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## Cognitive Health of Older Persons in Longitudinal Ageing Cohort Studies (Kajian Kohort Penuaan Longitud Kesihatan Kognitif dalam Kalangan Warga Emas)

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### ABSTRACT

*Dementia poses a major global burden of care to society and health systems in ageing populations. The majority (over 60%) of persons with dementia in the world are found in Asia and developing countries with rapid rates of population ageing. Improving and maintaining the cognitive health of older persons is vital to national strategies for dementia prevention. Increasing numbers of population-based ageing cohort studies in the past decade have provided a better understanding of the factors that contribute to cognitive function and decline in old age. The roles of major demographic, psychosocial, lifestyle, behavioral and cardiovascular risk factors contributing to cognitive health were discussed using examples from the Singapore Longitudinal Ageing Studies. They include socio-demographic factors, particularly education and marital status, leisure time activity such as physical activity, social engagement and mental activities, psychological factors such as depression, cardiovascular and metabolic risk factors: obesity, diabetes, hypertension and dyslipidemia, and the metabolic syndrome, under-nutrition, low albumin, low hemoglobin, nutritional factors such as blood folate, B12 and homocysteine, omega-3 poly-unsaturated fatty acids, tea drinking and curcumin-rich turmeric in curry meals. These factors are found to be associated variously with cognitive functions (memory and learning, language, visuospatial, attention and information processing speed), rates of cognitive impairment and cognitive decline, or increased risk of developing MCI and progression to dementia.*

*Keywords: Aging; cognitive function; dementia; older adult; risk factor*

### ABSTRAK

*Secara global, demensia menjadi beban jagaan utama terhadap masyarakat dan sistem kesihatan dalam kalangan populasi tua. Lebih daripada 60% individu yang mempunyai masalah demensia terdiri daripada masyarakat negara Asia serta negara-negara membangun yang mempunyai kadar kenaikan populasi tua yang mendadak. Langkah meningkatkan dan mengekalkan kesihatan mental bagi warga emas merupakan strategi yang amat penting sebagai pencegahan masalah demensia. Peningkatan jumlah kajian kohort berkenaan populasi ini telah meningkatkan pemahaman terhadap faktor yang boleh mempengaruhi fungsi kognitif dan penurunan fungsi kognitif di usia tua. Faktor yang mempengaruhi kesihatan kognitif yang dibincangkan adalah berdasarkan Kajian Penuaan Longitud Singapura iaitu faktor demografi, psikososial, gaya hidup, tingkah laku dan risiko kardiovaskular. Faktor sosiodemografi termasuklah pendidikan dan status perkahwinan manakala aktiviti masa lapang melibatkan aktiviti fizikal, penglibatan sosial dan aktiviti yang menggunakan daya mental. Faktor signifikan melibatkan psikososial seperti kemurungan bersama faktor risiko kardiovaskular dan metabolik termasuklah obesiti, diabetes, hipertensi dan dislipidemia dan sindrom metabolik, kekurangan nutrisi, paras albumin serta hemoglobin yang rendah. Selain itu, faktor pemakanan seperti paras folat dalam darah, B12 dan homosisteina, omega-3 asid lemak poli tak tepu, pengambilan minuman teh dan kunyit yang tinggi kandungan kurkumin dalam masakan berasaskan kari didapati penting. Faktor ini berkait dengan pelbagai fungsi kognitif (memori dan pembelajaran, bahasa, visuoreruag, perhatian dan kelajuan pemprosesan maklumat), kadar gangguan dan penurunan fungsi kognitif atau peningkatan risiko kemerosotan kognitif ringan dan progresi kepada masalah demensia.*

*Kata kunci: Demensia; faktor risiko; fungsi kognitif; penuaan; warga emas*

### INTRODUCTION

Dementia poses a major global burden of care to society in ageing populations. According to Alzheimer's Disease International, there were an estimated 46.8 million cases of dementia in 2015. With 9.9 million new cases of dementia annually, there will be a phenomenal increase over the next 15 years to 74.7 million cases in 2030. It is important to note that the majority of persons with dementia in the world (58%) were found in low and middle-income countries including much of Asia (Prince et al. 2015).

Dementia is not curable by any currently available treatment and available drug therapy provides only limited symptomatic and functional relief for up to 2 years. It is estimated that any therapeutic or lifestyle interventions that delay the onset of dementia by only one year is projected to lower worldwide prevalence of dementia by 9 million cases by 2050 (Brookmeyer et al. 2007). The onset of dementia could theoretically be delayed by slowing cognitive decline via modifying the underlying Alzheimer's disease and/or cardiovascular disease pathological processes and/or

