors and decision makings process influenced by the environment from the perspectives of the social determinants of health for effective prevention.

3 Disparities Related to Cognitive Health

The pathways to developing dementia and its countermeasures vary according to the types of dementia. Contributory factors to the development of dementia such as hypertension, obesity, type-2 diabetes, and hyperinsulinemia in middle and older age have been reported to have different effects on different types of dementia [69]; for example, Vascular dementia (VaD), Alzheimer's dementia (AD), Lewy Bodies (DLB) and others. However, sociodemographic factors have been reported to be risk factors for most types of dementia. Socioeconomic status and social disparities are argued to be related to the risk of dementia and unhealthy aging in the later stages of life. It is important to examine a broad range of primary, secondary and tertiary prevention measures to reduce the risk of dementia onset.

3.1 *Material and Information Disparities*

Researchers have discussed the pathways by which absolute and relative socioeconomic conditions affect individual health directly and indirectly: the materialist and the psychosocial pathways. The materialist pathway anticipates situations in which material deprivation relates to socioeconomic background. Conditions of deprivation can limit access to health resources such as healthy behaviors including diet and physical exercise, health screening and medical treatment [70]. A vulnerable group can also have difficulty in accessing accurate information and may suffer double or triple inequalities. Geographic and built environment can influence or design people's behavior and cognitive decisions. For example, 'walkability' [71] in the community may affect physical and cognitive health via difficulties in accessing shops that stock healthy food and in reaching a safe environment for physical activities and social interactions [72–74]. In order to support people in making healthier choices for physical and cognitive health, the following actions will be important; 1) Removing environmental barriers 2) Minimizing budget constraints 3) Improving information asymmetry 4) Leveraging social reinforcement 5) Designing individual behavioral plans 6) Constructing networks and build social capital. These approaches can be conducted on three levels: the individual, the community, and societal and policy levels.

It is anticipated that solutions to these structural or environmental disparities, will be generated through population-based approaches [75]. These may include imposing taxes on tobacco products and unhealthy foods [76], rather than approaching high-risk individuals and encouraging them to transform their behaviors by their own effort. For example, according to the results of a review of over 160 papers [77], raising the price of soft drinks by 10% causes consumption to fall by 8–10%. Further, a 20-year accumulation of data from the CARDIA Study showed that in the case of soft drinks and pizza, caloric intake decreased as price increases. When the price of these products was increased by \$1, total caloric intake decreased by 124 kcal, body weight by 1.05 kg, and glucose tolerance, according to HOMA-IR scores, by 0.42 points [78, 79]. Altering environments to support unconscious healthier choices of irrational individuals is important. Instead of expecting an individual to make rational behavioral change, attempts are being made to use behavioral economic theories and environmental changes, it is hoped, to be more effective [80]. If Goffman's frame analysis theory were incorporated, re-capture of existing frameworks would become necessary [81]. Kahneman [82] has pointed out that individual actions and behaviors are determined by two systems: 'System 1', based on intuition, and 'System 2', based on rationalization. Provision of existing health information and offering health education are System 2 approach oriented that work on cognitive understanding and justify behaviors based on rational thought. To change unhealthy behaviors that people already know are bad behavior, but cannot stop doing, it is important to build methodologies that act on the sensory and awareness frames, as well as the cognitive understanding frames. As part of their advertising strategies, tobacco companies and fast-food industries spend huge amounts of money to work on the sensation of pleasure–displeasure, as well as operating at the unconscious level. On the other hand, in terms of public health measures, the key tactic is to work at the cognitive level, for example by providing accurate information, based on the

results of epidemiological research on, say, the link between smoking and the high risk of developing lung cancer. With the latter method, however, differences in effects are seen; the technique is most effective among people with more education and in groups of people with a strong interest in health. Therefore, this technique has a risk to worsen health disparities. It is thus deemed imperative to recognize that there are disparities in people's access to socioeconomic resources, including information, and carry out health education and anti-poverty measures as a prelude to increasing basic opportunities, and to implement programs designed to narrow socioeconomic gaps.

Regarding social policies such as those related to education systems, Lynch and Kaplan [83] state that educational attainment is largely determined by the environment in which an individual is raised, and that it acts as an indicator when the individual moves from the socioeconomic background of their upbringing to new social and financial statuses which they themselves acquire. Considered from the perspective of life course epidemiology, a person's educational level, income, and occupation appear to influence different aspects of his or her life at different time points [27, 54, 61, 84, 85].

Many studies on occupation and income focus on a person's first job, as well as the longest held. However, it is necessary to study the different influences exerted by occupations and incomes during various life periods [61, 84, 85]. For example, the increased risk of developing AD attributable to high blood pressure and obesity was more strongly related to having these conditions during adolescence and midlife than in old age [86–88]. Enhancing educational opportunity is also likely to be significant in preventing dementia; although some researchers pointed out that emphasizing better education may counter-intuitively cause wider social gaps [89, 90]. Research suggests that a longer education reduces risks. However, improving public education during early childhood and supporting the rearing environment in infancy, rather than promoting higher education in adults, appears to guard more effectively against future dementia. Opportunities of higher education in adulthood can be effective for dementia prevention as it promotes social engagement and brain stimulation at a later stage of life. On the other hand, environment in infancy is a key factor in the development of person's physical, mental and cognitive health status in midlife and old age. For dementia prevention, treatment and care, early life and mid life support are important as well as old age interventions. There will inevitably be a considerable lag between the adoption of new policies including education and economic programs and the time when the affected persons reach old age. It will thus be necessary to monitor and evaluate the effects of these policies, taking the time axis into consideration.

