The relationship between dietary patterns and cognitive health among older adults

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A thesis in fulfilment of the requirements for the degree of

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Thesis submission for the degree of Doctor of Philosophy

Thesis Title and Abstract | **Declarations** | **Inclusion of Publications Statement**

Thesis Title

The relationship between dietary patterns and cognitive health among older adults

Thesis Abstract

Dementia and cognitive decline, most commonly secondary to Alzheimer's disease, affects over 50 million people globally, placing a significant financial and social burden on patients, carers and health care systems. As life expectancy is increasing and the population is ageing, the number of people living with dementia has been estimated to triple by 2050. No effective pharmaceutical treatment for most causes of dementia or cognitive decline is available so far. Prevention or delay onset holds more promise.

Among modifiable factors, diet may be a promising strategy to postpone, slow or prevent cognitive decline and reduce the risk of dementia. The overall aim of this thesis is to answer the important question as to whether, and how effective, different types of dietary patterns and related food groups are in protecting against neurocognitive decline in older adults?

This thesis presents a comprehensive systematic review by collating and evaluating the evidence from all human studies of RCTs and prospective cohorts conducted on a variety of dietary patterns and the outcome of cognitive function and/or dementia; examines cross-sectional relationship and longitudinal associations between dietary patterns and key food components within dietary patterns, and cognitive function and cognitive decline with ageing; examines dietary quality among Australian older adults and investigates association between diet quality indices and cognitive performance, using data from the Sydney Memory and Ageing Study, which is a well-characterized Australian ageing cohort. Finally, recommendations for future research are provided.

Overall, this thesis reveals that greater adherence to healthy dietary patterns which are plant based and rich in mono-/poly unsaturated fatty acids, were proven to be cross-sectionally associated with better cognition; and intake of legumes and nuts were positively linked both cross-sectionally and longitudinally to better performance and less decline in multiple cognition domains and global cognition. By contrast, a westernised diet was linked to overall poorer global function among men over years. No association between adherence to Australian Dietary Guidelines and cognitive performance was found, and future research is needed to provide further evidence and support specific dietary guidelines for neurocognitive health among Australian older adults.

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Publication Details #1

Full Title:	Dietary Patterns and Cognitive Health in Older Adults: A Systematic Review
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Journal or Book Name:	Journal of Alzheimer’s Disease
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Location of the work in the thesis and/or how the work is incorporated in the thesis:	This journal article is located in Chapter 3 of the thesis.

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Full Title:	Dietary Patterns and Cognitive Health in Older Adults: Findings from the Sydney Memory and Ageing Study
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Location of the work in the thesis and/or how the work is incorporated in the thesis:	This journal article is located in Chapter 5 of the thesis.

Publication Details #4

Full Title:	Association of adherence to Australian Dietary Guidelines with cognitive performance and cognitive decline in Sydney Memory and Ageing Study: a longitudinal analysis
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Abstract

Dementia and cognitive decline, most commonly secondary to Alzheimer's disease, affects over 50 million people globally, placing a significant financial and social burden on patients, carers and health care systems. As life expectancy is increasing and the population is ageing, the number of people living with dementia has been estimated to triple by 2050. No effective pharmaceutical treatment for most causes of dementia or cognitive decline is available so far. Prevention or delay onset holds more promise.

Among modifiable factors, diet may be a promising strategy to postpone, slow or prevent cognitive decline and reduce the risk of dementia. The overall aim of this thesis is to answer the important question as to whether, and how effective, different types of dietary patterns and related food groups are in protecting against neurocognitive decline in older adults?

This thesis presents a comprehensive systematic review by collating and evaluating the evidence from all human studies of RCTs and prospective cohorts conducted on a variety of dietary patterns and the outcome of cognitive function and/or dementia; examines cross-sectional relationship and longitudinal associations between dietary patterns and key food components within dietary patterns, and cognitive function and cognitive decline with ageing; examines dietary quality among Australian older adults and investigates association between diet quality indices and cognitive performance, using data from the Sydney Memory and Ageing Study, which is a well-characterized Australian ageing cohort. Finally, recommendations for future research are provided.

Overall, this thesis reveals that greater adherence to healthy dietary patterns which are plant based and rich in mono-/poly unsaturated fatty acids, were proven to be cross-sectionally associated with better cognition; and intake of legumes and nuts were positively linked both cross-sectionally and longitudinally to better performance and less decline in multiple cognition domains and global cognition. By contrast, a westernised diet was linked to overall poorer global function over years. No association between adherence to Australian Dietary Guidelines and cognitive performance was found, and future research is needed to provide further evidence and support specific dietary guidelines for neurocognitive health among Australian older adults.

Preface

This thesis aims to examine the relationship between dietary patterns and cognitive health among older adults. This thesis consisted of seven chapters, written in a manner to enable each chapter to be read independently. Ethical approval was obtained from the ethics committees of the University of New South Wales and the South Eastern Sydney and Irrewarra Area Health Service for Chapters Four, Five and Six.

Chapter One is an introduction which describes background of this research, contexts of this thesis, and provides an outline of thesis aims. Contents in this chapter are as following: i) global trend of dementia, ii) current dementia treatment, iii) modifiable risk factors for dementia, iv) diet as a promising approach for dementia prevention, and v) thesis aims and outlines.

Chapter Two is a description of the general methods and materials used in this thesis, comprised of the following: i) literature search and quality assessment methods for systematic review, ii) ethics approval and funding, iii) data source, data collection and measures from the Sydney Memory and Ageing study, and iv) statistical analysis approaches.

Chapter Three is a systematic review on the role of diet and nutrition in cognitive health among older adults, conducted following PRISMA guidelines. This chapter documents the existing evidence on efficacy of multiple dietary patterns on cognition, and pointed out that future research is needed to better understand the diet and cognition relationship.

Chapter Four is a cross-sectional study on the associations of dietary patterns, key food components and cognitive function based on the Sydney Memory and Ageing Study (MAS). Participants were community dwelling, non-demented, aged 70-90 years old, and recruited from Sydney, Australia.

Chapter Five is a longitudinal study that investigated the association of adherence to multiple dietary patterns and consumption of key food components, with cognitive performance and cognitive change over six years, among MAS participants.

Chapter Six is a longitudinal study that examined association of adherence to Australian Dietary Guidelines with cognitive performance and cognitive change over six years among MAS participants. Diet quality among MAS population was also assessed and discussed.

Chapter Seven is a conclusion chapter that summarises the key evidence arising from the body of research presented from Chapter 3 to Chapter 6, outlines future implications for dementia prevention, and suggests future research to provide further evidence supporting dietary changes for better neurocognitive health among older adults.

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Back in 2013, longing for research in dementia prevention, I first met Professor Henry Brodaty in his office at Dementia Centre for Research Collaboration (DCRC). I then enrolled in a master by research, which subsequently transferred into a PhD program. Towards submitting my PhD thesis, there are many people I would like to thank and acknowledge.

First and foremost, to my supervisor Professor Henry Brodaty, thank you for believing in me and providing such incredible research opportunities for me to pursue. Thank you for your great patience, brilliant guidance, constant support and encouragement even when I self-doubted. Words will not be enough to express my gratitude, and I am very lucky to be able to do my PhD under your supervision.

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Thank you to my family and friends, for your support throughout the years. To Yueyue, thank you for your great support and always being there for me. To Mengxue, thank you for always being such a loving sister. To Jiani, Maolin and Lina, thank you for your love and encouragement. To my dearest mum and dad, who has always supported me and encouraged my education endeavours and career as a health professional.

Finally, to my beloved grandparents, memory of whom have inspired my passionate research journey in fighting towards a world without dementia.

Publications

Journal articles

1. Chen X, Maguire B, Brodaty H& O'Leary F. Dietary Patterns and Cognitive Health in Older Adults: A Systematic Review. Journal of Alzheimer's Disease. 2019;67(2):583-619. doi:10.3233/JAD-180468

2. Chen X, Liu Z, Sachdev PS, Kochan NA, O'Leary F & Brodaty H. Dietary Patterns and Cognitive Health in Older Adults: Findings from the Sydney Memory and Ageing Study. Journal of Nutrition, Health & Aging. 2021;25(2):255-262. doi:10.1007/s12603-020-1536-8

3. Chen X, Liu Z, Sachdev PS, Kochan NA, O'Leary F & Brodaty H. Association of dietary patterns with cognitive function and cognitive decline in Sydney Memory and Ageing Study: a longitudinal analysis. Submitted to Journal of Academy of Nutrition and Dietetics. (Under review)

4. Chen X, Liu Z, Sachdev PS, Kochan NA, Brodaty H & O'Leary F. Association of adherence to Australian Dietary Guidelines with cognitive performance and cognitive decline in Sydney Memory and Ageing Study: a longitudinal analysis. Submitted to Journal of Nutritional Science. (Accepted)

Conferences abstracts

The following abstracts arose directly from research conducted as part of the PhD candidature:

1. Chen X, Maguire B, Brodaty H& O'Leary F. "Dietary Patterns and Cognitive Health in Older Adults: A Systematic Review". Poster presentation. Alzheimer's association international conference (AAIC) 2015, Washington DC, US

2. Chen X, Brodaty H& O'Leary F. "The relationship of nutrition to cognitive function in older adults: a systematic review of RCTs". Poster presentation. International psychogeriatric association (IPA) 2015, Berlin, Germany

3. Chen X, Liu Z, Sachdev PS, Kochan NA, O'Leary F & Brodaty H. "Association of Dietary Patterns with cognition in older adults: cross-sectional Findings from Sydney Memory and Aging study". Oral presentation. Alzheimer's dementia international (ADI) 2020, Online

4. Chen X, Liu Z, O'Leary F & Brodaty H. "Dietary Patterns and Cognitive health among Older Adults in Sydney Memory and Aging Study". Oral Presentation. Alzheimer's association international conference (AAIC) 2020, Online

5. Chen X, Liu Z, Sachdev PS, Kochan NA, Brodaty H & O'Leary F. "Legumes and nuts intake associated with less cognitive decline in older adults from Sydney Memory and Ageing study". Poster presentation. Alzheimer's dementia forum (ADF) 2020, Online

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Abbreviations

Aβ Amyloid beta

ABS Australian Bureau of Statistics

AD Alzheimer's Disease

ADG Australian Dietary Guidelines

AHEI Alternative Healthy Eating Index

APOE Apolipoprotein E

BMI Body Mass Index

CDR Clinical Dementia Rating

CDT Clock Drawing Test

CRP C-Reactive Protein

CSF Cerebrospinal Fluid

CVD Cardiovascular Disease

DASH Dietary Approaches to Stop Hypertension

DGI Dietary Guidelines Index

DQES v2 The Dietary Questionnaire for Epidemiological Studies Version 2

EVOO Extra Virgin Olive Oil

FFQ Food Frequency Questionnaire

GI Glycemia Index

HDI Healthy Diet Indicator

HEI Healthy Eating Index

IL Interleukin

MAR Missing at Random

MAS the Sydney Memory and Ageing Study

MCI Mild Cognitive Impairment

MI Multiple Imputation

MICE Multiple Imputation by Chained Equation

MIND the Mediterranean-DASH diet Intervention for Neurodegenerative Delay

MMSE Mini-Mental State Examination

MRI Magnetic Resonance Imaging

MUFA Monounsaturated Fatty Acid

NESB Non-English-Speaking Background

NFL Neurofilament Light Protein

NHMRC National Health & Medical Research Council

NUTTAB Nutrient Tables for use in Australia

PCA Principal Components Analysis

PET Positron Emission Tomography

PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RAVLT Rey Auditory Verbal Learning Test

RCT Randomized Controlled Trial

RFS Recommended Food Score

ROB Risk of Bias

SD Standard Deviation

SFA Saturated Fatty Acid

SNP Single Nucleotide Polymorphism

STROBE-nut STrengthening the Reporting of OBservational studies in Epidemiology-Nutritional Epidemiology

TIA Transient Ischaemic Attack

TMT Trail Making Test

TNF Tumour Necrosis Factor

WHO World Health Organisation

Chapter 1: Introduction

1.1 Introduction to chapter

This thesis aims to examine the relationship between dietary patterns and cognitive health among older adults. Chapter one describes background of this research, established contexts of this thesis, and provides an outline of thesis aims and the overall thesis direction.

1.2 Dementia and cognitive decline

Dementia and cognitive decline, most commonly secondary to Alzheimer's disease (1), affects over 50 million people globally (2, 3). Dementia places a significant financial and social burden on patients, carers and health care systems (4, 5), with annual global costs estimated at approximately $1 trillion (6). As life expectancy is increasing and the population is ageing, it is estimated that the total number of people with dementia worldwide will triple by 2050 (6).

In Australia, dementia is the greatest cause of disability among older adults (7). Three in 10 people over the age of 85 and almost one in 10 people over 65 (8), and more than half of the residents in aged care facilities are living with dementia (9). Dementia is the second leading cause of death in the older population, and the leading cause of death for older women (9). In 2020, about 459,000 Australians were living with dementia. Without effective pharmaceutical treatments, this number is expected to increase to 590,000 by 2028 and 1,076,000 by 2058 (10). The total cost due to dementia, which was calculated to exceed $15 billion in Australia in 2018, is projected to pass $18.7 billion by 2025 and $36.8 billion by 2056 (9).

1.3 Alzheimer's Disease

Alzheimer disease (AD), a neurodegenerative disorder that primarily affects older adults, is the most common type of dementia (11). The hallmarks of neuropathologic changes are neuritic plaques associated with neuronal injury; extracellular deposition of amyloid beta peptides; and neurofibrillary degeneration such as neurofibrillary tangles (12, 13). Nonmodifiable risk factors for AD include aging and carrying the epsilon 4 allele of the apolipoprotein E gene (APOE-ε4). Ageing is the most important risk factor of AD, and the incidence of AD increases exponentially after the age of 65 years (2, 14, 15).

Mild cognitive impairment (MCI), is an intermediate state between normal cognition and dementia, defined as cognitive decline greater than expected for an individual's age and education level but does not interfere significantly with daily activities (16). Although not all people with MCI progress to dementia, however, there has been increasing evidence that MCI is associated with risk of dementia, especially AD (17).

1.4 Treatment for dementia

No effective pharmaceutical treatment for most causes of dementia or cognitive decline is available. Symptomatic approaches are available: cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) help to increase cholinergic transmission and play a modest role in people living with mild to moderate Alzheimer's disease (2); memantine, an N-methyl-D-aspartate (NMDA) receptor antagonist, provides modest benefits in older adults with moderate and severe Alzheimer's disease (18-21). Disease modifying drug development has focussed on anti-amyloid and anti-tau protein strategies (9, 10, 22), unsuccessfully to date, although the anti-amyloid antibody aducanumab, may yet prove effective, but awaits further

clarification (23). As effective treatments for Alzheimer's disease remain elusive, prevention or delay in onset holds more promise (2). It has been estimated that an intervention that could delay the onset of dementia by 2 years and introduced in 2020, would decrease the cumulative number of people developing dementia between 2012 and 2050 by 13% in Australia; for an intervention capable of delaying onset by 5 years, the cumulative number would be almost one third less (approximately 935,000 fewer people by 2050) than projected in Australia (24).

1.5 Modifiable risk factors for dementia

Twelve potentially modifiable risk factors account for approximately 40% of the population attributable risk of dementia worldwide, as modelled by the Lancet Commission on dementia prevention, intervention and care (6). Those modifiable risk factors are: less education, hypertension, hearing impairment, smoking, obesity, depression, physical inactivity, diabetes, low social contact, excessive alcohol consumption, traumatic brain injury and air pollution (6). Furthermore, in recent years, the incidence of age-specific dementia and neurocognitive impairment has been reported to have declined in many countries such the USA, the UK, Sweden, the Netherlands and Canada, putatively because of improvements in education, nutrition, health care, and lifestyle (6, 25-31). These findings suggest that there is a cohort effect mediated by lifestyle factors including dietary patterns. Diet may be a promising strategy to postpone, slow, or prevent cognitive decline (32-38) and reduce the risk of dementia (39).

1.6 Nutrition as promising approach for prevention of dementia and cognitive decline

Strong associations have been reported of dementia and cognitive decline, with vascular and metabolic risk factors including diabetes, insulin resistance and cardiovascular disease (CVD) (40), suggesting efficient management of those risk factors are important for dementia

prevention. CVD and dementia share common risk factors, including obesity, physical inactivity, smoking, elevated blood pressure and cholesterol levels; and CVD may manifest as cerebrovascular disease, an independent predictor of cognitive dysfunction (41).

The onset of dementia in people with type 2 diabetes has been reported to be approximately 2.5 years earlier than those without diabetes. Impaired fasting glucose, insulin resistance, and higher glycosylated haemoglobin (HbA1c) concentrations were also reported to predict increased incidence of dementia (42). Additionally, both Alzheimer's disease and metabolic syndromes are strongly associated with oxidative metabolism which may lead to neuronal damage and cognitive decline (40, 42).

Healthy diets can effectively manage CVD and metabolic syndromes. For example, diets reported to effectively lower risk of CVD, are those with adequate fruits and vegetables, grains, monounsaturated fats and omega-3 fatty acids. In particular, emerging evidence shows that a Mediterranean-like diet is associated with reduced cardiovascular events (43, 44). Dietary Approaches to Stop Hypertension (DASH) diet has been reported to lower blood pressure in prehypertensive and hypertensive adults and is recommended as an effective nutritional strategy to prevent CVD (45). Diets with food choices of glycaemic index lower than 55 such as legumes and multigrain bread, have been shown to assist in managing blood glucose and insulin levels, as well as weight control (46-48).

Dietary factors can affect multiple brain processes by regulating neurotransmitter pathways, synaptic transmission, membrane fluidity and signal-transduction pathways (49). Diet and nutrition may also impact cognitive function, possibly via different mechanisms apart from prevention of CVD and metabolic syndromes. These include modulating oxidative stress that

is associated with neurodegeneration (50), impacting inflammation which if elevated may damage the blood-brain barrier and result in cognitive impairment (51), regulating gut microbiota and indirectly impacting cognition via gut-brain-axis (52, 53).

The association of diet and nutrition with dementia and cognitive decline, has attracted much research attention in recent years with a focus on dietary and supplemental micronutrients (54, 55), macronutrients (39, 56, 57) and dietary patterns (58, 59). Observational studies and clinical trials of single nutrients mostly focus on micronutrients including B vitamins (B6, B12 and folate) due to their effects on homocysteine metabolism which might indirectly affect cognitive decline (60); and nutrients with anti-oxidant and anti-inflammatory properties which possibly play a mediation role in pathogenesis of dementia and cognitive decline, including vitamin C, vitamin D, vitamin E, carotenoids and flavonoids (39). Macronutrient research has focussed on, poly-/mono-unsaturated fatty acids (39), because of their anti-inflammatory properties and association with cardiovascular health (61, 62). However, recent World Health Organisation (WHO) guidelines advise that Vitamin B and E, poly-unsaturated fatty acids and multi-complex supplementation should not be recommended to reduce dementia risk, as the majority of current evidence reports little to no benefit from such supplementation, and obtaining adequate nutrition from natural dietary sources are suggested (63-65).

It may be that single nutrients are not as important as an integral dietary pattern (32, 34). Within dietary patterns, the synergies and interactions between multiple nutrients and foods may play an important role to prevent or slow cognitive decline (32-35). An important question is how effective are different types of dietary patterns and related food groups in protecting against cognitive decline in older adults?

1.7 Dietary patterns and cognition

Evidence has been growing that the Mediterranean diet may protect against cognitive decline (66-69). The Mediterranean diet, which originated among countries bordering the Mediterranean Sea in southern Europe, is characterised by high intake of vegetables, fruits, olive oil, legumes, fish, whole grains, nuts and seeds, moderate wine consumption and low consumption of processed foods, dairy products, red meat and vegetable oils (70). WHO guidelines advise that a Mediterranean-like diet may be recommended to adults with normal cognition and mild cognitive impairment, for its potential benefits on cognitive health with moderate quality of evidence (65).

The Dietary Approaches to Stop Hypertension (DASH) diet, have also shown promising results (71). The DASH diet, the dietary pattern proven to be effective in lowering blood pressure in patients with hypertension or those at high risk (72, 73), is defined as a diet with high consumption of fruits, vegetables, low-fat dairy products, whole grains, poultry, fish and nuts, and low consumption of red meat, fats, sweets and sugary beverages. DASH requires lower consumption of saturated fat but higher consumption of low-fat dairy than the Mediterranean diet (74).

A combination of both Mediterranean and DASH diets, the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet, has demonstrated some benefits for cognition (75). The MIND diet specifies intake of ten brain healthy foods, including berries, nuts, beans, whole grains, seafood, poultry, green leafy vegetables, other vegetables, wine and olive oil; and low intake of five unhealthy foods (red meats, butter and margarine, cheese, pastries/sweets, fried/fast food) (76).

On the other hand, there is less research on dietary patterns derived by data reduction methods using principal components analysis (PCA), for example, the *Prudent healthy diet* (characterised by high intake of vegetables and fruits, whole grains, and legumes) as opposed to the Western diet (characterized by high intake of red meat and processed foods, energy dense foods that are high salt, sugar and saturated/trans-fat) (77-79). Research on diets recommended by national peak bodies such as the Australian Dietary Guidelines on effects on cognitive health of older people has been sparse (80-83).

Current evidence on the association between dietary patterns and cognitive health remains inconclusive. Although existing prospective studies in Mediterranean countries mostly supported that higher adherence to a Mediterranean diet was associated with better cognitive performance or less cognitive decline than those who had lower adherence (84-86), research conducted in western countries reported mixed findings (58, 87, 88). Studies on the association of other dietary patterns such as DASH diet (74, 88) and prudent diet (77, 78), with cognitive health in older populations also reported mixed results, therefore further investigation is required, particularly in Western dietary environments. Large-scale, well-characterised studies are urgently needed.

The development of dementia has a long pre-symptomatic period, estimated to be up to 25 years, between the onset of pathological changes (such as accumulation of amyloid beta plaques) in the brain and the development of clinical symptoms of dementia. Long-term epidemiological cohort studies are therefore a suitable study design to investigate the lifestyle and environmental risk factors for dementia, and allow data collection to begin prior to symptom onset (89).

1.8 Thesis outlines and aims

The overall aim of this thesis is to answer the question whether different types of dietary patterns and related food groups protect against neurocognitive decline in older adults and if so, how effective they are. This thesis has investigated the research questions below, using data from a well-characterized Australian ageing cohort of older adults who did not have dementia, from the Sydney Memory and Ageing Study.

The thesis has the following objectives: i) to provide a comprehensive update on the topic by collating and evaluating the evidence from all human studies of randomised controlled trials (RCTs) and prospective cohorts examining a variety of dietary patterns and their effects on cognitive function and/or dementia; ii) to examine the association of dietary patterns and key food components within dietary patterns, with cognitive function with ageing cross-sectionally; iii) to examine the association of dietary patterns and key food components, with cognitive decline with ageing longitudinally, and to examine association between diet and average cognition that was representative of average cognitive performance over time; and, iv) to examine dietary quality among Australian older adults, using data from the Sydney Memory and Ageing Study, which is a well-characterized Australian ageing cohort.

This thesis comprises four manuscripts (one published, one accepted and two manuscripts under review). Each manuscript answered the four main questions of this thesis:

1. What is the current evidence of the relationship between dietary pattern, food components and cognitive health in older adults?
2. What is the cross-sectional relationship between dietary patterns, food components with cognitive function in the Australian older population?
3. What is the longitudinal association between dietary patterns food components with

overall cognitive performance over time and cognitive decline with ageing?

4. What is diet quality and food consumption patterns among older adults, with regard to recommendations from the Australia Dietary Guidelines, and is there a longitudinal association between the score on a diet quality index and cognitive health among older Australians?

Outline of thesis follows:

Chapter 1 provides an introduction to thesis, with background and aims of this research.

Chapter 2 describes general methodologies of subsequent chapters.

Chapter 3 presents a comprehensive systematic review, examining up to date evidence and existing studies on dietary patterns and cognitive health among older adults.

