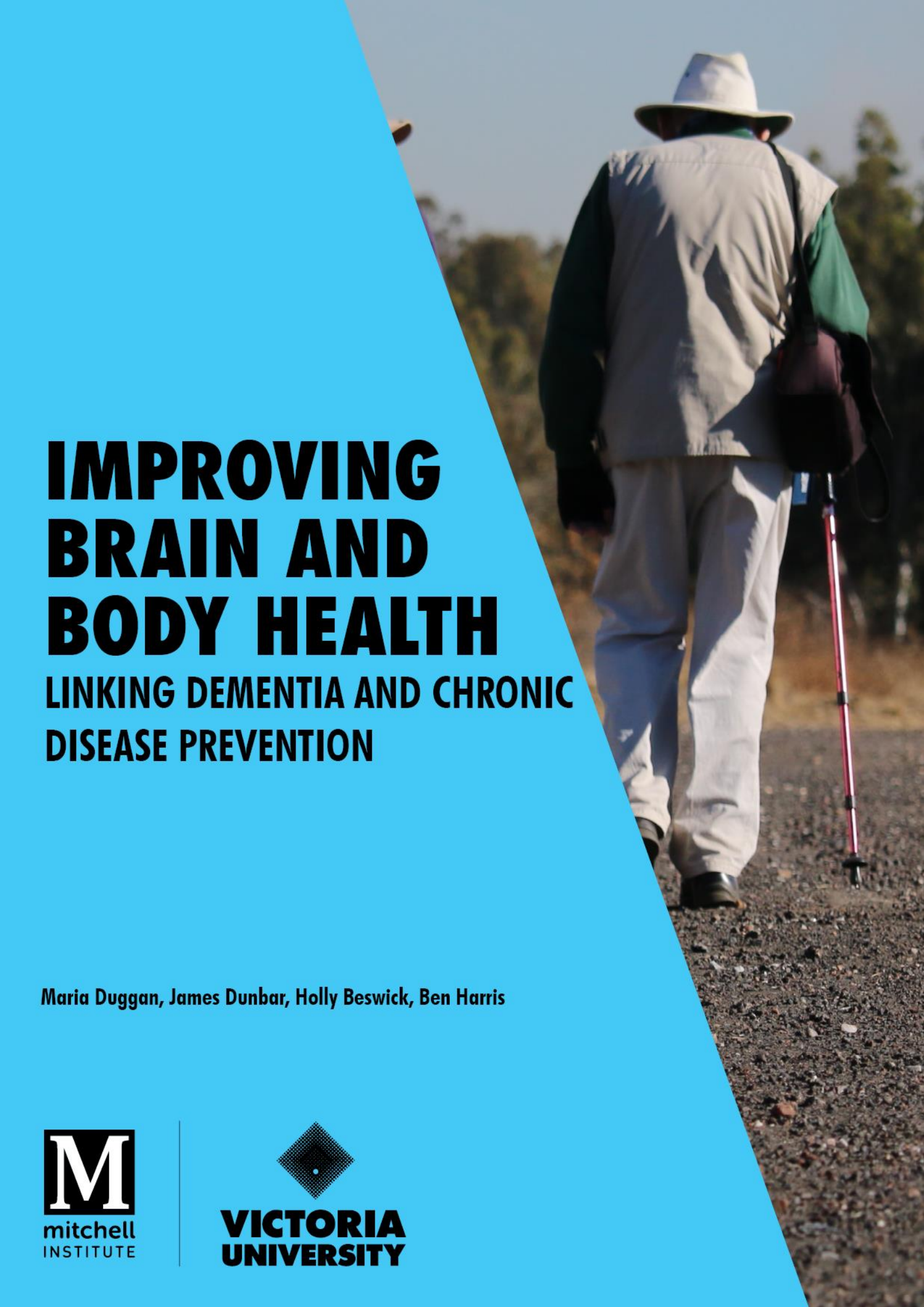

IMPROVING BRAIN AND BODY HEALTH

LINKING DEMENTIA AND CHRONIC DISEASE PREVENTION

Maria Duggan, James Dunbar, Holly Beswick, Ben Harris

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About us

The Mitchell Institute for Education and Health Policy at Victoria University is one of the country's leading education and health policy think tanks and trusted thought leaders. Our focus is on improving our education and health systems so more Australians can engage with and benefit from these services, supporting a healthier, fairer and more productive society.

The Australian Health Policy Collaboration is led by the Mitchell Institute at Victoria University and brings together leading health organisations and chronic disease experts to translate rigorous research into good policy. The national collaboration has developed health targets and indicators for preventable chronic diseases designed to contribute to reducing the health impacts of chronic conditions on the Australian population.

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List of acronyms and abbreviations

ACVR absolute cardiovascular risk assessment

AHPC Australian Health Policy Collaboration

AIHW Australian Institute of Health and Welfare

CALD culturally and linguistically diverse

COPD chronic obstructive pulmonary disease

CVD cardiovascular disease

FINGER Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability

NCD non-communicable disease

NESB non-English speaking backgrounds

Terminology

This paper uses the term dementia throughout. The authors recognise that there are many different kinds of dementia, that there may be progressive decline in cognitive functioning from mild cognitive impairment to severe dementia and that individual experiences will vary. Effective prevention will mean that more Australians reach their older years in the best possible health of brain and body.

Foreword

Societal ageing is a challenge for Australia and most countries in the world. Most health systems are poorly prepared to respond to the needs presented, including increasing dementia prevalence. However, fatalism in the face of these circumstances is not an appropriate response. Dementia is not, inevitably, a consequence of ageing. We could delay or prevent a significant proportion of this burden of disease and disability by tackling a number of known risk factors at individual and population levels. Several of these risk factors are common to chronic conditions of both the body and brain, especially cardiovascular disease. Yet there is poor public understanding of these risks and their impacts on both brain and body health.

The evidence cited in this paper makes a strong case for a new approach to risk reduction. Science is increasingly clarifying the pathways through which brain and body interactions take place and shedding light on the impacts of disease on the brain and other organs. Australia urgently needs a coordinated, integrated prevention strategy for brain and body health.

Rosemary Calder

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Summary

Purpose

This paper summarises some of the growing national and international evidence about the shared risk factors for brain and body health. Estimates suggest that over 30% of dementia cases can be prevented or delayed through a coordinated approach to tackling multiple risk factors for many chronic diseases, particularly cardiovascular disease (CVD).

The World Health Organisation (WHO) has recently (May 2019) summarised the existing evidence for risk-factor reduction and formulated guidelines for interventions based on this evidence. These new guidelines provide a strong, foundational knowledge base for governments, policymakers, health care providers and many other stakeholders to inform a national dementia risk-reduction strategy.

The evidence discussed in this paper has been reviewed and endorsed by a wide range of expert individuals and organisations working in the fields of dementia and population health. It will be followed by a policy issues paper, which will identify the ways in which national policy can begin to grasp the full preventative potential of an integrated, risk-reduction approach to brain and body health.

Dementia costs

The direct and indirect costs of dementia in Australia are projected to increase to $18.7 billion in today's dollars by 2025 and to **$36.8 billion by 2056**.

A third of the total dementia burden in Australia is attributable to the effect of vascular disease. The cost of services for dementia resulting from vascular disease over the next 20 years is estimated to reach $26.8 billion.

Whilst more research will shed further light on the causes of chronic disease, there is already more than enough compelling evidence to prompt focused and practical action to ensure that all Australians age as well as possible physically and cognitively. This will provide direct benefits for individuals and their families, society and the economy.

Dementia prevalence

Dementia in Australia is a substantial and growing public health challenge.

- An estimated **447,115 people have dementia**. Based on trends in population growth and ageing and the current lack of any curative interventions, the number of people with dementia will reach almost 1.1 million by 2056. [1]
- The Australian Bureau of Statistics (ABS) projects that dementia **will soon supplant heart disease as the leading cause of death in Australia.** Dementia is currently **the second leading cause of death,** contributing to 5.4% of all deaths in men and 10.6% of all deaths in women each year**.**[2]
- Around 244 people per day are newly diagnosed with dementia.[3]
- The number of **new cases of dementia** will increase to 318 per day by 2025 and over 650 per day
- An estimated **25,938 people have younger onset dementia**, expected to rise to 29,375 by 2025 and 42,252 by 2056. [4] This term describes any form of dementia diagnosed in people under the aged of 65. [5]
- The incidence of dementia in **Indigenous Australians** is 3–5 times that in non-Indigenous persons.[6]

- People with dementia aged 65 and over have **a substantially higher average number of health conditions** than all people in this age group (5.4 and 2.9 respectively).[7]

Public health measures to modify CVD risk factors have contributed to a large decline in heart disease and stroke in the past 50 years, and it would be possible to accelerate these efforts and achieve a greater health impact. There is some evidence of a reduction in age-specific dementia prevalence in some countries, including the Netherlands, France, and the United States, possibly as consequence of successful prevention efforts. However, the burden of dementia is still growing in most countries.

Dementia risk and protective factors

Multiple factors contribute to whether a person develops a chronic disease of body or brain – or both. Some of these, such as age, biological sex or genetic vulnerabilities, are non-modifiable. They cannot be changed. However, there is increasing evidence that many chronic diseases are associated with social, environmental and lifestyle risks and may be mitigated fully or in part. Modifiable risk factors include midlife obesity, raised cholesterol or blood pressure levels, smoking, physical inactivity, diabetes mellitus and depression. Low educational achievement, early school leaving and lack of access to lifelong learning opportunities are also associated in some studies with the development of dementia in later life. A recent report (July 2017) from The Lancet Commission on Dementia identifies other potentially modifiable risk factors for dementia, such as hearing loss and social isolation however the WHO has not found the current evidence sufficiently strong to propose acting in these areas yet.

The role of alcohol consumption as a risk factor for dementia is not yet fully determined. There is strong evidence that heavy drinking is associated with all types of dementia, including younger onset dementia, but the evidence of the impacts of moderate alcohol use is not conclusive. Several studies suggest that moderate use of alcohol (within national guidelines) may provide some protection – the 'J-shaped curve' – but recent evidence is beginning to challenge this understanding, leading some researchers to conclude that there is no level at which alcohol use is protective for either brain or body health. Further research will resolve this contentious issue. In the interim WHO recommends offering alcohol reduction support to individuals to reduce the risk of cognitive decline and dementia.

More information is required about the modifiable factors and interventions that may protect the brain against dementia, but emerging evidence indicates that these are similar to those known to be protective against a range of chronic diseases. It is important to note that the evidence suggests that no single protective intervention provides the much-needed 'magic bullet' in preventing cognitive decline or dementia but that a combination of these interventions, targeted at those at risk in mid-life or with mild cognitive impairment may reduce the risk of cognitive decline.

The WHO, the Lancet Commission, and many other studies suggest that these include:

- physical activity interventions
- tobacco cessation interventions
- nutritional interventions, specifically a Mediterranean diet
- interventions for alcohol use disorder
- timely detection and management of CVD risk factors including hypertension, obesity, diabetes mellitus and dyslipidaemia (high cholesterol).

Several protective social interventions, particularly higher educational attainment, also appear to exert a strong protective effect on dementia risk. People who leave high school before year

8 have a 2.2-fold higher risk of dementia in later life, and those leaving between years 8 and 11 have 1.5 times the risk of individuals who complete high school.

There is also increasing evidence that loneliness and isolation are associated with poorer cognitive function among older adults. Interventions to reduce social isolation, promote social engagement and increase levels of physical activity among older people may reduce dementia risk. Interventions that foster social connections may be particularly beneficial for individuals with low levels of education. The Lancet *Commission* suggests that the protective effect of education and social engagement is related to variations in levels of 'cognitive reserve' (brain resilience), which is enhanced by early-life experiences, including education and intellectual stimulation. The WHO has not supported this finding yet.

There is, additionally, good evidence that high-quality primary care and a robust approach to screening for CVD and support with managing risks to cardiovascular health is associated with better outcomes, particularly in areas of social disadvantage.

Strength of the evidence for prevention

The Lancet Commission estimated that, with coordinated action to address the known risk factors, **up to a third of cases of dementia could be prevented globally**. Other research claims that this is an underestimate.

Although the symptoms of dementia generally occur in later life, dementia is likely to be a clinically 'silent' (asymptomatic and unrecognised) disorder that begins at midlife (40–68 years of age), characterised by a slow and progressive deterioration in cognitive function. There is a **window of opportunity to intervene by addressing multiple dementia risk factors in middle age** through absolute cardiovascular risk assessment (ACVR), better management of cardiovascular risk factors and behaviour changes.

Integrating prevention policy

The Australian Government has established a wide-ranging National Strategic Framework for Chronic Conditions, which now needs to be extended to grasp the full potential of national investment in prevention to address brain health. Expert opinion in Australia and internationally identifies the importance of an integrated approach in achieving this benefit. In 2014, 190 leading international scientists, including several eminent Australians, wrote a letter to the *Journal of Alzheimer's Disease* making a compelling case for the preventability of dementia and calling upon the governments of the G8 countries to adopt an integrated, strategic approach to chronic disease prevention and risk reduction. This may be more effective than singular strategies focused on disease-specific chronic conditions. The evidence in support of this has accumulated in the intervening five years. There could be much to gain from the taking the following mix of population-wide and targeted actions.

1. Embedding the best evidence for dementia prevention interventions in all chronic disease policies and accompanying strategies including the forthcoming National Strategic Action Plan for Heart Disease and Stroke and the Absolute Cardio Vascular Risk Assessment Guidelines.
2. Ensuring that policies and guidelines reflect the evidence that the presence of vascular risk factors double the chances that asymptomatic, neurodegenerative pathology will lead to dementia. This requires identifying opportunities for intervention along the life course and targeting of screening and risk reduction interventions at people in their 40s and 50s who have vascular risk factors and earlier amongst Aboriginal and Torres Strait Islander groups.
3. Promoting and supporting the implementation of the WHO Guidelines on the prevention of Cognitive Decline and Dementia.