3.2 Psychosocial Influences

According to psychosocial theory, there are routes from stress to illness: direct and indirect [91]. Even in countries where little or no absolute poverty exists, stress and psychological ill health caused by relative deprivation can be harmful to physical

and cognitive health. A sense of social solidarity and consensus to invest in wealth redistribution may relate to avoid widening the disparities and the fixing of a person's ranking within a societal group. In a society where the haves and the have-nots are clearly delineated, a state of stress is likely to occur and persist as people compare themselves with those around them and find that they cannot obtain goods and services that should be within their reach. Psychological stress that comes from a sense of deficiency and dissatisfaction indirectly encourages unhealthy behaviors such as drinking and smoking, which worsen an individual's health status [92]. One study has also shown that stress increases the ingestion of sweets and high-salt, high-fat foods, although gender differences are seen [93]. A relationship between stress and obesity/diabetes, hypertension, cardiovascular disease and mortality is well reported [92, 94–98]. Researchers similarly point out that prolonged stress and accumulated allostatic load lead to the development of mental diseases such as depressive symptoms and suicide [99, 100]. Depressive states are also shown to increase the risk of dementia [101–103] and cardiovascular disease [104–106].

In addition to indirect influences mediated by unhealthy and risky behaviors, stress is known to exert a direct influence on the body. Stress cause the human body to accelerate or slow the action of the autonomic nervous system, endocrine system, and immune system [107, 108]. As a result, a variety of pathological responses can be observed, such as the elevation of blood pressure and blood sugar, a rise in blood aggregation capability, an increase in vascular load, a reduction in intestinal function, and a decline in immune function. The Whitehall II study shows that extended stressful states trigger inflammatory reactions, the progression of arteriosclerosis, and an increase in the risk of hypertension and coronary heart disease [98]. Countering stress is also thought to be a key factor for preventing the onset of dementia.

Folkman and Lazarus [109] used a two-stage stress source assessment and pointed out that identical events and challenges may or may not become a source of stress. It depends on an individual's coping strategy, empirical values and the quantity and quality of support resources available to them. Support resources include an individual's social network, social support and social capital in the community and workplace. Along with support resources that can be externalized, an individual's internal resources have also been noted. It has been reported that in addition to self-efficacy and self-esteem, an individual's ability to cope with stress through, resilience factors including optimistic personality traits, the ability to enjoy life, and positive emotions or so-called psychologically positive health resources, can alleviate the adverse effects of acute and prolonged stressors [108]. The accumulated effects of being loaded with stressors increase allostatic load [99]. These psychological traits and states are related to reducing the incidence of, and mortality from, cardiovascular disease [110–113] and dementia [114, 115]. Creating an environment that can readily foster rich social connection, positive emotions and enhance stress-coping skills may be an important measure for preventing dementia.

3.3 *Social Participation and Social Activities*

Social relations, social participation, and active engagement with society are one of the key components to maintaining the cognitive health of the older population. A meta-analysis examining social activity and dementia found that risk of incident dementia is elevated among people with lower participation in social activities (RR:1.41, 95%CI:1.31–1.75), and less frequent social contacts (RR:1.57, 95%CI: 1.32–1.85) [116]. Considering the ways that older people can participate socially and actively engage in life through social activities and creating forums in which they can play an active role may also be an important factor in reducing the risk of dementia. In the current literature on this topic based on the JAGES study which surveyed more than 100,000 older people in Japan, Saito T (2017) reported that diversity of social networks and support resources are related to a lower risk of dementia [117]. Nemoto M (2018) suggested that holding a responsible role in the occasion of social participation is related to a lower risk of dementia and loss of healthy life expectancy [118]. Takeda T (2010) has also reported on the relationship between older people's participation in hobbies and leisure activities and a reduced risk of developing dementia [119]. 'Silver human resources center' in Japan are public facilities that support older people's employment in order to support a sense of '*ikigai*' (*sense of life worth living, or purpose in life*), rather than financial gain. Such employment service centers for older people have been introduced internationally and are being adopted in some countries, learning from Japan's experience in order to support successful aging [120]. It has also been recognized that loneliness and social isolation are key factors for increased risk of declining cognitive and physical health [121]. In 2018, the UK government added the role of 'Minister for Loneliness' to the remit of the Minister for Sport and Civil Society, to tackle the problem of isolation in the UK. Social services and programs targeting the older population in Japan have mostly focused on providing support for the older people by positioning them as recipients of support. However, in the super-aged society, the idea of older population as providers of services and schemes to support people in care needs by older population in the community is gaining ground. Old and young generations in the community can work as community designers as well as service providers together to support people with dementia in the community. The diversity and heterogeneity of the older population have been increasing. People aged 65 years and over are entitled to receive social security benefits and referred to as 'older people' in the Japanese system. However, the roles they are expected to play in the society and in the community have been dramatically increased, and understanding the potential contribution of the older population themselves to constructing a dementia-friendly environment is one of the keys to providing support and preventing dementia in the community. According to the concept of 'productive aging' proposed by Butler [122] in 1985, having a place for older people to carry out activities, and having a role for them to play in the society, encourages them to 'adapt themselves to their own aging', will contribute to realizing a better 'aging in the society'. It is reported that among older people, they do not