Chapter 4 examines cross-sectional relationships between dietary patterns, key components within dietary patterns and baseline cognitive function among older adults.

Chapter 5 reports outcomes from longitudinal analysis between dietary patterns, key food components within dietary patterns and cognitive performance and cognitive decline over time.

Chapter 6 evaluates the diet quality of the study population, and examines the association between a diet quality index with cognitive performance and cognitive decline with ageing.

Chapter 7 provides conclusions, where findings from each chapter are synthesized and summarised to provide informed recommendations for future dietary intervention for protecting against cognitive decline and fostering better cognitive health among older adults; as well as provide insights for future research.

1.9 References

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Chapter 2: General methods

2.1 Introduction to chapter

This chapter comprises a description of the general methods and materials that are applicable to the subsequent chapters. This chapter explains methodology for the systematic review; data source, data collection and measures from the Sydney Memory and Ageing study, as well as statistical analysis methods.

2.2 Methodology for systematic review

A systematic review was carried out following PRISMA guidelines (1). An electronic literature search was conducted for articles published between January 1997 and September 2017, assisted by a librarian from UNSW library. Databases PubMed, Medline, Cochrane Library, Embase, and Scopus were searched. Key search terms were Diet/ Dietary pattern/ Mediterranean diet/ DASH diet/ MIND diet/ low GI diet/ low fat diet/ low calorie diet/ healthy diet/ prudent diet/ anti-inflammatory diet/ Western diet AND cognition/ cognitive function/ memory/ cognitive decline/ dementia/ MCI and Alzheimer's disease. References were managed using the Endnote X8 referencing software.

RCTs and longitudinal studies on both *a-priori* and *a-posteriori* patterns by data driven approach using statistical methods, were included in the systematic review, if they measured cognitive function or brain morphology and provided follow up regardless of the time frame, to test cognitive function or incident cases of mild cognitive impairment (MCI) or dementia in older populations (>50 years at baseline). Exclusion criteria were cross-sectional studies, those not published in English, or did not have full-text available, or used non-human participants.

For Quality assessment of eligible studies, Cochrane Risk of Bias tool and the SIGN 50 checklist were used. The Cochrane Risk of Bias tool (2), rates studies as having low, unclear, or high risk of bias (ROB) based on several criteria: random sequence generation, allocation concealment, selective reporting, blinding, and incomplete outcome data reporting and other biases. The SIGN 50 checklist (3) assesses selection, performance, attrition and detection bias, confounding and overall methodological quality in longitudinal studies (details in Chapter 3).

2.3 Data Source from the Sydney Memory and Ageing Study

Research described in this thesis (Chapter 4 to Chapter 6) is based on data from The Sydney Memory and Ageing Study (MAS). In MAS, community dwelling participants were recruited between 2005 and 2007 from Sydney, New South Wales, Australia, following a random approach to 8914 individuals on the electoral roll, who were invited by letter. 7142 declined and a sample of 1772 who responded in the affirmative went through further screening to assess eligibility. The screening checked if the person was willing to participate, aged between 70 and 90 years, and whether they had adequate English language skills to complete a psychometric assessment, and adequate visual acuity to complete psychometric testing, and were not meeting any exclusion criteria stated as below. After screening, 735 people were excluded, resulting in a final sample of 1037 participants who were required to be able to speak and write English sufficiently at baseline assessment (4).

Exclusion criteria for study entry were a previous diagnosis of dementia, psychotic symptoms or a diagnosis of schizophrenia or bipolar disorder, multiple sclerosis, motor neuron disease, developmental disability; progressive malignancy (active cancer or receiving treatment for

cancer, other than prostate – non-metastasized, and skin cancer); implausible energy intake (<500kcal or >4000kcal per day); a Mini-Mental State Examination score <24 after adjustment (+1 for age 80 years and older, +1 for ≤ 9 years education and +2 for non-English speaking background (NESB)) (5, 6); or other medical or psychological conditions that may prevent participants from completing assessment (4).

2.4 Ethics approval and funding

The Sydney Memory and Ageing study was approved by the institutional review boards of the University of New South Wales and the Ethics Committees of the South Eastern Sydney and Illawarra Area Health Service. All participants gave written consent.

The Sydney Memory and Ageing Study received funding from the National Health and Medical Research Council (NHMRC) Australia (grant number ID350833, ID568969). The sponsor had no role in the design, analysis and interpretation of data, or writing of this thesis.

2.5 Data collection and measurements

Participants' dietary intakes were assessed at baseline via completion of the Dietary Questionnaire for Epidemiological Studies Version 2 (DQES v2). DQES v2 is a validated food frequency questionnaire (FFQ) covering the past 12 months' dietary intake, modified from FFQ developed by the Cancer Council of Victoria for use in an ethnically diverse Australian population (7-9). The DQES v2 comprises 74 food items with 10 options on frequency of consumption ranging from 'never' to 'three or more times per day; and six alcoholic beverages with frequency choices from 'never' to 'every day'. Questions on portion sizes (assisted with sample pictures of varied portion sizes) were asked and responses were used to evaluate a single portion size factor indicating participant's average portion size compared to a median serving

size. Nutrient intakes were calculated by the Cancer Epidemiology Centre of the Cancer Council in Victoria using the Australian food composition NUTTAB database 2010 (10).

Cognitive assessments were conducted at baseline (wave 1), 2-year (wave 2), 4-year (wave 3) and 6-year (wave 4) follow-up. Assessments include a comprehensive neuropsychological battery that was administered according to standard protocols by trained psychology graduates, comprising six cognition domains including attention/processing speed, language, executive function, verbal memory, global memory (incorporating verbal and visual memory) and visuospatial function. Attention/ processing speed tests comprised Digit Symbol-Coding (11) and Trail Making Test (TMT) A (12). Verbal memory tests were the Logical Memory Story A delayed recall (13); Rey Auditory Verbal Learning Test (RAVLT) of total learning, immediate and delayed recall (12). Global memory included verbal memory measures and Benton Visual Retention Test recognition (14). Language tests were the Boston Naming Test (15) and Semantic Fluency (Animals) (12). To assess visuo-spatial cognition, the Block Design test was used (16). Executive function tests included Controlled Oral Word Association Test (12) and Trail Making Test (TMT) B (12). Global cognition scores were calculated by averaging the domain scores (4). A reference group was selected from 504 MAS participants from English-speaking background and classified as cognitively normal at baseline, to assist conversion from raw cognitive scores to standardized scores.

Data were collected by interviewing participants and informants who were the closest person to participants and preferably someone who cohabitated with them. Medical history was collected during the interview, including cardiovascular diseases and related risk factors at baseline and each following wave (including hypertension, hypercholesterolemia, diabetes, smoking, obesity, stroke or transient ischemic attack etc) (4). History of depression was defined

as one or more depressive episodes that required attention from a general practitioner, psychologist or psychiatrist. Assessment of physical activity was conducted using self-report questionnaires developed by the MAS team (17). Total physical activity scores were calculated based on the sum of metabolic equivalent minutes (18) per week of participation across listed physical activities which were walking, gardening, yoga, gym work, bowls, golf, tennis, swimming, dancing, bicycling, dancing, aerobics and other sports (19). Height and weight were measured to determine body mass index (BMI=weight in kg/height in m^2) by a research assistant using a tape measure and a scale on most occasions. Shoes were left on, while bulky clothing was asked to be removed. Where a participant could not stand unassisted or an assessment was done over the phone, height and weight were self-reported. Mild cognitive impairment (20) and dementia (21) were diagnosed at consensus meetings of at least three experienced clinicians according to international consensus criteria. Apolipoprotein (APOE) genotyping was undertaken by genotyping the two single nucleotide polymorphisms (SNPs, rs7412 and rs429358), which distinguish between the three APOE alleles ε2, ε3 and ε4. Genotyping was performed using Taqman assays (Applied Biosystems Inc.[ABI], Foster City, CA, USA) (4) . The validity of the APOE genotyping was confirmed in a subsample using an alternate genotyping method that uses polymerase chain reaction amplification and restriction digest analysis (22). All measurements were conducted at each wave.

2.6 Construction of dietary patterns

Mediterranean diet scores were constructed following two scoring systems which have been most commonly used: the 0-9 scoring system by Trichopolou et al (23, 24) and the 0-55 scoring system by Panagiotakos et al (25). Two scoring systems were used, as heterogeneity of the scoring systems assessing adherence to the Mediterranean diet has strongly impacted the published studies outcomes; and the scoring systems (definitions of components, cut-points,

and scoring schemes) played an important role in these differences in results which has hindered interpretation (26). Intake from food groups were calculated, adjusted for total energy intake using the residual method (27), and divided into either "beneficial" or "detrimental" factors according to characteristics of the Mediterranean dietary pattern. A value of either 1 (beneficial factor) or 0 (detrimental factor) were given for 9 food groups, if the individual consumption was at or above sex-specific population medians of food component in the 0-9 system; in the 0-55 system, a value ranging from 0 to 5 was assigned according to the predefined number of servings for each Mediterranean food group (25). Higher scores represented higher adherence to the Mediterranean diet (details in Chapter 4 and 5).

DASH diet scores were constructed using the 2017 scoring strategy of Berendsen (28), by grouping dietary and nutrient intake into nine DASH component (fruits, vegetables, legumes and nuts, red and processed meat, whole grain, low fat dairy, sodium intake, sugar intake and sum of monounsaturated fat and polyunsaturated fat intake) (28, 29). Beneficial component were scored 1 to 5, while detrimental components received reverse scoring (sodium intake, sugar intake, red and processed meat intake) (28-31). DASH scores ranged from 9 to 45, with a higher score indicating greater adherence to the DASH diet (details in Chapter 4 and 5).

A modified Dietary Guideline Index (DGI) 2013 was applied to assess diet quality and adherence to the 2013 Australian Dietary guidelines (32). It includes the Five Food Groups (grains and cereals, vegetables and legumes, fruits, dairy products or alternatives, lean meats or alternatives) as well as components to limit (including discretionary foods high in sugar, salt or saturated fat), with detrimental factors reversely scored (details as in Chapter 4 and 6).

Principal component analysis (PCA) was used to derive *a posterori* patterns (Kaiser-Meyer-Olkin Measure of Sampling Adequacy at 0.698, indicating suitability for PCA (33, 34)). The 74 FFQ food items were classified into 40 food groups based on the similarity of their nutrient profiles as described in the Australian Food Composition Database (10). A smaller number of underlying components from linear combinations of food group clusters, were derived by PCA. Varimax rotation was applied to improve the separation of components and interpretability of the pattern derived. Components with an eigenvalue of >1 were investigated, within which food groups with a factor loading ≥0.20 (35) considered as important contributors (36).

2.7 Analytical methods

In cross-sectional analysis, statistical analyses were performed with IBM SPSS statistics 23.0 software (37). A multivariable linear regression model was used to analyze the associations between global cognition and dietary patterns scores as primary outcome. The relationship between diet and six separate cognitive domains were explored as secondary outcomes.

In longitudinal analysis, statistical analyses were performed using R version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria) (38). Linear mixed effects models were used to examine the associations of dietary pattern score and key food components at baseline, with cognitive change over time, as primary outcome. The association of dietary pattern scores and food components, with overall cognitive performance over six years, was investigated as the secondary outcome. Missing values in the dataset were dealt with using multiple imputation (MI) by chained equation (MICE) appoach under assumption of missing at random (MAR) (39, 40) (details described in Chapter 4). The parameter estimates for the linear mixed effect model from the imputed datasets were combined to form a single inference following Rubin's rule (41). Variables used in the imputation model included age, sex, education (as a

continous vatiable), non-English speaking background, BMI, physical activity, smoking, CVD risk factors, history of depression, history of stroke, ethnicity and APOE ε4. In addition to listed covariates, global cognition and scores in each cognitve domain were included in multiple imputation process. The MI was conducted in R using R-package MICE (42-44). Interaction between dietary score and age, sex and education were investigated in longitudinal analysis (details in Chapter 4 and 5).

In both cross-sectional analysis and longitudinal analysis, two different models were applied: the basic model was adjusted for age, gender and education (continuous variable); and the fully adjusted model additionally adjusted for confounding variables, namely physical activity, Body Mass Index (BMI), metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), smoking, depression, ethnicity and APOE ε4 genotype. To determine the effect of covariates, changes in the β-coefficient were examined. Significance level of 0.05 was set for global cognition as primary outcomes, and level of 0.01 was set for individual cognitive domains to adjust for multiple testings.

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Chapter 3: Dietary Patterns and Cognitive Health in Older Adults- A Systematic Review

3.1 Publication details

This chapter contains identical text of the manuscript entitled "Dietary Patterns and Cognitive Health in Older Adults: A Systematic Review", published in the Journal of Alzheimer's Disease, 2019, Volume 76, Issue 2, Pages 583-619.

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Supplementary material of this manuscript can be found in Appendix A.

3.2 Author contribution statement

I, Xi Chen (the candidate) was the primary researcher involved in conducting the search, selecting the studies, extracting data, assessing study quality and writing the initial draft. Brook Maguire assisted with data extraction and quality assessment of studies on Mediterranean diet in this manuscript. Conception and design of this study was conducted by the candidate and co-authors Dr Fiona O'Leary and Professor Henry Brodaty. All co-authors contributed to writing of final manuscript, critically reviewed and approved the final manuscript.

3.3 Introduction to chapter

Chapter 3 is a systematic review on the role of diet and nutrition in cognitive health and dementia prevention in older adults, conducted following PRISMA guidelines. The literature search initiated from 2015 and the manuscript was finally completed and published in Jan 2019, with much efforts on data extraction and quality assessment of studies. This chapter documents the existing evidence on

efficacy of diet on cognition, not only from the most studied Mediterranean diet, but also other dietary patterns of Dietary Approach to Stop Hypertension (DASH) diet, the Mediterranean-DASH diet Intervention for Neurodegenerative Delay (MIND) diet, Anti-inflammatory diet, Healthy diet recommended by national guidelines, or Prudent healthy diets generated via statistical approaches.

3.4 Manuscript: Dietary Patterns and Cognitive Health in Older Adults- A Systematic Review

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Dietary Patterns and Cognitive Health in Older Adults: A Systematic Review

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Abstract. While the role of diet and nutrition in cognitive health and prevention of dementia in older adults has attracted much attention, the efficacy of different dietary patterns remains uncertain. Previous reviews have mainly focused on the Mediterranean diet, but either omitted other dietary patterns, lacked more recent studies, were based on cross-sectional studies, or combined older and younger populations. We followed PRISMA guidelines, and examined the efficacy of current research from randomized controlled trials and cohort studies on the effects of different dietary patterns. We reviewed the Mediterranean diet, Dietary Approach to Stop Hypertension (DASH) diet, the Mediterranean-DASH diet Intervention for Neurodegenerative Delay (MIND) diet, Anti-inflammatory diet, Healthy diet recommended by guidelines via dietary index, or *Prudent healthy diet*s generated via statistical approaches, and their impact on cognitive health among older adults. Of 37 studies, the Mediterranean diet was the most investigated with evidence supporting protection against cognitive decline among older adults. Evidence from other dietary patterns such as the MIND, DASH, Anti-inflammatory, and *Prudent healthy diets* was more limited but showed promising results, especially for those at risk of cardiovascular disease. Overall, this review found positive effects of dietary patterns including the Mediterranean, DASH, MIND, and Anti-inflammatory diets on cognitive health outcomes in older adults. These dietary patterns are plant-based, rich in poly- and mono-unsaturated fatty acids with lower consumption of processed foods. Better understanding of the underlying mechanisms and effectiveness is needed to develop comprehensive and practical dietary recommendations against age-related cognitive decline among older adult.

Keywords: Alzheimer's disease, anti-inflammatory, cognitive decline, DASH, dementia, dietary pattern, mild cognitive impairment, Mediterranean, MIND, nutrition

INTRODUCTION

Dementia is a global concern, placing a significant financial and social burden on patients, carers, and health care systems [1, 2]. Cardiovascular risk factors, psychosocial factors, lifestyle behaviors, education and social networking, have been consistently linked to cognitive health among older adults [3, 4]. Approximately 30% of the population attributable risk for Alzheimer's disease (AD), the most common cause of dementia, has been calculated to be determined by modifiable environmental factors [5]. In addition, the incidence of neurocognitive decline

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in the older population appears to be declining, suggesting a cohort effect with lifestyle factors having an impact, and diet may also be a promising strategy to postpone, slow, or prevent cognitive decline [6–12].

Despite research into the relationships between single nutrients or food with cognitive decline among older adults, it has been suggested that single nutrients or food are not as important as an integral dietary pattern [6, 8]. Within dietary patterns, the synergies and interactions between multiple nutrients and foods may play an important role to prevent or slow cognitive decline [6–9]. An important question is, whether and how effective different types of dietary patterns are in protecting against neurocognitive decline in older adults?

One of these dietary patterns, the Mediterranean diet originated among countries bordering the Mediterranean Sea in southern Europe. It is characterized by high intake of vegetables, fruits, olive oil, legumes, fish, whole grains, nuts and seeds, moderate wine consumption and low consumption of processed foods, dairy products, red meat, and vegetable oils [13]. A variety of tools to score adherence to the Mediterranean diet exist. Commonly used scoring systems are the 0–9 scoring system by Trichopolou et al. [14] or the 0–55 scoring system by Panagiotakos et al. [15]. The systems are similar in that they both score food component characteristics and include fruit, vegetable, legume, and alcohol intake. However, Trichopolou et al. used population sex-specific cut-offs around the median, while Panagiotakos et al. used pre-defined cut-offs based on frequency of consumption of foods relative to recommended amounts from the Mediterranean diet pyramid [15]. Furthermore, the 0–9 scoring system uses monounsaturated: saturated fat ratio (MUFA: SFA) while the 0–55 scoring system uses olive oil consumption. The 0–9 scoring system scores meat and meat products and fish as two components while the 0–55 system scores fish, poultry, red meat and meat products separately. Instead of non-specific intake of "cereal" and "dairy intake" in the 0–9 scoring system, the 0–55 scoring system redefined the component characteristics as "non-refined cereal" and "full fat dairy".

The DASH diet, the dietary pattern proven to be effective in lowering blood pressure in patients with hypertension or those at high risk [16, 17], is defined as a diet with high consumption of fruits, vegetables, low-fat dairy products, whole grains, poultry, fish and nuts, and low consumption of red meat, fats, sweets, and sugary beverages. DASH requires low consumption of saturated fat but high consumption of low-fat dairy when compared to the Mediterranean diet [18].

The MIND diet, on the other hand, specifies intake of 10 brain healthy food groups, including berries, nuts, beans, whole grains, seafood, poultry, green leafy vegetables, other vegetables, wine, and olive oil. There is little emphasis on overall fruit or dairy intake, compared to the Mediterranean diet. The MIND diet also scores a low intake of 5 unhealthy foods (red meats, butter and margarine, cheese, pastries and sweets, fried/fast food) [19].

Overall, the Mediterranean, MIND, and DASH diets have been associated with lower plasma levels of inflammatory markers [20–22], which suggests diets impact inflammation and therefore may also indirectly affect cognitive health in older adults [23]. Inflammation has been viewed as an important risk factor of neurodegenerative diseases including cognitive impairment and dementia [24], as higher levels of circulating inflammatory markers, especially interleukin-6 (IL-6), tumor necrosis factor-α [TNF-α], and C-Reactive protein (CRP), are associated with brain atrophy and greater cognitive decline [25–28]. In general, anti-inflammatory diets include foods such as vegetables, legumes, fruits, whole grains, and seafood. These foods are naturally rich in vitamins, bioactive nutrients including antioxidants and poly-/mono- unsaturated fatty acids, which have been reported to reduce systemic inflammation [29, 30]. By contrast, an inflammatory diet is characterized by high consumption of red and processed meats, sweets, desserts, fries, and refined grains which may increase inflammation [31, 32].

The low GI diet, classified as food choices with glycemic index (GI) lower than 55 such as legumes, low GI whole grains and fruits, has been shown to assist in managing blood glucose and insulin levels [33].

Other dietary patterns that utilize data reduction methods (e.g., using principle components analysis (PCA), factor analysis, cluster analysis, or reduced rank regression) [34] have also been studied. An example is *the Prudent healthy diet,* characterized by high intake of vegetables and fruits, nuts, whole grains, fish, poultry, and low-fat dairy. *The Prudent healthy diet* is a healthier pattern, and contrasts with the Western diet which is characterized by high intake of red meat and processed foods, refined grains, high fat dairy, and high saturated/trans-fat [35–37].

There is growing evidence that the Mediterranean diet may protect against cognitive decline [38–41]. The MIND diet and the DASH diet, have also shown promising results [42]. On the other hand, the effects of diets such as the low GI diet, commonly used to treat diabetes [43], and to reduce cardiovascular risk factors [44, 45], on cognitive decline in the older population have been little studied. Similarly, there is limited research on the effects of the Anti-inflammatory diet, the *Prudent healthy diet* as opposed to the Western diet, and diets recommended by the World Health Organization or national peak bodies such as the Dietary Guidelines for Americans and the Australian Dietary Guideline on cognitive health of older people [46–49].

Most reviews on the association of dietary patterns with cognitive function have been from studies focusing on the Mediterranean diet [38–41]; very few have reviewed the full variety of dietary patterns. The most recent published systematic review [42] covered Mediterranean, DASH, and MIND diets but only assessed cross-sectional and longitudinal cohort studies, and omitted randomized control studies (RCTs). No recent review has synthesized findings from studies with higher level evidence [50–52] including cohort studies and RCTs, nor examined the full range of dietary patterns and association with cognitive function.

The aim of this systematic review is to provide a comprehensive update on the topic by collating and evaluating the evidence from all human studies of RCTs and prospective cohorts conducted on a variety of dietary patterns and the outcome of cognitive function and/or dementia.

METHODS

Literature search

Process and search terms

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [53]. An electronic literature search was conducted for articles published between January 1997 and September 2017. Databases PubMed, Medline, Cochrane Library, Embase, and Scopus were searched. Key search terms were Diet/ Dietary pattern/ Mediterranean diet/ DASH diet/ MIND diet/ low GI diet/ low fat diet/ low calorie diet/ healthy diet/ prudent diet/ anti-inflammatory diet/ Western

Table 1
Quality assessment of RCTs included in the review (Cochrane Risk of Bias Tool)

Article	Random Sequence generation (Risk of bias)	Allocation concealment (Risk of bias)	Selective reporting (Risk of bias)	Other source of bias	Blinding (participants and personnel) (Risk of bias)	Blinding (outcome assessment)	Incomplete outcome data	Overall bias assessment
Martínez-Lapiscina et al. [64]	Low	Low	Unclear	Yes - performance bias	High	Low	High	High
Valls-Pedret et al. [65]	Low	Unclear	Low	Yes- performance bias	High	Low	Low	High
Knight et al. [71]	Low	Unclear	Low	Unclear	High	Low	Low	High
Lehtisalo et al. [86] & Ngandu et al. [90]	Low	Unclear	Low	Unclear	High	Low	Low	High
Kowk et al. [87]	Unclear	High	Low	Unclear	High	Low	Low	High
Bayer-Carter et al. [92]	Unclear	Low	Unclear	Unclear	Unclear	Low	Low	Unclear

diet AND cognition/ cognitive function/ memory/ cognitive decline/ dementia/ MCI and Alzheimer's disease. Systematic reviews and meta-analyses were included. References were managed using the Endnote X8 referencing software. Papers and systematic literature reviews were hand searched for additional relevant studies.

Study selection

Abstracts, keywords, and titles were screened by XC, if unable to obtain adequate information then full texts were assessed. We included peer reviewed studies from level I and II levels of evidence ranking, i.e., RCTs and longitudinal studies according to NHMRC level of Evidence [51], if they measured cognitive function or brain morphology and provided follow up regardless of the time frame, to test cognitive function or incident cases of mild cognitive impairment (MCI) or dementia in older populations (>50 years at baseline). We excluded studies that were cross-sectional, not published in English, did not have full-text available, or used non-human participants.