4. Integrating dementia prevention goals in the narrative and scope of relevant health improvement initiatives including physical activity and nutritional strategies and programmes, and tobacco and alcohol reduction programmes.
5. Identifying effective, cultural and gender-sensitive methods for raising public understanding of the shared risk factors for brain and body health with appropriate targeting of at-risk groups, particularly in areas of disadvantage.
6. Maintaining and extending support for dementia prevention research through the NHMRC's Boosting Dementia Research initiative and Medical Research Future Fund, and enlarging the scope to address the impact of social, economic and environmental risk factors and preventative interventions.

Introduction

The scientific and policy literature documents significant associations between the risk factors for dementia and those for other major chronic diseases, including heart disease, stroke, chronic obstructive pulmonary disease (COPD), diabetes, some cancers and falls. High blood pressure, high cholesterol and obesity in midlife are strong risk factors for dementia. Estimates suggest that over 30% of dementia cases could be prevented or delayed through a coordinated approach to tackling the shared risk factors for many chronic diseases, particularly cardiovascular disease (CVD). Achieving this potential for disease reduction requires the integration of dementia prevention initiatives into the Australian Government's ambitious chronic disease policy and accompanying strategies.

A growing volume of research and expert opinion highlights the effectiveness of adopting an integrated approach to chronic disease reduction. Policy and interventions focused on understanding and responding to the shared, underlying risk factors for preventable chronic diseases may have more impact than those focused on disease-specific chronic conditions.[8] [9] [10] The World Health Organisation (WHO) has recently (May 2019) summarised the existing evidence for risk-factor reduction and formulated guidelines for interventions based on this evidence.[11] These new guidelines provide a strong, foundational knowledge base for governments, policymakers, health care providers and many other stakeholders to inform a national dementia risk-reduction strategy.

The evidence base is more than adequate to support the implementation of a bold new approach to identifying and reducing risk factors in individuals through evidence-based interventions. Such an approach could prevent much of the dementia burden of vascular origin, whilst simultaneously reducing rates of CVD, diabetes, obesity and other chronic diseases in the Australian population.

The evidence discussed in this paper has been reviewed and endorsed by a wide range of expert individuals and organisations working in the fields of dementia and population health. It will be supplemented by a policy issues paper, which will identify the ways in which national policy can begin to grasp the full preventative potential of linking brain and body health.

The key facts

Dementia is a public health crisis

Dementia is a group of disorders characterised by a decline from a previously attained cognitive level. Dementia may be diagnosed at any time of life and in any population, but it is more common after the age of 65. Dementia is one of the main causes of disability in later life in Australia, affecting the ability to undertake the activities of daily living with symptoms including memory loss, confusion, and problems with speech, understanding, and controlling emotions.[12] Comorbid vascular disease is commonly observed in both older and younger people with dementia, including 80% of cases of people with Alzheimer's disease.[13 14 15]

People living with dementia

2019: 50 million

2030: 82 million

2050: >152 million

The growing incidence of dementia is a global public health crisis, posing significant challenges to health and social care systems worldwide. The World Health Organization (WHO) estimates that 50 million people (5% of the world's population of people over 60 years of age) are living with dementia; with this number expected to more than triple by 2050 (see Figure 1 below).16

Dementia is feared

Research by Dementia Australia (formerly Alzheimer's Australia) has shown that dementia is the most feared condition after cancer.17 A survey of over 1000 adult Australians in 2014 suggests that whilst people think that dementia is very important, many people consider it an inevitable part of ageing and do not understand the role of vascular health in dementia risk-reduction. 18 There is an urgent need for proactive efforts to transform fatalistic attitudes by informing the community of the association between dementia and cardiovascular risk factors and to raise public awareness of the possibilities and options for prevention.19 20

Dementia Australia has urged the Australian Government to develop and implement a National Dementia Strategy to ensure a comprehensive and coordinated approach to addressing cognitive decline. Dementia Australia makes the important case that this would slow the rise in the number of people over 65 who have Alzheimer's disease or other dementias.[21] However, dealing with brain health in isolation from the broader framework of policies on chronic disease may mean that other preventive health strategies and approaches fail to grasp the added potential for brain health.[22 23] Growing evidence and expert opinion suggests a need to engage policy and practice in focusing on the shared risk factors that contribute to a range of preventable chronic diseases, including dementia.[24 25 26]

Dementia in Australia: current trends

- An estimated **447,115** people have dementia. Based on trends in population growth and ageing and the current lack of any curative interventions, the number of people with dementia will reach 1.1 million by 2056 [27]
- **The Australian Bureau of Statistics (ABS) projects that dementia will soon supplant heart disease as the leading cause of death in Australia. Dementia is, currently, the second leading cause of death, contributing to 5.4% of all deaths in men and 10.6% of all deaths in women each year.**[28]
- Around 244 people per day are newly diagnosed with dementia.[29]
- The number of new cases of dementia will increase to 318 per day by 2025 and over 650 per day by 2056.[30]
- An estimated 25,938 people have younger onset dementia, expected to rise to 29,375 by 2025 and 42,252 by 2056.[31] This term describes any form of dementia diagnosed in people under the aged of 65 by.[32]
- The number of persons with dementia in 2017 was estimated to range from 1,663 individuals living in the Northern Territory to 138,721 persons living in New South Wales**. The greatest percentage increase in the number of persons with dementia over the next 40 years is expected to occur in the Northern Territory, followed by Western Australia.**[33]
- The risk of dementia in Indigenous Australians is 3–5 times that in non-Indigenous persons.[34]
- People with dementia aged 65 and over have **a substantially higher average number of health conditions** than all people in this age group (5.4 and 2.9 respectively).[35]

Number of Australians newly diagnosed with dementia per day

2015: 244

2025: 318

2056: 650

Costs of dementia

Predicted cost of dementia in Australia

2025: $18.7 billion

2056 $36.8 billion

The direct and indirect costs of dementia in Australia are estimated by the National Centre or Social and Economic Modelling (NATSEM) to increase to **$18.7 billion in today's dollars by 2025** and to **$36.8 billion by 2056**.[36] This will place health care systems under significant additional strain. NATSEM suggests that a 5% reduction in the numbers of people over 65 with dementia could achieve immediate savings of nearly $6 billion to 2025 and a 'staggering' cumulative $120.4 billion by 2056.

Dementia also generates substantial health and social costs for carers, family members, and others affected by it indirectly. In response to the anticipated enormous social and economic burden, the Australian Government's 2014 Budget gave an additional $200 million over five years to boost Australia's dementia research capacity.[37] The National Health and Medical Research Council's Dementia Research Initiative maintains a focus on "*strengthening coordination of Australia's dementia research effort, implementing research findings into policy and practice and evaluating impacts*." This focus includes dementia prevention.

Dementia and population characteristics

Sex and gender

Currently dementia is the leading cause of death in women and the second leading cause of death in the population overall**,** contributing to 5.4% of all deaths in men and 10.6% of all deaths in women each year.[38] There are, in addition, measurable differences between men and women in dementia prevalence.[39] Most people with dementia are women (64%). Half of those with dementia living in the community are women but, in residential accommodation, 72% of people with dementia are women. Given the increasing prevalence of dementia with age, and the longer life expectancy of women, it is unsurprising that people with dementia are mostly older women, but it should not be assumed that the incidence of dementia amongst older women is attributable to longevity in isolation from other factors.[40 41]

Very little is understood about the range and interactions of both biological sex and gender-associated risk factors for dementia across the life course.[42] There is some evidence about the impacts of both biological sex and gender on the development of cognitive impairment and progression to dementia; this highlights the need for additional, high-quality longitudinal research. There is good evidence that women and men have different risk profiles in relation to CVD, diabetes, obesity, musculoskeletal problems and mental illnesses, all of which are established risk factors for dementia in later life.

One large-scale French study (>6000 participants) found that both men and women classified as having mild cognitive impairment were more likely to have depressive symptomatology and to be taking anticholinergic drugs.[1] Men were also more likely to have a higher body mass index, diabetes and stroke, whereas women were more likely to have poor subjective health, to be disabled, to be socially isolated and to suffer from insomnia.[43] Other studies have identified that in women aged >75 years, rates of hypertension, hyperlipidaemia and diabetes are higher than in similarly aged men.[44] Genetic and pathological factors also appear to have a greater deleterious effect on the brain and memory performance in women than men.[45] Midlife hypertension and hypercholesterolemia in both sexes predict a higher risk of developing mild cognitive impairment or dementia in later life.[46 47 48] Diabetes is increasing in incidence to a greater extent in women than in men, and is associated with a substantial risk of cognitive impairment.[49 50 51] Dementia in women is probably, and in men possibly, influenced by obesity in midlife.[52 53] All of these biological factors interact with social and cultural aspects of gender, which also influence differential exposure to and impacts from risks for both men and women. These gender-associated risks relate to differences in health-related behaviours, including smoking and the use of alcohol, and years of formal education.[54 55 56 57]

[1] Anticholinergic drugs inhibit the transmission of parasympathetic nerve impulses, thereby reducing spasms of smooth muscles (for example, muscles in the bladder). Side effects of anticholinergic medications include dry mouth and related dental problems, blurred vision, tendency toward overheating (hyperpyrexia), and in some cases, dementia-like symptoms

Aboriginal and Torres Strait Islander People

In 2008, a study found that the prevalence of dementia in Indigenous people aged over 45 years in the Kimberley was 12.4%, some five times greater than the overall Australian population rate of 2.4% (age standardised).[58] Another study has confirmed the high prevalence of dementia in rural and urban-dwelling Indigenous people in NSW.[59] In both studies, the most common specific form of dementia was Alzheimer's disease. A five-year follow-up of the original Kimberly study confirmed the risk factors associated with dementia and cognitive impairment as age, head injury, hypertension and stroke.[60] Of the original participants with dementia, 77% had died by the five-year follow-up. Overall, the major predictors of mortality were age, male sex, poor mobility and cognitive impairment. These studies are the largest community studies of population prevalence of dementia performed in Australia over the last 25 years, confirming that dementia and cognitive impairment pose major challenges for Australian Indigenous and Torres Strait Islander people.

Country of birth

Little epidemiological data about dementia has been collected in Australia over the past 30 years, and data on the incidence or prevalence of dementia among culturally and linguistically diverse (CALD) communities in Australia is even scarcer. It has been suggested that dementia incidence rates are lower in developing regions than in developed countries due to variations in genes, environment, chemical neurotoxins, diet, vascular disease and its risk factors, lifestyles, and interactions between genes and the environment.[61] However, lower incidence rates in developing countries may be attributable to under-detection of mild dementia due to difficulties in determining cognitive impairment.

Some studies have identified variations in the prevalence of dementia between different ethnic groups. However, there is a dearth of Australian studies focusing on how ethnicity influences dementia, with a preponderance of studies looking at service and treatment access for people from minority ethnic groups who face well-documented barriers. It is not possible at this stage to identify precise correlations between ethnicity, which is unmodifiable, and the modifiable risks for dementia, but it is suggested that a variety of biopsychosocial factors cause ethnic differences in dementia incidence.

A major systematic review compared the use of health and social services and treatments for dementia and involvement in dementia research between different ethnic groups. The researchers found consistent evidence, mostly from the United States, that people from minority ethnic groups accessed diagnostic services later in their illnesses, and once they received a diagnosis, were less likely to access anti-dementia medication or 24-hour care, or participate in trials.[62] Similarly, research conducted in Australia found that patients from non-English-speaking backgrounds (NESB) were less likely to visit a memory clinic than their English-speaking counterparts.[63] Patients of NESB were younger and less educated, and those who presented with dementia did so at a later stage of the disease. These findings highlight the difficulty that some people of NESB have in understanding preventive information and accessing appropriate disease management services. They may point to a need to strengthen CVD risk assessment and chronic disease management approaches in minority communities, as well as develop linguistically and culturally appropriate services for people from these backgrounds.

Remoteness

Australia is a large country with a minority of the population residing in remote or rural areas. Health is poorer in remote areas than in metropolitan areas and exposure to all risk factors for brain and body health is higher.[64] Age-standardised data for premature deaths (under 75) show that these are twice as likely in the Northern Territory, for example, as in Australia as a whole.[65] ABS data (2008) shows that dementia is the fourth leading cause of death in remote areas. There is good international evidence of geographical variation in the prevalence or incidence of dementia. [66] Little is known about the impact of remoteness in the development of dementia, but it is arguable that the incidence may reflect the geographical disparities that exist for CVD outcomes. Some variations may be explained by socio-economic factors, with risks of adverse CVD events rising as remoteness increases. Reduced access to high-quality community health services is also implicated in health variations.[67] [68] [69] Remoteness is a known risk factor for hospital admission and prolonged hospitalisation and is strongly associated with longer duration of hospitalisation in dementia cases.[70] [71] It is possible that geographical isolation plays a bigger role for people with dementia in their last year of life than for the general population.[72] A robust national approach to risk reduction, which addresses the particular needs of people living in remote and rural areas, could have significant preventive potential and reduce health service costs, particularly the costs of inpatient care.[73] [74]

Psychosocial factors

There is strong evidence of the significant mediating effects of education and depression, suggesting that modifiable psychosocial factors may influence an individual's vulnerability to dementia.[75] [76] [77] [78] Hence, timely diagnosis and appropriate and effective treatment of depression, as well as management of cardiovascular risks, may prevent and reduce the rate of cognitive impairment and dementia in old age. There is evidence that high-quality primary care, involving robust assessment and management of risks, is associated with better outcomes in CVD and that this effect is particularly marked in areas of high deprivation and in areas of ethnic diversity.[79] [80]

Causes of dementia

Despite much research into the causes of dementia, many unanswered questions remain. The current evidence demonstrates that multiple factors, including age, genes, environment and lifestyle factors, contribute to whether a person develops dementia.

Biomedical risk factors

Risk factors for some dementias are similar to those for other major chronic diseases, including heart disease, stroke, COPD, diabetes and some cancers.

Risk factors for dementia, as for heart disease and other chronic diseases, are classified as modifiable and non-modifiable. The scientific and policy literature documents significant associations between the modifiable risk factors for some dementias and those for other major chronic diseases, including heart disease, stroke, chronic obstructive pulmonary disease, diabetes and some cancers.[81] The WHO has recently reviewed the evidence on risk factors and provided guidelines for preventive interventions where the evidence is considered strong enough. Sufficient evidence was found in relation to the following risks.