only receive support but also provide it for others and that engaging with these two aspects of support in a well-balanced manner reduces an individual's risk of developing dementia [117, 118, 123, 124]. At present, services and programs for dementia prevention and treatments are implemented based on the "Comprehensive Strategy to Accelerate Dementia Countermeasures (New Orange Plan)" in Japan established by the Japanese Government in January 2015. And the establishment of the integrated community care system for a sustainable social security system is essential in Japan. Kondo and Hirai [125] pointed out the importance of the broader population approach in the community.

As a measure for coping with older people who require long-term care, it is essential to reinforce both the formal and informal long-term care support systems. From the perspective of prevention, encouraging participation in social activities such as engaging in community salon which targets older people, encouraging them to participate, become community volunteers and working broadly to establish a society in which older people can play active roles may be generally adopted as measures to counter dementia in a super-aged society.

4 Social Determinants of Health and Dementia Prevention

This chapter attempted to provide an overview of research which examines the relationship between socioeconomic background and dementia. However, numerous researches and societal challenges remain undiscussed regarding the identification of social determinants of healthy aging.

In order to tackle the issue of dementia, collaboration among the health, medical, and welfare sectors are important when we consider relationship between prevention, treatment, and long-term care. Dementia countermeasures must be discussed not only in the medical and public health sector, but in the context of a broad range of social policies such as education, employment, economy, social participation, and the creation of *'ikigai'* among the older population. Through our review of the literature and discussions in this chapter, the perspective of social determinants of health (SDH) was discussed as an important part of these multifaceted dementia countermeasures.

Challenges concerning SDH and dementia are likely to become the touchstones for realizing a sustainable society in today's Japan, in which we aim to ensure mature social growth and development. Life-course perspective that spans from infancy, middle age to old age is also important to understand dementia. The relationship between early years deprivation and later non-communicable diseases (NCDs) in developing countries has been attracting increased attention in recent years; for example, we are increasingly aware that children who suffer from poor nutrition during infancy have an increased risk of developing obesity and cardio-metabolic disease in middle to old age. Moreover, adverse childhood experiences were reported to be associated with an increased risk of dementia among older people [126, 127]. For

dementia prevention, securing education and a healthy environment in childhood, and mentally and socially integrated lifestyle in late life could be both important as cognitive reserve factors. In other words, closing the disparities gaps that begin in infancy and focusing on lifestyle-related diseases are regarded as essential strategies for enhancing indexes of health in middle and old age, and for improving quality of life. We consider measures against dementia not as a medical challenge but rather as a complex challenge that society must meet from a SDH perspective. In addition, with a sharp increase in the number of dementia patients predicted in low- to medium-income nations in the coming years, Japan, as an advanced nation in terms of dementia prevention, treatment and care, will be expected to play an important role in the international community.

The perspective of SDH is essential for Japan, a super-aged society, to create a sustainable society and is increasingly needed worldwide.

5 Summary

Dementia is a significant public health issue in Japan and throughout the world. It is a major challenge for governments and policymakers given its growing incidence and high prevalence rate, primarily due to population aging worldwide. It is one of the principal causes of disability and dependency in the later stages of life, and is associated with physical, psychosocial, and economic burdens on individuals and society. However, several papers, especially from high-income countries, have reported declining trends in age-specific incidence rates of dementia cases [15–18], although the total number of dementia patient has sharply increased worldwide. Moreover, a Lancet commissioned paper suggested 35% of dementia cases are preventable. Modifiable risk factors for dementia include short education in early life, hearing loss, hypertension, obesity in midlife, smoking, depression, physical inactivity, social isolation, and diabetes in late life [3]. Specifically, education, smoking, physical activity, diabetes are reported as a modifiable risk factor related to the cognitive decline and dementia in several large cohort studies [128]. This chapter mainly reviewed the association between SES including the length of education and risks of dementia incidence and prevalence as one of the major social determinants of healthy aging. Further investigation is required to examine modifiable factors which may prevent dementia in Japan and the rest of the world. Also, the establishment of reliable evidence to understand dementia and to construct systems to support current and potential dementia patients and their families in society are required.

Acknowledgement The authors are grateful to Professor Ichiro Kawachi for his inspiring lectures and fruitful suggestions at T.H. Chan Harvard School of Public Health (HSPH) for this chapter. Original manuscript of this chapter was written during a research period in the HSPH as a research fellow.