Data extraction and quality assessment

Study and participant characteristics, exposure assessment, length of follow-up, confounders, cognitive assessment methods, key statistical results, and overall quality rating were inserted into a customized extraction table. An extraction table was generated for recent systematic reviews, included as a supplementary table.

Data extraction and quality assessment were first assessed by a single reviewer (XC), cross checked by a second reviewer (FOL), with discrepancies discussed with a third reviewer (HB). Cochrane Risk of Bias tool and the SIGN 50 checklist [54] were used.

The Cochrane Risk of Bias tool [55], rates studies as having low, unclear, or high risk of bias (ROB) based on several criteria: random sequence generation, allocation concealment, selective reporting, blinding, and incomplete outcome data reporting and other biases.

The SIGN 50 checklist assesses selection, performance, attrition and detection bias, confounding and overall methodological quality in longitudinal studies [54]. This assessment tool has 14 questions targeting internal validity and four questions covering overall evaluation of quality. The questions prompt a "Yes", "No", or "Can't Say" answer [56]. Overall, articles were scored Low Quality (–) if they had 1–6 "yes" scores, Acceptable (+) for 7–9 "yes" scores and High Quality (++) for 10–14 "yes" scores.

RESULTS

Study selection

Study selection flow chart is shown in Fig. 1 and PRISMA Checklist is provided as Supplementary Material. From 1,765 articles obtained, 37 studies were eligible for inclusion. Study characteristics and outcomes can be found in Tables 1 and 2. Thirty-one were cohort studies emanating from the US ($n=17$), France ($n=2$), Australia ($n=3$), UK ($n=2$), Italy ($n=1$), Sweden ($n=2$), Asia ($n=2$), Greece ($n=1$), and Spain ($n=1$). Six studies were RCTs; they came from Spain ($n=2$), Finland ($n=1$), Australia ($n=1$), US ($n=1$), and Hong Kong ($n=1$). Most papers (5/6 for RCTs and 31/31 for cohorts) assessed community-dwelling older adults.

A priori and a posteriori studies

Most cohort studies included in this review used *a priori* ($n=26$) approaches by assessing dietary adherence scores to a specific dietary pattern based on consumption of key food components. Patterns included the Mediterranean diet, which was the most studied dietary pattern with three RCTs (two conducted in the Mediterranean area) and 19 cohort studies (4 conducted in Mediterranean countries) using 0–9 [14] or 0–55 scoring system [15]. Other *a priori* studies were the DASH diet ($n=3$) using 8–40 [37] or 0–10 DASH scoring system [57], and the MIND diet ($n=3$ studies) using a 0–15 scoring system [58]. Other less studied patterns were the Anti-inflammatory diet ($n=2$), the Low GI diet ($n=1$), and the Healthy diet recommended by dietary guidelines ($n=7$) (see Fig. 2).

By contrast, only seven studies ($n=2$ overlapped with *a priori* group as reported both *a priori* and *a posteriori* patterns) used *a posteriori* approaches to investigate dietary profiles of a target population (see Fig. 2), including studies on *the Prudent healthy diet* compared to the Western diet ($n=3$ using PCA [59] or factor analysis [35, 36]), and wheat based diet ($n=1$, using PCA [60]). Other studies used reduced rank regression [61], cluster analysis [62], and factor analysis [63] to derive population-specific dietary patterns (see Table 3 for details).

Table 2
Characteristics of RCTs included in the review

Author, year, Location, length of follow up	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Martínez-Lapiscina et al. 2013 [64] Spain follow up: 6.5 years	N = 522 from PREDIMED Age: mean 74.6 ± 5.7 years Male: 44.6% Clinical Status: Participants initially free of CVD but at high vascular risk, because of the presence of either type-2 diabetes or at least three of the following major risk factors: current smoking, hypertension, dyslipidemia, overweight or family history of premature CVD.	Med Diet with EVOO (1L/ wk), or Med diet with mixed nuts (30g/ d) versus control diet (advice to reduce dietary fat). Foods provided to the Intervention Group but not Control Group	Validated 137 item FFQ questionnaire and a 14-item short questionnaire of adherence to the Med Diet, interview with a trained dietitian	Sex, age, education, APOEε4 genotype, family history of cognitive impairment/ dementia, smoking, physical activity, body mass index, HTN, dyslipidemia, diabetes, alcohol and total energy intake	Cognition/ Incidence of Dementia or MCI Test used: MMSE and CDT; Incidence of Dementia or MCI from medical records	Participants in the Med Diet + EVOO had higher mean MMSE and CDT scores versus control (adjusted differences: +0.62 95% CI +0.18, +1.05, $p = 0.005$ for MMSE, and +0.51 95% CI +0.20, +0.82, $p = 0.001$ for CDT). MMSE and CDT scores were also higher for participants in the Med Diet + Nuts versus control (adjusted differences: +0.57 (95% CI +0.11, +1.03), $p = 0.015$ for MMSE and +0.33 (95% CI +0.003, +0.67), $p = 0.048$ for CDT).
Valls-Pedret et al. 2015 [65] Spain follow up: 4.1 years	N = 447 from PREDIMED Age: mean 66.9 years Male: 47.9% Clinical Status: cognitively healthy, free of CVD but at high cardiovascular risk, because of the presence of either type-2 diabetes or at least three of the following major risk factors: current smoking, hypertension, dyslipidemia, overweight or family history of premature CVD.	Med Diet with EVOO (1L/ wk), or a Mediterranean diet with mixed nuts (30 g/ d) versus a control diet (advice to reduce dietary fat). Foods were provided to the intervention but not control Group	Validated 137 item FFQ questionnaire and a 14-item short questionnaire of adherence to the Med Diet, interview with a trained dietitian.	Sex, baseline age, years of education, APOEε4 genotype, smoking, BMI, energy intake, physical activity, diabetes, hyperlipidemia, the ratio of total cholesterol to HDL cholesterol, statin treatment, HTN, and use of anticholinergic drugs	Cognition/Cognitive decline Test used: MMSE RAVLT The verbal paired associates test - a subtest of Wechsler Memory Scale The animal fluency test the Digit Span subtest of the Wechsler Adult Intelligence Scale the Colour Trail Test	Participants allocated to a Med diet plus EVOO scored better on the RAVLT: 4.50 (95% CI: 3.24, 5.77, $p = 0.049$) and Colour Trail Test part 2: 5.66 (95% CI: –10.23, 21.55, $p = 0.04$) compared with controls. Memory composite score was higher in the Mediterranean diet plus nuts 0.09 (95% CI: –0.05 to 0.23, $p = 0.04$); frontal cognition composite score was higher in the Med Diet plus EVOO 0.23 (95% CI: 0.03, 0.43, $p = 0.003$); global cognition composite was higher in the Med Diet plus EVOO 0.05 (95% CI: –0.11, 0.21, $p = 0.005$) compared to controls. All cognitive composite scores significantly ($p < 0.05$) decreased from baseline in controls.

(*continued*)

Table 2
(*Continued*)

Author, year, Location, length of follow up	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Knight et al. 2016 [71] Australia follow up: 6 months	N = 137 the MedLey study Age: mean 72.1 ± 5.0 years Male: 46.7% Clinical Status: normal cognitive function, no previous or current conditions that may cause cognitive impairment without potential health issues	Mediterranean Diet versus control diet - habitual dietary intake (HabDiet). Foods provided to Intervention Group and supermarket gift vouchers for Control Group	Validated FFQ Cancer Council Victoria and 3-day weighed food record, a semi-quantitative daily food check list; fortnightly meeting with a dietitian to provide education and monitor compliance	Age, sex, BMI, education, APOE ε4 allele, self-rated depressive symptoms, sleep quality, anxiety symptoms and stress levels, family history of dementia, AD, incidence of heart attack, high blood pressure, stroke and diabetes, physical activity and the dependent variables (i.e., all individual cognitive test scores, and composite scores for: overall age-related cognitive performance, executive function, speed of processing, memory, visual-spatial ability.	Cognition/Cognitive decline Test used: Executive function by the following four tests: Dodrill's version of the Stroop Test, Initial Letter Fluency (ILF) and Excluded Letter Fluency (ELF) and D-KEFS version of the Tower of London (TOL); Memory by Rey and Schmidt's, RAVLT, Digit Span Forward (DSF) Digit Span Backward (DSB) and the Letter-Number sequencing (LNS) subtest tasks from the Wechsler Adult Intelligence Scale (WAIS-IV) Speed of processing by: Symbol Search and Coding core subtests from WAIS IV Visual-spatial memory ability, The Benton Visual Retention Test (BVRT).	No difference for executive functioning, speed of processing, memory, visual-spatial ability and overall age-related cognitive performance. Executive functioning ($p = 0.33$; 95%CI: –2.58, 7.65); speed of processing ($p = 0.15$; 95%CI: –1.21, 7.70); Memory ($p = 0.50$; 95%CI: –3.88, 7.88); Visual-spatial ability ($p = 0.48$; 95%CI: –0.38, 0.81); overall age-related cognitive performance ($p = 0.19$; 95%CI: –4.00, 19.9).

(*continued*)

Table 2
(*Continued*)

Author, year, Location, length of follow up	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Lehtisalo et al., 2017 [86] & Ngandu et al., 2015 [90] Finland Follow up 2 years	N = 1260 from the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) Age: 60–77 years Male: 56 Clinical Status: those have a CAIDE (Cardiovascular Risk Factors, Aging and Dementia) Risk Score of 6 points or higher (score based on age, sex, education, systolic blood pressure, BMI, total cholesterol, and physical activity; range 0–15 points). Exclude previously diagnosed dementia/suspected dementia, MMSE <20, disorders affecting safe engagement in the intervention (e.g., malignant disease, major depression, symptomatic cardiovascular disease, revascularization within 1 year previously); severe loss of vision, hearing, or communicative ability	Nutrition Intervention based on national Finnish Dietary Recommendation	Food record in 3 consecutive days completed close to annual visits, include 2 weekdays and 1 weekend day (Thursday to Saturday or Sunday to Tuesday). Dietary adherence score to national dietary recommendations range (0–9)	Age, education, sex and study center, baseline BMI, systolic blood pressure, fasting glucose, LDL-cholesterol and depressive symptoms.	Intake and changes in intake of nutrients during the intervention/cognition Cognition Test used: comprehensive neuropsychological test battery; The executive functioning domain included category fluency test, 19-digit span, concept shifting test, trail making test, and a shortened 40-stimulus version of the original Stroop test. The processing speed domain included letter digit substitution test, concept shifting test, and Stroop test. The memory domain included visual paired associates test, immediate and delayed recall; logical memory immediate and delayed recall; and word list learning and delayed recall.	Composite dietary intervention adherence score range (0–9 points) was 5 0 at baseline and increased in the intervention group after the 1st ($p < 0.001$) and 2nd ($p = 0.005$) year. The difference in change compared with the control group was significant at both years ($p < 0.001$ and $p = 0.018$). Intake of several nutrients decreased in the control group but remained unchanged or increased in the intervention group, significant difference in fiber, w-3/w-6 fatty acids, vitamin C/D/E/folic acid/magnesium. After diet Intervention together with exercise, cognitive training and monitoring of vascular risk for two years, improvement in comprehensive neuropsychological test total score after 24 months was 25% higher in the intervention group than in the control group ($p = 0.03$). Improvement in executive functioning was 83% higher, and in processing speed 150% higher, in the intervention group than in the control group. Significant intervention effect for executive functioning ($p = 0.039$) and processing speed ($p = 0.029$).

(*continued*)

Table 2
(*Continued*)

Author, year, Location, length of follow up	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Kwok et al., 2012 [87] Hong Kong follow up: mean 25 months (range 24–33 months)	N = 429 Age: mean 83 years Male: 15.4% Clinical Status: Tube-fed residents and those on special diet due to chronic renal failure were excluded. non-demented subjects in old age hostels,	Dietary interventions promote intakes of fruit, vegetable, fish and lower salt intake add this in - to either regular group dietary counselling and menu changes or advice on hostel menu only.	24-h recall or food record via face to face interview by RA in those with intact memory or via observation at 3 main meals for MCI subjects For those with impairment in the memory domain of CDR, food intakes during the three main meals were recorded by direct observation by RA. Quantification of nutrients was determined by a dietary computer program 'Food processor', which was based on food tables for Hong Kong and Mainland China.	Baseline characteristics and dietary intakes: age, sex, HTN, diabetes mellitus, education, intakes of fruit, vegetable, fish, and saturated fat	Cognition/Cognitive decline test used: Cognitive tests included clinical dementia rating scale, Chinese MMSE and category fluency test.	Dietary interventions in older people were effective in maintaining fruit and fish intake, but no significant effect on cognition. Subgroup analysis found fewer cognitively normal subjects in intervention group had cognitive decline at 24 months versus control group ($p = 0.065$).
Bayer-Carter et al. 2012 [92] USA follow up: 4 weeks	N = 49 Age: mean age 68.3 years Male: 46.9% Clinical Status: free of major psychiatric disorders, alcoholism, neurologic disorders other than amnesic MCI ($n = 29$), renal or hepatic disease, diabetes mellitus 2, chronic obstructive pulmonary disease, and unstable cardiac disease. None taking cholesterol-lowering medications.	High saturated fat/ high GI (HIGH) diet versus a low saturated fat/low GI (LOW) diet	All food was delivered to the homes of participants twice weekly. Menus were designed by a nutritionist Study participants recorded all food consumed each day to assess adherence. Not validated.	Age, baseline BMI, educational level, and APOE-ε4 status	Cognition/Cognitive decline Test used: Tests of immediate and delayed memory (story recall, word list, and the Brief Visuospatial Memory Test), executive function (Trail-Making Test, part B; Stroop test/interference condition; and Verbal Fluency Test), and motor speed (Trail-Making Test, part A and Stroop test/ matching condition).	The healthy control and amnesic MCI groups showed improved delayed visual recall with the LOW GI diet ($p = 0.04$), but other delayed memory measures did not change significantly. No diet-related changes were observed for immediate memory, executive, or motor speed domains.

AD, Alzheimer's Disease; APOE, Apolipoprotein E; BMI, body mass index; CI, confidence interval; CDT, the Clock Drawing Test; CVD, cardiovascular disease; EVOO, extra virgin olive oil; FFQ, Food frequency questionnaire; GI, glycemic index; HTN, hypertension; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MCI, mild cognitive impairment; Med Diet, Mediterranean diet; MMSE, Mini-Mental Status Examination; PREDIMED, the PREvención con DIeta MEDiterránea study; RAVLT, Rey Auditory Verbal Learning Test; WAIS-IV, the Wechsler Adult Intelligence Scale.

Table 3
Characteristics of cohort studies in this review

Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Berendsen et al. 2017 [18] USA Follow up 6 years Acceptable (+)	N = 16,144 from the Nurses' Health Study. Age: Mean 74.3 ± 2.3 years first cognitive assessment Male (%): 0% Clinical status: free of stroke	DASH diet	116 item FFQ and validation DASH scoring system range 8–40, based on intake of 9 food components	Age and education, and additionally for long-term energy intake and physical activity, BMI, smoking status, alcohol intake, history of depression, multivitamin use, and cardiovascular risk factors (history of diabetes, hypertension, hypercholesterolemia, and/or myocardial infarction. In a subset of 5,822 participants, APOE ε4 alleles tested for interaction	Cognition/cognitive decline Cognition test used: The cognitive battery included: TICS, immediate and delayed recalls of the East Boston Memory test, delayed recall of the TICS 10-word list, category fluency, digit span backward test	Greater adherence to long term DASH score was associated with better average cognitive function, irrespective of APOE ε4 status. For mean z-scores between highest and lowest DASH quintiles $p = 0.04$ (95% CI 0.01, 0.07), $p = 0.009$ for global cognition: 0.04 (9% CI 0.01, 0.07), p trend for verbal memory and 0.16 (95%CI 0.03, 0.29), and $p = 0.03$ for TICS. Those differences were equivalent to being 1 year younger in age. Adherence to DASH score was not associated with change in cognitive function over 6 years.
Berendsen et al. 2017 [19] USA Follow up 6 years High Quality (++)	N = 16,058 from the Nurses' Health Study. Age: 70 and older mean 74.3 ± 2.3 years Male (%): 0% Clinical status: exclude dementia not MCI	MIND diet	116-item Food Frequency Questionnaire The 0–15 MIND score includes ten brain-healthy foods and five unhealthy foods.	Age and education, and additionally for long-term energy intake and physical activity, BMI, smoking status, alcohol intake, history of depression, multivitamin use, and cardiovascular risk factors (history of diabetes, hypertension, hypercholesterolemia, and/or myocardial infarction. In a subset of 5,822 participants, a variable indicating the product of the number of ApoE ε4 alleles (0,1,2) was used to test for effect modification by ApoE ε4. Energy intake adjusted	Cognition/cognitive decline Cognition test used: The cognitive battery included TICS, immediate and delayed recalls of the East Boston Memory test, delayed recall of the TICS 10-word list, category fluency and digit span backward test.	Greater long-term adherence to the MIND diet was associated with a better verbal memory score (multivariable-adjusted mean differences between highest and lowest MIND quintiles = 0.04 (95%CI 0.01, 0.07), $p = 0.006$), but not with cognitive decline over 6 years in global cognition, verbal memory or TICS.

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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Ozawa et al. 2017 [23] UK Follow up 10 years High Quality (++)	N = 5083, British civil servant Whitehall II Perspective Cohort Study Age: age 35–79 years baseline mean 56 years Male (%): 71.3% Clinical status: Nil Subjects with implausible total energy intake Excluded.	Inflammatory Dietary pattern characterized as higher intake of red processed meat, peas, legumes and fried food, and lower intake of whole grains	127 item FFQ Validated. Reduced rank regression to determine dietary pattern associated with Interleukin-6.	Age, sex, ethnicity, education and total energy intake. Health related variables included BMI, diabetes mellitus, HTN, smoking, leisure time physical activity, ethnicity, occupational position, education, smoking history. Energy intake adjusted	Cognition/Cognitive decline Cognitive test used: 4 standard tasks: Alice Heim 4-I, short term verbal memory, phonemic fluency, and semantic fluency. Global cognitive score, MMSE	Greater inflammatory diet associated with accelerated cognitive decline at older ages. Greatest decline in highest tertile of inflammatory diet for reasoning (–0.37 SD, 95% CI –0.40, –0.33) compared to lowest tertile (–0.31 SD, 95% CI –0.34, –0.28) global cognition: highest tertile –0.35 (–0.38, –0.32) compared to lowest tertile –0.31 (–0.33, –0.28). Stronger association in those less than 56 years.
Gardener et al. 2015 [35] Australia Follow up 3 years Acceptable (+)	N = 527 participants from the AIBL study. Over 79% were born in Australia Age: mean age 69.3 years Male (%): 39.8% Clinical status: cognitive intact, average BMI of 26.3 kg/m^2	Modified Australian Mediterranean diet (AusMeDi), *Prudent healthy diet* and Western diet derived by factor analysis	Cancer Council of Victoria food frequency questionnaire 101 food items, 0–9 Med Diet scoring system	APOE ε4 status, BMI, country of birth (Australia or other), years of education ($\leqslant$12 years or 412 years), past smoking status, energy intake, history of angina, stroke, HTN, heart attack and diabetes	Cognition/cognitive decline Cognition test used: Composite scores constructed for a global cognitive score and six cognitive domains (verbal memory, visual memory, executive function, language, attention, and visuospatial functioning). The full battery comprised the MMSE, California Verbal Learning Test – Second edition, Logical Memory I and II (Story A only), D-KEFS verbal fluency, 30-item Boston Naming Test, Wechsler Test of Adult Reading, Digit Span and Digit Symbol-Coding subtests of the Wechsler Adult Intelligence Scale – Third edition (WAIS– III), the Stroop task (Victoria version), and the Rey Complex Figure Test	Higher baseline adherence to the AusMeDi associated with better performance in the executive function cognitive domain in APOE ε4 allele carriers ($p < 0.01$). Higher baseline Western diet adherence was associated with greater cognitive decline in the visuospatial cognitive domain in APOE ε4 allele non-carriers ($p < 0.01$). All other results were not significant.

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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Shakersain et al. 2016 [36] Sweden Follow up 6 years High Quality (++)	N = 2223 Community based From the Swedish National study on Aging and Care-Kungsholmen (SNAC-K). Age: aged ≥60 mean 70.6 ± 8.9 Male (%): 39.2% Clinical status: dementia-free	Prudent healthy diet versus western diet identified via exploratory factor analysis (principle component)	Validated FFQ with 98 items.	Age, sex, education, civil status, BMI, physical activity, smoking, vascular and other chronic diseases, dietary supplements use, APOE ε4 genotype, energy intake	Cognition Cognition test used: MMSE	Compared with the lowest adherence to each pattern, the highest adherence to prudent pattern was related to less MMSE decline ($p = 0.011$) where highest adherence to western pattern was associated with more MMSE decline ($p < 0.001$). Western diet (β = –0.045 95%CI 0.071, 0.019) and *prudent healthy diet* (β = 0.043 95%CI 0.017, 0.068)
Morris et al. 2015 [58] USA Follow up 4.7 years High Quality (++)	N = 960 participants From retirement communities and senior public housing, the Rush Memory and Aging Project Age: mean age 81.4 ± 7.2 Male (%): 25% Clinical status: free of dementia	MIND diet	144-item validated semi-quantitative FFQ. The 0–15 MIND score includes ten brain-healthy foods and five unhealthy foods.	Age, sex, education, APOE ε4 genotyping, physical activity, total energy intake, smoking, participation in cognitive activity, BMI, depressive symptoms, HTN history, Myocardial Infarction history, diabetes history, medication, stroke	Cognition/cognitive decline Cognition test used: 21 neuropsychological tests included 19 measures cognition in 5 cognitive domains (episodic memory, working memory, semantic memory, visuospatial ability and perceptual speed).	The MIND score was positively associated with slower decline in global cognitive score (β = 0.0092; $p < 0.0001$) and with each of five cognitive domains. The difference in decline rates for being in the top tertile of MIND diet scores versus the lowest was equivalent to being 7.5 years younger in age.
Jacka et al. 2015 [59] AU Follow up 4 years High Quality (++)	N = 255 from the Personality and Total Health Through Life Study Age: mean 62.6 ± 1.42 Male: 56% Clinical status: excluded those with MRI abnormality, stroke or epilepsy	Prudent (healthy) diet versus Western (unhealthy) diet derived using PCA	188-item Commonwealth Scientific and Industrial Research Organisation FFQ	Age, gender, education, labor-force status, depressive symptoms and medication, physical activity, smoking, hypertension and diabetes	hippocampal volume Test used: Magnetic resonance imaging	Every one SD increases in healthy "prudent" dietary pattern was associated with a 45.7 mm^3 (standard error 22.9 mm^3) larger left hippocampal volume, while higher consumption of an unhealthy "Western" dietary pattern was (independently) associated with a 52.6 mm^3 (standard error 26.6 mm^3) smaller left hippocampal volume. While hippocampal volume declined over time, there was no evidence that dietary patterns influenced this decline. No relationships were observed between dietary patterns and right hippocampal volume.