Physical inactivity

Physical activity has many health benefits and is a key modifiable factor involved in the development of many chronic diseases including dementia.[82] [83] [84] There is evidence that the highest levels of physical activity are the most protective and may have direct beneficial effects on brain structures. [85] [86] [87] Indirectly, it is suggested that the impacts of physical activity on brain health arise from the underlying impacts on cardiovascular risk factors including hypertension, insulin resistance, high cholesterol and other biological mechanisms.[88] Therefore, maintaining physical activity levels and muscle mass, strength and function throughout the life course may reduce the prevalence of dementia and prevent (or slow) cognitive decline among the Australian population.

Smoking

Tobacco is still the leading cause of preventable deaths globally, incurring billions of dollars on healthcare and welfare costs.[89] Smoking is a major risk factor for a number of chronic conditions including heart disease, respiratory diseases, and many cancers. A large body of evidence highlights associations between smoking in mid-life and subsequent disorders in later life including cognitive decline and dementia.[90] [91] There is good evidence for the effectiveness of smoking cessation interventions in reducing all of these health risks. [92] [93]

Nutrition

Healthy eating is an important contributor to optimal health across the life course as well as in the prevention of chronic diseases, including those that increase the risk of dementia.[94] Evidence suggests that diet may be involved both directly and indirectly in the development of dementia through its effect on other risk factors. [95] A range of high-quality studies have concluded that high levels of adherence to a Mediterranean diet, including consumption of fruit, vegetables, fish, nuts, olive oil and other unsaturated fats, whole grains and coffee may be associated with better cognitive performance and reduced incidence of dementia. [96] [97]

Alcohol

Evidence is increasing about the complex relationship between alcohol use and cognitive health and dementia. Previous reviews point to a possible beneficial effect of light to moderate alcohol use on cognitive health.[98] However, even moderate drinking has been associated with detrimental effects on brain structure, and heavy drinking is detrimentally related to dementia risk, whatever the dementia type.[99] [100] [101] [102] [103] There is increasing evidence in support of the contention that heavy alcohol use (>12g per day) is associated with increased dementia risk.[104] Alcohol use disorders are characterised by the harmful and chronic consumption of alcohol. People who consume harmful amounts of alcohol are three times more likely to develop younger onset dementia. [105] [106] [107] [108] Alcohol use disorders are also associated with a range of associated risk factors for dementia, including smoking and poor nutrition and physical inactivity. [109]

Weight management

Overweight and obesity are direct risks for a wide range of chronic diseases including Type 2 diabetes and cancer.[110] [111] They are also indirect risks for other cardiovascular risk factors including high cholesterol and hypertension.[112] There is evidence that obesity at mid-life increases the subsequent risk of dementia.[113]

Diabetes mellitus management

Late life diabetes has been linked to an increased risk of cognitive decline and dementia.[114] [115] In addition, secondary health problems arising from diabetes including kidney disease, eye disease, hearing impairments and CVD have all been associated with increased risk of dementia. [116] [117] There is only inconsistent evidence yet for a direct impact on cognitive outcomes from glucose-control interventions.[118] There is evidence that treating the cardiovascular comorbidities associated with diabetes may mediate risks for dementia. [119]

Hypertension management

Hypertension in mid-life has been associated with an increased risk of dementia later in life.[120] The evidence for a direct impact on blood pressure reduction in mid or later life on subsequent cognitive decline or dementia is not yet established. However, it is clear that reducing hypertension is highly beneficial in reducing cardiovascular disease and premature mortality and therefore on improving the overall health of the older population. [121]

Cholesterol management

Dyslipidaemia (high cholesterol) is an important modifiable risk factor, linked to a third of the burden of heart disease globally as well as premature mortality and disability. A number of epidemiological studies have found a link between high cholesterol and dementia, although this has not yet been demonstrated definitively. Other studies have identified an association between the control of cholesterol and a reduction of dementia risk.

A summary of the WHO recommendations in relation to each of these risks is provided at Appendix 1.

The WHO has not provided guidelines for the management of depression and mid-life hearing loss although a number of studies, including the Lancet Commission, have identified these as additional, modifiable risks for cognitive impairment and dementia. [122] [123]

Social risk factors

The World Health Organization guidelines do not address the influence of broader social determinants on dementia risk. Many other studies have, however, explored and described an inverse association between socioeconomic position and chronic conditions such as cardiovascular disease (CVD) and dementia.[124] The biological and other pathways that lead to these conditions are known although the ways in which they exert their cumulative impact is not well understood. The social gradient in CVD persists even after adjustment for health behaviours and clinical indicators, suggesting that other processes are involved.[125] [126]

Compared with people who complete high school, those who leave between years 8 and 11 have 1.5 times the risk of dementia, and those leaving before year 8 have 2.2-fold higher risk.

Immune responses to chronic 'social stress' may explain some of the socioeconomic gradient in CVD and other inflammation-associated conditions, including dementia.[127] Providing a measure of support for this argument, there is some evidence that social interventions, particularly the promotion of higher educational attainment, may exert a protective impact. People who leave high school before year 8 have a 2.2-fold higher risk of dementia in later life and those leaving between years 8 and 11 have 1.5 times the risk of individuals who complete high school.[128] [129] [130] [131] [132] There is increasing evidence that loneliness and isolation are associated with poorer cognitive function among older adults.[133] [134] Interventions to reduce social isolation, promote social engagement and increase levels of physical activity among older people reduce dementia risk.[135] Interventions that foster social connections may be particularly beneficial for individuals with low levels of education.[136] In addition, hearing loss is associated with both social isolation and the incidence of dementia.[137] [138]

The Lancet Commission suggests that the protective effect of education and social engagement is related to variations in levels of 'cognitive reserve' (brain resilience), which is enhanced by early-life experiences, including education and intellectual stimulation.[139] [140] [141] There is evidence that higher socioeconomic status during gestation and early childhood has a protective association with late-life dementia risk.[142] [143]

Cost benefits of a risk reduction approach

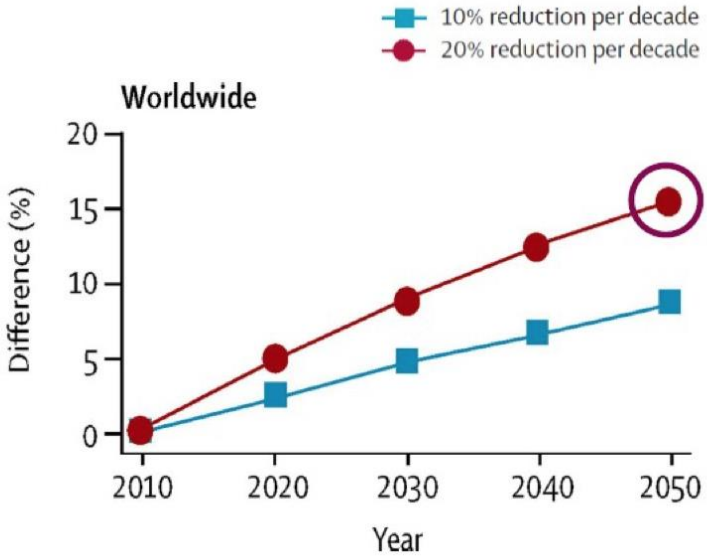
Up to half of the total dementia burden in Australia may be due to the effect of vascular and other modifiable risk factors.[144 145 146] A reduction in these risk factors would lower the cost of dementia by $24.8 billion over the next 20 years (by avoiding direct costs of $17.6bn and indirect costs of $7.2bn) and $120.4 billion by 2056 (by avoiding direct costs of $76.6bn and indirect costs of $43.8bn).[147] A decline in the physical inactivity rate by 5% every five years would reduce dementia prevalence by 11% in 2051,[148] meaning 100,000 fewer Australians living with dementia by addressing just one risk factor.

A much larger, cumulative reduction would be expected if more than one risk factor were reduced simultaneously, and these benefits would be enhanced by concurrent reductions in the incidence and prevalence of CVD and other chronic diseases affecting the body.[149 150] Mounting international evidence supports these findings. Norton et al. (2009) suggest that reducing the incidence of seven risk factors (diabetes, hypertension, obesity, physical inactivity, depression, smoking and low education) by 25% would prevent three million cases of Alzheimer's disease per decade worldwide (see Figure 2).[151]

Figure 1. Potential for prevention of Alzheimer's disease. Source: Norton et al. 2015 [152]

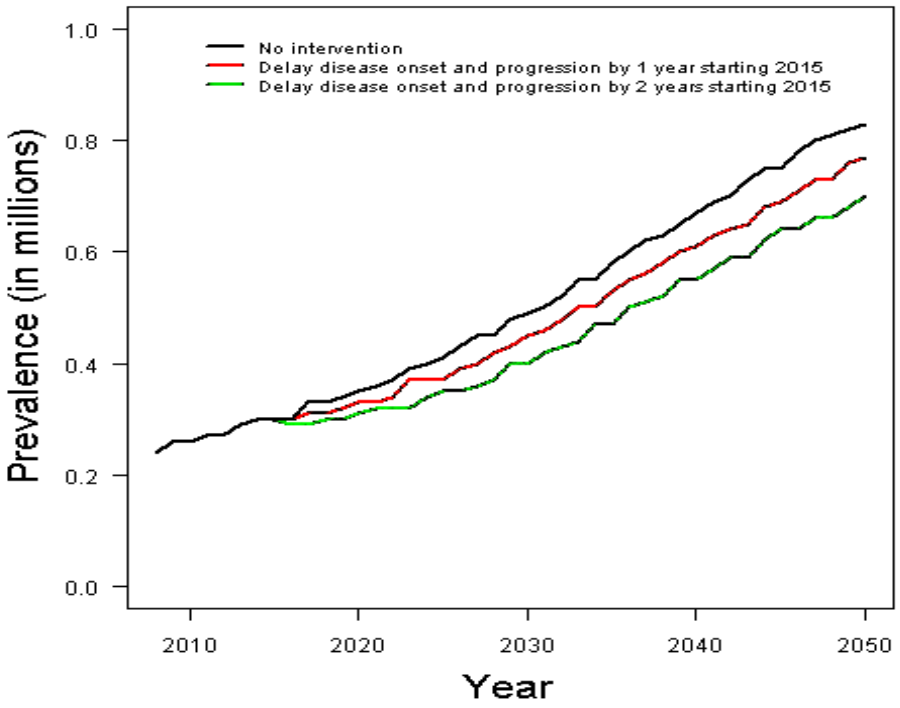
Risk factor	PAR
Diabetes mellitus	2.9%
Midlife hypertension	5.1%
Midlife obesity	2.0%
Physical inactivity	12.7%
Depression	7.9%
Smoking	13.9%
Low education	19.1%
Combined PAR*	28.2%

PAR=population-attributable risk.
*Adjusting for non-independence of the risk factors.



Other studies estimate that a one-year delay in the average age of onset of Alzheimer's disease due to preventive strategies could result in nearly 12 million fewer cases worldwide by 2050.[153] See Figure 2 for modelled comparisons between disease onset and progression with no risk reduction intervention and with a hypothetical risk reduction intervention from 2015.

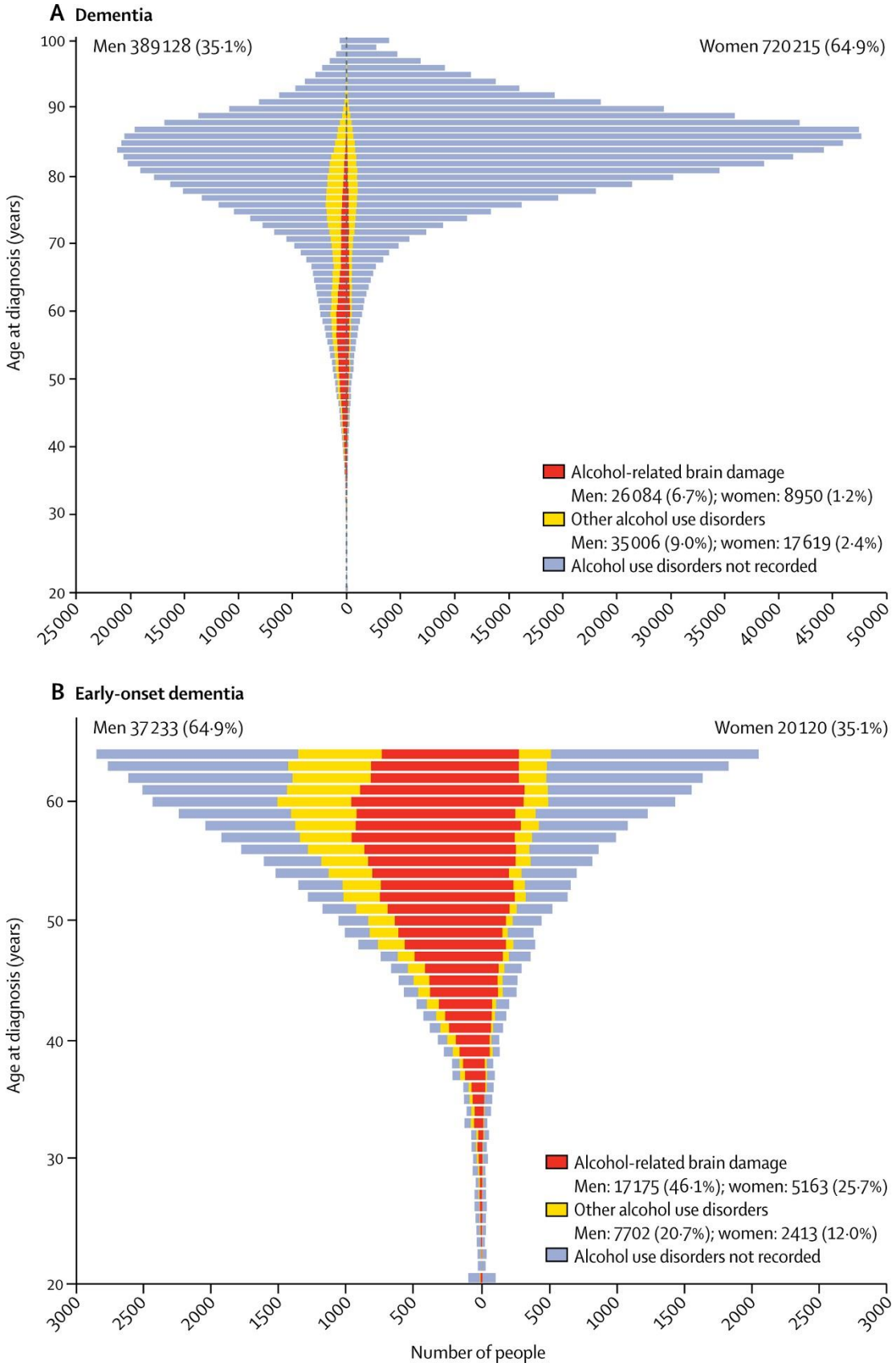
Figure 2. Modelling data on impacts of postponing the onset and progression of Alzheimer's disease in Australia. Adapted from Access Economics 2009.[154]



Tackling alcohol abuse

There is some evidence that dementia prevention could produce even greater results if it includes action to reduce levels of heavy drinking in the Australian population. The evidence base for the impact of alcohol on brain health is not yet established, but it is accumulating. Figure 3 shows the population pyramid of alcohol-related dementia prevalence identified in this study. [155]

Figure 3. Population pyramid of dementia (A) and early-onset dementia (B), overall and by alcohol use disorders (A) Prevalent cases of dementia (n=1 109343). (B) Prevalent cases of early-onset dementia (n=57 353). Source: Schwarzinger et al. 2018.