References

1. Scholzel-Dorenbos CJ, Ettema TP, Bos J, et al. Evaluating the outcome of interventions on quality of life in dementia: selection of the appropriate scale. *Int J Geriatr Psychiatry*. 2007;22(6):511–9.
2. Tariq S, Barber PA. Dementia risk and prevention by targeting modifiable vascular risk factors. *J Neurochem*. 2018;144(5):565–81.
3. Livingston G, Sommerlad A, Orgeta V, et al. Dementia prevention, intervention, and care. *Lancet*. 2017;390(10113):2673–734.
4. Prince M, Ali GC, Guerchet M, et al. Recent global trends in the prevalence and incidence of dementia, and survival with dementia. *Alzheimers Res Ther*. 2016;8(1):23.
5. Alzheimer's Disease International. *World Alzheimer Report 2018: the state of the art of dementia research: new frontiers*. London: Alzheimer's Disease International; 2018.
6. Noda H, Yamagishi K, Ikeda A, et al. Identification of dementia using standard clinical assessments by primary care physicians in Japan. *Geriatr Gerontol Int*. 2018;18(5):738–44.
7. Ohara T, Hata J, Yoshida D, et al. Trends in dementia prevalence, incidence, and survival rate in a Japanese community. *Neurology*. 2017;88(20):1925–32.
8. Dodge HH, Buracchio TJ, Fisher GG, et al. Trends in the prevalence of dementia in Japan. *Int J Alzheimers Dis*. 2012;2012:956354.
9. Meguro K, Ishii H, Yamaguchi S, et al. Prevalence of dementia and dementing diseases in Japan: the Tajiri project. *Arch Neurol*. 2002;59(7):1109–14.
10. Meguro K, Ishii H, Kasuya M, et al. Incidence of dementia and associated risk factors in Japan: the Osaka-Tajiri Project. *J Neurol Sci*. 2007;260(1–2):175–82.
11. Kasai M, Nakamura K, Meguro K. Alzheimer's disease in Japan and other countries: review of epidemiological studies in the last 10 years (in Japanese). *Brain Nerve*. 2010;62(7):667–78.
12. Okamura H, Ishii S, Ishii T, Eboshida A. Prevalence of dementia in Japan: a systematic review. *Dement Geriatr Cogn Disord*. 2013;36(1–2):111–8.
13. Yamada M, Sasaki H, Mimori Y, et al. Prevalence and risks of dementia in the Japanese population: RERF's adult health study Hiroshima subjects. *Radiation Effects Research Foundation. J Am Geriatr Soc*. 1999;47(2):189–95.
14. Ahmadi-Abhari S, Guzman-Castillo M, Bandosz P, et al. Temporal trend in dementia incidence since 2002 and projections for prevalence in England and Wales to 2040: modelling study. *BMJ*. 2017;358:j2856.
15. Wu YT, Beiser AS, Breteler MMB, et al. The changing prevalence and incidence of dementia over time current evidence. *Nat Rev Neurol*. 2017;13(6):327–39.
16. Matthews FE, Stephan BC, Robinson L, et al. A two decade dementia incidence comparison from the Cognitive Function and Ageing Studies I and II. *Nat Commun*. 2016;7:11398.
17. Satizabal CL, Beiser AS, Chouraki V, et al. Incidence of dementia over three decades in the Framingham Heart Study. *N Engl J Med*. 2016;374(6):523–32.
18. Stephan BCM, Birdi R, Tang EYH, et al. Secular trends in dementia prevalence and incidence worldwide: a systematic review. *J Alzheimers Dis*. 2018;66(2):653–80.
19. Schrijvers EM, Verhaaren BF, Koudstaal PJ, et al. Is dementia incidence declining?: trends in dementia incidence since 1990 in the Rotterdam Study. *Neurology*. 2012;78(19):1456–63.
20. Qiu C, von SE, Backman L, Winblad B, Fratiglioni L. Twenty-year changes in dementia occurrence suggest decreasing incidence in central Stockholm, Sweden. *Neurology*. 2013;80(20):1888–94.
21. Alzheimer's Disease International. *World Alzheimer Report 2010. The global economic impact of dementia*. London: Alzheimer's Disease International; 2010.
22. Hurd MD, Martorell P, Delavande A, et al. Monetary costs of dementia in the United States. *N Engl J Med*. 2013;368(14):1326–34.
23. Sado M, Ninomiya A, Shikimoto R, et al. The estimated cost of dementia in Japan, the most aged society in the world. *PLoS One*. 2018;13:e0206508.