increasing brain and cognitive reserve (Stern 2002), that is creating surplus buffering capacity to raise the threshold at which dementia symptoms would manifest (Figures 1 and 2). Thus, improving and maintaining the cognitive health of older persons is vital to national strategies for dementia prevention. Increasing number of population-based ageing cohort studies in the past decade have provided a better understanding of the factors that contribute to cognitive function and decline in old age. The psychosocial, lifestyle, behavioral and cardiovascular risk factors include in particular education, marital status, physical activity, social engagement and mental activities, depression, cardiovascular and metabolic risk factors including obesity, diabetes, hypertension and dyslipidemia and the metabolic syndrome and nutritional factors (under-nutrition, physical frailty, blood folate, B12 and homocysteine, omega-3 polyunsaturated fatty acids, dietary intake of plant flavonoids in tea, fruits and turmeric). These risk and protective factors are known to influence cognitive functioning and health of older persons with varying magnitude and direction throughout the life course (Launer 2005; Muller et al. 2014). Cognitive outcomes studied in longitudinal cohort studies include cognitive impairment, cognitive decline, mild cognitive impairment and dementia and its pathological subtypes including Alzheimer's disease and vascular dementia. In this paper, the major risk and protective factors contributing to the risks and progression of dementia are reviewed and summarized, with examples from the Singapore Longitudinal Ageing Studies in particular.

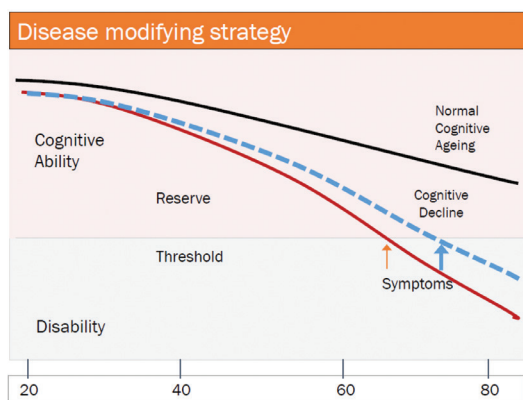


FIGURE 1. Strategy to modify disease

#### SOCIO-DEMOGRAPHIC FACTORS

**Age** The level of cognitive function, the prevalence of cognitive impairment, rate of cognitive decline and risk of developing mild cognitive impairment (MCI) and dementia are related to increasing age. The risk of Alzheimer's disease in particular is shown to increase exponentially with age, doubling for every decade of age after 65 (Qiu et al. 2007). The findings across many studies are equivocal in regard to the influence of *sex* and is probably related

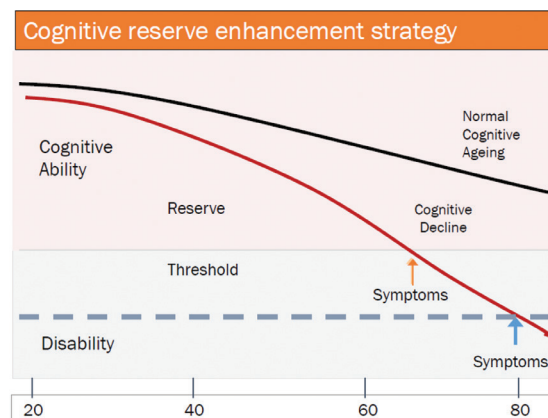


FIGURE 2. Strategy to enhance cognitive reservation

to their level of education in different population studies. *Ethnicity* has been shown in multi-ethnic population studies to influence the level of cognitive function and dementia in several countries (Hamid et al. 2010; Ng et al. 2010; Tang et al. 2001). Higher prevalence rates of dementia are reported for African-Americans versus Caucasians in New York (Tang et al. 2001) and Bumiputeras, Malays and Indians versus Chinese in Malaysia (Hamid et al. 2010) and Singapore (Ng et al. 2010). The studies in Singapore in particular indicate that the differentials in dementia prevalence and the level of cognitive function among ethnic groups vary with education, being most marked among those with no or little education and virtually none among those with secondary and higher education. *Education* is well documented to be an important strong factor for cognitive function and dementia risk (Ng et al. 2010; Qiu et al. 2007). The profound impact of education on cognitive health throughout the life span undergirds the strong emphasis on life-long learning in active ageing programs throughout the world. A number of studies have shown that older persons who were *single, widowed or divorced* were more likely to be cognitively impaired or at increased risk of developing dementia (Feng et al. 2014; Håkansson et al. 2009). This reflects the important influence of social isolation and loneliness among psychosocial factors that has impact on cognitive health in late life (Boyle et al. 2010; Johansson et al. 2010). A large number of studies consistently showed that a higher level of *leisure time participation in physical activities, social activities and mentally stimulating activities* are protective against cognitive decline and risk of dementia (Boyle et al. 2010; Fratiglioni et al. 2004; Karp et al. 2006; Niti et al. 2008; Qiu et al. 2010; Wang et al. 2002).

#### PSYCHOSOCIAL FACTORS

**Depression** Studies which show that a lifetime history of clinical depression was associated with increased risk of dementia suggest that depression is a risk factor for developing dementia (Bassuk et al. 1998; Speck et al. 1995). Among patients with mild cognitive impairment

or dementia, depression or depressive symptoms is also known to be present concurrently or develop within ten years preceding the onset of cognitive symptoms, indicating that it could also be a prodrome or comorbidity of dementia (Geerlings et al. 2000). The Singapore Longitudinal Ageing Studies showed that depressive symptoms was associated with greater likelihood of cognitive decline particularly in men but not women (Ng et al. 2009b), suggesting a greater vulnerability to the impact of social isolation and/or cardiovascular risk factors which are more prevalent among men.