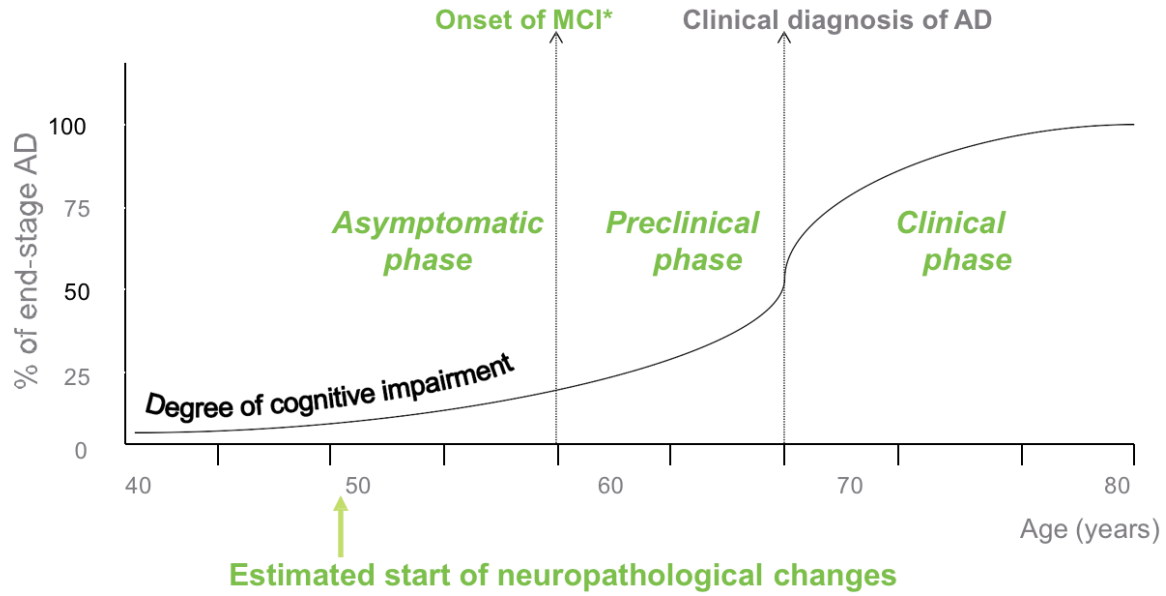


Alcohol use disorders are also associated with a range of other risk factors for dementia, including smoking, depression and poor lifestyle choices, all of which are absolute cardiovascular risk factors.[156] A recent Lancet publication (2018) on the relationship between alcohol and dementia prevention underscores the importance of alcohol use disorders in relation to people with younger onset dementia, finding that 57% of people with this diagnosis also had an alcohol use disorder.[157]

Life course effects

There are important life course considerations for both risk and protective factors for dementia. These diseases have a long latency period and pathology may be present for decades before cognitive symptoms are evident. The life course progression of Alzheimer's disease is described in Figure 4.

Figure 4. Life course progression of Alzheimer's disease. Source: Ngandu et al. 2015.[158]



***MCI** - mild cognitive impairment

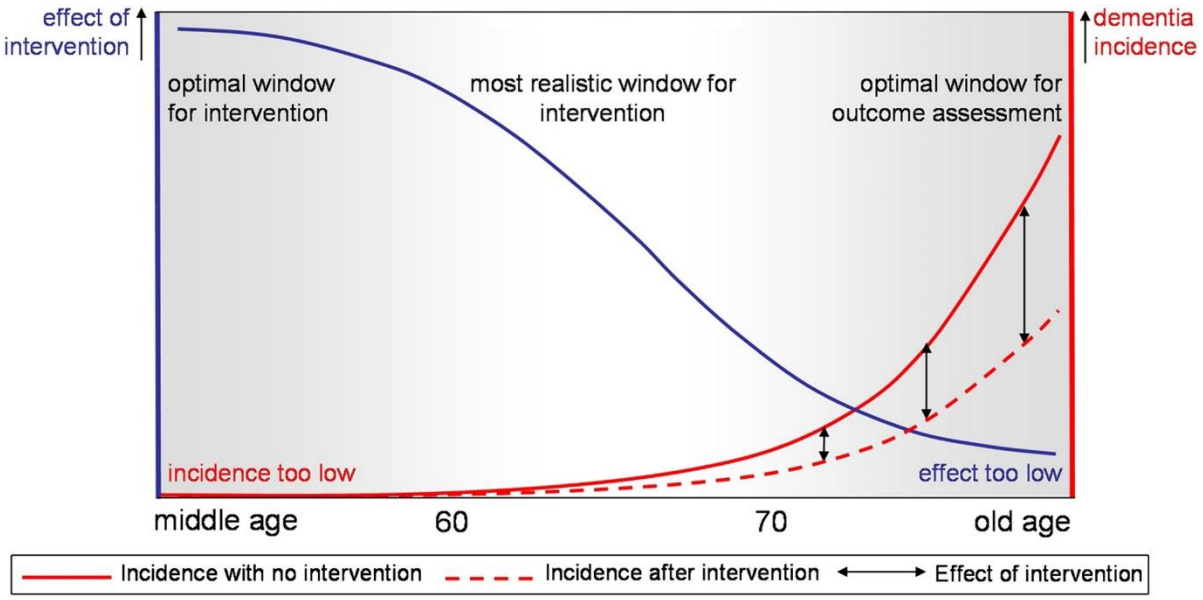
The life course nature of disease onset and progression means that there may be optimal 'windows' for intervention. Research increasingly indicates that the presence of risk factors in midlife, but not late life, is associated with an increased risk of dementia.[159] There is international evidence that even at age 50, cognition is affected by risk behaviours. However, most dementia studies recruit participants over the age of 70, because of the assumption that dementia is an older person's disease, but the age of an individual at diagnosis provides no guide to the length of time that brain pathology was present.[160] Figure 5 identifies the optimal life course periods for preventive dementia intervention based on current knowledge. Further research, focusing on cognition in younger population cohorts, not just diagnosed dementia in older populations, is required to improve understanding of how and when to target preventive interventions. [161]

Other research indicates that middle-aged people with multiple vascular risk factors such as obesity, hypertension, diabetes, high cholesterol and smoking have elevated levels of brain amyloid (the plaques and tangles in the brain associated with Alzheimer's disease and other dementias) in later life.[162] These researchers recommend aligning policy and clinical practice to target cardiovascular screening and risk reduction strategies at people in middle age. Their

findings reinforce the recommendations of a wide range of expert bodies including the WHO regarding the importance of assessing cardiovascular risk for all adults aged 40–75 and for offering lifestyle modification advice, medication or both to those at high risk.[163] [164] Bodies which have already made such calls include the Royal Australian College of General Practitioners[165] the National Health and Medical Research Council, and the National Vascular Disease Prevention Alliance.[166]

The need for a life course approach has been acknowledged by the Australian Government. In 2016 the Parliament of the Commonwealth of Australia stated that the absence of longitudinal data (and in particular longitudinal biomedical data) about people's health as they progress from midlife into later life is an impediment to tackling the chronic disease epidemic in Australia. [167]

Figure 5. Optimal time window for preventive interventions. Source: Richard et al. 2012. [168]



The Finnish National Memory Program

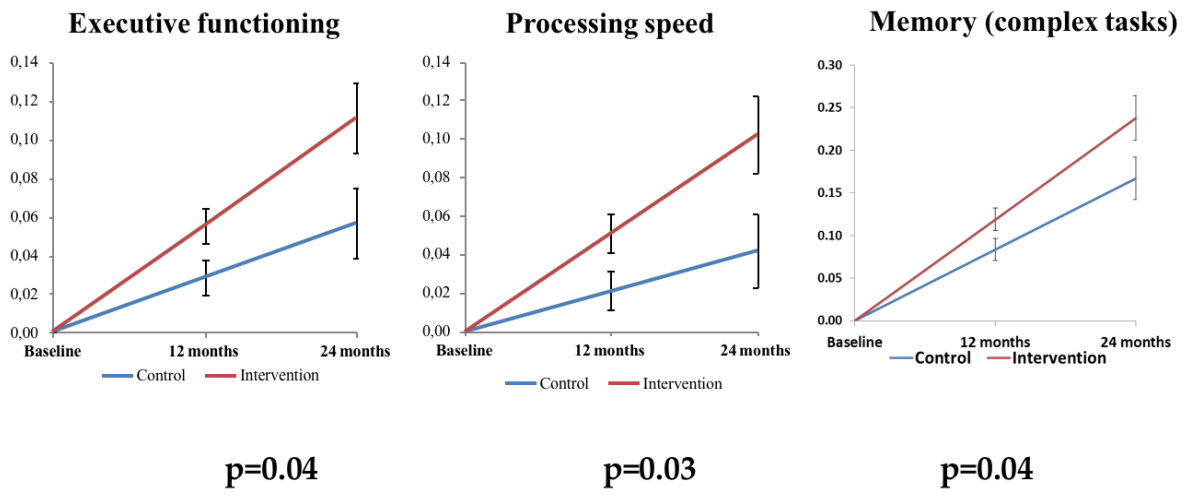
Finland has taken a unique and effective national strategic approach to the prevention of dementia and the promotion of brain health, which could provide an evidence-based model for similar initiatives in Australia. In 2013, the Finnish Ministry of Social Affairs and Health published its national plan, *Creating a Memory-Friendly Finland*, which addresses both dementia and brain health.[169] A 'memory-friendly' Finland is a society that takes the promotion of brain health and the early detection of cognitive symptoms seriously. It is a society in which "*anyone diagnosed with a cognitive problem or dementia has access to appropriate treatment, care and rehabilitation"* and it ensures that "*patients can lead their lives with dignity, and they will not be left without support"*.

It is important to note that the Finns' emphasis on the term 'memory' as opposed to dementia points to the expected outcomes of the National Programme, which is improved cognitive functioning at the population level. The use of this word also avoids the potential for stigma and discrimination associated with the term 'dementia'.

Evidence of the effectiveness of the Finnish model has been demonstrated through the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER). The FINGER Study was a multi-centre controlled trial involving 1,200 people with several vascular risk factors and unhealthy lifestyle-related factors who were assessed to be at risk of cognitive decline.[170] They participated in a two-year, intensive multi-domain intervention consisting of nutritional guidance, exercise, cognitive training and social activity, and management of metabolic and vascular risk factors. At the end of the study, the intervention group had improved several aspects of cognitive functioning compared with the control group.[171] These findings are summarised in Figure 7 below.

Finland has promoted ACVR assessment by primary care clinicians for over a decade as part of a comprehensive range of national policy measures to improve diets, reduce smoking and ensure that the whole population has access to evidence-based prevention and treatment regimes.[172] This has led to a significant decline in CVD.[173] [174] The National Memory Programme is therefore taking place in a countrywide context in which risks to brain and body health are being proactively addressed. This approach may be replicable lessons in Australia.

Figure 6. Outcomes from the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability. Source: Ngandu et al. 2015.



Barriers to a risk reduction approach

Apart from the notable example of the Finnish National Memory Programme, national dementia policies worldwide tend not to address prevention, and when they do, the reach and extent of dementia prevention is restricted and under-funded compared with prevention of other major chronic diseases.[175] The primary focus of most current research is to improve understanding of the biological causes and to develop treatments and cures. Even in this context, dementia research has gaps in several critical areas, including the role of and interactions with other conditions such as diabetes and the effects of interventions to control vascular risk factors for declining cognition or the impact of depression, and hearing loss or biological sex.[176] There are also large research gaps in relation to social risk factors including gender, ethnicity, socio-economic status and geography on the development and progression of dementia.

Like biomedical research, chronic disease prevention programs often operate in silos, addressing risk factors for single chronic physical diseases such as diabetes or CVD without attending to the risks these pose for other disorders, particularly those affecting the brain.[177] In addition, there is little integrated reporting on Australia's progress in preventing chronic diseases.[178] [179]

Policies tend to emphasise social care and other service provision, clinical and management practices for people with dementia, support for carers and 'information', broadly defined.[180] These are essential to address the needs of individuals with dementia, carers and communities. However, complementary policies and further investment in prevention is urgently required to avoid the costs, both human and economic, which will accrue by 2050.

Is the evidence strong enough?