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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Qin et al. 2015 [60] China Follow up 7 years Acceptable (+)	N = 1,650 community dwelling, from China Health and N1utrition Survey Age: ≥55 years of age Mean age 64 years Male (%): 49.7% Clinical status: Nil specific	Chinese adapted Mediterranean Diet and two dietary pattern scores derived from PCA	24 h food recall for 3 consecutive days, Adapted 0–9 Med Diet scoring system	Age, gender, region, urbanization index, education, annual household income per capita, physical activity, current smoking, total energy intake, time, BMI, HTN	Cognition/cognitive decline Cognition test used: cognitive screening items from part of the TICS-modified., immediate and delayed recall of a 10-word list (10 points each); counting backward and serial 7's (seven points); orientation assessed by asking the participant the current date (one point each for year, month, and date); and naming the tool used to cut paper (one point).	In those ≥65 years of age, Q3 versus Q1 of adapted Med Diet Q3 had slower rate of cognitive decline (β = 0.042; 95% CI: 0.002, 0.081) and wheat-based diverse diet Q3 versus Q1 had slower annual decline in global cognitive function (β = 0.069 SU/year; 95% CI: 0.023, 0.114). No associations in adults <65 years of age.
Gu et al. 2010 [61] USA Follow up 3.9 years Acceptable (+)	N = 2148 northern Manhattan residents, from Washington/Hamilton Heights-Inwood Columbia Aging Project II: WHICAP II Age: mean 77.2 ± 6.6 Male: 32% Clinical status: without dementia	DPs based on 7 AD-related nutrients: saturated fatty acids, vitamin E, vitamin B12, and folate, MUFA/PUFA, derived using reduced rank regression	61-item version of Willett's SFFQ	Recruitment cohort, age, sex, ethnicity, education, smoking status, BMI, caloric intake, comorbidity index, and APOE ε4 genotype	Incidence of dementia Cognition test used: Clinical Dementia Rating (CDR). Diagnosis for the dementia using the neuropsychological battery of tests, the Blessed Dementia Rating Scale, the Schwab and England Activities of Daily Living Scale, and the physician's assessment, and evidence of cognitive and social/occupational function decline as compared with the past, as required by the DSM-III-R.	DP that strongly associated with lower AD risk is characterized by higher intakes of salad dressing, nuts, fish, tomatoes, poultry, cruciferous vegetables, fruits, and dark and green leafy vegetables and a lower intake of high-fat dairy products, red meat, organ meat, and butter. Compared with subjects in the lowest tertile of adherence to this pattern, the AD hazard ratio (95% CI) for subjects in the highest DP tertile was 0.62 (0.43, 0.89) after multivariable adjustment ($p = 0.01$)

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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Granic et al. 2016 [62] UK Follow up 5 years Acceptable (+)	N = 791 (302 men and 489 from Northeast UK from The Newcastle 85 + Study Living in community or aged home Age: ≥85 Male (%): 38% Clinical status: nil. Very old adults >= 85 years	3 Dietary Patterns derived by cluster analysis that differed in intake of red meat, potato, gravy, and butter and varied with key health measures, derived using SPSS 2-step clustering	Two day (non-consecutive) 24-h multiple pass dietary recall	Sex; education; marital status; social class, smoking; physical activity; BMI, APOE ε4 status. Chronic diseases included arthritis, HTN, cardiac disease, respiratory disease, cerebrovascular disease, diabetes, and cancer. sex-specific energy quartiles, supplement intake, and number of medications, in sensitivity analysis.	Cognition Cognition test used: SMMSE and the cognitive drug research attention battery.	Compared with DP1 (high red meat) and DP3 (high butter), DP2 (low meat) had better SMMSE ($p < 0.001$) better initial attention ($p < 0.005$) at baseline and follow ups. DP1 and DP3 was associated with overall worse SMMSE scores ($\beta = 0.09$, $p = 0.01$ and $\beta = 0.08$, $p = 0.02$, respectively) than DP2 after adjustment. Additional adjustment for APOE ε4 genotype attenuated the association to non significant in women but not in men in DP1 ($\beta = 0.13$, $p = 0.02$). DP1 and DP3 also had worse concentration ($\beta = 0.04$, $p = 0.002$ and $\beta = 0.028$, $p = 0.03$, respectively) and focused attention ($\beta = 0.02$, $p = 0.01$ and $\beta = 0.02$, $p = 0.03$, respectively), irrespective of APOE ε4
Chen et al. 2017 [63] Taiwan Follow up 2 years Acceptable (+)	N = 475 from the elderly health checkup program at National Taiwan University Hospital (NTUH) Age: 65 and older, mean 73 Male (%): 17% Clinical status: excluded use of medication for AD treatment, history of stroke, vegetarians, total energy intake <650 kcal/d, physical activities >10,000 kcal/d.	Three Dietary Patterns (vegetable, meat, and traditional) derived using factor analysis.	44-item semi-quantitative FFQ (which represents a shortened version of a validated 64-item FFQ for Taiwanese) at baseline, a factor analysis based on 24 food groups performed to identify DPs	Age, sex, years of education, and APOE ε4 status, disease history (e.g., HTN,, diabetes mellitus, and hyperlipidemia), and supplement use (e.g., multivitamin and calcium). Physical activity. Depressive symptoms energy intake adjusted	Cognition/cognitive decline Cognition test used: Global cognition determined by the Montreal Cognitive Assessment-Taiwan version. the Wechsler Memory Scale-Third Edition (WMS-III) to assess logical memory and attention (digit span) domains. Verbal fluency tests. Trail making tests (A and B) used to assess executive function. Eleven domain-specific cognitive variables were obtained.	Moderate/high-score "vegetable" DP significantly protected against decline of logical memory (recall I: $\beta = 0.16$–0.18, OR = 0.42–0.48; recall II: $\beta = 0.17$–0.21); high-score "vegetable" DP increased executive function decline ($\beta = -0.22$). A high-score "meat" DP related to decline of verbal fluency-total score ($\beta = -0.19$); moderate/high-score "meat" DP protected against attention decline ($\beta = 0.20$–0.22). High-score "traditional" DP protected against decline of logical memory-recall I ($\beta = 0.18$). No significant association was observed for global cognition.

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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Feart et al. 2009 [66] France Follow up 4.1 years Acceptable (+)	N = 1410 from 3 City Study Age: mean 75.9 years Male (%): 37.4% Clinical status: non-demented non-institutionalized	Mediterranean Diet	FFQ with 40 item foods and beverages, administered by trained dietitian and a 24-hour dietary recall. The 10-point (0 to 9) Med Diet Score	Age, sex, education, marital status, caloric intake, APOE ε4 genotype, physical activity, >5 medications/day, depression score, BMI, diabetes, HTN, tobacco use, hypercholesterolemia, stroke	Cognitive decline/ dementia risk Cognitive test used: MMSE, The Isaacs Set Test (IST), The Benton Visual Retention Test (BVRT), and The Free and Cued Selective Reminding Test (FCSRT)	A higher Med Diet score associated with fewer MMSE errors (β = –0.006; 95% CI –0.01, –0.0003; $p = 0.04$ for 1 point of the Mediterranean diet score). No association with performance on the IST, BVRT, or FCSRT over time. No association with risk for incident dementia (HR, 1.12; 95% CI 0.60, 2.10; $p = 0.72$).
Trichopoulou et al. 2015 [67] Greece Follow up 7 years Acceptable (+)	N = 401 from The European Prospective Investigation into Cancer and Nutrition (EPIC-Greece). Age: mean 74 years Male (%): 36% Clinical status: nil specific, generally healthy	Mediterranean diet	validated semiquantitative FFQ with approximately 150 foods and beverages, interviewer administered, The 10-point (0 to 9) Med Diet Score	Age, education, BMI, physical activity, alcohol, smoking, HTN, diabetes, no APOE ε4 adjusted	Cognition/cognitive decline Cognition test used: MMSE	Decline in MMSE performance inversely associated with adherence to Med Diet. For mild versus no decline, OR high versus low 0.46 [95% CI 0.25, 0.87, $p = 0.012$]. For substantial versus no decline, OR high versus low adherence 0.34 (95% CI 0.13, 0.89, $p = 0.025$). Of the nine MDS components, only vegetable consumption exhibited a significant inverse association with cognitive decline
Galbete et al. 2015 [68] Spain Follow up 2 years Acceptable (+)	N = 823 participants from SUN project Age: mean 62 ± 6 years Male (%): 71% Clinical status: Nil total energy intake outside of predefined values (<800 kcal/d for men,<500 kcal/d for women and >4000 kcal/d for men, >3500 kcal/d for women) and were excluded	Mediterranean Diet	A validated 136-item FFQ. The 10-point (0 to 9) Med Diet Score	Age, gender, APOε4, total energy intake, follow up time between baseline and cognitive evaluation, BMI, smoking status, physical activity, diabetes, HTN, hypercholesterolemia, history of CVD, and years of university education	Cognition/cognitive decline Cognition test used: Telephone Interview of Cognitive Status-modified (TICS-m, range 0 to 54 points), not validated in Spanish population	Greater cognitive decline observed among participants with low or moderate adherence to the Med Diet versus those with better adherence (adjusted difference = –0.56 points in TICS-m, 95% CI = –0.99, –0.13).

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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Kesse-Guyot et al. 2013 [70] France Follow up 2 years Acceptable (+)	$n = 3083$ from Supplementation with Vitamins and Mineral Antioxidants (SUVIMAX) study Age: mean 52 ± 4.6 years Male (%): 53.7 Clinical status: not specified, community dwelling individuals	Mediterranean diet	24-h dietary records The 10-point (0 to 9) Med Diet Score	Age, sex, education, follow-up time, supplementation group during the trial phase, number of 24-h dietary records, energy intake, BMI, occupational status, tobacco use status, physical activity, memory difficulties at baseline, depressive symptoms, diabetes, HTN, cardiovascular disease.	Cognition Cognitive test used: Neuropsychological evaluation by trained neuropsychologists at baseline. Battery included RI-48, verbal (semantic and phonetic) fluency tasks, forward and backward digit span, Delis-Kaplan trail-making test.	A lower phonemic fluency score with decreasing MSDPS ($p = 0.048$) and a lower backward digit span score with decreasing MDS ($p = 0.03$). A low MDS related to a lower composite cognitive score in subsample of manual workers ($n = 178$, p-interaction = 0.04) hypothesized to have low cognitive reserve. Med Diet adherence did not interact with educational level in relation to cognitive function.
Vercambre et al. 2012 [72] USA Follow up 5 years Acceptable (+)	N = 2504 from Women's Antioxidant Cardiovascular Study (WACS) Age: mean 72.5 years Male (%): 0 Clinical status: vascular disease or >3 coronary risk factors	Mediterranean diet	The 116 item semi-quantitative FFQ, The 10-point (0 to 9) Med Diet Score	Age at initial cognitive assessment, educational attainment, energy intake, WACS randomization assignments, depression, numerous lifestyle and health variables and incident vascular events during follow-up	Cognitive decline Cognitive test used: TICS, the East Boston Memory Test category fluency- animal test	Consuming a Mediterranean style diet was not related to cognitive decline. No effect modification was detected by age, education, depression, cardiovascular disease severity at WACS baseline, or level of cognition at initial assessment. The mean multivariable-adjusted difference 95%CI in rates of change in the global composite score was 0.01 (–0.01, 0.02) between the second tertile and the first tertile of Mediterranean diet score, and 0.00 (–0.02, 0.01) between the top tertile and the first tertile ($p = 0.88$).

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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Cherbuin et al. 2012 [73] Australia Follow up 4 years High Quality (++)	N = 1528 from PATH Through Life study Age: 60–64 years baseline Male (%): 48.2 Clinical status: no cognitive impairment in first wave	Mediterranean diet	Commonwealth Scientific and Industrial Research Organisation 215 item FFQ The 10-point (0 to 9) Med Diet Score	Age, sex, education, APOE ε4, genotype, body mass index, physical activity, stroke, diabetes, HTN, and total caloric intake	Cognitive decline/Incidence of MCI or dementia Test used: Clinical Dementia Rating 0.5 global cognition was computed (average z-scores for immediate and delayed recall, digits backward, spot-the-word, symbol-digit modalities test, simple and complex reaction time) DSM-IV criteria were used to assess dementia and delirium.	No protective effect of Adherence to Mediterranean diet against cognitive decline. Excessive caloric intake, and high intake of monounsaturated fats are predictive of MCI ($p < 0.01$).
Samieri et al. 2013 [74] US Follow up 13 years High Quality (++)	N = 16,058, from Nurses' Health Study (1976) Age: 74.3 ± 2.3 Male (%): 0 Clinical status: free of stroke	Mediterranean Diet	The 61 item Semi-quantitative FFQ The 10-point (0 to 9) Med Diet Score	Age and education, long-term energy intake and physical activity, BMI, smoking, history of depression, multivitamin use, and vascular risk factors (history of diabetes, HTN, hypercholesterolemia, and myocardial infarction)	Cognition/ Cognitive decline Test used: TICS, immediate and delayed recalls of the East Boston Memory test (EBMT), delayed recall of the TICS 10-word list, category fluency and digit span-backward.	The Med diet not associated with decline in global cognition or verbal memory. In a secondary approach examining cognitive status in older age, each higher quintile of long-term Med Diet score was linearly associated with better multivariable-adjusted mean cognitive scores (differences in mean Z-scores between extreme quintiles of Med Diet = 0.06 (95% CI: 0.01–, 0.11); = 0.05 (95% CI: 0.01, 0.08); and = 0.06 (95% CI: 0.03, 0.10) standard units; $p = 0.004$, 0.002, and <0.001 for TICS, global cognition, and verbal memory, respectively).

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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Olsson et al. 2015 [75] Sweden Follow up 12 years Acceptable (+)	N = 1,038 from Uppsala longitudinal study of adult men Age: mean 71 years Male (%): 100% Clinical status: excluded those with substantial weight loss (10%) between 60–70 years, excluding extremes with a reported energy intake <800 or >4200kcal per day was applied. subgroup of 564 classified using Goldberg's cut-off	Mediterranean like Diet, low CHO high protein diet (LCHP), WHO recommendation diet (Healthy Diet Indicator)	Seven-day food record validated; 0–9 Med Diet scoring system; 1–10 LCHP scoring system; –1 to 8 HDI scoring	Blood pressure, CRP, BGL, HDL, LDL, triglycerides, weight, height, BMI, APOE ε4 genotype, smoking status, educational level, health status, and physical activity, energy intake	Cognition/ Incidence of MCI or dementia Test used: MMSE AD defined according (NINCDS-ADRDA and DSM-IV criteria.	No association found between Healthy Diet Indicator and any outcomes. HR associated with 1 SD increment in the LCHP score were 1.16 (95% CI: 0.95,1.43) for AD and 1.16 (95%CI: 0.99,1.37) for all-type dementia. Modified MDS was not associated with dementia diagnosis. OR/1 SD increase for modified MDS and all-type cognitive impairment was 0.82 (95% CI: 0.65, 1.05). Subgroup classified by Goldberg method OR for modified MDS and all-type cognitive impairment was 0.32 (95% CI: 0.11, 0.89).
Haring et al., 2016 [76] US Follow up 9.11 years High Quality (++)	N = 6425 from Women's health initiative (WHI) Memory study Age: 65–79 years Male (%): 0% Clinical status: Post-menopausal women cognitively intact at baseline excessive or low energy intake	Dietary patterns characterized by alternate Mediterranean diet (aMED), HEI-2010 and AHEI 2010) and DASH	122 item WHI food frequency questionnaire. Dietary patterns 0–9 aMED score; 0–110 aHEI-2010 score; 8–40 DASH score	Age, race, education, family income, BMI, smoking, HTN, physical activity, diabetes, depression, history of cardiovascular disease, hormone replacement, modified MMSE score, total energy intake. APOE ε4 adjustment in a sub-sample of 5,180 white women.	Cognitive decline/Incidence of MCI or PD Cognition test used: 3MS Diagnosis of MCI/PD made following "four phase protocols as outlined by WHIMS trial and WHIMS extension study" in person or validated telephone cognitive assessment. Physician classify MCI/PD according to DSM– IV criteria.	No relationship across dietary patterns and MCI/PD was found ($p = 0.30$, 0.45, 0.44 and 0.23). In Subset of white women with APOE ε4 adjusted and found higher adherence to Med diet and AHEI-2010 was associated with lower risk of MCI incidence ($p = 0.03$).

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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Buhushan et al. 2017 [77] USA Follow up 4 years Acceptable (+)	N = 27,842 male health professionals From the Health Professionals' Follow-up Study Age: 40–75 years at baseline, mean age 51 years Male (%): 100% Clinical status: no self-reported Parkinson's disease excluding individuals with energy intake of <800 or >4200 kcal/day	Mediterranean diet	self-administered mailed FFQ 131 items 0–9 Med Diet scoring system	Age, smoking history, diabetes, HTN, depression, and hypercholesterolemia. BMI, physical activity. Total energy intake not adjusted	Cognition/cognitive decline Cognition test used: Subjective Cognitive Function (SCF) scores are based on 6 yes/ no questions	Compared with men having a MD score in the lowest quintile, those in the highest quintile had a 36% lower odds of a poor SCF score (OR 0.64, 95% CI 0.55, 0.75; $p < 0.001$) and a 24% lower odds of a moderate SCF score (OR 0.76, 95% CI 0.70, 0.83; $p < 0.001$). Both remote and more recent diet contributed to this relationship. Long-term adherence to the Mediterranean diet pattern was strongly related to lower subjective cognitive function decline.
Gu et al., 2010 [78] USA Follow up 4 years Acceptable (+)	N = 1219 northern Manhattan residents, from Washington/Hamilton Heights-Inwood Columbia Aging Project II: WHICAP II Age: mean 76.7 ± 6.4 Male: 33.4% Clinical status: without dementia	Mediterranean diet	61-item version of Willett's semi-quantitative FFQ 0–9 Med Diet scoring system	Age, education, caloric intake, BMI, gender, smoking status at baseline, ethnic groups (non-Hispanic Black, Hispanic, non-Hispanic White or Other). APOE ε4 status	Cognition/Incidence of AD Cognition test used: the Selective Reminding Test; the Benton Visual Retention Test; the WAIS-R similarities subtest; the Dementia Rating Scale; the Rosen drawing test; the Boston Naming Test; the Boston Diagnostic Aphasia Examination; the phonemic fluency and category fluency test; AD criteria for the DSM-III-R and the NINCDS-ADRDA	Better adherence to MD tended to be associated with significantly lower risk for AD After adjustment for age, gender, race, and education, compared to subjects in the lowest tertile of MD score, HR (95% CI) for subjects in the highest tertile was 0.66 (0.41, 1.04) after multivariable adjustment, $p = 0.04$. Additional adjusting for other factors (including APOE ε4, comorbidity, smoking status, caloric intake, and BMI), the results were essentially the same: the HR (95% CI) comparing subjects in the highest tertile to the lowest was 0.66 (0.41, 1.06), $p = 0.06$.

(*continued*)

Table 3
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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Koyama et al., 2015 [79] US Follow up 7.9 years Acceptable (+)	N = 2,326, from the Health, Aging, and Body Composition (Health ABC) study Male (%): 48.7% Age 70–79 years Clinical status: Exclude non-AD dementia, schizophrenia, bipolar disorder, significant current depression, Parkinson's disease, cancer (other than basal cell skin carcinoma) within the last 2 years, symptomatic stroke, insulin-dependent diabetes, uncontrolled diabetes mellitus or current regular alcohol use exceeding two standard drinks per day women or four per day men	Mediterranean diet (from Mediterranean Diet score)	modified 108-item Block FFQ. interviewed by trained examiners. 0–55 Med Diet score;	APOE ε4 status, BMI, current smoking, physical activity, depression, and diabetes, age, sex, education, total energy intake	Cognition/cognitive decline Cognition test used: Repeated 3MS score, validated interviewer-administered instrument measuring several cognitive domains including orientation, registration, attention, recall, and visuospatial ability.	Among blacks, participants with high Med Diet scores had a significantly lower mean rate of decline on the 3MS compared with participants with lower Med Diet scores (middle and bottom tertiles). The mean difference in points per year was 0.22 (95% CI: 0.05, 0.39; $p = 0.01$) after adjustment. No association between Med Diet scores and change in 3MS score was seen among white participants ($p = 0.14$).
Morris et al., 2015 [80] USA Follow up 4.5 years High Quality (++)	N = 923 participants From retirement communities and senior public housing, the Rush Memory and Aging Project Age: 58–98 mean age 81 Male (%): 25% Clinical status: free of dementia	MIND diet DASH diet Mediterranean diet	144-item validated SFFQ. 0–15 MIND diet scoring system, 0–10 DASH dit scoring system, and 0–55 Med Diet scoring system	Age, education, APOE ε4 genotyping, physical activity, BMI, depressive symptoms, HTN history, Myocardial Infarction history, diabetes history, medication, stroke, total energy intake	Cognition/cognitive decline Cognition test used: 19 neuropsychological tests included measures of orientation, attention, memory, language and visual perception. AD diagnosis- criteria of the joint working group of the National Institute of Neurological and Communicative Disorders and stroke and AD and related disorders association.	In basic adjusted + cardiovascular condition model: Compared to 1st tertile, higher tertiles had lower rates of AD. For MIND diet: 2nd tertile (HR = 0.64, 95% CI 0.42, 0.97) and 3rd tertiles (HR = 0.48, 95% CI 0.29, 0.79) For DASH 3rd tertile (HR = 0.60, 95% CI 0.37, 0.96) For Mediterranean diet 3rd tertile (HR = 0.49, 95 % CI 0.29, 0.85) were associated with lower AD rates.

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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Scarmeas et al., 2009 [81] USA Follow up 4.5 ± 2.7 years High Quality (++)	N = 2364 from the Washington Heights-Inwood Columbia Aging Project (WHICAP) Age: mean 76.9 years Male (%): 32 Clinical status: Non-demented, community dwellers	Mediterranean diet	61-item version of Willett's semi-quantitative FFQ, 0–9 Med Diet scoring system	Cohort, age, sex, ethnicity, education, APOE ε4 genotype, caloric intake, BMI, and duration between baseline dietary assessment and baseline diagnosis	MCI /AD incidence Cognitive test used: The neuropsychological battery: tests of memory (short and long-term verbal and nonverbal); orientation; abstract reasoning (verbal and non-verbal); language (naming, verbal fluency, comprehension and repetition); and construction (copying and matching). Clinical Dementia Rating (CDR) assigned. AD diagnosis by consensus clinical judgment, criteria of the NINCDS-ADRDA and DSM-III-R	Compared with subjects in the lowest Med Diet adherence tertile, subjects in the middle tertile had 17% less risk (HR = 0.83; 95% CI 0.62, 1.12; $p = 0.24$) of developing MCI and those in the highest tertile had 28% less risk (HR = 0.72; 95% CI 0.52, 1.00; $p = 0.05$) of developing MCI (HR = 0.85; 95% CI 0.72–1.00; $p = 0.05$). Assessment of the conversion from MCI to AD, showed compared with subjects in the lowest Med Diet adherence tertile, the middle tertile had 45% less risk (HR = 0.55; 95% CI 0.34, 0.90; $p = 0.01$) of developing AD and those in the highest tertile had 48% less risk (HR = 0.52; 95% CI 0.30, 0.91; $p = 0.02$) of developing AD (HR = 0.71; 95% CI 0.53, 0.95; $p = 0.02$).
Scarmeas et al., 2006 [82] USA Follow up 4 ± 3.0 years High Quality (++)	N = 2258 from the Washington Heights-Inwood Columbia Aging Project (WHICAP) Age: mean 77.2 ± 6.6 years Male (%): 32 Clinical status: community-based, non-demented	Mediterranean diet	61-item version of Willett's semi-quantitative FFQ, 0–9 Med Diet scoring system	Cohort, age, sex, ethnicity, education, APOE ε4 genotype, caloric intake, smoking, medical comorbidity index, and BMI	Cognition/ Incidence of AD Cognitive test used: Cognitive battery administered covering memory, orientation, abstract reasoning, language and construction. AD diagnoses were made by consensus clinical judgment, criteria of the NINCDS-ADRDA and DSM-III-R	Higher adherence to the Med Diet was associated with lower risk for AD (HR, 0.91; 95% CI, 0.83, 0.98; $p = 0.015$). Compared with subjects in the lowest Med Diet tertile, subjects in the middle Med Diet tertile had a HR of 0.85 (95% CI, 0.63, 1.16) and those at the highest tertile had a HR of 0.60 (95% CI, 0.42, 0.87) for AD ($p = 0.007$).