24. Livingston G, Franchis H. A global perspective on dementia care: a Lancet Commission. *Lancet*. 2015;386(9997):933–4.
25. Corder EH, Saunders AM, Strittmatter WJ, et al. Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's disease in late onset families. *Science*. 1993;261:921–3.
26. Reiman EM, Caselli RJ, Yun LS, et al. Preclinical evidence of Alzheimer's disease in personshomozygous for the epsilon 4 allele for apolipoprotein E. *N Engl J Med*. 1996;334:752–8.
27. Ritchie K, Carriere I, Ritchie CW, et al. Designing prevention programmes to reduce incidence of dementia: prospective cohort study of modifiable risk factors. *BMJ*. 2010;341:c3885.
28. Cobb JL, Wolf PA, Au R, et al. The effect of education on the incidence of dementia and Alzheimer's disease in the Framingham Study. *Neurology*. 1995;45(9):1707–12.
29. Yip AG, Brayne C, Matthews FE, Study MCFaA. Risk factors for incident dementia in England and Wales: the Medical Research Council Cognitive Function and Ageing Study. A population based nested case-control study. *Age Ageing*. 2006;35(2):154–60.
30. Gatz M, Mortimer JA, Fratiglioni L, Johansson B, Berg S, Andel R, Crowe M, Fiske A, Reynolds CA, Pedersen NL. Accounting for the relationship between low education and dementia: a twin study. *Physiol Behav*. 2007;92:232–7.
31. Gilleard CJ. Education and Alzheimer's disease: a review of recent international epidemiological studies. *Aging Ment Health*. 1997;1(1):33–46.
32. Sharp ES, Gatz M. Relationship between education and dementia: an updated systematic review. *Alzheimer Dis Assoc Disord*. 2011;25(4):289–304.
33. Valenzuela MJ, Sachdev P. Brain reserve and dementia: a systematic review. *Psychol Med*. 2006;36(4):441–54.
34. Russ TC, Stamatakis E, Hamer M, et al. Socioeconomic status as a risk factor for dementia death: individual participant meta-analysis of 86 508 men and women from the UK. *Br J Psychiatry*. 2013;203(1):10–7.
35. Sattler C, Toro P, Schonknecht P, Schroder J. Cognitive activity, education and socioeconomic status as preventive factors for mild cognitive impairment and Alzheimer's disease. *Psychiatry Res*. 2012;196(1):90–5.
36. Harrison SL, Sajjad A, Bramer WM, et al. Exploring strategies to operationalize cognitive reserve: a systematic review of reviews. *J Clin Exp Neuropsychol*. 2015;37(3):253–64.
37. Caamano-Isorna F, Corral M, Montes-Martinez A, Takkouche B. Education and dementia: a meta-analytic study. *Neuroepidemiology*. 2006;26(4):226–32.
38. Letenneur L, Launer LJ, Andersen K, et al. Education and the risk for Alzheimer's disease: sex makes a difference. EURODEM pooled analyses. EURODEM Incidence Research Group. *Am J Epidemiol*. 2000;151(11):1064–71.
39. Letenneur L, Gilleron V, Commenges D, et al. Are sex and educational level independent predictors of dementia and Alzheimer's disease? Incidence data from the PAQUID project. *J Neurol Neurosurg Psychiatry*. 1999;66(2):177–83.
40. Ott A, van Rossum CT, van Harskamp F, et al. Education and the incidence of dementia in a large population-based study: the Rotterdam Study. *Neurology*. 1999;52(3):663–6.
41. Lindsay J, Laurin D, Verreault R, et al. Risk factors for Alzheimer's disease: a prospective analysis from the Canadian Study of Health and Aging. *Am J Epidemiol*. 2002;156(5):445–53.
42. Qiu C, Karp A, von Strauss E, et al. Lifetime principal occupation and risk of Alzheimer's disease in the Kungsholmen project. *Am J Ind Med*. 2003;43(2):204–11.
43. Karp A, Kareholt I, Qiu C, et al. Relation of education and occupation-based socioeconomic status to incident Alzheimer's disease. *Am J Epidemiol*. 2004;159(2):175–83.
44. Evans DA, Hebert LE, Beckett LA, et al. Education and other measures of socioeconomic status and risk of incident Alzheimer disease in a defined population of older persons. *Arch Neurol*. 1997;54(11):1399–405.
45. Reuser M, Willekens FJ, Bonneux L. Higher education delays and shortens cognitive impairment: a multistate life table analysis of the US Health and Retirement Study. *Eur J Epidemiol*. 2011;26(5):395–403.