There is good evidence from Australia and internationally that preventive interventions have significant returns on investment at both individual and population levels, particularly when compared with investment in healthcare.[181] [182] [183] [184] There is convincing evidence of the cost-effectiveness of interventions targeted at people at highest risk of chronic diseases.[185] As the population ages the costs of chronic diseases of the body and brain will continue to rise.[186] [187] The available evidence suggests that it is feasible to attempt to prevent or delay up to a third of the anticipated rise in incidence of dementia through a mix of population and individual-level interventions. Moreover, an integrated focus on better population health will reduce the prevalence of multiple chronic diseases which are cumulatively responsible for substantial disability and loss of independence in ageing and which are extremely costly economically, socially and individually.[188] If the potential for prevention can be grasped, there will be significant returns on investment for the Australian taxpayer arising from increased productivity and reduced costs of health and social care.[189] [190]

In 2014, 190 leading international scientists, including several eminent Australians, wrote a letter to the *Journal of Alzheimer's Disease* making a compelling case for the preventability of dementia and calling upon the governments of the G8 countries to adopt an integrated, strategic approach to dementia prevention.[191] These scientists were unequivocal in stating that "*there is already sufficient evidence to justify immediate action.*" The WHO and the Lancet Commission have both reinforced this position.

The evidence about dementia prevention is now sufficiently robust to be made more widely available and acted upon. The public should know what the scientific evidence demonstrates: certain healthy behaviours are known to be effective for preventing diabetes, CVD, cancer and for reducing the risk of dementia and other forms of cognitive decline.

Australia's International Commitments on Dementia

Signatory to the G8 Dementia Summit Declaration, 2013 [192]

Signatory to the first WHO Ministerial Conference on Global Action against Dementia 2015.[193]

Signatory to the WHO Global Action Plan for Prevention and Control of NCDs 2013–2020[194]

Signatory to WHO Global Action Plan on the Public Health Response to Dementia 2017–2025.[195]

In 2018, the OECD reviewed progress on translating these aspirations into meaningful action amongst member nations. The OECD has concluded that '*The priority given to dementia is too low given its impact on society'.*[196]

Australia has a proud history of achievements in ambitious, focused strategies to reduce health risks for our population, such as prevention strategies related to sun exposure and tobacco smoking. The same ambition and commitment now needs to be applied to an integrated prevention agenda for brain and body health.

Next steps

The AHPC and collaborating experts are in the process of developing an evidence based policy framework for brain health. In the interim, the evidence suggests that the following achievable components, which are aligned with current policy approaches in Australia would signal serious national commitment to the prevention of dementia and cognitive decline:

1. Embedding the best evidence for dementia prevention interventions in all chronic disease policies and accompanying strategies including the forthcoming National Strategic Action Plan for Heart Disease and Stroke and the Absolute Cardio Vascular Risk Assessment Guidelines.

2. Ensuring that policies and guidelines reflect the evidence that the presence of vascular risk factors double the chances that asymptomatic, neurodegenerative pathology will lead to dementia. This requires identifying opportunities for intervention along the life course and targeting of screening and risk reduction interventions at people in their 40s and 50s who have vascular risk factors and earlier amongst Aboriginal and Torres Strait Islander groups.

3. Promoting and supporting the implementation of the WHO Guidelines on the prevention of Cognitive Decline and Dementia.

4. Integrating dementia prevention goals in the narrative and scope of relevant health improvement initiatives including physical activity and nutritional strategies and programmes, and tobacco and alcohol reduction programmes.

5. Identifying effective, cultural and gender-sensitive methods for raising public understanding of the shared risk factors for brain and body health with appropriate targeting of at-risk groups.

6. Maintaining and extending support for dementia prevention research through the NHMRC's Boosting Dementia Research initiative and enlarging the scope to address the impact of social, economic and environmental risk factors and preventative interventions.

Appendix 1: WHO Guidelines: Reduction of Risk of Cognitive Decline and Dementia

Summary of key recommendations

1. Physical Inactivity

The WHO recommends that adults aged 65 years and over should do at least 150 minutes (rising to 300 minutes) of moderate intensity aerobic physical activity on at least three days each week, involving muscle strengthening and balance training. Adults of this age group whose health conditions prevent them from doing the recommended levels of activity should be as physically active as their abilities and conditions allow.

2. Smoking

The WHO recommends that interventions for tobacco cessation should be offered to all adults who use tobacco to reduce the risks of cognitive decline and dementia as well as other health benefits.

3. Nutrition

The WHO recommends offering a Mediterranean -like diet to adults to with normal cognition or mild cognitive impairment to reduce the risk of cognitive decline and/or dementia.

4. Alcohol

The WHO recommends that interventions aimed at ceasing or reducing harmful drinking should be offered to adults with normal cognition or mild cognitive impairment to reduce the risk of cognitive decline and/or dementia as well as other health benefits.

5. Weight Management

The WHO recommends that interventions for mid-life overweight and/or obesity be offered to reduce the risk of cognitive decline and dementia but emphasises that lifestyle interventions that include dietary changes and increased physical activity have the best results.

6. Diabetes Management

The WHO recommends that management of diabetes in the form of medications and/or lifestyle interventions should be offered to adults with diabetes to reduce the risk of cognitive decline and/or dementia.

7. Hypertension Management

The WHO recommends that hypertension reduction interventions be offered to adults with hypertension to reduce the risk of cognitive decline and/or dementia.

8. Dyslipidaemia Management

The WHO recommends that management of dyslipidaemia at mid-life should be offered to reduce the risk of cognitive decline and dementia.

Source: World Health Organization 2019, Risk Reduction of Cognitive Decline and Dementia*: WHO Guidelines.*
https://www.who.int/mental_health/neurology/dementia/guidelines_risk_reduction/en/

References

[1] Dementia Australia 2018, Dementia Prevalence Data 2018-2058, commissioned research undertaken by NATSEM, University of Canberra.
[2] Australian Bureau of Statistics 2015, *Causes of Death, Australia, 2015,* cat. no. 3303.0, ABS, Canberra.
[3] Australian Bureau of Statistics 2015, *Causes of Death, Australia, 2015,* cat. no. 3303.0, ABS, Canberra.
[4] Dementia Australia (2018). Dementia Prevalence Data 2018-2058, commissioned research undertaken by NATSEM, University of Canberra. *https://www.dementia.org.au/information/statistics/prevalence-data*.
[5] Australian Bureau of Statistics 2015, *Causes of Death, Australia, 2015,* cat. no. 3303.0, ABS, Canberra.
[6] Australian Bureau of Statistics 2013, Census of Population and Housing: *Socio-economic Indexes for Areas (SEIFA*), *Australia, 2011,* cat. 2033.0.55.001, ABS, Canberra.
[7] Australian Institute of Health and Welfare 2012, *Dementia in Australia*, cat. no. AGE 70, AIHW, Canberra.
[8] Barnes, DE & Yaffe, K 2011, The projected effect of risk factor reduction on Alzheimer's disease prevalence, *The Lancet Neurology*, vol. 10, no. 9, pp. 819-828.
[9] Profenno, LA, Porsteinsson, AP & Faraone, SV 2010, Meta-analysis of Alzheimer's disease risk with obesity, diabetes, and related disorders, *Biological Psychiatry*, vol. 67, no. 6, pp. 505-512.
[10] Access Economics 2009, *Keeping dementia front of mind: incidence and prevalence 2009–2050,* Alzheimer's Australia, http://www.alzheimers.org.au/common/files/NAT/20090800_Nat__AE_FullKeepDemFrontMind.pdf
[11] World Health Organization 2019, Risk Reduction of Cognitive Decline and Dementia*: WHO Guidelines. https://www.who.int/mental_health/neurology/dementia/guidelines_risk_reduction/en/*
[12] Australian Institute of Health and Welfare 2012, *Dementia in Australia*, http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=10737422943
[13] Hachinski, V 2015*,* Stroke and potentially preventable dementias proclamation, *Stroke*, pp. 3039–3040, http://stroke.ahajournals.org/content/46/11/3039
[14] Kling, MA, Trojanowski, JQ, Wolk, DA, Lee, VM & Arnold, SE 2013, Vascular disease and dementias: paradigm shifts to drive research in new directions, *Alzheimer's & Dementia*, vol. 9, no. 1, pp. 76–92.
[15] Toledo, JB, Arnold, SE, Raible, K, Brettschneider, J, Xie, SX, Grossman, M, Monsell, SE, Kukull, WA & Trojanowski, JQ 2013, Contribution of cerebrovascular disease in autopsy confirmed neurodegenerative disease cases in the National Alzheimer's Coordinating Centre. *Brain*, vol. 136, no. 9, pp. 2697-2706.
[16] World Health Organization 2019, Risk Reduction of Cognitive Decline and Dementia*: WHO Guidelines. https://www.who.int/mental_health/neurology/dementia/guidelines_risk_reduction/en/*
[17] Phillipson, L, Magee, C, Jones, S & Skladzie, E 2012, *Exploring dementia and stigma beliefs: a pilot study of Australian adults aged 40 to 65*, Paper 28, Alzheimer's Australia, https://www.fightdementia.org.au/files/20120712_US_28_Stigma_Report.pdf
[18] Smith, B.J., Ali, S. and Quach, H., 2014. Public knowledge and beliefs about dementia risk reduction: a national survey of Australians. *BMC Public Health*, *14*(1), p.661.
[19] Schomerus, G, Schwahn, C, Holzinger, A, Corrigan, PW, Grabe, HJ, Carta, MG & Angermeyer, MC 2012, Evolution of public attitudes about mental illness: a systematic review and meta-analysis, *Acta Psychiatrica* Scandinavica, vol. 12, iss. 5, no. 6, pp. 440–452.
[20] Hachinski, V 2015*,* Stroke and potentially preventable dementias proclamation, *Stroke*, vol. 46, pp. 3039–3040, http://stroke.ahajournals.org/content/46/11/3039
[21] Alzheimer's Australia 2015, *Urgent call for a national dementia strategy*, 12 August, https://www.fightdementia.org.au/national/media-releases/urgent-call-for-a-national-dementia-strategy
[22] Smith, AD & Yaffe, K 2014, Dementia (including Alzheimer's disease) can be prevented: statement supported by international experts*, Journal of Alzheimer's Disease*, vol. 38, pp. 699–703
[23] Hachinski, V 2015, Stroke and potentially preventable dementias proclamation, *Stroke*, vol. 46, pp. 3039-3040, http://stroke.ahajournals.org/content/46/11/3039
[24] Barnes, DE & Yaffe, K 2011, The projected effect of risk factor reduction on Alzheimer's disease prevalence, *The Lancet Neurology*, vol. 10, no. 9, pp. 819-828.

[25] Profenno, LA, Porsteinsson, AP & Faraone, SV 2010, Meta-analysis of Alzheimer's disease risk with obesity, diabetes, and related disorders, *Biological Psychiatry*, vol. 67, no. 6, pp. 505-512.
[26] Access Economics 2009, *Keeping dementia front of mind: incidence and prevalence 2009–2050,* Alzheimer's Australia, http://www.alzheimers.org.au/common/files/NAT/20090800_Nat__AE_FullKeepDemFrontMind.pdf
[27] Dementia Australia (2018) Dementia Prevalence Data 2018-2058, commissioned research undertaken by NATSEM, University of Canberra
[28] Australian Bureau of Statistics 2015, *Causes of Death, Australia, 2015,* cat. no. 3303.0, ABS, Canberra.
[29] Australian Bureau of Statistics 2015, *Causes of Death, Australia, 2015,* cat. no. 3303.0, ABS, Canberra.
[30] Australian Bureau of Statistics 2015, *Causes of Death, Australia, 2015,* cat. no. 3303.0, ABS, Canberra.
[31] Australian Bureau of Statistics 2015, *Causes of Death, Australia, 2015,* cat. no. 3303.0, ABS, Canberra.
[32] Australian Bureau of Statistics 2015, *Causes of Death, Australia, 2015,* cat. no. 3303.0, ABS, Canberra.
[33] ABS 2013, Census of Population and Housing: *Socio-economic Indexes for Areas (SEIFA*), *Australia, 2011,* cat. 2033.0.55.001, ABS, Canberra.
[34] ABS 2013, Census of Population and Housing: *Socio-economic Indexes for Areas (SEIFA*), *Australia, 2011,* cat. 2033.0.55.001, ABS, Canberra.
[35] Australian Institute of Health and Welfare 2012, *Dementia in Australia*, cat. no. AGE 70, AIHW, Canberra.
[36] The National Centre for Social and Economic Modelling 2016, *Economic cost of dementia in Australia 2016-2056, https://www.fightdementia.org.au/files/NATIONAL/documents/The-economic-cost-of-dementia-in-Australia-2016-to-2056.pdf*
[37] Department of Health 2017, *Portfolio Budget Statements (2017-18) Budget Related Paper No. 1.10 Health Portfolio*, https://www.health.gov.au/internet/budget/publishing.nsf/Content/2017-2018_Health_PBS_sup4/$File/2017-18_Health_PBS_Complete.pdf, p. 390
[38] Australian Bureau of Statistics 2015, *Causes of Death, Australia, 2015,* cat. no. 3303.0, ABS, Canberra.
[39] Ruitenberg, A, Ott, A, van Swieten, JC, Hofman, A & Breteler, MM 2001, Incidence of dementia: does gender make a difference? *Neurobiology of Aging*, vol. 22, no. 4, pp. 575-580.
[40] Australian Institute of Health and Welfare 2010, *Analysis of the ABS 2009 Survey of Disability, Ageing and Carers*, AIHW, Canberra.
[41] Bamford, SM & Walker, T 2012, Women and dementia – not forgotten, *Maturitas*, vol. 73, no. 2, pp. 121–126.
[42] Milne, A & Williams, J 2000, Meeting the mental health needs of older women: taking social inequality into account, *Ageing and Society*, vol. 20, no. 6, pp. 699–723.
[43] Artero, S, Ancelin, M, Portet F, Dupuy, A, Berr, C, Dartigues, J-F, Tzourio, C, Rouaud, O, Poncet, M, Pasquier, F, Auriacombe, S, Touchon, J & Ritchie K 2008, Risk profiles for mild cognitive impairment and progression to dementia are gender specific, *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 79, pp. 979-984.
[44] Azad, NA, Al Bugami, M & Loy-English, I 2007, Gender differences in dementia risk factors, *Gender Medicine*, vol. 4, no. 2, pp. 120-129.
[45] Rocca, WA, Mielke, MM, Vemuri, P & Miller, VM 2014, Sex and gender differences in the causes of dementia: a narrative review, *Maturitas*, vol. 79, no. 2, pp. 196-201.
[46] Skoog, I, Lernfelt, B, Landahl, S, Palmertz, B, Andreasson, LA, Nilsson, L, Persson, G, Oden, A & Svanborg, A 1996, 15-year longitudinal study of blood pressure and dementia, *The Lancet*, vol. 347, pp. 1141–1145.
[47] Tervo, S, Kivipelto, M, Hänninen, T, Vanhanen, M, Hallikainen, M, Mannermaa, A & Soininen, H 2004, Incidence and risk factors for mild cognitive impairment: a population-based three-year follow-up study of cognitively healthy elderly subjects, *Dementia and Geriatric Cognitive Disorders*, vol. 17, no. 3, pp. 196-203.
[48] Kivipelto, M, Helkala, EL, Hänninen, T, Laakso, MP, Hallikainen, M, Alhainen, K, Soininen, H, Tuomilehto, J & Nissinen, A 2001, Midlife vascular risk factors and late-life mild cognitive impairment: a population-based study, *Neurology*, vol. 56, no. 12, pp. 1683–1689.
[49] Sowers, JR 2004, Diabetes in the elderly and in women: cardiovascular risks, *Clinical Cardiology*, vol. 22, pp. 541-551.