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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Tangney et al., 2011 [83] USA Follow up 7.6 years Acceptable (+)	N = 3790 from Chicago Health and Aging Project Age: mean 75.4 ± 6.2 year Male (%): 38.3 Clinical status: Nil. 60.2% of the sample was black	Mediterranean type diet or Healthy Eating Index 2005 (HEI-2005)	Modified Harvard 139 question food frequency questionnaire. 0–55 Med Diet score; The HEI-2005 is a 12-component measure of dietary quality range 0–100 scores	Age, sex, race, education, participation in cognitive activities and total energy intake (kcal; for Med Diet and Med Diet wine scores), and the interaction between time and each variable, estimate the influence of adherence to Med Diet wine score on rates of within-person change in cognitive score over time also included total alcohol intake.	Cognition/Cognitive decline Cognitive test used: East Boston tests of immediate and delayed recall, the MMSE, and the Symbol Digit Modalities Test.	Higher Med Diet scores and Med Diet wine scores associated with reduced declines in cognitive function ($p = 0.0004$, and $p = 0.0009$, respectively). No associations observed for HEI-2005 scores.
Tsivgoulis et al., 2013 [84] USA Follow up 4.0 ± 1.5 years High Quality (++)	N = 17,478 from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort Age: 64.4 ± 9.1 (range 45–98) Male (%): 43 Clinical status: No history of stroke, non-impaired cognition at baseline	Mediterranean diet	Self-administered Block 98 FFQ and two 24-hour recalls 0–9 Med Diet scoring system	Age, race, sex, region of residence, BMI, waist circumference, household income, education, smoking status, alcohol use, physical activity level, history of heart disease, diabetes mellitus, atrial fibrillation, systolic blood pressure, diastolic blood pressure, high cholesterol, antihypertensive regimen, perceived general health status, and depressive symptoms.	Cognition/ Incident Cognitive Impairment (ICI) Cognitive test used: Six-item Screener (SIS)	Higher adherence to Med Diet was associated with lower likelihood of(ICI)(OR 0.87; 95% CI 0.76, 1.00). There was no interaction between race ($p = 0.2928$) and association of adherence to Med Diet with cognitive status. Interaction effect of diabetes found ($p = 0.0134$) on the relationship between adherence to Med Diet with ICI; high adherence to Med Diet was associated with a lower likelihood of ICI in nondiabetic participants (OR 0.81; 95%CI 0.70, 0.94; $p = 0.0066$) but not in diabetic individuals (OR 1.27; 95% CI 0.95, 1.71; $p = 0.1063$).

(*continued*)

Table 3
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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Hayden et al. 2017 [85] USA Follow up 9.7 years Acceptable (+)	N = 7085 women From Women's Health Initiative Memory Study (WHIMS) Age: (65–79 years), mean age 71 Male (%): 0% Clinical status: Without MCI	Inflammatory diet, by Dietary Inflammatory Index (DII) scores	WHI FFQ based on block FFQ, 32 food parameters Dietary pattern analyzed using DII method to generate weighted scores for inflammatory effect	Age, education, total energy intake, BMI, physical activity, history of non-steroidal anti-inflammatory drug APOE ε4, race, baseline self-reported diabetes, high cholesterol, HTN and smoking	Cognitive decline/Incidence of MCI and PD Cognition test used: MMSE, the Consortium to Establish a Registry for Alzheimer's Disease battery, Trail making test part A and B, Structured psychiatric interview (PRIME-MD), cognitive and behavioral changes interview, Modified TICS, East Boston Memory Test, Digit Span and Verbal Fluency -Animals, Dementia Questionnaire	High Dietary Inflammatory scores associated with greater cognitive decline and earlier onset of MCI. Adjusted hazard ratios comparing lower (anti-inflammatory; group 1 referent) to higher dietary Inflammatory scores were group 2-HR: 1.01 (0.86, 1.20); group 3-HR:0.99 (0.82, 1.18); group 4- HR:1.27 (1.06, 1.52)
Wengreen et al. 2009 [88] USA Follow up 11 years High Quality (++)	*n* = 3634 from the Cache County Study on Memory and Aging (CCMS) study Age: >65 mean 74.6 years Male (%): 42.7 Clinical status: non-demented	Overall diet quality and variety from recommended food score (RFS) according to dietary guidelines for Americans	142-item modified version of the FFQ used in the Nurses' Health Study	Education, age at baseline, gender, APOE ε4 genotype, physical activity, use of multivitamin/mineral supplements, total energy intake, activity of daily living, BMI, history of usual alcohol intake, smoking, and history of diabetes, stroke, and heart attack at the baseline interview	Cognitive function and cognitive decline Cognitive test used: The 100-point 3MS for dementia screening and cognitive function	After 11 y of follow-up, those with the highest RFS declined by 3.4 points over 11 y compared with the 5.2-point decline experienced by those with the lowest RFS ($p = 0.0013$).

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Table 3
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Author, year, Location, Length of follow-up, Quality of Study	Participants and setting	Type of diet studied	Dietary intake assessment	Confounders accounted for	Outcome/Measurement of outcome	Key Findings
Smyth et al. 2015 [89] Canada Follow up 56 months Acceptable (+)	N = 27860 From the ONTARGET (Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial) and TRANSCEND (Telmisartan Randomised Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease) Age: mean 66.2 ± 7.1 Male: 70.8% Clinical Status: with a history of one or more of coronary, cerebral, or peripheral artery disease, or high-risk diabetes. Exclude acute coronary syndrome, acute stroke, congestive heart failure, or important renal insufficiency	Diet quality measured using the modified AHEI	20- item FFQ. The mAHEI was developed to measure overall diet quality according to dietary guidelines	Age, BMI, blood pressure, baseline MMSE score, sex, trial enrolment, treatment allocation, geographical region, education, smoking, physical activity, medical history including stroke/TIA, hypertension, diabetes mellitus, and myocardial infarction], and medication use -statin, β-blocker, antithrombotic.	Cognition/cognitive decline Cognition test used: MMSE Cognitive decline defined as 3 or more points decrease in MMSE any anytime during follow-up.	During 56 months of follow-up, 4,699 cases of cognitive decline occurred. Lower risk of cognitive decline among those in the healthiest dietary quintile of modified Alternative Healthy Eating Index compared with lowest quintile (HR 0.76, 95% CI 0.66, 0.86, Q5 versus Q1). ($p < 0.01$). Lower risk of cognitive decline was consistent regardless of baseline cognitive level.

3MS, Modified Mini mental State Examination; AD, Alzheimer's disease; AHEI, Alternate Healthy Eating Index; APOE, Apolipoprotein E; BMI, body mass index; CHO, carbohydrate; CVD, cardiovascular disease; CI, confidence interval; CRP, C-reactive protein; DASH, Dietary Approach to Stop Hypertension; DSM, the Diagnostic and Statistical Manual of Mental Disorders; DSM-III-R, the Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-III-R); FFQ, Food frequency questionnaire; GI, glycemic index; HEI, Healthy Eating Index; HDI, Healthy Diet Indicator; HTN, hypertension; HR, hazard ratio; MMSE, Mini-Mental Status Examination; Med Diet, Mediterranean diet; MCI, mild cognitive impairment; MIND, the Mediterranean-DASH diet Intervention for Neurodegenerative Delay; MDS, Mediterranean Diet Score; MSDPS, Mediterranean-Style Dietary Pattern Score; NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association; OR, odds ratio; PCA, principal component analysis; PD, probable dementia; RFS, Recommended Food Score; SD, standard deviation; SFFQ, semi-quantitative food frequency questionnaire; SMMSE, Standardized Mini-Mental State Examination; TIA, transient ischemic attack; TICS, Telephone Interview for Cognitive Status.

Overall eight articles published results of more than one dietary pattern from the same cohort, and these are discussed separately under the appropriate dietary patterns.

Exposure and outcome assessment

Nutritional assessment tools to determine dietary pattern exposure varied. The most commonly used were the semi-quantitative Food Frequency Questionnaire (FFQ), or a food record or 24-h recall, either self-administered or researcher-administered, for both RCTs and cohort studies.

Most studies focused on cognitive change and used the Mini-Mental State Examination (MMSE) score or a neuropsychological test battery. Tests generally covered a broad range of cognitive skills including language, memory (short-term and working), visual perception, executive function, cognitive flexibility, global cognitive function, and cognitive processing. In detail, memory tests included recognition, immediate recall, delayed recall, face-name recall, paired associates, and semantic memory. Executive function tests included working memory, verbal fluency, reasoning, attention, and processing speed. Composite measures of episodic memory (e.g., immediate and delayed recall) were also included. Global cognition was measured using composite measures of cognitive function. Studies also investigated brain morphology using magnetic resonance imaging, or diagnosis of incident cases of MCI or dementia as assessed by neurologists or neurophysiologists.

Quality assessment

Except for one study with unclear risk of bias, all other RCTs received a high risk of bias due to the long-term nature of nutrition interventions and impossibility of complete double blinding. Among longitudinal studies thirteen received "High Quality" with remaining nineteen articles assessed as "Acceptable" (see Table 1 for results from the Cochrane Risk of Bias and table 3 and Supplementary data for the SIGN 50 quality assessment).

Dietary patterns and cognitive health: A priori patterns

Mediterranean diet

RCTs in Mediterranean countries: Two RCTs which investigated the Mediterranean diet in Spain and reported positive outcomes, targeted those at high cardiovascular risk but without cardiovascular disease at baseline [64, 65], from the multicenter randomized prevention trial PREDIMED (PREvención con DIeta MEDiterránea) study. Both studies had high risk of bias due to the difficulty of blinding.

The earlier PREDIMED study [64] reported a positive link between Mediterranean diet supplemented with either extra virgin olive oil (EVOO) 1 L/week or raw mixed nuts (walnuts, hazelnuts, and almonds) 30 g/day and cognition which was assessed by MMSE and Clock Drawing Test (CDT) after 6.5 years, as well as a lower incidence of MCI and dementia compared to a control diet. In the more recent clinical trial conducted in a subcohort from PREDIMED, two intervention groups followed the Mediterranean diet supplemented with either EVOO (1 L/week) or mixed nuts (30 g/d) [65]. They were compared to a control group of those receiving dietary advice on a reduced fat diet. After a median follow up of 4.1 years, participants allocated to a Mediterranean diet plus EVOO scored significantly better than controls on the Rey Auditory Verbal Learning Test (RAVLT) and Colour Trail Test part2. The Mediterranean diet plus nuts group had significantly improved memory composite, while Mediterranean diet plus EVOO group had significantly better performance of the frontal and global cognition composites than control group.

Cohort studies in Mediterranean countries: Four cohort studies evaluated the Mediterranean diet and were conducted in the Mediterranean area (France $n = 2$, Spain $n = 1$, and Greece $n = 1$). All had acceptable study quality, and all supported a positive link between Mediterranean diet and better cognitive health in older adults.

Among those, three studies used MMSE or Telephone Interview of Cognitive Status (TICS) to measure cognition. The Three-City study reported that a higher Mediterranean diet score was associated with better MMSE performance but not with other cognitive tests on verbal/visual function or with incidence of dementia [66]. Similarly, The European Prospective Investigation into Cancer and Nutrition (EPIC) [67] reported an inverse association between adherence to the Mediterranean Diet and decline in MMSE scores. The Spanish SUN (Seguimiento Universidad de Navarra) cohort study [68] reported greater cognitive decline (as assessed by the TICS) in participants with low or moderate adherence to the

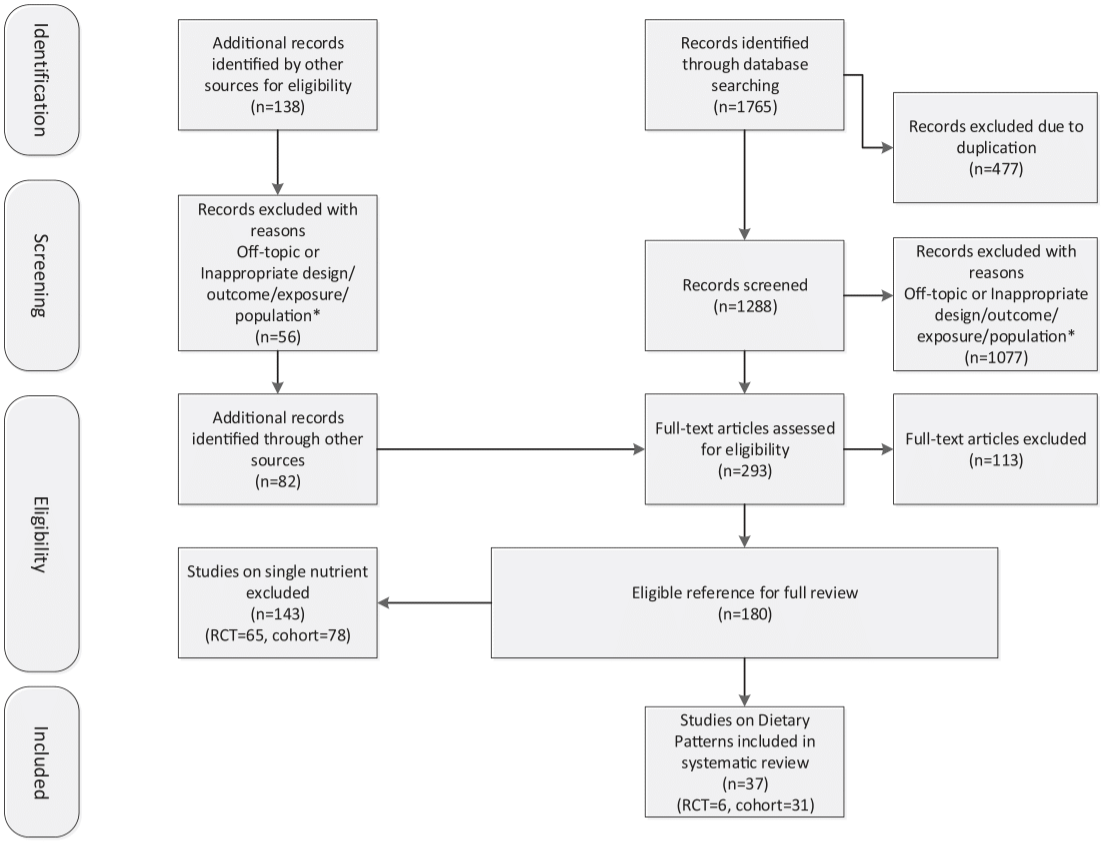

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

Mediterranean Diet compared to those with higher adherence.

In the SU.VI.MAX (Supplementation with Vitamins and Mineral Antioxidants) study, lower backward digit span and lower phonemic fluency scores were associated with poorer adherence to Mediterranean diet over 13 years [70], no effect was observed on composite cognition score.

RCTs in non-Mediterranean Western countries: The only RCT completed in a non-Mediterranean area was the Australian Medley study [71], which reported no evidence that Mediterranean diet benefited cognitive function compared to a habitual dietary intake after 6 months.

Cohort studies in non-Mediterranean Western countries: Fourteen cohort studies were undertaken in non-Mediterranean western countries, the majority from the US ($n = 11$). Five studies reported little to no association of adherence to the Mediterranean diet with cognitive decline [72–76]. However, the majority, nine studies [35, 77–84] provided evidence of statistically significant positive associations between the Mediterranean diet and the protection of cognitive health.

Among those studies finding no effect, most received "High Quality" ($n = 3$) while the rest were "acceptable" ($n = 2$). Two studies that measured cognitive function using a cognitive test battery, were the Women's Antioxidant Cardiovascular Study (WACS) [72] which followed 2,504 participants with vascular disease or coronary risk factors for five years, and the US Nurses' Health Study which followed 16,058 stroke free female nurses at baseline for six years [74]. Three of these five studies looked at incidence of MCI or dementia as the primary outcome, including the PATH Through Life study in Australia which followed 1528 community dwelling participants for 4 years [73], the Uppsala longitudinal study that followed older men for 12 years [75], and the US Women's Health Initiative Memory (WHI) study which followed cognitively intact (at baseline) post-menopausal white women aged more than 65 years for 9 years [76]. Most results of the five studies were adjusted for apolipoprotein E (APOE) $\varepsilon 4$

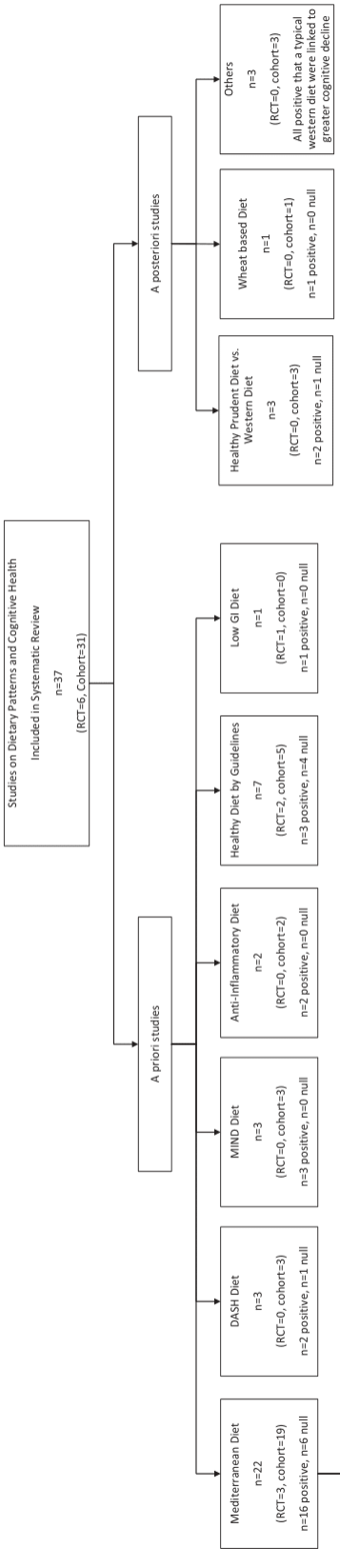

Fig. 2. Dietary patterns and study outcomes.

genotype except for Nurses' Health Study [74] and WACS [72].

By contrast, nine cohort studies, of which five received "acceptable" study quality and four were ranked as "high quality", revealed statistically significant associations that the Mediterranean diet protected against cognitive decline in older adults.

Four of the nine studies assessed cognitive decline using either cognitive tests averaged for composite measure of global cognition [83], or modified MMSE (3MS) [79], a comprehensive neuropsychological battery [35], or a Subjective cognitive function questionnaire [77]. The Chicago Health and Aging Project (CHAP) reported higher Mediterranean diet scores were associated with slower rates of cognitive decline after an average 7.6 years follow up on 3790 participants aged 75.4 years on average at baseline [83], while The Health, Aging and Body Composition study in the US [79] reported varied findings among racial groups and positive effects from the Mediterranean diet was only observed among black but not white participants. By contrast, the Australian Imaging Biomarkers and Lifestyle study of Ageing reported no significant effects in subjects without MCI or AD at baseline, except for APOE $\varepsilon 4$ allele carriers, in whom higher Mediterranean diet scores were associated with less decline in executive functioning after 36 months [35]. The (male) Health Professionals' Follow-up study [77] reported that long-term adherence to the Mediterranean diet was strongly linked to lower subjective ratings of change in cognitive function. A limitation of this study is that cognitive function results had relied on subjective self-reporting of six "yes" or "no" questions, rather than performance-based methods [77].

Among the nine studies, five assessed incidence of MCI or AD as the clinical outcome [78, 80–82, 84]. The US study Washington/Hamilton Heights-Inwood Columbia Aging Project (WHICAP) 1992 and WHICAP 1999 [78, 81, 82] found that higher adherence to the Mediterranean diet was associated with reduced risk for developing MCI or AD. Similar conclusions were drawn from The Reasons for Geographic and Racial Differences in Stroke Study (REGARDS) which followed up 17,478 participants, mean age 64.4 years and cognitively intact with no history of stroke at baseline, for 4 years [84], and reported high adherence to Mediterranean diet was associated with a lower likelihood of incident cognitive impairment in nondiabetic but not diabetic individuals. Moreover, in the Rush Memory and Aging Project (MAP), the highest tertile of Mediterranean diet scores were found to have lower AD rates [80].

Cohort study in Asian countries: Only one longitudinal cohort study conducted in Asia [60] with acceptable study quality found a benefit for a Mediterranean-like diet, modified to suit local eating habits (Table 5). The diet shared similar characteristics with the Mediterranean diet such as high consumption of fruits, vegetables, and grains, as well as low consumption of meat and dairy foods. Qin et al. reported that among the 1,650 community dwelling persons more than 65 years old followed for 5.3 years, those in the highest tertile had a slower rate of cognitive decline than people in the lowest tertile of the adapted Mediterranean diet.

DASH diet

The three studies that examined the effect of adherence to the DASH diet on cognitive health in later life reported mixed results [18, 76, 80]. The majority of the studies received a "high quality" rating ($n = 2$).

Two studies reported positive effects from the DASH diet [18, 80]. The Rush Memory and Aging Project followed-up 923 elderly men and women mean aged 81.4 years old, and reported modest but positive links between the highest tertile of DASH diet adherence and lower rates of AD [80]. The Nurse's Health Study computed a long-term DASH score from five previous dietary assessments and reported greater adherence was associated with better composite scores of global cognition and verbal memory irrespective of APOE $\varepsilon 4$ [16]. However, during the next six years, no association between DASH scores and change in cognition were found [18]. By contrast, the Women's Health Initiative Memory Study (WHIMS) [76] reported that DASH scores were not associated with incidence of MCI or dementia in older women generally or in those with hypertension. Various cut-off scores for highest quintiles were selected including 28 [76] and 31 [18], respectively, for the 8–40 DASH scoring system [37] and 5 [80] was used for 0–10 DASH scoring system [57].

MIND diet

Three cohort studies, all with high study quality, found protective effects of the MIND diet on cognition.

The Rush Memory and Aging Project reported that moderate adherence to the MIND diet was associated

with lower rates of AD [80], slower decline in a global cognitive score and five cognitive domains (episodic memory, semantic memory, perceptual organization, perceptual speed, working memory) [58]. The difference between highest and lowest quintiles in MIND scores was calculated to be equivalent to being 7.5 years younger in cognitive health [58, 80]. In addition, the US Nurse's Health Study [19], where 16,058 older women aged 70 and over were followed up for 6 years with multiple assessments of dietary intake and cognition, reported long-term adherence to the MIND diet was moderately associated with better verbal memory in later life, but not with global cognition, verbal memory or TICS. All studies adjusted for multiple covariates including APOE $\varepsilon 4$ and used the same 0–15 MIND scoring system [58], but had different MIND score cut-offs for highest quintiles [58, 80].

Anti-inflammatory / inflammatory diet

Two studies that investigated dietary patterns associated with inflammation, characterized by high consumption of foods such as red and processed meats, sweets, deserts, chips, and refined grains [31, 32], found significant impacts on cognitive function; however, divergence in results were reported for different age groups [23, 85]. Among the two studies, one was of high quality while the other received an "acceptable" quality assessment rating.

The Whitehall II cohort study [23] followed 5,083 participants whose median age was 56 years for 10 years. They reported higher intake of an inflammatory dietary pattern was associated with accelerated cognitive decline. The greatest decline in global cognition and reasoning was found in the highest tertile of inflammatory diet when compared to the lowest tertile. In an age-stratified analysis, higher inflammatory scores were linked to significantly faster cognitive decline in reasoning in the age <56 group, while no significant association was found among those aged 56 and older.

The WHIMS researched the inflammatory pattern [85] by following up 7,085 women aged at 65–79 years for 9.7 years with annual cognitive function assessments. They found that higher dietary pro-inflammatory scores were associated with greater cognitive decline and earlier onset of MCI, after adjustment for multiple covariates. This study suggested the existence of a possible threshold effect.

Healthy diet recommended by dietary guidelines

Two RCTs [86, 87] (both with high risk of bias) and five cohort studies (high quality $n = 2$ and acceptable quality $n = 3$) investigated diets complying with the dietary guidelines of national peak bodies or the World Health Organization's Healthy Diet Indicator tool. Mixed results were reported and three studies [86, 88, 89] found associations with cognitive benefits.