46. De Ronchi D, Fratiglioni L, Rucci P, et al. The effect of education on dementia occurrence in an Italian population with middle to high socioeconomic status. *Neurology*. 1998;50(5):1231–8.
47. Cadar D, Lassale C, Davies H, et al. Individual and area-based socioeconomic factors associated with dementia incidence in England: evidence from a 12-year follow-up in the English longitudinal study of ageing. *JAMA Psychiatry*. 2018;75(7):723–32.
48. Yoshitake T, Kiyohara Y, Kato I, et al. Incidence and risk factors of vascular dementia and Alzheimer's disease in a defined elderly Japanese population: the Hisayama Study. *Neurology*. 1995;45(6):1161–8.
49. Takeda T, Kondo K, Hirai H. Psychosocial risk factors in certifying the need for long-term care accompanied by dementia in the elderly living in the community: AGES Project, a 3-year cohort study. *J Jpn Publ Health*. 2010;57:1054–65.
50. Shirai K, Hirai H, Kondo K, et al. Socioeconomic status and its association with incidence of dementia among older Japanese men and women: JAGES study. *Intel Epidemiol Assoc World Congr Epidemiol*. 2017;46(1):60.
51. Takasugi T, Tsuji T, Kondo K, et al. Socio-economic status and dementia onset among older Japanese: a 6-year prospective cohort study from the Japan Gerontological Evaluation Study. *Int J Geriatr Psychiatry*. 2019;34(11):1642–50.
52. Chen RL, Ma Y, Wilson K, et al. A multicentre community-based study of dementia cases and subcases in older people in China—the GMSAGECAT prevalence and socio-economic correlates. *Int J Geriatr Psychiatry*. 2012;27(7):692–702.
53. Zhang ZX, Zahner GE, Román GC, et al. Socio-demographic variation of dementia subtypes in China: methodology and results of a prevalence study in Beijing, Chengdu, Shanghai, and Xian. *Neuroepidemiology*. 2006;27(4):177–87.
54. Chiao C, Botticello A, Fuh JL. Life-course socio-economic disadvantage and late-life cognitive functioning in Taiwan: results from a national cohort study. *Int Health*. 2014;6(4):322–30.
55. Bonaiuto S, Rocca WA, Lippi A, et al. Education and occupation as risk factors for dementia: a population-based case-control study. *Neuroepidemiology*. 1995;14(3):101–9.
56. Helmer C, Letenneur L, Rouch I, et al. Occupation during life and risk of dementia in French elderly community residents. *J Neurol Neurosurg Psychiatry*. 2001;71(3):303–9.
57. Del Ser T, Hachinski V, Merskey H, Munoz DG. An autopsy-verified study of the effect of education on degenerative dementia. *Brain*. 1999;122(Pt 12):2309–19.
58. Seidler A, Nienhaus A, Bernhardt T, et al. Psychosocial work factors and dementia. *Occup Environ Med*. 2004;61(12):962–71.
59. Kroger E, Andel R, Lindsay J, et al. Is complexity of work associated with risk of dementia? *Am J Epidemiol*. 2008;167(7):820–30.
60. Andel R, Crowe M, Hahn EA, et al. Work-related stress may increase the risk of vascular dementia. *J Am Geriatr Soc*. 2012;60(1):60–7.
61. Marden JR, Tchetgen Tchetgen EJ, et al. Contribution of socioeconomic status at 3 life-course periods to late-life memory function and decline: early and late predictors of dementia risk. *Am J Epidemiol*. 2017;186(7):805–14.
62. Lang IA, Llewellyn DJ, Langa KM, et al. Neighborhood deprivation, individual socioeconomic status, and cognitive function in older people: analyses from the English Longitudinal Study of Ageing. *J Am Geriatr Soc*. 2008;56(2):191–8.
63. Kim GH, Lee HA, Park H, et al. Effect of individual and district-level socioeconomic disparities on cognitive decline in community-dwelling elderly in Seoul. *J Korean Med Sci*. 2017;32(9):1508–15.
64. Meyer OL, Mungas D, King J, et al. Neighborhood socioeconomic status and cognitive trajectories in a diverse longitudinal cohort. *Clin Gerontol*. 2018;41(1):82–93.
65. Stern Y. What is cognitive reserve? Theory and research application of the reserve concept. *J Int Neuropsychol Soc*. 2002;8(3):448–60.
66. Schmand B, Smit JH, Geerlings MI, Lindeboom J. The effects of intelligence and education on the development of dementia. A test of the brain reserve hypothesis. *Psychol Med*. 1997;27(6):1337–44.