[50] Kannel, WB 2001, Risk factors for cardiovascular disease in women, *Cardiology Review*, vol. 18, pp. 11-16.
[51] Okereke, O, Hankinson, SE, Hu, FB & Grodstein, F 2005, Plasma C peptide level and cognitive function among older women without diabetes mellitus, *Archives Internal Medicine*, vol. 165, pp. 1651-1656.
[52] Whitmer, RA, Gunderson, EP, Barett-Connor, E, Quesenberry, CP Jr & Yaffe, K 2005, Obesity in middle age and future risk of dementia: a 27 year longitudinal population based study, *BMJ*, vol. 330, pp. 1360.
[53] Gustafson, D, Rothenberg, E, Blennow, K, Steen B & Skoog, I 2003, An 18-year follow-up of overweight and risk of Alzheimer disease, *Archives of Internnational Medicine*, vol. 163, pp. 1524-1528.
[54] Deeks, A, Lombard, C, Michelmore, J & Teede, H 2009, The effects of gender and age on health related behaviors, *BMC Public Health*, vol. 9, no. 1, p. 213.
[55] Di Marco, LY, Marzo, A, Muñoz-Ruiz, M, Ikram, MA, Kivipelto, M, Ruefenacht, D, Venneri, A, Soininen, H, Wanke, I, Ventikos, YA & Frangi, AF 2014, Modifiable lifestyle factors in dementia: a systematic review of longitudinal observational cohort studies, *Journal of Alzheimer's Disease*, vol. 42, no. 1, pp. 119-135.
[56] Karp, A, Andel, R, Parker, MG, Wang, HX, Winblad, B & Fratiglioni, L 2009, Mentally stimulating activities at work during midlife and dementia risk after age 75: follow-up study from the Kungsholmen Project, *The American Journal of Geriatric Psychiatry*, vol. 17, pp. 227–36.
[57] Ryan, CL & Siebens, J 2012, *Current Population Reports, Educational Attainment in the United States: 2009*, US Department of Commerce, US Census Bureau, Washington DC, http://www.census.gov/prod/2012pubs/p20-566.pdf
[58] Smith, K, Flicker, L, Lautenschlager, NT, Almeida, OP, Atkinson, D, Dwyer, A and LoGiudice, D 2008, High prevalence of dementia and cognitive impairment in Indigenous Australians, *Neurology*, vol. 71, no. 19, pp. 1470-1473.

[59] Radford, K, Mack, HA, Draper, B, Chalkley, S, Daylight, G, Cumming, R, Bennett, H, Delbaere, K and Broe, GA 2015, Prevalence of dementia in urban and regional Aboriginal Australians,. *Alzheimer's & dementia: the journal of the Alzheimer's Association*, vol. 11, no. 3, pp. 271-279.

[60] Giudice, DL, Smith, K, Fenner, S, Hyde, Z, Atkinson, D, Skeaf, L, Malay, R and Flicker, L 2016, Incidence and predictors of cognitive impairment and dementia in Aboriginal Australians: a follow-up study of 5 years, *Alzheimer's & Dementia: the Journal of the Alzheimer's Association*, vol. 12, no. 3, pp. 252-261.

[61] Ferri, CP, Prince, M, Brayne, C, Brodaty, H, Fratiglioni, L, Ganguli, M, Hall, K, Hasegawa, K, Hendrie, H, Huang, Y & Jorm, A 2005, Global prevalence of dementia: a Delphi consensus study, *The Lancet*, vol. 366, no. 9503, pp. 2112-2117.
[62] Cooper, C, Tandy, AR, Balamurali, TB & Livingston, G 2010, A systematic review and meta-analysis of ethnic differences in use of dementia treatment, care, and research, *The American Journal of Geriatric Psychiatry*, vol. 18, no. 3, pp. 193-203.
[63] LoGiudice, D, Hassett, A, Cook, R, Flicker, L and Ames, D 2001, Equity of access to a memory clinic in Melbourne? Non-English speaking background attenders are more severely demented and have increased rates of psychiatric disorders. *International Journal of Geriatric Psychiatry*, vol. 16, no. 3, pp. 327-334.

[64] National Rural Health Alliance Inc, November 2010, Fact Sheet 23: Measuring the metropolitan-rural inequity,
[65] Australian Institute of Health and Welfare 2017, *Mortality Over Regions and Time (MORT) books*. https://www.aihw.gov.au/reports/life-expectancy-death/mort-books/contents/mort-books
[66] Russ, T.C., Batty, G.D., Hearnshaw, G.F., Fenton, C. and Starr, J.M., 2012. Geographical variation in dementia: systematic review with meta-analysis. *International journal of epidemiology*, *41*(4), pp.1012-1032.
[67] Pong, R.W., DesMeules, M. and Lagacé, C., 2009. Rural–urban disparities in health: How does Canada fare and how does Canada compare with Australia?. *Australian Journal of Rural Health*, *17*(1), pp.58-64.

[68] Chowdhury, R, Lawrence, R, van Daalen, K, Hawkes, S and Feldmann, J 2018, Reducing NCDs globally: the under-recognised role of environmental risk factors, *The Lancet*, vol. 392, no. 10143, p. 212

[69] COAG Reform Council. Healthcare 2010–11: comparing outcomes by remoteness. Sydney: COAG Reform Council; 2012.

[70] Hall, S.E., Holman, C.D.A.J., Wisniewski, Z.S. and Semmens, J., 2005. Prostate cancer: socio-economic, geographical and private-health insurance effects on care and survival. *BJU international*, *95*(1), pp.51-58.

[71] Zilkens, R, Spilsbury, K, Bruce, D & Semmens, J 2009, Clinical epidemiology and in-patient hospital use in the last year of life (1990–2005) of 29,884 Western Australians with dementia, *Journal of Alzheimer's Disease*, vol. 17, pp. 399–407.

[72] Bail, K, Hudson, C, Grealish, L, Shannon, K, Ehsen, S, Peut, A, Gibson, D, Draper, B & Karmel, R 2013, Characteristics of rural hospital services for people with dementia: findings from the Hospital Dementia Services Project, *Australian Journal of Rural Health*, vol. 21, no. 4, pp. 208-215.

[73] Bail, K, Hudson, C, Grealish, L, Shannon, K, Ehsen, S, Peut, A, Gibson, D, Draper, B & Karmel, R 2013, Characteristics of rural hospital services for people with dementia: findings from the Hospital Dementia Services Project, *Australian Journal of Rural Health*, vol. 21, no. 4, pp. 208-215.

[74] Burgess, CP, Sinclair, G, Ramjan, M, Coffey, PJ, Connors, CM and Katekar, LV 2015, Strengthening Cardiovascular Disease Prevention in Remote Indigenous Communities in Australia's Northern Territory, *Heart, Lung and Circulation*, vol. 24, no. 5, pp. 450-457.

[75] Manly, JJ & Mayeux, R 2004, Ethnic differences in dementia and Alzheimer's disease, in NB Anderson, RA Bulatao & B Cohen (eds.), *Critical perspectives on racial and ethnic differences in health in late life*, National Research Council, the National Academies Press, Washington DC.

[76] Geda, YE 2010, Blowing hot and cold over depression and cognitive impairment, *Neurology*, vol. 75, pp. 12–14.

[77] Butters, MA, Young, JB, Lopez, O, Aizenstein, HJ, Mulsant, BH, Reynolds, CF III, DeKosky, ST & Becker, JT 2008, Pathways linking late-life depression to persistent cognitive impairment and dementia, *Dialogues Clinical Neuroscience*, vol. 10, pp. 345–357.

[78] Korczyn, AD & Halperin I 2009, Depression and dementia, *Journal of Neurological Science*, vol. 283, pp. 139-142.

[79] Kiran, T, Hutchings, A, Dhalla, IA, Furlong, C & Jacobson, B 2010, The association between quality of primary care, deprivation and cardiovascular outcomes: a cross-sectional study using data from the UK Quality and Outcomes Framework, *Journal of Epidemiology & Community Health*, vol. 64, no. 10, pp. 927-934.

[80] Bhopal, R, Fischbacher, C, Vartiainen, E, Unwin, N, White, M & Alberti, G 2005, Predicted and observed cardiovascular disease in South Asians: application of FINRISK, Framingham and SCORE models to Newcastle Heart Project data, *Journal of Public Health*, vol. 27, no. 1, pp. 93-100.

[81] World Health Organization and Alzheimer's International 2012, *Dementia. A public health priority,* http://www.who.int/mental_health/publications/dementia_report_2012/en/

[82] Lee, IM, Shiroma, EJ, Lobelo, F, Puska, P, Blair, SN, Katzmarzyk, PT and Lancet Physical Activity Series Working Group 2012, Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy, *The Lancet*, vol. 380, no. 9838, pp. 219-229.

[83] Gallaway, P., Miyake, H., Buchowski, M., Shimada, M., Yoshitake, Y., Kim, A. and Hongu, N., 2017. Physical activity: a viable way to reduce the risks of mild cognitive impairment, Alzheimer's disease, and vascular dementia in older adults. *Brain sciences*, *7*(2), p.22.

[84] Hamer, M. and Chida, Y., 2009. Physical activity and risk of neurodegenerative disease: a systematic review of prospective evidence. *Psychological medicine*, *39*(1), pp.3-11.

[85] Hamer, M. and Chida, Y., 2009. Physical activity and risk of neurodegenerative disease: a systematic review of prospective evidence. *Psychological medicine*, *39*(1), pp.3-11.

[86] Sofi, F., Valecchi, D., Bacci, D., Abbate, R., Gensini, G.F., Casini, A. and Macchi, C., 2011. Physical activity and risk of cognitive decline: a meta-analysis of prospective studies. *Journal of internal medicine*, *269*(1), pp.107-117.

[87] Rovio, S., Spulber, G., Nieminen, L.J., Niskanen, E., Winblad, B., Tuomilehto, J., Nissinen, A., Soininen, H. and Kivipelto, M., 2010. The effect of midlife physical activity on structural brain changes in the elderly. *Neurobiology of aging*, *31*(11), pp.1927-1936.

[88] World Health Organization, WHO Global recommendations on physical activity for health. Geneva: World Health Organization; 2011.
[89] Lightwood, J., Collins, D., Lapsley, H. and Novotny, T.E., 2000. 4 Estimating the costs of tobacco use.
[90] Beydoun, M.A., Beydoun, H.A., Gamaldo, A.A., Teel, A., Zonderman, A.B. and Wang, Y., 2014. Epidemiologic studies of modifiable factors associated with cognition and dementia: systematic review and meta-analysis. *BMC public health*, *14*(1), p.643.
[91] Di Marco, L.Y., Marzo, A., Muñoz-Ruiz, M., Ikram, M.A., Kivipelto, M., Ruefenacht, D., Venneri, A., Soininen, H., Wanke, I., Ventikos, Y.A. and Frangi, A.F., 2014. Modifiable lifestyle factors in dementia: a systematic review of longitudinal observational cohort studies. *Journal of Alzheimer's disease*, *42*(1), pp.119-135.
[92] Pirie, K., Peto, R., Reeves, G.K., Green, J., Beral, V. and Million Women Study Collaborators, 2013. The 21st century hazards of smoking and benefits of stopping: a prospective study of one million women in the UK. *The Lancet*, *381*(9861), pp.133-141.
[93] Taylor, G., McNeill, A., Girling, A., Farley, A., Lindson-Hawley, N. and Aveyard, P., 2014. Change in mental health after smoking cessation: systematic review and meta-analysis. *Bmj*, *348*, p.g1151.
[94] Tuomilehto, J., Lindström, J., Eriksson, J.G., Valle, T.T., Hämäläinen, H., Ilanne-Parikka, P., Keinänen-Kiukaanniemi, S., Laakso, M., Louheranta, A., Rastas, M. and Salminen, V., 2001. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine*, *344*(18), pp.1343-1350.
[95] Swaminathan, A. and Jicha, G.A., 2014. Nutrition and prevention of Alzheimer's dementia. *Frontiers in aging neuroscience*, *6*, p.282.
[96] Singh, B., Parsaik, A.K., Mielke, M.M., Erwin, P.J., Knopman, D.S., Petersen, R.C. and Roberts, R.O., 2014. Association of mediterranean diet with mild cognitive impairment and Alzheimer's disease: a systematic review and meta-analysis. *Journal of Alzheimer's disease*, *39*(2), pp.271-282.
[97] Wu, L. and Sun, D., 2017. Adherence to Mediterranean diet and risk of developing cognitive disorders: An updated systematic review and meta-analysis of prospective cohort studies. *Scientific reports*, *7*, p.41317.
[98] Britton, A, Singh-Manoux, A & Marmot, M 2004, Alcohol consumption and cognitive function in the Whitehall II Study, *American Journal of Epidemiology*, vol. 160, no. 3, pp. 240-7.
[99] Schwarzinger, M, Pollock, B, Hasan, O, Dufouil, C, Rehm, J for the QalyDays Study Group 2018, Contribution of alcohol use disorders to the burden of dementia in France 2008-13: a nationwide retrospective cohort study, *Lancet Public Health*, vol. 3, no. 3, pp. e124-e132, doi:10.1016/S2468-2667(18)30022/7.
[100] Ballard, C & Lang I 2018, Alcohol and dementia: a complex relationship with potential for dementia prevention, *Lancet Public Health*, vol. 3, no. 3, pp. e103-e104, doi:10.1016/S2468-2667(18)30031-8.
[101] Verbaten, MN 2009, Chronic effects of low to moderate alcohol consumption on structural and functional properties of the brain: beneficial or not? *Human Psychopharmacology: Clinical and Experimental*, vol. 24, no. 3, pp. 199-205.
[102] Topiwala, A, Allan, CL, Valkanova, V, Zsoldos, E, Filippini, N, Sexton, C, Mahmood, A, Fooks, P, Singh-Manoux, A, Mackay, CE, Kivimäki, PM & Ebmeier KP 2017, Moderate alcohol consumption as risk factor for adverse brain outcomes and cognitive decline: longitudinal cohort study, *British Medical Journal*, vol. 357, p. j2353.
[103] Gupta, S & Warner J 2008, Alcohol-related dementia: a 21st-century silent epidemic? *British Journal of Psychiatry*, vol. 193, pp. 351–53.
[104] Kadlecová, P, Andel, R, Mikulík, R, Handing, EP and Pedersen, NL, 2015, Alcohol consumption at midlife and risk of stroke during 43 years of follow-up: cohort and twin analyses, *Stroke*, vol. 46, no. 3, pp. 627-633.
[105] Schwarzinger, M, Pollock, BG, Hasan, OS, Dufouil, C, Rehm, J, Baillot, S, Guibert, Q, Planchet, F and Luchini, S 2018, Contribution of alcohol use disorders to the burden of dementia in France 2008–13: a nationwide retrospective cohort study, *The Lancet Public Health*, vol. 3, no. 3, pp.e124-e132.
[106] Oslin, D, Atkinson, RM, Smith, DM & Hendrie, H 1998, Alcohol related dementia: proposed clinical criteria, *International Journal of Geriatric Psychiatry*, vol. 13, pp. 203–12.
[107] Ridley, NJ, Draper, B & Withall, A 2013, Alcohol-related dementia: an update of the evidence, *Alzheimer's Research & Therapy*, vol. 5, p. 3.
[108] Nordstrom, P, Nordstrom, A, Eriksson, M, Wahlund, LO & Gustafson, Y 2013, Risk factors in late adolescence for young-onset dementia in men: a nationwide cohort study, *JAMA Internal Medicine*, vol. 173, pp. 1612-18.