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER), a randomized 2-year multi-domain lifestyle intervention trial [86, 90], assessed cognitive decline in 1,260 participants aged 60–77 years at baseline. This study reported cognitive benefits in groups which received dietary intervention together with exercise, cognitive training, and monitoring of vascular risk. In FINGER, dietary counselling was based on the Finish Nutrition Recommendations and a composite dietary intervention adherence score was generated based on the consumption of fruit, vegetables, fish, whole grain cereals, low fat milk, and meat products, as well as the limiting of sucrose intake and using vegetable margarine and rapeseed oil instead of butter [90] (see Table 2 for details).

A Hong Kong RCT [87] included 419 participants with mean age of 83 years living in old age hostels, and provided nutrition intervention including counselling and menu change, with a mean follow up time of 25 months. They reported that although nutrition interventions were effective in maintaining fruit and fish intake compared to control group, this did not result in a significant reduction in cognitive decline.

Four studies researched the effect of adherence to the dietary guidelines for Americans, using either the Recommended Food Score (RFS) [88], modified Alternative Healthy Eating Index (mAHEI) [89], HEI (Healthy Eating Index) -2005 [83], or HEI-2010 [76, 89]. The Cache County Study on Memory and Aging in US [88] evaluated effects on cognition of adherence to the RFS, which was developed to assess diet quality and food variety related to the dietary guidelines for Americans [91]. After 11 years follow up, those in the highest RFS quartile declined by 3.4 points compared with the 5.2 point decline in those in the lowest RFS quartile [88]. With regards to the mAHEI, lower risk of cognitive decline was found among those in the healthiest dietary quintile, compared with lowest quintile, regardless of baseline cognitive level [89].

No association with cognition change was observed in the CHAP study using HEI-2005 scores [83]. Similarly, the WHIMS reported no significant relationship between adherence to HEI-2010 or Alternate HEI-2010, with incidence of MCI or probable dementia in older women [76].

One of the five studies, the Uppsala longitudinal study, examined the HDI by following 1038 older men over 12 years and found no association between HDI and any of the cognition outcomes [75].

Low GI diet

Only one RCT (unclear risk of bias) examined the effect of GI on cognition by comparing healthy older adults or those with amnestic MCI allocated to high saturated fat, high GI or low saturated fat, low GI diets [92]. Both cognitive healthy and amnestic MCI participants had better scores on delayed visual recall with the low saturated fat, low GI combined diet, although not in immediate memory, executive and motor speed domains. However, a major limitation of this study is the small sample size ($n = 49$) and short intervention time (4 weeks) and the combination of effect from saturated fat and GI.

Dietary patterns and cognitive health: A posterori patterns

Prudent healthy diet versus Western diet

Findings from three cohort studies (high quality $n = 2$ and acceptable quality $n = 1$) of the *Prudent healthy diet* (see Table 3) reported mixed findings [35, 36, 59].

Two studies used factor analysis (principle components) to extract dietary patterns [35, 36]. The Australian Imaging, Biomarkers and Lifestyle (AIBL) Study of Ageing [35] reported no significant relationships between adherence to a computer generated *Prudent healthy diet* and cognition, measured by a comprehensive battery of neuropsychological tests either for global or single domain scores (see Table 3 for details) [93]. By contrast, The Swedish National study on Aging and Care-Kungsholmen (SNAC-K) [36] found that the highest adherence to their *Prudent healthy diet* was related to less MMSE decline, and highest adherence to a Western dietary pattern was associated with greater MMSE decline. The decline associated with the Western diet was attenuated when accompanied by higher adherence to *Prudent healthy diet* [36, 93]. However, as these diet patterns were computer generated and based on the subjects consumption patterns, the definition of the *Prudent healthy diets* differed between studies with AIBL emphasizing nuts, tomatoes, potatoes and garlic as single food groups whereas SNAC-K study defined a *Prudent healthy diet* by the inclusion of cereals legumes, rice/pasta, water and cooking/dressing oil [35, 36].

In addition, the first and only human longitudinal study that investigated the impact of diet on changes in magnetic resonance imaging (MRI) over time is the Personality and Total Health Through Life Study, which focused on a subsample of 255 participants aged 60–64 years at baseline with two MRI scans 4 years apart. This study reported that a Western diet, characterized by lower intakes of naturally nutrient-dense foods and higher intakes of unhealthy foods was associated with smaller left hippocampal volume [59].

Wheat-based diverse diet

The China Health and Nutrition Survey, with acceptable study quality, assessed a wheat-based diverse diet, derived by factor analysis. The top tertile was associated with slower annual decline in global cognitive function [60] among adults 65 years and older. The wheat based diverse diet shared some features of the Mediterranean diet, and was characterized by high intakes of wheat buns, deep-fried wheat, nuts, fruits, moderate- to high-fat red meat, poultry and game, egg, fish, dairy, sugar, vinegar, soy sauce, plant oil, and with low intake of animal-source cooking fat.

Others

Three cohort studies [61–63] investigated the impact of other dietary patterns from *a posteriori* statistical approaches, and reported mixed results. Overall dietary patterns that shared features of a typical Western diet were linked to greater cognitive decline consistently across all studies.

Among the prospective cohort studies, Gu et al. reported in 2010 that the dietary pattern which was found to be protective against the development of AD had higher consumption of salad dressing, nuts, fish, tomatoes, poultry, cruciferous vegetables, fruits, dark and green leafy vegetables, with lower intake of high-fat dairy, red meat, organ meat, and butter [61]. Dietary patterns were derived by reduced rank regression, using predetermined food groups as predictor variables and seven potentially AD-related nutrients as response variables (see Table 3 for details).

In the UK Newcastle 85+ cohort study, dietary patterns (DPs) derived by cluster analysis that differed in intake of red meat, potato, gravy, and butter, were studied for their effect on cognition [62]. When compared with DP2 group (low meat intake, high intake of fruits, vegetables, fish, nuts, whole grains and dairy), men in DP1 group (high red meat, gravy and potato dishes, low in butter) scored worse in initial attention and MMSE, and DP3 (high butter intake and low in unsaturated fats, moderate intake of red meat) was associated with a 3.2-fold increased risk of cognitive decline despite APOE ε4 status. Both DP1 and DP3 had overall worse concentration and focused attention.

A prospective cohort study in Taiwan researched three dietary patterns characterized as vegetable, meat based, or traditional. High score "traditional" pattern was found to protect against decline in logical memory-recall I [63]. Mixed results were reported on the other two patterns: the moderate or high score "vegetable" pattern was significantly associated with less decline of logical memory, although high score "vegetable" pattern was linked to greater decline in executive function. A high-score "meat" pattern was related to decline of verbal fluency, but protection against attention decline [63].

DISCUSSION

Of studies included in this review, the Mediterranean diet was the most investigated with evidence supporting protection against cognitive decline among older adults. Research on other diets such as the MIND, DASH, and Anti-inflammatory diets was more limited but showed promising beneficial results, especially for the MIND diet which received a high quality rating for all three studies [94].

Within studies on the Mediterranean diet, there were differences in outcomes between Mediterranean and non-Mediterranean countries. This suggests that the effects of diet on cognition are complex and likely to vary across geographic, cultural, or sociodemographic contexts [95–98]. For example, cultural values and lifestyle in the Mediterranean area, such as social connection and sense of community, meals being traditionally cooked at home using slower cooking methods such as boiling and stewing, enjoyed slowly and mindfully, meal times shared with family and friends rather than rushing through the meals or eating in front of a screen [8], may partly explain the discrepancies observed in studies. The supportive evidence of a modified Mediterranean diet in Asian countries, suggests the possibility of adapting the principles of a Mediterranean diet to suit local foods, culture, and eating habits [60].

Discrepancies of results in western countries may result from cultural and demographic diversity of the populations being studied [95]. For example, the Australian RCT Medley study, while based on a multicultural population, included only 70 of 137 (51%) participants born locally, and the comparison habitual diet may not have been a typical Western diet. Secondly, more highly educated participants (such as in [72, 74, 99]), are more likely to be living a healthier lifestyle and perform better on cognitive tasks. Many studies controlled for education and lifestyle factors but residual confounding and the impact of clustering of health behaviors may remain. Cognitive decline may be harder to detect in these groups requiring sensitive cognition tests and longer follow up [71]. Studies that excluded people with potential underlying health issues, targeting generally healthy participants [74, 79] may be less likely to detect a protective effect from the Mediterranean diet on cognition than those that included participants at risk of cardiovascular disease, as modification of cardiovascular risk factors may alter rates of cognitive decline [76]. In summary, differences in protective outcomes with the Mediterranean diet may result from differences in populations with respect to their culture or education, general health, level of physical activity, and specifically their risk of cardiovascular disease, and baseline cognition.

One potential mechanism by which the Mediterranean diet may protect against cognitive decline is through improving vascular health and preventing cardiovascular diseases due to its richness in poly-/mono- unsaturated fats [100]. A diet rich in poly-/mono-unsaturated fat improves insulin sensitivity, has an anti-diabetic effect [101–103] and lowers cardiovascular disease risk. Anti-diabetic effects of diet may also benefit cognition by maintaining relatively stable brain glucose levels; even small changes in glucose levels can alter metabolic homeostasis, which has been consistently linked to insulin resistance and cognitive impairment in older individuals [33, 104]. In support of the impact of fat quality, the positive association between the Mediterranean diet and cognition disappeared when monounsaturated fat: saturated fat ratio (MUFA:SFA) was excluded from the Mediterranean diet scoring system [105], suggesting that there is an important role of high MUFA:SFA ratio for protection of cognition [68].

The positive link between the Mediterranean diet and cognition protection may be also due to the higher consumption of antioxidants, as brain oxidative stress is associated with neurodegeneration [38]. Antioxidants in Mediterranean diets include phenolic compounds, and anti-inflammatory agents such as omega 3 fatty acids. Importantly urinary polyphenol excretion, a biomarker of adherence to the Mediterranean diet [106], has been associated with better memory, indicating the likelihood that phenolic compounds may benefit cognition in older adults [107]. In addition, EVOO consumption, compared to regular olive oil and other vegetable oils [108, 109], has resulted in significantly lower plasma inflammatory markers and increased anti-oxidant capacity [110, 111]. This is consistent with the PREDIMED study [64, 65] findings that a Mediterranean diet plus EVOO, or nuts, resulted in better cognition performance, indicating that the quality of oil as determined by the level of anti-oxidant and anti-inflammatory agents is important. It remains unclear as to what is an adequate therapeutic amount of EVOO and how long it needs to be taken to protect against cognitive decline, despite a recent trial reporting that 12 months of EVOO (26 g) to replace all vegetable oil (olive oil, high-oleic safflower oil, high-oleic sunflower oil, canola oil and hydrogenated vegetable oils) in Mediterranean diet may benefit-cognition [112].

Likewise, long-term inflammation might damage the blood-brain barrier leading to cognitive impairment, and increase the risk of neurodegenerative diseases [24], as higher levels of circulating inflammatory markers are associated with greater cognitive decline [113, 114]. Anti-inflammatory diets were associated with slower cognitive decline in older adults, however, the effect varied with age [23, 85]. Ozawa et al. reported a significant protective effect only in those under 56 years [23] while Hayden et al. reported protection against cognitive decline for those above 65 years [85]. Contributing factors to the difference may include different research methods such as selection of inflammatory diet scoring system. While one is based on specific food-based loading factors associated with one inflammatory marker [23], the other used the DII (Dietary Inflammatory Index) system, which includes a set of eight pro-inflammatory nutrients, 19 anti-inflammatory nutrients, and "10 whole foods and spices, caffeine, flavones, flavonols, flananones, anthocyanidins and isoflavones" [32, 85]. Selection of cut-points for tertiles may also make a difference as a possible threshold effect was suggested [85].

Similarly, the benefits of MIND and DASH diets could also be related to their richness in mono-/poly-unsaturated fats, anti-oxidant, anti-inflammatory, and anti-diabetic effects. The low GI diet has also been commonly used for its anti-diabetic effects [33]. Additionally, the DASH diet is effective in managing hypertension [17], which may confer greater benefit in older people at higher cardiovascular risk [16]. Interestingly, when comparing low-fat dairy intake, the DASH diet requires "moderate to high consumption, 2-3 serves daily", while the Mediterranean diet requires "low consumption". The role of low-fat dairy with a Mediterranean diet remains uncertain, and differences in dairy intake might contribute to inconsistent results from the Mediterranean diet in western countries when compared to DASH diet, thus further research on the role of low-fat dairy on cognitive health is required [115]. When compared to the Mediterranean diet, the MIND diet emphasizes berry and nut intake, as well as scoring unhealthy food groups, and whilst it has shown consistent protective effects [57, 80], this requires further investigation.

Divergent results from research on *the Prudent healthy diet* may be due to the nature of *a posteriori* studies, as dietary patterns were generated by data reduction methods, based on different populations and different subjects consumption patterns. Other factors may include dietary assessment tools and differences in cut-off and factor loadings selected [35, 36]. In brain imaging studies, longer follow-up time may be needed particularly to separate dietary and aging effects on brain atrophy [59].

Encouragingly, the potential detrimental effects on cognition in older adults from unhealthy foods in a Western diet such as fast food meals, sugary drinks, and fatty snacks may be corrected greatly by adding healthier options such as fruits, vegetables, nuts, and whole grains [36]. This suggests the importance of more healthy dietary patterns with foods naturally rich in nutrients, even when Western diets have been mostly followed previously.

Overall, the dietary patterns that were found to be protective against cognitive decline, are plant-based, rich in poly- and mono-unsaturated fatty acids with reduced consumption of processed foods. As we focused on dietary patterns, a comprehensive review of the effects of single food groups on cognition among older adults is outside the scope of this article. However, several studies of dietary patterns further analyzed their results to determine which components may be key to cognitive protection, and mixed

results have been reported. For example, vegetable consumption, compared to other Mediterranean food components [105], was shown to have a significant inverse association with cognitive decline [67], which is in line with earlier research on vegetables and cognition [116, 117]. On the other hand, moderate alcohol consumption and a high ratio of MUFA:SFA were also found to have a weak association with cognition. Of DASH diet components, vegetables, nuts, and legumes appear to be the key components [18]. Examination of MIND food group components and their impact on outcomes demonstrated that excluding high saturated fat components attenuated the association between the MIND score and verbal memory, perhaps because less saturated fat results in a higher MUFA:SFA [19]. Relationships of other foods with anti-inflammatory effects and cognitive health were also studied [116–121]. A link between fermented food and pickles and protection against logical memory decline is currently under investigation [63]. The effect may be seen as an anti-inflammatory effect [122], or explained by anti-oxidants and possibly probiotics like lactic acid bacteria in pickled foods, highlighting the need for further research on the relationship between probiotics, gastrointestinal health, and cognition [63].

We identified limitations common to many studies. Firstly, long-term medications, e.g., hypolipidemic, anti-hypertensive, anti-diabetic, and anti-cholinergic drugs, were only adjusted for in a few studies [64, 65]. Secondly, most studies only assessed dietary intake at baseline, which introduces performance bias, as dietary intake may change over the years of a trial, due to a change of eating habits secondary to medications, influences from society, friends, and family members and high risk for or diagnoses of medical conditions such as diabetes, hypertension, and cardiovascular disease [72]. In some studies, cognitive function was not assessed at baseline precluding assessment of the impact of the intervention on cognitive change over the years, although inferences may be drawn from looking at differences in cognitive function between groups at follow up [64]. Thirdly, for those with shorter follow up times the findings may reflect reverse causality, as cognitive impairment and AD are preceded by relatively long periods of subclinical cognitive decline which could influence eating patterns [70]. Fourthly, only 20 of the 38 studies adjusted for the APOE ε4 allele which is a major genetic risk factor for more rapid cognitive decline and earlier onset of dementia. Fifthly, it is not possible to adjust for all known risk factors, and future studies should consider including physical activity levels, obesity, diabetes, smoking, and alcohol as covariates. Sixthly, there are no standard cut-offs for diet adherence scores, for example, Mediterranean diet adherence scores. As tertiles were used, cut-off points varied [19, 35, 60, 76–80]. Future research is needed to determine the cut-off points for the level of adherence required to generate an effect [60, 79]. Seventhly, a common limitation among all RCT studies is, the single blinded nature, as due to the nature of nutrition trials using foods, it is not feasible to double blind RCTs for long term studies into nutrition interventions. Finally, there is limited evidence from longitudinal or intervention studies on associations between dietary patterns and neuro imaging outcomes [59]. Continuing research with longer follow up of older people may provide insight and better understanding on the changes in brain morphology, activity and function, in addition to cognitive function tests outcomes.

Future trials and observational studies should investigate the effectiveness of food components as well as the whole diet, take APOE ε4 genotype into consideration as well as multiple covariates, such as gender, age group (from >50 years to >85), medical conditions, gastrointestinal health, and report use of medications or nutrition supplements due to chronic conditions. Validated dietary assessment tools should be employed multiple times throughout long follow ups with analysis on dietary change over the years, and a comprehensive cognitive battery and neuro imaging included for outcome assessment.

Conclusion

This review adds to previous reviews in that it includes for the first time, higher level of evidence from six RCTs and 31 cohorts which were classified into different dietary patterns and investigated the potential effect of different diets on cognitive function among older adults. Overall, the findings support positive relationships between dietary patterns which are plant-based, rich in poly/monounsaturated fatty acids with reduced consumption of processed foods and cognitive health in older adults. More research is required for better understanding of the underlying mechanisms and effectiveness, in order to develop comprehensive and practical nutrition interventions and dietary recommendations to protect against cognitive decline and dementia with aging.

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SUPPLEMENTARY MATERIAL

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Chapter 4: Dietary Patterns and Cognitive Health in Older Adults- Findings from the Sydney Memory and Ageing Study

4.1 Publication details

This chapter contains identical text of the manuscript entitled "Dietary Patterns and Cognitive Health in Older Adults: Findings from the Sydney Memory and Ageing Study", published in the Journal of Nutrition, Health & Aging, 2021, Volume 25, Issue 2, Pages 255-262. doi:10.1007/s12603-020-1536-8

Supplementary material of this manuscript can be found in Appendix B.

4.2 Author contribution statement

I, Xi Chen (the candidate) designed the research protocol, conducted data analysis, drafted the protocol and report, including creating reference list and tables. Dr Zhixin Liu was responsible for technical support on statistical analysis, interpreting results and providing comments on manuscript. Professor Perminder Sachdev was responsible for co-designing the Memory and Ageing Study (MAS) and Dr Nicole Kochan were responsible for project design of neuropsychological tests for MAS, data collection and study coordination, critical revision of manuscript. Dr Fiona O'Leary provided support on dietary pattern score construction, data analysis, interpretation of results, critical revision of manuscript and approval of report. Professor Henry Brodaty was responsible for co-designing the research protocol for MAS, interpreting results, critical revision and final approval of report. All authors reviewed the final manuscript.

4.3 Introduction to chapter

As highlighted in Chapter 3, although existing study results remained inconsistent, dietary patterns that may be beneficial for cognitive health are plant-based, rich in poly- and mono-unsaturated fatty acids with lower consumption of processed foods. As presented in Chapter 4, we examined this hypothesis with cross-sectional analysis, on associations between dietary patterns, key food components and cognitive health among older adults from a well-characterized community-dwelling ageing cohort in Sydney Memory and Ageing study.

4.4 Modification to manuscript: Dietary Patterns and Cognitive Health in Older Adults- Findings from the Sydney Memory and Ageing Study

The reviewers of this thesis have pointed out that, the results section does not clearly state that there were no association found with the 0-9 Mediterranean score. As a result, a clear statement that no significant associations between Mediterranean diet scores by 0-9 scoring system and cognitive outcomes should be added in the results section (page70, first paragraph under 'A-priori diets and cognition'): "No association has been observed between Mediterranean scores constructed using the 0-9 scoring system, and global cognition (β=-0.005; 95% CI: -0.098, 0.088; P = 0.918) or cognitive performance in any domains. Although there was a positive trend observed in the visuospatial domain (β=0.086; 95% CI: 0.008, 0.164; P = 0.030), however this did not reach statistical significance after adjustment for multiple comparison where p value <0.01 was required for significance for individual domains."

Reviewer comments were received regarding the results section does not clearly state whether or not individual components of the DASH diet were associated with cognitive outcomes. In results section, a clear statement that no significant associations of DASH diet components

except for legumes and nuts, with cognitive outcome should be added in the results section (page 71, second paragraph under 'A-priori diets and cognition'): "Individual components of the DASH diet were not associated with cognitive performance, except for the legumes and nuts group. This food group is equivalent to the Mediterranean diet legume and nuts group and was significant as reported above."

As suggested by reviewers, additional discussion should be added on why one Mediterranean score by 0-55 system found associations with cognitive outcomes, but the other Mediterranean score by 0-9 system did not find any significant associations in the discussion section (page 72, second paragraph): "In this study, we have observed significant association of Mediterranean scores constructed by the 0-55 scoring system with visuospatial function, however the Mediterranean scores constructed by the 0-9 scoring system were not linked to performance in any cognitive domains. The difference in results may be due to the heterogeneity of the scoring systems (1). For example, the 0-9 system uses population sex-specific cut-offs around the median, and provides a relative ranking only within a given study population. The 0-55 system uses pre-defined cut-offs based on frequency of consumption of foods relative to recommended amounts from the Mediterranean diet pyramid (2, 3), so is more characteristic of a Mediterranean dietary pattern. Furthermore, differences in grouping food components may also contribute to the discrepancy in findings. 0-9 system used non-specific intake of "cereal" and "dairy intake", whilst the 0–55 scoring system redefined the component characteristics as "non-refined cereal" and "full fat dairy". Poultry and potatoes were list as two individual food groups in 0-55 system, while in 0-9 system poultry consumption was counted within the meat group and potato was counted within cereal group; and legumes and nuts were combined as one component in 0-55, when compared to 0-9 scoring system where legumes were an individual component and nuts were included with fruit (4)".

With references to:

1. Limongi F, Siviero P, Bozanic A, Noale M, Veronese N, Maggi S. The Effect of Adherence to the Mediterranean Diet on Late-Life Cognitive Disorders: A Systematic Review. Journal of the American Medical Directors Association. 2020;21(10):1402-9.

2. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med. 2003;348(26):2599-608.

3. Panagiotakos DB, Pitsavos C, Arvaniti F, Stefanadis C. Adherence to the Mediterranean food pattern predicts the prevalence of hypertension, hypercholesterolemia, diabetes and obesity, among healthy adults; the accuracy of the MedDietScore. Prev Med. 2007;44(4):335-40.

4. Chen X, Liu Z, Sachdev PS, Kochan NA, O'Leary F, Brodaty H. Dietary Patterns and Cognitive Health in Older Adults: Findings from the Sydney Memory and Ageing Study. The journal of nutrition, health & aging. 2021;25(2):255-62.

In additional, reviewer has kindly pointed out missing spaces in Table 5, column of 'DP by PCA', where spaces should be added before brackets and contents in this column should read: 'Prudent healthy diet (female)' and 'Western diet (male)'.