67. Fratiglioni L, Wang H-X. Brain reserve hypothesis in dementia. *J Alzheimers Dis.* 2007;12(1):11–22.
68. Katzman R. Education and the prevalence of dementia and Alzheimer's disease. *Neurology.* 1993;43(1):13–20.
69. Dufouil C, Richard F, Fievet N, et al. APOE genotype, cholesterol level, lipid-lowering treatment, and dementia: the Three-City Study. *Neurology.* 2005;64(9):1531–8.
70. Murata C, Yamada T, Chen C-C, et al. Barriers to health care among the elderly in Japan. *Int J Environ Res Public Health.* 2010;7(4):1330–41.
71. Frank LD, Sallis JF, Saelens BE, et al. The development of a walkability index: application to the Neighborhood Quality of Life Study. *Br J Sports Med.* 2010;44(13):924–33.
72. Morland K, Wing S, Diez Roux A, et al. Neighborhood characteristics associated with the location of food stores and food service places. *Am J Prev Med.* 2002;22(1):23–9.
73. Kikuchi H, Nakaya T, Hanibuchi T, et al. Objectively measured neighborhood walkability and change in physical activity in older Japanese adults: a five-year cohort study. *Int J Environ Res Public Health.* 2018;15(9):E1814.
74. Hanibuchi T, Kondo K, Nakaya T, et al. Does walkable mean sociable? Neighborhood determinants of social capital among older adults in Japan. *Health Place.* 2012;18(2):229–39.
75. Rose G. Sick individuals and sick populations. *Int J Epidemiol.* 2001;30(3):427–32.
76. Brownell KD, Farley T, Willett WC, et al. The public health and economic benefits of taxing sugar-sweetened beverages. *N Engl J Med.* 2009;361(16):1599–605.
77. Andreyeva T, Long MW, Brownell KD. The impact of food prices on consumption: a systematic review of research on the price elasticity of demand for food. *Am J Public Health.* 2010;100(2):216–22.
78. Duffey KJ, Gordon-Larsen P, Shikany JM, et al. Food price and diet and health outcomes: 20 years of the CARDIA Study. *Arch Intern Med.* 2010;170(5):420–6.
79. Meyer KA, Guilkey DK, Ng SW, et al. Sociodemographic differences in fast food price sensitivity. *JAMA Intern Med.* 2014;174(3):434–42.
80. Glanz K, Rimer BK, Viswanath K. Health behavior and health education: theory, research, and practice. 4th ed. San Francisco, CA: Jossey-Bass; 2008.
81. Johnston H. A methodology for flame analysis: from discourse to cognitive schemata. In: Johnston H, Klandermans B, editors. *Social movements and culture.* 4th ed. London: Routledge; 1995.
82. Kahneman D. Maps of bounded rationality: psychology for behavioral economics. *Am Econ Rev.* 2003;93(5):1449–75.
83. Lynch J, Kaplan G. Socioeconomic position. In: Berkman LF, Kawachi I, editors. *Social epidemiology.* Oxford: Oxford University Press; 2000. p. 13–35.
84. Marengoni A, Fratiglioni L, Bandinelli S, Ferrucci L. Socioeconomic status during lifetime and cognitive impairment no-dementia in late life: the populationbased aging in the Chianti area (InCHIANTI) Study. *J Alzheimers Dis.* 2011;24(3):559–68.
85. Sha TT, Yan Y, Cheng WW. Associations of childhood socioeconomic status with mid-life and late-life cognition in Chinese middle-aged and older population based on a 5-year period cohort study. *Int J Geriatr Psychiatry.* 2018;33(10):1335–45.
86. Bendlin BB, Carlsson CM, Gleason CE, et al. Midlife predictors of Alzheimer's disease. *Maturitas.* 2010;65:131–7.
87. Qiu C, Winblad B, Fratiglioni L. The age-dependent relation of blood pressure to cognitive function and dementia. *Lancet Neurol.* 2005;4:487–99.
88. Whitmer RA, Gunderson EP, Quesenberry CP Jr, et al. Body mass index in midlife and risk of Alzheimer disease and vascular dementia. *Curr Alzheimer Res.* 2007;4:103–9.
89. Kawachi I, Adler NE, Dow WH. Money, schooling, and health: mechanisms and causal evidence. *Ann N Y Acad Sci.* 2010;1186:56–68.
90. Vera MR. France's educational attainment inflation and disparate society. Tokyo: Akashi Shoten; 2007. Hayashi, M. (translated).