[109] Ott, A, Slooter, AJC, Hofman, A, van Harskamp, F, Witteman, JCM, Van Broeckhoven, C, Van Duijn, CM and Breteler, MMB 1998, Smoking and risk of dementia and Alzheimer's disease in a population-based cohort study: the Rotterdam Study. *The Lancet*, vol. 351, no. 9119, pp. 1840-1843.
[110] WHO (2019b) Global Health Observatory data: Obesity. https://www.who.int/gho/ncd/risk_factors/overweight_obesity/obesity_adults/en/ Accessed 29th May 2019
[111] Renehan, A.G., Zwahlen, M. and Egger, M., 2015. Adiposity and cancer risk: new mechanistic insights from epidemiology. *Nature Reviews Cancer*, *15*(8), p.484.
[112] Fontana, L. and Hu, F.B., 2014. Optimal body weight for health and longevity: bridging basic, clinical, and population research. *Aging cell*, *13*(3), pp.391-400.
[113] Albanese, E., Davis, B., Jonsson, P.V., Chang, M., Aspelund, T., Garcia, M., Harris, T., Gudnason, V. and Launer, L.J., 2015. Overweight and obesity in midlife and brain structure and dementia 26 years later: the AGES-Reykjavik Study. *American journal of epidemiology*, *181*(9), pp.672-679.
[114] Luchsinger, J.A., 2010. Diabetes, related conditions, and dementia. *Journal of the neurological sciences*, *299*(1-2), pp.35-38.
[115] Prince, M., Albanese, E., Guerchet, M. and Prina, M., 2014. Dementia and risk reduction: an analysis of protective and modifiable factors. *World Alzheimer Report*, pp.66-83.
[116] Bruce, D.G., Davis, W.A., Starkstein, S.E. and Davis, T.M., 2014. Mid-life predictors of cognitive impairment and dementia in type 2 diabetes mellitus: the Fremantle Diabetes Study. *Journal of Alzheimer's Disease*, *42*(s3), pp.S63-S70.
[117] Exalto, L.G., Biessels, G.J., Karter, A.J., Huang, E.S., Katon, W.J., Minkoff, J.R. and Whitmer, R.A., 2013. Risk score for prediction of 10 year dementia risk in individuals with type 2 diabetes: a cohort study. *The Lancet Diabetes & Endocrinology*, *1*(3), pp.183-190.
[118] Launer, L.J., Miller, M.E., Williamson, J.D., Lazar, R.M., Gerstein, H.C., Murray, A.M., Sullivan, M., Horowitz, K.R., Ding, J., Marcovina, S. and Lovato, L.C., 2011. Effects of intensive glucose lowering on brain structure and function in people with type 2 diabetes (ACCORD MIND): a randomised open-label substudy. *The Lancet Neurology*, *10*(11), pp.969-977.
[119] Johnson, M.L., Parikh, N., Kunik, M.E., Schulz, P.E., Patel, J.G., Chen, H., Aparasu, R.R. and Morgan, R.O., 2012. Antihypertensive drug use and the risk of dementia in patients with diabetes mellitus. *Alzheimer's & Dementia*, *8*(5), pp.437-444.
[120] Kivipelto, M., Helkala, E.L., Laakso, M.P., Hänninen, T., Hallikainen, M., Alhainen, K., Iivonen, S., Mannermaa, A., Tuomilehto, J., Nissinen, A. and Soininen, H., 2002. Apolipoprotein E ϵ4 allele, elevated midlife total cholesterol level, and high midlife systolic blood pressure are independent risk factors for late-life Alzheimer disease. *Annals of internal medicine*, *137*(3), pp.149-155.
[121] Musini, V.M., Tejani, A.M., Bassett, K. and Wright, J.M., 2009. Pharmacotherapy for hypertension in the elderly. *Cochrane Database of Systematic Reviews*, (4).
[122] Norton, S, Matthews, FE, Barnes, DE, Yaffe, K & Brayne, C 2014, Potential for primary prevention of Alzheimer's disease: an analysis of population-based data, *The Lancet Neurology*, vol. 13, no. 8, pp. 788-794.
[123] Livingston, G., Sommerlad, A., Orgeta, V., Costafreda, S.G., Huntley, J., Ames, D., Ballard, C., Banerjee, S., Burns, A., Cohen-Mansfield, J. and Cooper, C., 2017. Dementia prevention, intervention, and care. *The Lancet*, *390*(10113), pp.2673-2734.
[124] McMunn, A, Nazroo, J & Breeze, E 2009, Inequalities in health at older ages: a longitudinal investigation of the onset of illness and survival effects in England, *Age and Ageing*, vol. 38, no. 2, pp. 181–187.
[125] Lin, J, Epel, E & Blackburn, E 2012, Telomeres and lifestyle factors: roles in cellular aging, *Mutation Research*, vol. 730, no. 1, pp. 85–89.
[126] Lantz, PM, House, JS, Lepkowski, JM, Williams, DR, Mero, RP & Chen, J 1998, Socioeconomic factors, health behaviors, and mortality: results from a nationally representative prospective study of US adults, *JAMA*, vol. 279, no. 21, pp. 1703–1708.
[127] Lin, J, Epel, E & Blackburn, E 2012, Telomeres and lifestyle factors: roles in cellular aging, *Mutation Research,* vol. 730, no. 1, pp. 85–89.
[128] Beydoun, MA, Beydoun, HA, Gamaldo, AA, Teel, A, Zonderman, AB & Wang Y 2014, Epidemiologic studies of modifiable factors associated with cognition and dementia: systematic review and meta-analysis, *BMC Public Health*, vol. 14, no.1, p. 643.
[129] Caamaño-Isorna, F, Corral, M, Montes-Martínez, A & Takkouche, B 2006, Education and dementia: a meta-analytic study, *Neuroepidemiology*, vol. 26, no. 4, pp. 226–232.
[130] Anstey, KJ, Cherbuin, N & Herath, PM 2013, Development of a new method for assessing global risk of Alzheimer's disease for use in population health approaches to prevention, *Prevention Science*, vol. 14, no. 4, pp. 411–421.

[131] Baumgart, M, Snyder, HM, Carrillo, MC, Fazio, S, Kim, H and Johns, H, 2015 Summary of the evidence on modifiable risk factors for cognitive decline and dementia: a population-based perspective, *Alzheimer's & Dementia*, vol. 11, no. 6, pp. 718-726.
[132] Kivipelto, M, Ngandu, T, Laatikainen, T, Winblad, B, Soininen, H & Tuomilehto, J 2006, Risk score for the prediction of dementia risk in 20 years among middle aged people: a longitudinal, population-based study, *Lancet Neurol*. vol. 5, pp. 735–41
[133] Holwerda, TJ, Deeg, DJ, Beekman, AT, van Tilburg, TG, Stek, ML, Jonker, C & Schoevers, RA 2012, Feelings of loneliness, but not social isolation, predict dementia onset: results from the Amsterdam Study of the Elderly (AMSTEL), *J Neurol Neurosurg Psychiatry*, p. jnnp-2012.
[134] Shankar, A, Hamer, M, McMunn, A & Steptoe, A 2013, Social isolation and loneliness: relationships with cognitive function during 4 years of follow-up in the English Longitudinal Study of Ageing, *Psychosomatic Medicine*, vol. 75, no. 2, pp. 161-170.
[135] Karp, A, Paillard-Borg, S, Wang, HX, Silverstein, M, Winblad, B & Fratiglioni, L 2006, Mental, physical and social components in leisure activities equally contribute to decrease dementia risk, *Dementia and Geriatric Cognitive Disorders*, vol. 21, no. 2, pp. 65–73.
[136] Kuiper, JS, Zuidersma, M, Voshaar, RCO, Zuidema, SU, van den Heuvel, ER, Stolk, RP & Smidt, N 2015, Social relationships and risk of dementia: a systematic review and meta-analysis of longitudinal cohort studies, *Ageing Research Reviews*, vol. 22, pp. -57.
[137] Lin, FR, Metter, EJ, O'Brien, RJ, Resnick, SM, Zonderman, AB & Ferrucci, L 2011, Hearing loss and incident dementia, *Archives of Neurology*, vol. 68, no. 2, pp. 214-220.
[138] Lin, FR, Ferrucci, L, Metter, EJ, An, Y, Zonderman, AB & Resnick, SM 2011, Hearing loss and cognition in the Baltimore Longitudinal Study of Aging, *Neuropsychology*, vol. 25, no. 6, p. 763.
[139] Livingston, G, Sommerlad, A, Orgeta, V, Costafreda, SG, Huntley, J, Ames, D, Ballard, C, Banerjee, S, Burns, A, Cohen-Mansfield, J & Cooper, C 2017, Dementia prevention, intervention, and care, *The Lancet*, vol. 390, no. 10113, pp. 2673-2734.
[140] Stern, Y 2005, Lifestyle and other risk factors: *Cognitive reserve. Alzheimer's & Dementia*, vol. 1, iss. 1, p. S93.
[141] Prince, M, Acosta, D, Ferri, CP, Guerra, M, Huang, Y, Rodriguez, JJL, Salas, A, Sosa, AL, Williams, JD, Dewey, ME & Acosta, I 2012, Dementia incidence and mortality in middle-income countries, and associations with indicators of cognitive reserve: a 10/66 Dementia Research Group population-based cohort study, *The Lancet*, vol. 380, no. 9836, pp. 50-58.
[142] Borenstein, A & Mortimer, J 2016, *Alzheimer's disease: life course perspectives on risk reduction* (1st ed.), Academic Press, Cambridge MA.
[143] Larson, EB 2010, Prospects for delaying the rising tide of worldwide, late-life dementias, *International Psychogeriatrics*, vol. 22, pp. 1196-1202.
[144] Australian Institute of Health and Welfare 2016, Contribution of vascular diseases and risk factors to the burden of dementia in Australia: Australian Burden of Disease Study 2011, Australian Burden of Disease Study series no. 9, cat. no. BOD 10, AIHW, Canberra, http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=60129557756
[145] Farrow, M & O'Connor, E 2012, *Targeting brain, body and heart for cognitive health and dementia prevention, current evidence and future directions*, Paper 29, Alzheimer's Australia, https://www.fightdementia.org.au/sites/default/files/YBM_evidence_paper_29_lores.pdf
[146] Ashby-Mitchell, K, Burns, R, Shaw, J and Anstey, KJ 2017, Proportion of dementia in Australia explained by common modifiable risk factors, *Alzheimer's Research & Therapy*, vol. 9, no. 1, p. 11.
[147] The National Centre for Social and Economic Modelling 2016, *Economic cost of dementia in Australia 2016-2056*, NATSEM, Canberra, https://www.fightdementia.org.au/files/NATIONAL/documents/The-economic-cost-of-dementia-in-Australia-2016-to-2056.pdf
[148] Nepal, B, Brown, L & Ranmuthugala, G 2010, Modelling the impact of modifying lifestyle risk factors on dementia prevalence in Australian population aged 45 years and over, 2006-2051, *Australasian Journal on Ageing*, vol. 29, no. 3, pp. 111–116.
[149] Access Economics 2009, *Keeping dementia front of mind: incidence and prevalence 2009–2050,* Alzheimer's Australia, http://www.alzheimers.org.au/common/files/NAT/20090800_Nat__AE_FullKeepDemFrontMind.pdf
[150] Gorelick, PB, Scuteri, A, Black, SE, DeCarli, C, Greenberg, SM, Iadecola, C, Launer, LJ, Laurent, S, Lopez, OL, Nyenhuis, D & Petersen, RC 2011, Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the American Heart Association/American Stroke Association, *Stroke*, vol. 42, no. 9, pp. 2672-2713.