4.5 Manuscript: Dietary Patterns and Cognitive Health in Older Adults- Findings from the Sydney Memory and Ageing Study

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DIETARY PATTERNS AND COGNITIVE HEALTH IN OLDER ADULTS: FINDINGS FROM THE SYDNEY MEMORY AND AGEING STUDY

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Abstract: *Objectives:* Systematic reviews report dietary patterns may be associated with cognitive health in older adults. However, inconsistent findings have been reported and relevant research lacks large scale studies. This study aims to examine the associations of dietary patterns and cognitive function among older adults in an Australian ageing cohort. *Design:* A population-based, cross-sectional analysis of the baseline phase of the Sydney Memory and Ageing Study, a well-characterised Australian ageing study. *Setting:* The Sydney Memory and Ageing Study was initiated in 2005 to examine the clinical characteristics and prevalence of mild cognitive impairment (MCI). *Participants:* Non-demented community-dwelling individuals from English-speaking background (N = 819) aged 70-90 recruited from two areas of Sydney, following a random approach to 8914 individuals on the electoral roll in the Sydney Memory and Ageing study. *Measurements:* The Cancer Council of Victoria Food Frequency Questionnaire was used to assess dietary intake. Scores for Mediterranean diet, Dietary Approaches to Stop Hypertension (DASH) diet and the Dietary Guidelines Index (DGI 2013) were generated. Two patterns - a Prudent healthy and a Western dietary pattern - were derived using principal components analysis (PCA). Neuropsychological tests were used to assess global cognition and six cognitive domains. Multivariate linear modelling assessed the relationship between dietary patterns and cognitive domain scores. *Results:* Mediterranean diet and DASH diet were both positively linked to visuospatial cognition (P=0.002 and P=0.001 respectively). Higher intake of legumes and nuts was related to better performance in global cognition (β=0.117; 95% CI:0.052, 0.181; P<0.001) and language and visuospatial cognitive domains. The Prudent healthy diet was associated with better global cognition (β=0.307; 95% CI: 0.053, 0.562; P=0.019) in women and a Western diet was related to poorer global function (β=-0.242; 95% CI: -0.451,-0.034; P=0.023) and executive function (β=-0.325; 95% CI: -0.552,-0.099; P=0.005) in men. *Conclusion:* In this analysis, higher adherence to the Mediterranean diet, DASH diet, Prudent healthy diet and greater consumption of legumes and nuts were associated with better cognition among older adults.

Key words: Cognitive health, dietary pattern, nutrition.

Introduction

Dementia is a global concern. Over 50 million people worldwide are currently living with dementia, and this is estimated to triple by 2050 (1). Cardiovascular risk factors, psychosocial factors, lifestyle behaviours, education and social networking, have been consistently linked to cognitive health among older adults (2, 3). Of the modifiable factors, nutrition has been recognised as a possible strategy for the prevention of cognitive decline among older adults (4-10).

A considerable body of research has examined the relationships between single nutrients or foods and cognitive decline among older adults (11). However, nutrients or specific foods are not consumed in isolation (4, 6) but within dietary patterns, where the synergies and interactions between multiple nutrients and foods may play an important role to prevent or slow cognitive decline (4-7). Our systematic review reported that dietary patterns with positive effects on cognition in older adults are mostly plant-based, rich in poly-/ mono-unsaturated fatty acids and low in processed foods (11). However, the association has not been fully investigated due to limited number of large-scale studies. The review revealed mixed findings with respect to Western dietary environments, with 5 out of 14 cohort studies from Western countries finding that Mediterranean diets had little to no effect on cognitive health, while 1 out of 3 cohort studies observing Dietary Approaches to Stop Hypertension (DASH) diets were not associated with cognition. By contrast the majority of studies conducted in Mediterranean regions reported significant associations between dietary patterns and at least one cognitive domain, or the incidence of Mild Cognitive Impairment (MCI) or dementia. These differences suggest culture and eating habits may play a role, and further investigation of the relationship between diet and cognition is needed, particularly in western countries (11).

Our study examines the associations of dietary patterns and cognitive function among Sydney Memory and Ageing Study (MAS) participants. Specific dietary patterns assessed include the Mediterranean diet, DASH diet, healthy diet as recommended by the 2013 Australian Dietary Guidelines, and dietary patterns derived by principal components analysis (PCA).

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Methods

Participants

The Sydney Memory and Ageing Study (MAS) commenced in 2005 to investigate the rate of cognitive decline, predictors and protectors for cognitive health, as well as incidence and prevalence of Mild Cognitive Impairment (MCI) and dementia among older adults. Participants were non-demented, community dwelling (n=1037) persons aged 70-90 years at baseline assessment from 2005 to 2007, recruited from two areas of Sydney, Australia. Participants underwent detailed neuropsychological and medical assessments and donated blood for clinical chemistry, proteomics and genomics (12).

Those with a previous diagnosis of dementia, psychotic symptoms, schizophrenia or bipolar disorder were excluded. Other exclusionary conditions were multiple sclerosis, motor neuron disease, developmental disability, and progressive malignancy. Our study population consisted of 819 MAS participants from English-speaking background (able to speak English at a basic conversational level by the age of 10 years) with complete neuropsychological testing and dietary assessment.

The study was approved by the Ethics Committees of the University of New South Wales and the South Eastern Sydney and Illawarra Area Health Service.

Cognitive Assessment

A comprehensive neuropsychological battery was administered according to standard protocols. Six major cognitive domains were assessed: attention/processing speed, language, executive function, verbal memory, global memory (consisted of verbal and visual memory) and visuospatial function. Tests for each domain were: Attention/ processing speed - Digit Symbol-Coding (13) and Trail Making Test (TMT) A (14); global memory - Logical Memory Story A delayed recall (15), Rey Auditory Verbal Learning Test (RAVLT) (14) and Benton Visual Retention Test recognition (16); Language - Boston Naming Test (17) and Semantic Fluency (Animals) (14); visuo-spatial-- Block Design test (18) and executive function - Controlled Oral Word Association Test (14) and Trail Making Test (TMT) B (14). Global cognition scores were calculated using composite z scores in all domains (12).

Dietary Assessment

The Dietary Questionnaire for Epidemiological Studies Version 2 (DQES v2) was used to assess dietary intake at baseline. This 80-item Food Frequency Questionnaire (FFQ), developed by the Cancer Council of Victoria, includes 74 food items and six alcoholic beverages and has been validated against weighed food records (19-21).

DQES v2 was self-administered. Nutrient intakes were calculated by the Cancer Epidemiology Centre of the Cancer Council in Victoria using an Australian food composition NUTTAB database (22).

Dietary Patterns

A priori patterns

Mediterranean diet scores were constructed following commonly used scoring systems, i.e. the 0-9 scoring system by Trichopolou et al (23, 24) and the 0-55 scoring system by Panagiotakos et al (23-25) (Supplementary Table 1). Both systems score food group components including fruit, vegetable, legumes and alcohol intake, using population sex-specific cut-offs (23, 24) or pre-defined cut-offs based on recommended food group amounts from the Mediterranean diet pyramid (25). Intakes from food groups were categorised as "beneficial" or "detrimental" according to characteristics of a Mediterranean dietary pattern. We used monounsaturated: saturated fat ratio (MUFA: SFA) in both systems to replace olive oil. Food intake (g) was adjusted for total energy intake using the residual method (26). For both scores a higher Mediterranean score represented higher adherence to the Mediterranean diet (see Supplementary Table 1).

To construct DASH diet scores, dietary and nutrient intake were grouped into nine categories (fruits, vegetables, legumes and nuts, red and processed meat, whole grain, low fat dairy, sodium intake, sugar intake and sum of monounsaturated fat and polyunsaturated fat intake) (27, 28). Food intake (g) was adjusted for total energy intake (26). Participants were classifed into quintiles according to consumption of each food category. Among the nine food categories, beneficial food categories were scored 1 to 5, with higher scores indicating greater adherance to the DASH diet and three detrimental factors received reverse scoring (sodium intake, sugar intake, red and processed meat intake) (27-30).

The Dietary Guideline Index (DGI) 2013 is developed to reflect diet quality and adherence to the 2013 Australian Dietary guidelines (31). It includes the Five Food Groups (grains and cereals, vegetables and legumes, fruits, dairy products or alternatives, lean meats or alternatives) as well as components to limit (including discretionary foods high in sugar, salt or saturated fat), with detrimental factors reversely scored (Supplementary Table 2).

A posterori patterns

All 74 FFQ food items were classified into 40 food groups (Supplemental Table 3) based on the similarity of their nutrient profiles as described in the Australian Food Composition Database (22) to reduce the number of input variables before analysis. Intake of each food group was calculated by adding the intakes of member food items. We used PCA for dimension reduction so that linear combinations of food group clusters with fewer underlying components were identified. Varimax rotation was applied to improve the separation of components and interpretability of the pattern derived, resulting in higher factor loadings for a smaller number of food groups and lower factor loadings for the rest. We considered components with an eigenvalue of >2 for female and male participants separately

Table 1
Demographic and clinical characteristics of participants from Sydney Memory and Ageing study (N=819)

Variables	All (n=819) Mean±SD Or N(%)	Female(n=459) Mean±SD Or N(%)	Male(n=360) Mean±SDOr N(%)
Age (year)	78.6±4.8	78.7±4.9	78.4±4.6
Years of education	11.6±3.5	11.0±3.0	12.5±3.9
CVD risk score[a]	4.1±3.1	4.2±3.4	4.0±2.6
Sum of physical activity	1.6±1.1	1.5±1.1	1.7±1.1
BMI, kg/m^2	25.7±4.5	25.3±4.6	26.2±4.2
Vitamin D level (nmol/L)	62.7±25.1	58.0±24.0	68.0±25.0
Total cholesterol (mmol/L)	4.8±1.0	5.0±1.0	4.5±0.9
Triglyceride (mmol/L)	1.1±0.6	1.1±0.5	1.1±0.6
HDL-chol (mmol/L)[b]	1.5±0.5	1.6±0.4	1.3±0.4
LDL-chol (mmol/L)[c]	2.8±0.9	3.0±0.9	2.7±0.8
CRP (mg/L)[d]	3.1±5.7	3.0±5.0	3.0±6.0
Vitamin A (umol/L)	3.1±0.8	3.0±0.8	3.2±0.8
Vitamin E (umol/L)	35.4±12.9	37.5±12.4	32.9±13.0
Beta- carotene (umol/L)	0.7±0.6	0.9±0.7	0.6±0.5
Total energy intake (KJ/day)	6943.2±2265.0	6107.6±1858.9	8026.4±2287.7
History of hypertension, N (%)	499(60.9%)	295(64.3%)	204(57.1%)
History of diabetes, N (%)	88(10.7%)	32(7.0%)	56(15.6%)
History of hyperlipidaemia, N (%)	478(58.4%)	262(57.3%)	216(60.3%)
History of depression, N (%)	129(15.8%)	81(18.2%)	48(13.7%)
History of stroke, N (%)	33(4.0%)	11(2.4%)	22(6.2%)
History of TIA, N (%)	57(7%)	34(7.6%)	23(6.5%)
Current smoker, N (%)	252(30.8%)	139(38.6%)	113(24.6%)
APOE4 genotype, N (%)	183(22.3%)	93(20.3%)	90(25.0%)

Notes: SD= Standard deviation; a. The CVD Risk Factor data is computed based on the research of the Framingham Stroke Study (http://www.framinghamheartstudy.org/index.html) and based on the 10-year risk prediction of general cardiovascular disease (http://www.framinghamheartstudy.org/risk/gencardio.html); b. How-density-lipoprotein cholesterol
c. Low-density-lipoprotein cholesterol
d. C-reactive protein

(32), based on scree plots (Supplementary figure 1 and 2). Food components with a factor loading ≥0.2 (33) were considered as important contributors to each pattern.

Other Measurements

At baseline and subsequent interviews, participants provided information on medical history including cardiovascular diseases and related risk factors (including hypertension, hypercholesterolemia, diabetes, atrial fibrillation, smoking, obesity, stroke or transient ischemic attack etc) and alcohol consumption (12). Assessment of levels of physical activities was also undertaken using self-report questionnaires, where types of physical activities included walking, gardening, yoga, gym work, bowls, golf, tennis, swimming, dancing, bicycling, dancing, aerobics and other sports.

Statistical Analysis

Means, standard deviations and percentages are provided for the entire cohort as well as stratification by sex. Two sample t tests (for continuous variables) and chi-square tests (for categorical variables) were used to compare means, and proportions of demographic, clinical characteristics, dietary intake, cognitive functions, and other variables between female and male participants.

A multivariable linear regression model was used to analyze the associations between global cognition and dietary patterns scores. The relationship between diet and six separate cognitive domains were explored as secondary outcomes. The basic model adjusted for age, gender and education (basic model). The fully adjusted model additionally adjusted for confounding variables, namely physical activity, Body Mass Index (BMI), metabolic syndrome, hypertension, diabetes,

Table 2
Cognitive function at baseline in the Sydney Memory and Ageing study (N=819)

Cognition Domains	All (n=819)	Female(n=459)	Male(n=360)	P value*
Attention/Processing Speed	-0.31±1.16	-0.29±1.14	-0.34±1.18	0.605
Language	-0.49±1.36	-0.59±1.37	-0.37±1.33	0.022
Executive	-0.40±1.25	-0.45±1.26	-0.33±1.24	0.180
Visuo-Spatial	-0.27±1.08	-0.44±1.04	-0.06±1.09	<0.0001
Global Memory	-0.42±1.17	-0.22±1.18	-0.66±1.11	<0.0001
Verbal Memory	-0.37±1.16	-0.14±1.15	-0.68±1.10	<0.0001
Global Cognition	-0.53±1.30	-0.57±1.29	-0.48±1.30	0.333

Notes: statistical significance by gender using independent t test. Raw scores were converted to Z-scores using the baseline mean and standard deviation (SD) values for a reference group (reference group was selected from 504 MAS participants with fluent English before 10 years old and classified as cognitive normal at baseline). If necessary, the signs of the z-scores were reversed so that higher scores reflect better performance. Domain scores were calculated by averaging z-scores of the component tests with the exception of the visuo-spatial domain represented by a single test. Global cognition scores were calculated by averaging the domain scores. All domain and global cognition scores were standardised. *P < 0.05 is significant.

Table 3
Significant associations of food group and cognition in fully adjusted model: Sydney Memory and Ageing study (N=819)

Cognition Domains	Food Groups	β	95% CI		P value*
Attention/ Processing Speed	Legumes and Nuts	.035	-.048	.119	.407
Language	Legumes and Nuts	.113	.038	.189	.003
Visuo-Spatial	Legumes and Nuts	.105	.047	.163	<.001
Executive	Legumes and Nuts	.041	-.051	.133	.364
Global Memory	Legumes and Nuts	.077	.006	.160	.068
Verbal Memory	Legumes and Nuts	.055	-.013	.123	.111
Global cognition	Legumes and Nuts	.117	.052	.181	<.001

Notes: Values are β(95% CI), n = 819. β - Coefficients show a 1 serve increase in food intake is associated with higher cognitive score (positive β) or lower cognitive score (negative β). CI= Confidence Interval. Results were fully adjusted with age, gender, education, as well as physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype. *P value<.05 is significant for global cognition and p <.01 for subdomains.

hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), smoking, depression, ethnicity and apolipoprotein E (APOE) ε4 genotype. To determine the effect of covariates, changes in the β-coefficient were examined. Significance level of 0.05 was set for global cognition as primary outcomes, and level of 0.01 was set for multiple secondary outcomes including individual cognitive domains to adjust for multiple testings. Statistical analyses were performed with IBM SPSS statistics 23.0 software.

Results

Baseline Characteristics

This cohort of 819 participants (56% female) had an average age of 78.7 years, mean education level of 11.6 years (11.0 years for women and 12.6 years for men), and mean BMI of 25.7 kg/m^2 (25.3 kg/m^2 for women and 26.2 kg/m^2 for men). Of the participants 22.3% were carriers of the APOE ε4 allele (genotypes ε2/4, ε3/4 or ε4/4), and 30.8% were current smokers (Table 1). Cognitive scores are described in Table 2. Male participants performed better on the visuo-spatial function tests and females on memory tests.

Dietary pattern scores and intake from food groups for the whole group and stratified for men and women are presented in Supplementary Tables 4 and 5. Mean Mediterranean diet scores were in the mid-range on both scoring systems (4.4 for men and 4.3 for women using 0-9 scoring system (23, 24), and 27.9 for men and 27.5 for women on a 0-55 scoring system (25). Mean DASH diet scores, 26.6 for male and 27.3 for female participants (27, 28), were also about half of the maximum DASH score (range from 9 to 45).

A -priori diets and cognition

A higher Mediterranean diet score constructed by the 0-55 scoring system, was associated with better visuospatial cognition (β=0.045; 95% CI:0.017, 0.072; P=0.002) (supplementary table 7). Further analysis of food groups (25) showed that after full adjustment, consumption of the legume

Table 4
Major dietary patterns derived by PCA*: Prudent Healthy Diet (female) and Western Diet (male): Sydney Memory and Ageing study (N=819)

Prudent Healthy Diet (female)		Western Diet (male)	
Food items	**Factor Loading**	**Food items**	**Factor Loading**
Yellow vegetables	0.342	Yellow vegetables	-0.401
Green vegetables	0.429	Cruciferous vegetables	-0.310
Cruciferous vegetables	0.391	Nuts	0.234
Other vegetables	0.395	Legumes	-0.302
Tomato	0.222	Low fat dairy	-0.482
Legumes	0.204	Full fat dairy	0.356
Nuts	0.270	Margarine	-0.456
Garlic	0.244	Butter	0.270
Full fat dairy	-0.217	Chocolate	0.226
Poultry	-0.420	Vegemite	0.214
Meat pies	-0.228	Cakes and biscuits	0.759
Fried fish	-0.603	Flavoured milk	0.238
Chips	-0.366	Fruit juice	0.271
Sugar	-0.211	Tinned fruit	0.357

Notes: *PCA Principal Components Analysis

and nuts group was positively related to better performance in global cognition (β=0.117; 95% CI:0.052, 0.181; P<0.001) and cognitive domains of language and visuospatial (Table 3). A positive association between alcohol intake and baseline cognition observed in the basic model did not reach significance after full adjustment of covariates (Supplementary Table 8).

The DASH diet score, was associated with better performance on the visuospatial test (β=0.053; 95% CI: 0.023, 0.083; P=0.001). No significant associations were found between level of adherence to the Dietary Guideline Index 2013 with global cognition or performance in any other cognitive domains (Supplementary Tables 6 and 7).

A posteriori diets and cognition

Analysis of PCA dietary patterns were stratified by participants' sex, given significant differences in food group consumption and cognitive performances between men and women (Table 2 and Table 4). One major dietary pattern was generated and examined for each sex, the Prudent healthy diet for women and the Western diet for men (see Table 4 and Supplementary figure 1 and 2).

For women, the Prudent healthy diet pattern was associated with better performance in global cognition (β=0.307; 95% CI: 0.053,0.562; P=0.019) (Table 5). In men, a Western dietary pattern appeared to relate to poorer performance in global function (β=-0.242; 95% CI: -0.451, -0.034; P=0.023), as well as in executive function tests (β=-0.325; 95% CI: -0.552, -0.099; P=0.005) (Table 5).

Discussion

This study investigated the cross-sectional associations of dietary patterns and cognition in the Sydney Memory and Ageing Study. Main findings were that both the Mediterranean and DASH diets were positively linked to visuospatial cognition, and that higher consumption of the legumes and nuts food group was associated with better overall performance in global cognition and in multiple cognition domains. The Prudent healthy diet, derived by PCA, was positively associated with global cognition among women while the Western diet was associated with poorer global cognition and executive function in men.

Our analysis of food groups found significant positive associations between legume and nut consumption and better global cognition and higher scores in multiple cognitive domains, consistent with other research reporting positive links between high legume (34) and nut intake with cognition of older adults (35, 36). The underlying mechanism may be due to their low glycaemic index (GI) properties which benefit cognition by stabilizing brain glucose levels (37). Research also suggests the brain-gut-microbiome connection and interplay between food and gut microbiota influences

Table 5
A-posterori dietary patterns and cognition by sex: Sydney Memory and Ageing study (N=819)

Cognition Domains	DP by PCA	β	95% CI		P value*
Attention Processing Speed	Prudent healthy Diet (female)	.451	.08	.823	.018
	Western Diet(male)	-.221	-.498	.055	.114
Language	Prudent healthy Diet (female)	.25	-.042	.543	.093
	Western Diet(male)	-.176	-.439	.087	.186
Executive	Prudent healthy Diet(female)	.082	-.203	.366	.57
	Western Diet(male)	-.325	-.552	-.099	.005
Visuospatial	Prudent healthy Diet(female)	.265	.043	.488	.02
	Western Diet(male)	-.146	-.268	-.024	.02
Global Memory	Prudent healthy Diet(female)	.107	-.193	.407	.479
	Western Diet(male)	.008	-.268	.285	.954
Verbal Memory	Prudent healthy Diet(female)	.101	-.191	.393	.492
	Western Diet(male)	.111	-.179	.040	.451
Global cognition at baseline	Prudent healthy Diet(female)	.307	.053	.562	.019
	Western Diet(male)	-.242	-.451	-.034	.023

Notes: Results were fully adjusted for age, sex, education, as well as physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype.
*P < 0.05 for global cognition or P<0.01 for individual cognitive domains, is significant.

neurocognitive health (38). Nuts and legumes are rich in plant based protein, fibre, anti-inflammatory agents such as polyphenols, poly-/mono-unsaturated fatty acids and may improve intestinal microbiota composition, positively affecting cognition (38).

Despite reports of cognitive benefits from the Mediterranean diet, putatively explained by the diet's anti-inflammatory, anti-oxidant properties (11), no associations were found in global cognition or cognition in individual domains apart from visuospatial cognition. It may be that visuospatial cognition is more susceptible to diet influence (39). Our dietary assessment tool was limited in measuring Mediterranean diet adherence, as it did not assess intake of olive oil which is a key component of the Mediterranean diet. In addition, the mostly Australian-born study population in Sydney, differed greatly from Mediterranean populations in various aspects including lifestyle, attitude towards foods and eating habits which could have impacted the overall outcome (11). Furthermore, higher adherence to the Mediterranean diet may be critical (40) and adherence in this study was low when compared to Mediterranean countries, with a mean score at only half of highest possible Mediterranean diet score (Supplementary Table 4).

Similarly, the link between higher adherence to DASH diet and visuospatial cognition (28, 41) was observed. However this result should be interpreted with caution. We performed multiple analyses and did not adjust for anti-hypertensive medications which may be linked to dementia-related pathophysiological pathways (42). Possible effects may be explained through the low sodium, low sugar and high vegetable focus of the DASH diet (30) with richness in mono-/ poly-unsaturated fats, beneficial for vascular health and insulin sensitivity (43, 44) for stable brain glucose levels (37).

A Prudent healthy diet generated using dimension reduction methods has been associated with improved cognition among older adults in our systematic review (11). Our results from MAS, again showed association of a Prudent healthy dietary pattern with better performance in global cognition in older women. This cognition-friendly diet was high in yellow, green leafy, cruciferous and other vegetables, as well as nuts, legumes and garlic. By contrast, a western dietary pattern found to be associated with worse global cognition among men, comprised foods high in saturated fat and sugar, including full fat dairy, butter, flavoured milk and cakes.

This study is among the first few, to our knowledge to investigate adherence to the Australian Dietary Guidelines and cognitive performance among older Australians. Similar to other international dietary guideline index studies we found no associations (Supplementary Table 6 and 7) (45, 46). The Dietary Guidelines are based on evidence for the prevention of chronic disease such as diabetes and obesity (31), and not specifically designed for the prevention of cognitive decline. Within the guidelines the mono-/poly- unsaturated fats including olive oil, because of their high energy density, have only a small allowance (approximately 20 g spread or 14g oil) (33), much lower than the level of daily consumption reported

to be beneficial for cognitive health among older adults. For example, in the PREDIMED study 1 Litre/week extra virgin olive oils were provided (40). In addition, detrimental factors specified in the Mediterranean and DASH diets, such as red and processed meat, are counted positively as an essential protein source in the DGI and foods linked to better brain health such as fish, legumes and nuts are also counted within the protein group. This suggests that more specific dietary guidelines for cognition may be needed for education and policy around better cognitive health for adults.

Mild to moderate alcohol intake was positively related to better cognition at baseline in the basic model, but not after adding cardiovascular disease (CVD) risk factors as covariates (Supplementary Table 8). Whether this is due to confounding effects or CVD risk factors as a mediator between alcohol intake and cognition, is uncertain, especially lacking data of lifetime alcohol consumption in this analysis. Some previous reviews and meta-analysis have reported light to moderate alcohol intake may be associated with reduced risk (47), however, this requires further research (1, 48).

Our study has multiple strengths, including comprehensive neurocognitive tests in multiple cognition domains, a validated dietary assessment tool, dietary patterns constructed by a qualified dietitian, statistical adjustments for important confounding factors such as cardiovascular risk factors and APOE ε4 genotype, analysis on both a-priori and a-posterori dietary patterns, as well as investigation into key Mediterranean food groups, rather than dietary patterns alone.