#### CARDIOVASCULAR RISK FACTOR

The role of *cardiovascular and metabolic risk factors* (CVRF) in the development of dementia were first investigated in pre-existing population-based studies with baseline data collected in the 1960s-1990s on CVRF in middle-aged people and followed up in late-life (65 years and over) for incident dementia and its subtypes, including such studies as the Goteborg study, Cardiovascular Risk Factors Ageing and Dementia study, Honolulu-Asia Aging Study, and Hisayama Study (Kivipelto et al. 2001; Launer et al. 2000; Ninomiya et al. 2011; Skoog et al. 1996). These studies have consistently shown hypertension in mid-life predicted incident dementia in late life; diabetes in both mid-life and late life has also been consistently shown to be associated with increased risk of incident dementia (Posner et al. 2000; Prince et al. 2014; Qiu et al. 2010; Skoog 2003). Other CVRFs namely high body mass and dyslipidaemia are less consistently found to be associated, possibly because of changes in body mass and lipid levels associated with the development of dementia and frailty in late life (Anstey et al. 2011; Beydoun et al. 2008; Buchman et al. 2005; Luchsinger et al. 2006; Qiu et al. 2010; Reitz et al. 2004). More recently, studies including the SLAS, have shown that the *metabolic syndrome* predicted a greater rate of cognitive decline and incident mild cognitive decline and dementia (Ho et al. 2008; Ng et al. 2016) in particular, the presence of the metabolic syndrome among older persons with MCI predicted a four-fold increased likelihood of conversion to dementia (Ng et al. 2016; Solfrizzi et al. 2011). Interestingly, data in the SLAS showed that treatment with *metformin* among diabetic older persons was associated with a reduced risk of cognitive decline and dementia (Ng et al. 2014).

#### DIET AND NUTRITION

A *Mediterranean-like diet* has been reported to be associated with a reduced risk of cognitive impairment and Alzheimer's disease (Singh et al. 2014). No study of a healthy Asian diet has yet been reported. On the other hand, various studies have suggested that a poor diet or a lifestyle and behavior risk profile predisposing to risk of *malnutrition*, as well as *low albumin or hemoglobin* was associated with poorer cognitive functioning and impairment (Ng et al. 2009a, 2008b).

The level of blood *folate and B12 and homocysteine* (which is elevated when folate or B12 are low) play vital roles in the 4-carbon methylation cycle which is involved in the synthesis of bioactive amines and neurotransmitters such as serotonin and dopamine in the brain. They have been found in a good number of studies to be associated with cognitive function, impairment and dementia (O'leary et al. 2012). In particular, low blood folate has been shown to be associated with poorer performance on tasks of memory recall and learning and language, whereas high homocysteine was shown to be related to deficits in processing speed and visuo-spatial construction, as well as with smaller white matter volume of the brain (Feng et al. 2013, 2006). Findings from recent systematic reviews of randomized double-blind trials, however, have not found any evidence of potential benefit of vitamin supplementation.

The role of *poly-unsaturated fatty acids* in cognitive health and dementia has received much attention given that DHA and EPA are constituents of the neuronal membrane and are mostly derived from exogenous sources in seafood and plant sources. Earlier studies of an association of consumption of fish with lower risk of dementia have not been consistently replicated in other population studies, probably due to lower levels of PUFA consumed from predominant sources of seafood other than tuna, salmon or cod, as well as different methods of food preparation (Sydenham et al. 2012). Although no association with fish consumption was found, the SLAS study however, found that daily intake of fish oil capsules reported by the respondents was associated with lower risk of cognitive decline (Gao et al. 2011).

*Tea consumption* The role of anti-oxidant plant flavonoids has received much attention with laboratory experimental studies showing positive neuronal and cognitive effects of components of pigmented fruits and vegetables. Tea, both green and fermented black and oolong, is a common source of anti-oxidant polyphenols (catechins & theaflavins) and has been shown in several recent studies in Japan, Singapore and China to be associated with lower rates of cognitive impairment and decline (Feng et al. 2012, 2010; Ng et al. 2008a; Song et al. 2012).

*Curcumins* are another group of polyphenols with powerful anti-oxidants and anti-inflammatory actions, found richly in turmeric commonly used in curry meals. The SLAS study is the only study so far that has shown an association of frequent intake of curry with lower prevalence of cognitive impairment in non-demented subjects (Ng et al. 2006).

#### LIFESTYLE

Epidemiological studies have contributed a great amount of information about lifestyle and behavioural factors influencing the risk and severity of neurocognitive disorder. However, many more studies are needed to firmly establish the roles of these risk and protective factors for cognitive

health. In particular, findings from interventional studies are needed to establish the evidence base for primary and secondary preventions of dementia.

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