[151] Norton, S, Matthews, FE, Barnes, DE, Yaffe, K & Brayne, C 2014, Potential for primary prevention of Alzheimer's disease: an analysis of population-based data, *The Lancet Neurology*, vol. 13, no. 8, pp. 788-794.
[152] Norton, S, Matthews, FE, Barnes, DE, Yaffe, K & Brayne, C 2014, Potential for primary prevention of Alzheimer's disease: an analysis of population-based data*, The Lancet Neurology*, vol. 13, no. 8, pp. 788-794.
[153] Brookmeyer, R, Johnson, E, Ziegler-Graham, K & Arrighi, HM 2007, Forecasting the global burden of Alzheimer's disease*, Alzheimer's & Dementia*, vol. 3, no. 3, pp. 186–191.
[154] Access Economics 2009, *Keeping dementia front of mind: incidence and prevalence 2009–2050,* Alzheimer's Australia, http://www.alzheimers.org.au/common/files/NAT/20090800_Nat__AE_FullKeepDemFrontMind.pdf
[155] Schwarzinger, M, Pollock, B, Hasan, O, Dufouil, C, Rehm, J for the QalyDays Study Group 2018, Contribution of alcohol use disorders to the burden of dementia in France 2008-13: a nationwide retrospective cohort study, *Lancet Public Health*, vol. 3, no. 3, pp. e124-e132, doi:10.1016/S2468-2667(18)30022/7.
[156] Ott A, Slooter AJC, Hofman A, van Harskamp F, Witteman JCM, Van Broeckhoven C, et al. 1998, Smoking and risk of dementia and Alzheimer's disease in a population-based cohort study: the Rotterdam Study, *The Lancet*, vol. 351, no. 9119, pp. 1840-3.
[157] Schwarzinger, M, Pollock, B, Hasan, O, Dufouil, C, Rehm, J for the QalyDays Study Group 2018, Contribution of alcohol use disorders to the burden of dementia in France 2008-13: a nationwide retrospective cohort study, *Lancet Public Health*, vol. 3, no. 3, pp. e124-e132, doi:10.1016/S2468-2667(18)30022/7.
[158] Ngandu, T, Lehtisalo, J, Solomon, A, Levälahti, E, Ahtiluoto, S, Antikainen, R, Bäckman, L, Hänninen, T, Jula, A, Laatikainen, T, Lindström, J, Mangialasche, F, Paajanen, T, Pajala, S, Peltonen, M, Rauramaa, R, Stigsdotter-Neely, A, Strandberg, T, Tuomilehto, J, Soininen, H & Kivipelto, M 2015, A 2-year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial, *The Lancet*, vol. 385, no. 9984, pp. 2255–2263.
[159] Abell, JG, Kivimäki, M, Dugravot, A, Tabak, AG, Fayosse, A, Shipley, M, Sabia, S and Singh-Manoux, A 2018, Association between systolic blood pressure and dementia in the Whitehall II cohort study: role of age, duration, and threshold used to define hypertension, *European Heart Journal*, vol. 39, no. 33, pp. 3119-3125.
[160] Lim, YY, Villemagne, VL, Pietrzak, RH, Ames, D, Ellis, KA, Harrington, K, Snyder, PJ, Martins, RN, Masters, CL, Rowe, CC and Maruff, P 2015, APOE ε4 moderates amyloid-related memory decline in preclinical Alzheimer's disease, *Neurobiology of Aging*, vol. 36, no. 3, pp. 1239-1244.
[161] Villemagne, VL, Burnham, S, Bourgeat, P, Brown, B, Ellis, KA, Salvado, O, Szoeke, C, Macaulay, SL, Martins, R, Maruff, P and Ames, D 2013, Amyloid β deposition, neurodegeneration, and cognitive decline in sporadic Alzheimer's disease: a prospective cohort study, *The Lancet Neurology*, vol. 12, no. 4, pp. 357-367.
[162] Gottesman, R, Schneider, A, Zhou, Y, Coresh, J, Green, E, Gupta, N, Knopman, DS, Mintz, A, Rahmim, A, Sharrett, AR, Wagenknecht, LE, Wong, DF & Mosley, TH 2017, Association between midlife vascular risk factors and estimated brain amyloid deposition*, JAMA,* vol. 317, no. 14, pp. 1443-1450, doi:10.1001/jama.2017.3090.
[163] National Vascular Disease Prevention Alliance 2012, *Guidelines for the management of absolute cardiovascular disease risk,* http://www.cvdcheck.org.au/pdf/Absolute_CVD_Risk_Full_Guidelines.pdf
[164] World Health Organization (2013) *Global Action Plan for the Prevention and Control of NCDs 2013-2020. Case for Action*- Proposal to NHMRC. Research Translation Faculty Primary Health Care Steering Group 2014. http://www.who.int/nmh/events/ncd_action_plan/en
[165] The Royal Australian College of General Practitioners 2016, *Guidelines for preventive activities in general practice* (9th ed.), RACGP, East Melbourne, http://www.racgp.org.au/download/Documents/Guidelines/Redbook9/17048-Red-Book-9th-Edition.pdf
[166] National Vascular Disease Prevention Alliance 2012, *Guidelines for the management of absolute cardiovascular disease risk*, http://www.cvdcheck.org.au/pdf/Absolute_CVD_Risk_Full_Guidelines.pdf
[167] House of Representatives Standing Committee on Health 2016, Inquiry into Chronic Disease Prevention and Management in Primary Health Care, Submission 143, p. 32, Dept of Health ed. Canberra, Australia: The Parliament of the Commonwealth of Australia
[168] Richard, E, Andrieu, S, Solomon, A, Mangialasche, F, Ahtiluoto, S, Moll van Charante, EP, Coley, N, Fratiglioni, L, Neely, AS, Vellas, B, van Gool, WA & Kivipelto, M 2012, Methodological challenges in designing dementia prevention trials – the European Dementia Prevention Initiative (EDPI), *Journal of the Neurological Sciences*, vol. 322, no. 1, pp. 64–70.

[169] Finnish Ministry of Social Affairs and Health 2013, *National Memory Programme 2012–2020: Creating a "memory-friendly" Finland*, http://julkaisut.valtioneuvosto.fi/handle/10024/74501
[170] Kivipelto, M, Solomon, A, Ahtiluoto, S, Ngandu, T, Lehtisalo, J, Antikainen, R, Bäckman, L, Hänninen, T, Jula, A, Laatikainen, T, Lindström, J, Mangialasche, F, Nissinen, A, Paajanen, T, Pajala, S, Peltonen, M, Rauramaa, R, Stigsdotter-Neely, A, Strandberg, T, Tuomilehto, J, Soininen, H 2013, The Finnish geriatric intervention study to prevent cognitive impairment and disability (FINGER): study design and progress, *Alzheimer's & Dementia*, vol. 9, no. 6, pp. 657–665.
[171] Ngandu, T, Lehtisalo, J, Solomon, A, Levälahti, E, Ahtiluoto, S, Antikainen, R, Bäckman, L, Hänninen, T, Jula, A, Laatikainen, T, Lindström, J, Mangialasche, F, Paajanen, T, Pajala, S, Peltonen, M, Rauramaa, R, Stigsdotter-Neely, A, Strandberg, T, Tuomilehto, J, Soininen, H & Kivipelto, M 2015, A 2-year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial, *The Lancet*, vol. 385, no. 9984, pp. 2255–2263.
[172] Laatikainen, T, Critchley, J, Vartiainen, E, Salomaa, V, Ketonen, M & Capewell, S 2005, Explaining the decline in coronary heart disease mortality in Finland between 1982 and 1997, *American Journal of Epidemiology*, vol. 162, no. 8, pp. 764-773.
[173] Salomaa, V, Ketonen, M, Koukkunen, H, Immonen-Raiha, P, Jerkkola, T, Karja-Koskenkari, P, Mahonen, M, Niemela, M, Kuulasmaa, K, Palomaki, P & Arstila, M 2003, Trends in coronary events in Finland during 1983–1997; The FINAMI study, *European Heart Journal*, vol. 24, no. 4, pp. 311-319.
[174] Pajunen, P, Pääkkönen, R, Juolevi, A, Hämäläinen, H, Keskimäki, I, Laatikainen, T, Moltchanov, V, Niemi, M, Rintanen, H & Salomaa, V 2004, Trends in fatal and non-fatal coronary heart disease events in Finland during 1991–2001, *Scandinavian Cardiovascular Journal*, vol. 38, no. 6, pp. 340-344.
[175] UK Health Forum 2014, Promoting brain health: Developing a prevention agenda linking dementia and other non-communicable diseases, UK Health Forum, London.
[176] Snyder, HM, Corriveau, RA, Craft, S, Faber, JE, Greenberg, SM, Knopman, D, Lamb, BT, Montine, TJ, Nedergaard, M, Schaffer, CB & Schneider, JA 2015, Vascular contributions to cognitive impairment and dementia including Alzheimer's disease, *Alzheimer's & Dementia*, vol. 11, no. 6, pp. 710-717.
[177] Duggan, M 2015, *Beyond the fragments: preventing the costs and consequences of chronic physical and mental diseases,* Australian Health Policy Collaboration Issues paper No. 2015-05, Australian Health Policy Collaboration, Melbourne.
[178] Tolhurst, P 2015, *Development of Australian chronic disease targets & indicators,* Australian Health Policy Collaboration Issues paper No. 2015-04, AHPC, Melbourne.
[179] Lindberg, R, Fetherston, H, Calder, R, McNamara, K, Knight, A, Livingston, M, Kypri, K, Malo, J, Roberts, L, Stanley, S, Grimes, C, Bolam, B, White, S, Purcell, K, Daube, M, O'Reilly, S, Colagiuri, S, Peeters, A, Batterham, P, Harvey, C, Dunbar, JA 2016, *Getting Australia's health on track 2016*, AHPC, Melbourne.
[180] UK Health Forum 2014, Promoting brain health: Developing a prevention agenda linking dementia and other non-communicable diseases, UK Health Forum, London.
[181] Barton, P, Andronis, L, Briggs, A, McPherson, K & Capewell, S 2011, Effectiveness and cost effectiveness of cardiovascular disease prevention in whole populations: modelling study, *BMJ*, vol. 343, p. d4044.
[182] Jørgensen, T, Capewell, S, Prescott, E, Allender, S, Sans, S, Zdrojewski, T, De Bacquer, D, De Sutter, J, Franco, OH, Løgstrup, S & Volpe, M 2013, Population-level changes to promote cardiovascular health, *European Journal of Preventive Cardiology*, vol. 20, no. 3, pp. 409-421.
[183] Owen, L, Morgan, A, Fischer, A, Ellis, S, Hoy, A & Kelly, MP 2012, The cost-effectiveness of public health interventions*, Journal of Public Health*, vol. 34, iss. 1, pp. 37–45, https://doi.org/10.1093/pubmed/fdr075
[184] Masters, R, Anwar, E, Collins, B, Cookson, R & Capewell, S 2017, Return on investment of public health interventions: a systematic review, *Journal of Epidemiology and Community Health*, vol. 71, no. 8, pp. 827-834.
[185] Lim, SS, Gaziano, TA, Gakidou, E, Reddy, KS, Farzadfar, F, Lozano, R & Rodgers, A 2007, Prevention of cardiovascular disease in high-risk individuals in low-income and middle-income countries: health effects and costs, *The Lancet*, vol. 370, no. 9604, pp. 2054-2062.
[186] Willcox, S 2014, *Chronic diseases in Australia: the case for changing course*, Australian Health Policy Collaboration Issues paper no. 2014-02, AHPC, Melbourne, https://www.vu.edu.au/sites/default/files/AHPC/pdfs/Chronic-diseases-in-Australia-the-case-for-changing-course-sharon-willcox.pdf
[187] Commonwealth of Australia 2016, *Inquiry into Chronic Disease Prevention and Management in Primary Health Care*, House of Representatives Standing Committee on Health, https://www.aph.gov.au/Parliamentary_Business/Committees/House/Health/Chronic_Disease/Report

[188] Mangialasche, F, Kivipelto, M, Solomon, A & Fratiglioni, L 2012, Dementia prevention: current epidemiological evidence and future perspective, *Alzheimer's Research & Therapy*, vol. 4, no. 1, p. 6.
[189] Wimo, A, Jönsson, L, Bond, J, Prince, M & Winblad, B 2013, The worldwide economic impact of dementia 2010*, Alzheimer's & Dementia*, vol. 9, no. 1, pp. 1-11.
[190] The National Centre for Social and Economic Modelling 2016, *Economic cost of dementia in Australia 2016-2056*, NATSEM, Canberra, *https://www.fightdementia.org.au/files/NATIONAL/documents/The-economic-cost-of-dementia-in-Australia-2016-to-2056.pdf*
[191] Smith, AD & Yaffe, K 2014, Dementia (including Alzheimer's disease) can be prevented: statement supported by international experts, *Journal of Alzheimer's Disease*, vol. 38, pp. 699–703.
[192] G8 Health and Science Ministers 2013, *G8 Dementia Summit Declaration*, http://www.g8.utoronto.ca/healthG8/g8-dementia-summit-declaration-2013.pdf
[193] World Health Organization 2015, *First WHO ministerial conference on global action against dementia: meeting report,* WHO Headquarters, Geneva, 16-17 March, http://apps.who.int/iris/bitstream/10665/179537/1/9789241509114_eng.pdf
[194] World Health Organization 2015, *Global action plan for the prevention and control of NCDs 2013-2020*, WHO, Geneva, http://www.who.int/nmh/events/ncd_action_plan/en/
[195] World Health Organization 2016, *Global Action Plan on the Public Health Response to Dementia 2017-2025*, WHO, Geneva, http://www.who.int/mental_health/neurology/dementia/action_plan_2017_2025/en/
[196] OECD 2018 Policy Brief. Renewing Priority for Dementia: Where do we stand? http://www.oecd.org/health/health-systems/Renewing-priority-for-dementia-Where-do-we-stand-2018.pdf