91. Rozanski A, Kubzansky LD. Psychologic functioning and physical health: a paradigm of flexibility. *Psychosom Med.* 2005;67:S47–53.
92. Torres SJ, Nowson CA. Relationship between stress, eating behavior, and obesity. *Nutrition.* 2007;23:887–94.
93. Mikolajczyk RT, El Ansari W, Maxwell AE. Food consumption frequency and perceived stress and depressive symptoms among students in three European countries. *Nutr J.* 2009;8:31.
94. McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med.* 1998;338:171–9.
95. Kivimäki M, Steptoe A. Effects of stress on the development and progression of cardiovascular disease. *Nat Rev Cardiol.* 2017;15:215–29.
96. Arnold SV, Smolderen KG, Buchanan DM, et al. Perceived stress in myocardial infarction: long-term mortality and health status outcomes. *J Am Coll Cardiol.* 2012;60:1756–63.
97. Hackett RA, Steptoe A. Type 2 diabetes mellitus and psychological stress—a modifiable risk factor. *Nat Rev Endocrinol.* 2017;13:547–60.
98. Stansfeld SA, Fuhrer R, Shipley MJ, Marmot MG. Psychological distress as a risk factor for coronary heart disease in the Whitehall II Study. *Int J Epidemiol.* 2002;31(1):248–55.
99. Logan JG, Barksdale DJ. Allostasis and allostatic load: expanding the discourse on stress and cardiovascular disease. *J Clin Nurs.* 2008;17:201–8.
100. Edelstein BA, Heisel MJ, McKee DR, et al. Development and psychometric evaluation of the reasons for living-older adults scale: a suicide risk assessment inventory. *Gerontologist.* 2009;49:736–45.
101. Byers AL, Yaffe K. Depression and risk of developing dementia. *Nat Rev Neurol.* 2011;7:323–31.
102. Underwood EA, Davidson HP, Azam AB, et al. Sex differences in depression as a risk factor for Alzheimer’s disease: a systematic review. *Innov Aging.* 2019;3(2):igz015.
103. Diniz BS, Butters MA, Albert SM, et al. Late-life depression and risk of vascular dementia and Alzheimer’s disease: systematic review and meta-analysis of community-based cohort studies. *Br J Psychiatry.* 2013;202(5):329–35.
104. Van der Kooy K, van Hout H, Marwijk H, et al. Depression and the risk for cardiovascular diseases: systematic review and meta analysis. *Int J Geriatr Psychiatry.* 2007;22(7):613–26.
105. Fan AZ, Strine TW, Jiles R, Mokdad AH. Depression and anxiety associated with cardiovascular disease among persons aged 45 years and older in 38 states of the United States, 2006. *Prev Med.* 2008;46(5):445–50.
106. Gan Y, Gong Y, Tong X, et al. Depression and the risk of coronary heart disease: a meta-analysis of prospective cohort studies. *BMC Psychiatry.* 2014;14:371.
107. Cohen S, Kessler RC, Gordon LU. *Measuring stress: guide for health and social scientists.* Oxford: Oxford University Press; 1995.
108. Steptoe A, Wardle J, Marmot M. Positive affect and health-related neuroendocrine, cardiovascular, and inflammatory processes. *Proc Natl Acad Sci U S A.* 2005;102:6508–12.
109. Folkman S, Lazarus RS. Coping as a mediator of emotion. *J Pers Soc Psychol.* 1988;54(3):466–75.
110. Kubzansky LD, Sparrow D, Vokonas P, Kawachi I. Is the glass half empty or half full? A prospective study of optimism and coronary heart disease in the Normative Aging Study. *Psychosom Med.* 2001;63:910–6.
111. Giltay EJ, Kamphuis MH, Kalmijn S, et al. Dispositional optimism and the risk of cardiovascular death: the Zutphen Elderly Study. *Arch Intern Med.* 2006;166:431–6.
112. Shirai K, Iso H, Ohira T, et al. Perceived level of life enjoyment and risks of cardiovascular disease incidence and mortality: the Japan public health center-based study. *Circulation.* 2009;120:956–63.
113. Chida Y, Steptoe A. Positive psychological well-being and mortality: a quantitative review of prospective observational studies. *Psychosom Med.* 2008;70:741–56.
114. Sutin A, Stephan Y, Terracciano A. Psychological well-being and risk of dementia. *Int J Geriatr Psychiatry.* 2018;33(5):743–7.

115. Gawronski KAB, Kim ES, et al. Dispositional optimism and incidence of cognitive impairment in older adults. *Psychosom Med.* 2016;78(7):819–28.
116. Kuiper JS, Zuidersma M, Oude Voshaar RC, et al. Social relationships and risk of dementia: a systematic review and meta-analysis of longitudinal cohort studies. *Ageing Res Rev.* 2015;22:39–57.
117. Saito T, Murata C, Saito M, et al. Influence of social relationship domains and their combinations on incident dementia: a prospective cohort study. *J Epidemiol Community Health.* 2018;72(1):7–12.
118. Nemoto Y, Saito T, Kanamori S, et al. An additive effect of leading role in the organization between social participation and dementia onset among Japanese older adults: the AGES cohort study. *BMC Geriatr.* 2017;17(1):297.
119. Takeda T, Kondo K, Hirai H. Relations between the onset of dementia and the content of hobbies of elderly local residents based on a cohort study, AGES Project. In: *The 68th Meeting of the Japanese Society of Public Health, Nara City.* Tokyo: JPHA; 2009.
120. Rowe JW, Kahn RL. Successful aging. *Gerontologist.* 1997;37:433–40.
121. Evans I, Martyr A, Collins R, et al. Social isolation and cognitive function in later life: a systematic review and meta-analysis. *J Alzheimers Dis.* 2019;70(S1):S119–44.
122. Butler RN. The study of productive aging. *J Gerontol B Psychol Sci Soc Sci.* 2002;57:S323.
123. Murata C, Saito T, Saito M, et al. The association between social support and incident dementia: a 10-year follow-up study in Japan. *Int J Environ Res Public Health.* 2019;16(2):239.
124. Shirai K, Iso H, Aida J, et al. Reciprocal social support and onset of dementia—relationship with a loss of healthy life expectancy; AGES Project. *Nihon Kosshu Eisei Zasshi.* 2009;56(10):510.
125. Kondo K, Hirai H. To what extent is high-risk strategy of preventing long-term care effective?—a study based on a cohort research. In: *The 18th Annual Scientific Meeting of the Japan Epidemiological Association, January 25–26, 2008, National Center for Sciences, Tokyo.* Tokyo: JPHA; 2008.
126. Tani Y, Fujiwara T, Kondo K. Association between adverse childhood experiences and dementia in older Japanese adults. *JAMA Netw Open.* 2020;3(2):e1920740.
127. Ritchie K, Jaussent I, Stewart R, et al. Adverse childhood environment and late-life cognitive functioning. *Int J Geriatr Psychiatry.* 2011;26(5):503–10.
128. Lipnicki DM, Makkar SR, Crawford JD, et al. Determinants of cognitive performance and decline in 20 diverse ethno-regional groups: a COSMIC collaboration cohort study. *PLoS Med.* 2019;16(7):e1002853.

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