However, potential limitations suggest caution is needed in interpreting the findings. This is a cross-sectional analysis so causality cannot be determined. Our results may be impacted by limitations of the dietary assessment tool and scoring methods used. Firstly, DQES v2 did not assess olive oil intake, an essential component of Mediterranean diet, and our proxy of monounsaturated to saturated fat ratio may not fully compensate, as studies reported lower plasma inflammatory markers and increased anti-oxidant capacity when compared to other vegetable oils (49). Secondly, the Mediterranean diet 0-55 system scored alcohol intake linearly as a detrimental factor, while studies suggested a non-linear relationship and gender differences (50), and Mediterranean diet encourages mild to moderate alcohol intake (23). Thirdly, the study assessed current dietary patterns; lifetime patterns may be more revealing.

Conclusion

We found that greater adherence to the Mediterranean diet and DASH diet were both associated with better visuospatial function, and legumes and nuts were positively linked to better performance in multiple cognition domains and global cognition. Among dietary patterns derived by PCA, a Prudent healthy diet was positively associated with global cognition among older women. A Western diet was linked to poorer global function and executive among men. Future longitudinal analysis is needed to further investigate the relationship of diet and cognition change over time.

Conflict of interest: Henry Brodaty is an Advisory Board member for Nutricia. None declared by other authors.

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Author contributions: XC designed the research protocol, conducted data analysis, drafted the protocol and report, including creating reference list and tables. ZXL was responsible for technical support on statistical analysis, interpreting results and providing comments on manuscript. PS and NK were responsible for project design, data collection and study coordination, critical revision of manuscript. FOL provided support on dietary pattern score construction, data analysis, interpretation of results, critical revision of manuscript and approval of report. HB was responsible for designing the research protocol, interpreting results, critical revision and final approval of report. All authors reviewed the final draft.

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Chapter 5: Association of dietary patterns with cognitive function and cognitive decline in Sydney Memory and Ageing Study- a longitudinal analysis

5.1 Publication details

This chapter is a formatted for the Journal of Academy of Nutrition and Dietetics and contains identical text to the prepared manuscript entitled "Association of dietary patterns with cognitive function and cognitive decline in Sydney Memory and Ageing Study: a longitudinal analysis".

Supplementary material of this manuscript can be found in Appendix C.

5.2 Author contribution statement

I, Xi Chen (the candidate) designed the research protocol, conducted data analysis, drafted the protocol and report, including creating reference list and tables. Dr Zhixin Liu was responsible for technical support on statistical analysis, interpreting results and providing comments on manuscript. Professor Perminder Sachdev contributed to acquisition of research funds, co-design of research protocol for the Memory and Ageing Study (MAS), supervision of data acquisition and review of manuscript. Dr Nicole Kochan contributed to design of neuropsychological test protocol for MAS, supervision of data acquisition and review of manuscript. Dr Fiona O'Leary provided support on the data analysis protocol, dietary pattern score construction, data analysis, interpretation of results, critical revision of manuscript and was responsible for final approval of report. Professor Henry Brodaty was responsible for co-designing the research protocol for MAS, interpreting results, critical revision and final approval of report. All authors reviewed the final draft.

5.3 Introduction to chapter

In the last chapter, cross-sectional association between dietary patterns, key food component and baseline cognition was explored with promising results. In this chapter, longitudinal relationship between dietary patterns, key food components and cognitive performance over time are examined, with a hypothesis that healthier patterns and higher intake of legumes and nuts are linked not only to cognitive health cross-sectionally, but importantly, to slower cognitive decline with ageing over time.

5.4 Manuscript: Association of dietary patterns with cognitive function and cognitive decline in Sydney Memory and Ageing Study- a longitudinal analysis

RESEARCH SNAPSHOT

Research Question:

What are the associations between dietary patterns and food components with cognitive performance and cognitive decline over time among older adults?

Key findings:

In this prospective Sydney Memory and Ageing study that followed up 1037 participants aged 70-90 years at baseline for six years, the *Prudent healthy diet* was associated with better overall global cognition and visuo-spatial function. There were no associations of Mediterranean or DASH dietary scores with overall cognition and cognitive decline over six years. Higher intake of legumes and nuts was positively related to better global cognition, and to less cognitive decline with age.

Association of dietary patterns with cognitive function and cognitive decline in Sydney Memory and Ageing Study: a longitudinal analysis

ABSTRACT

Background: The relationship of dietary patterns to cognitive health in older adults has attracted much research attention. However, results from existing studies were inconclusive.

Objective: The aim of this study was to investigate the association between multiple dietary patterns and overall cognitive performance and cognitive change over time.

Design: This analysis was conducted as part of the longitudinal Sydney Memory and Ageing study with six years follow up. Mediterranean diet and Dietary Approaches to Stop Hypertension (DASH) diet scores were generated based on dietary intake for each individual, assessed by the Dietary Questionnaire for Epidemiological Studies Version 2. Using principal component analysis (PCA), *a-posterori* patterns were derived.

Participants/Setting: This longitudinal study comprised 1037 community dwelling non-demented participants aged 70-90 years at baseline, recruited from Sydney, Australia.

Main outcome measures: Neuropsychological tests assessed global cognition and 6 cognitive domains on four occasions, at baseline and 2, 4 and 6 years later.

Statistical analyses performed: Linear mixed model analyses were conducted to examine the relationship between dietary scores, food components and overall cognitive function and cognitive change over six years.

Results: No associations of Mediterranean or DASH dietary scores with overall cognition and cognitive decline over six years were found. The *Prudent healthy* diet derived by PCA was

associated with better overall global function (β=0.108; 95% CI: 0.039, 0.177; P=0.002) and visuospatial function (β=0.079; 95% CI: 0.021, 0.137; P=0.008). Higher intake of legumes and nuts was positively related to better overall performance in global cognition (β=0.091; 95% CI:0.035, 0.146; P=0.001) and multiple cognitive domains, and to less decline in global cognition (β=-0.016; 95% CI: -0.032, -0.001; P=0.032).

Conclusion: Our findings indicated *Prudent healthy* diet was associated with better overall cognitive performance over years, and greater consumption of legumes and nuts maybe important to slow cognitive decline with age.

Keywords: Dementia, Cognition, Dietary pattern, Legumes and nuts

INTRODUCTION

Cognitive decline is an increasing global concern, placing a significant financial and social burden on patients, caregivers and health care systems [1-3]. Over 50 million people worldwide are currently living with dementia, and this number is estimated to triple by 2050 [3]. With the ageing population, the importance of dementia prevention via modifiable risk factors has been recognised, and diet has received much research attention as a possible non-pharmaceutical strategy for the prevention of cognitive decline in older adults [3-10]. Within dietary patterns, the synergies and interactions between multiple nutrients and foods may play an important role to protect cognitive health [4-7], particularly those which are plant-based, rich in poly-/ mono-unsaturated fatty acids and low in processed foods [11].

However, evidence remains inconclusive. Although existing prospective studies in Mediterranean countries mostly supported that higher adherence to a Mediterranean diet was associated with better cognitive performance or less cognitive decline than those who had lower adherence[12-14], research conducted in western countries reported mixed findings [11,15,16]. Studies on the association between the DASH diet and cognitive decline in older populations also reported mixed results [16,17], therefore further investigation is required, particularly in western dietary environments. Among research on the prudent diet, Australian Imaging, Biomarkers and Lifestyle (AIBL) study of Ageing reported no significant relationships between the prudent diet and cognitive performance [18], contrasting the Swedish National study on Aging and Care-Kungsholmen (SNAC-K) which found that the highest adherence to prudent diet was related to less MMSE decline [19]. Moreover, when those diets were examined in cross-sectional analysis from the Sydney Memory and Ageing Study, promising results were found [20], however the longitudinal relationship between diet and cognitive performance has not yet been

explored in this cohort.

The aims of this study were twofold. The first aim was to investigate the associations between dietary patterns with overall cognitive function and cognitive decline in the ageing cohort of the Sydney Memory and Ageing Study. The second aim was to explore effects of food components on overall cognition and cognitive decline. Dietary patterns investigated were *a priori* patterns, i.e. Mediterranean diet, Dietary Approaches to Stop Hypertension (DASH) diet, and *a posterori* patterns i.e. *Prudent healthy diet* and *Western diet* derived by Principle Component Analysis (PCA) from the Sydney Memory and Ageing Study data.

The hypothesis was that higher adherence to a healthy diet such as Mediterranean diet, DASH diet, or *Prudent healthy* diet and higher intake of healthy food components would be associated with better cognitive performance and less cognitive decline over time when compared to those who had lower adherence to those diets and lower intake of healthy food components, while *Western* diet would be associated with poorer overall cognitive performance and greater cognitive decline over six years.

MATERIALS AND METHODS

Participants

The Sydney Memory and Ageing Study (MAS) is a longitudinal study of 1037 community dwelling participants (that is, living in their own home) aged 70-90 years without dementia recruited between 2005 and 2007 at baseline. MAS investigated the rate of cognitive decline, predictors of and protectors against cognitive decline, and incidence and prevalence of Mild Cognitive Impairment (MCI)/ dementia among older adults[21]. Participants were recruited from two areas of Sydney, New South Wales, Australia, following a random approach to 8914

individuals on the electoral roll, who were invited by letter to join this study. 7142 declined and a sample of 1772 responded in affirmative went through further screening to assess eligibility, where 735 people were excluded or declined to participate, resulting in a final sample of 1037 participants who were required to have conversational English at baseline assessment [21]. Participants provided demographic data, underwent extensive assessment including medical and lifestyle history, neuropsychological and medical assessments and donated blood samples for clinical chemistry, proteomics and genomics [21]. Informants (relatives or close friends of participants) were interviewed by phone or in person and completed questionnaires by mail afterwards, for a 6-year period.

Exclusion criteria for study entry were a previous diagnosis of dementia, psychotic symptoms or a diagnosis of schizophrenia or bipolar disorder, multiple sclerosis, motor neuron disease, developmental disability; progressive malignancy (active cancer or receiving treatment for cancer, other than prostate – non-metastasized, and skin cancer); implausible energy intake (<500kcal or >4000kcal per day); a Mini-Mental State Examination score <24 after adjustment (+1 for age 80 years and older, +1 for ≤ 9 years education and +2 for non-English speaking background (NESB))[22,23]; or other medical or psychological conditions that may prevent assessment. Further study details have been described [21].

The Sydney Memory and Ageing study was approved by the institutional review boards of the University of New South Wales and the Ethics Committees of the South Eastern Sydney and Illawarra Area Health Service. All participants gave written consent.

Dietary Assessment and Dietary Patterns

Participants' dietary intake were assessed at baseline via completion of the Dietary Questionnaire for Epidemiological Studies Version 2 (DQES v2). DQES v2 is a validated food

frequency questionnaire (FFQ), modified from FFQ developed by the Cancer Council of Victoria for use in an ethnically diverse Australian population [24-26]. The DQES v2 covers the past 12 months' dietary intake and comprises 74 food items with 10 options on frequency of consumption ranging from 'never' to 'three or more times per day'; and six alcoholic beverages with frequency choices from 'never' to 'every day'. Questions on portion sizes were asked and responses were used to evaluate a single portion size factor indicating participant's average portion size compared to a median serving size. Nutrient intakes were calculated by the Cancer Epidemiology Centre of the Cancer Council in Victoria using an Australian food composition NUTTAB database 2010 [27].

Mediterranean diet scores at baseline were constructed following two scoring systems which have been most commonly used: the 0-9 scoring system by Trichopolou et al [13,28] and the 0-55 scoring system by Panagiotakos et al [29]. Intake from food groups were calculated, adjusted for total energy intake using the residual method [30], and divided into either "beneficial" or "detrimental" factors according to characteristics of the Mediterranean dietary pattern. A value of either 1 (beneficial factor) or 0 (detrimental factor) were given for 9 food groups, if the individual consumption was at or above sex-specific population medians of food component in the 0-9 system; in the 0-55 system, a value ranging from 0 to 5 was assigned according to the predefined number of servings for each Mediterranean food group [29]. For details of similarities and differences between the two Mediterranean scoring systems, see Supplementary Table 1. Monounsaturated: saturated fat ratio (MUFA/ SFA) was used to replace olive oil in Mediterranean score construction. Higher scores represented higher adherence to the Mediterranean diet.

DASH diet scores were constructed using the 2017 scoring strategy of Berendsen [17], by

grouping dietary and nutrient intake into nine DASH component (fruits, vegetables, legumes and nuts, red and processed meat, whole grain, low fat dairy, sodium intake, sugar intake and sum of monounsaturated fat and polyunsaturated fat intake) [17,31]. As sweetened beverages were not assessed in the DQES v2, sugar intake was used in construction of the DASH score. Beneficial components were scored 1 to 5, while detrimental components received reverse scoring (sodium intake, sugar intake, red and processed meat intake) [17,31-33]. DASH scores ranged from 9 to 45, with a higher DASH score indicating greater adherence to the DASH diet.

Principal component analysis (PCA) was used to derive *a posterori* patterns (Kaiser-Meyer-Olkin Measure of Sampling Adequacy at 0.698, indicating suitability for PCA [34,35]). The 74 FFQ food items were classified into 40 food groups (Supplementary Table 2) based on the similarity of their nutrient profiles as described in the Australian Food Composition Database [27]. PCA was conducted to identify a smaller number of underlying components from linear combinations of food group clusters. Varimax rotation was applied to improve the separation of components and interpretability of the pattern derived. Components with an eigenvalue of >1 were investigated based on scree plots (Supplementary Figure 1), within which food groups with a factor loading ≥0.35 [36] considered as important contributors (Supplementary Table 3) [37].

The reporting of this work has been compliant with STROBE-nut guidelines (STrengthening the Reporting of OBservational studies in Epidemiology- Nutritional Epidemiology) [38].

Cognitive Assessment

Cognitive assessments were conducted at baseline (wave 1), 2-year (wave 2), 4-year (wave 3) and 6-year (wave 4) follow-up. Assessments include a comprehensive neuropsychological battery that was administered according to standard protocols by trained psychology graduates,

comprising six cognition domains including attention/processing speed, language, executive function, verbal memory, global memory (incorporating verbal and visual memory) and visuospatial function. Attention/ processing speed tests comprised Digit Symbol-Coding [39] and Trail Making Test (TMT) A [40]. Verbal memory tests were the Logical Memory Story A delayed recall [41]; Rey Auditory Verbal Learning Test (RAVLT) of total learning, immediate and delayed recall[40]. Global memory included verbal memory measures and Benton Visual Retention Test recognition [42]. Language tests were the Boston Naming Test [43] and Semantic Fluency (Animals) [40]. To assess visuo-spatial cognition, the Block Design test was used [44]. Executive function tests included Controlled Oral Word Association Test [40] and Trail Making Test (TMT) B [40].

In detail, raw cognitive scores were converted to z-scores using the baseline mean and standard deviation (SD) values for a reference group (selected from 504 MAS participants with fluent English before 10 years old and classified as cognitively normal at baseline). If necessary, the signs of the z-scores were reversed so that higher scores reflected better performance. Domain scores were calculated by averaging z-scores of the component tests except for the visuo-spatial domain which was represented by a single test. Global cognition scores, as primary outcomes, were calculated by averaging the domain scores [21]. All domain and global cognition scores were standardised so that reference groups had means of 0 and SDs of 1 (Supplementary Table 4).

Other Measurements

Participants were interviewed to gather information on medical history including cardiovascular diseases and related risk factors at baseline and each following wave (including hypertension, hypercholesterolemia, diabetes, atrial fibrillation, smoking, obesity, stroke or transient ischemic attack etc, a detailed medical history [21]), mental health issues, current

medications and oral supplements. History of depression was defined as one or more depressive episodes that required attention from a general practitioner, psychologist or psychiatrist. Assessment of physical activity was conducted using self-report questionnaires developed by the MAS team[45]. Total physical activity scores were calculated based on the sum of metabolic equivalent minutes [46] per week of participation across listed physical activities which were walking, gardening, yoga, gym work, bowls, golf, tennis, swimming, dancing, bicycling, dancing, aerobics and other sports [47]. Height and weight were measured to determine body mass index (BMI=weight in kg/height in m^2) by a research assistant using a tape measure and a scale on most occasions. Shoes were left on, while bulky clothing was asked to be removed. Where a participant could not stand unassisted or an assessment was done over the phone, height and weight were self-reported. Mild cognitive impairment [48] and dementia [49] were diagnosed at consensus meetings of at least three experienced clinicians according to international consensus criteria. The level of dementia was also measured by the Clinical Dementia Rating (CDR) scale [50]. All measurements were conducted at each wave.

Statistical Analysis

Statistical analyses were performed using R version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria) [51]. Missing values in the dataset were dealt with using multiple imputation (MI) by chained equation (MICE) appoach under assumption of missing at random (MAR) [52,53] (details of missing data as in Supplementary Table 5). The multilevel imputation model was used and 100 imputed data sets were generated. The parameter estimates for the linear mixed effect model from the imputed datasets were combined to form a single inferrence following Rubin's rule [54]. Variables used in the imputation model included age, sex, education, non-English speaking background, BMI, physical activity, smoking, CVD risk factors (hypertention, diabetes and hypercholestromia), history of depression, history of stroke,

ethnicity and APOE ε4. In addition to listed covariates, global cognition and scores in each cognitve domain were included in multiple imputation process. The MI was conducted in R using R-package MICE [55-57]. A sensitivity analysis without imputation was also conducted.

Linear mixed effects models were used to examine the associations between dietary pattern score and intakes of food groups at baseline, with cognitive change over time, as the primary outcome. The interaction of dietary intake by time was of interest. As secondary exploration, association between diet and overall cognitive performance across four waves was investigated, in answering the question about the association between diet and average cognition over a certain time frame, which is six years for this study. Overall cognitive performance is representative of average cognitive performance over years, which attenuates variability in each single cognitive assessment, and may be helpful when cognition is measured over a relatively short follow-up in community-dwelling and non-demented participants [58,59]. Model 1 adjusted for age, sex and education (basic model), and model 2 additionally adjusted for non-English speaking background, physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression, race and APOE ε4 genotype (fully adjusted model). Probability value <0.05 were considered as statistically significant for overall global cognition (average global cognition over four waves), and change in global cognition over six years, while probability value <0.01 was considered significant for other individual cognitive domains to adjust for multiple comparisons. Means, standard deviations and percentages are provided for characteristics of the entire cohort in Sydney Memory and Ageing study as well as stratified by sex. Independent t tests (for continuous variables) and chi-square tests (for categorical variables) were used to compare group differences in terms of means, and proportions of

demographic, clinical characteristics, dietary intake, cognitive functions, and other variables between female and male participants.

The interaction of dietary score by sex, age and education were also tested in this study. Analyses were planned to repeat following stratification by sex, if there was evidence of a dietary score and sex interaction, using dietary score * sex as an interaction term (p interaction < 0.05). Additional exploration was also conducted to investigate each tertile of Mediterranean diet and DASH diet (analysed as categorical variables) and cognition in fully adjusted model, with the lowest tertile as reference group.

RESULTS

General Characteristics

This cohort consisted of 1037 participants (55.2% female) with an average age of 78.8 years, a mean education level of 11.6 years (11.0 years for women and 12.3 years for men) and mean BMI of 25.7 kg/m^2 (25.3 kg/m^2 for women and 26.1 kg/m^2 for men) at baseline. About 21.4% of participants were carriers of the APOE ε4 allele (genotypes ε2/4, ε3/4 or ε4/4), 36.7% were current smokers (Table 1) and 15.8% were from a non-English speaking background. Global cognition at each wave and changes over six years are shown in Supplementary Figure 2. As expected, mean cognitive composite domain scores gradually declined over time. Overall male participants were more likely to perform better in visuo-spatial function tests (95% CI: 0.215,0.373, p<0.0001) while female participants scored more highly in memory tests (95% CI:-0.688,-0.513, p<0.0001). Approximately 9.5% (N=31) of participants developed dementia during 6-year follow-up. Dietary data were missing in 6.1%, and increasing missing cognition data were observed over waves, from 0.5% (N=5) at baseline to 38.9% at final wave (N=403) (Supplementary Table 5).

Table 1. Baseline demographic and clinical characteristics of participants from the Sydney Memory and Ageing study (N=1037)

Variables	All (n=1037) Mean±SD Or N(%)	Female(n=572) Mean±SD Or N(%)	Male(n=465) Mean±SD Or N(%)	P value for between sex differences
Age (year)	78.8±4.8	78.9±4.9	78.8±4.7	0.659
Years of education	11.6±3.5	11.0±3.1	12.3±3.8	<0.001
Sum of physical activity	1.6±1.1	1.5±1.1	1.7±1.1	0.003
BMI, kg/m2	25.7±4.4	25.3±4.7	26.1±4.0	0.011
Total cholesterol (mg/dL) [a]	181.7±38.7	193.4±38.7	170.1±34.8	<0.001
Triglyceride (mg/dL) [b]	97.4±44.3	97.4±44.3	97.4±53.1	0.900
HDL-chol (mg/dL) [c]	54.1±15.5	61.9±15.5	50.3±15.5	<0.001
LDL-chol (mg/dL) [d]	108.3±34.8	112.1±34.8	104.4±30.9	<0.001
Total energy intake (Kcal/day)	1647.8±534.5	1456.1±445.2	1890.9±539.8	<0.001
History of hypertension, N (%)	629(60.7)	359(62.8)	270(58.1)	0.121
History of diabetes, N (%)	126(12.2)	48(8.4)	78(16.7)	<0.001
History of hyperlipidaemia, N (%)	623(60.1)	344(60.1)	279(60.1)	0.976
History of depression, N (%)	163(15.7)	102(17.8)	61(13.1)	0.036
History of stroke, N (%)	41(4.0)	14(2.4)	27(5.8)	0.005
History of TIA, N (%)	69(6.7)	40(7.0)	29(6.2)	0.608
Current smoker, N (%)	381(36.7)	172(30.1)	209(54.9)	0.060
Metabolic syndrome, N (%)	506(48.8)	242(42.3)	264(56.8)	<0.001
APOE4 genotype, N (%)	222(21.4)	118(20.6)	104(22.4)	<0.001
NESB [e]	164(15.8)	82(14.4)	83(17.6)	0.148
Ethnicity				
White	1016(98.0)	566(99.0)	450(96.8)	0.025
Asian	10(1.0)	3(0.5)	7(1.5)	
Other	11(1.1)	3(0.5)	8(1.7)	
Dietary Pattern scores				
Mediterranean diet score (0-9)	4.4±1.7	4.3±1.7	4.5±1.7	0.172
Mediterranean diet score (0-55)	27.7±6.2	27.5±6.2	27.9±6.3	<0.001
DASH diet score (9-45)	27.0±4.1	27.3±3.9	26.7±4.3	0.016
Baseline Cognition (z score)				
Global cognition	-0.72±1.38	-0.71±1.34	-0.74±1.41	0.75
Attention processing speed	-0.42±1.22	-0.39±1.22	-0.45±1.22	0.41
Language function	-0.74±1.53	-0.80±1.50	-0.68±1.58	0.22
Executive function	-0.46±1.27	-0.48±1.26	-0.44±1.28	0.63
Visuo-Spatial function	-0.34±1.09	-0.48±1.03	-0.16±1.14	<0.0001
Global Memory	-0.52±1.21	-0.29±1.20	-0.81±1.15	<0.0001
Verbal Memory	-0.47±1.18	-0.20±1.17	-0.80±1.11	<0.0001

Notes: SD, Standard Deviation.

a. To convert to mmol/L, multiply by 0.02586

b. To convert to mmol/L, multiply by 0.0113

c. High-density-lipoprotein cholesterol

d. Low-density-lipoprotein cholesterol

e. non-English-speaking background

Differences by sex in food group intake were found (Supplementary Table 6). Female participants consumed more low fat dairy foods (95% CI: -0.25,0.04; p=0.008), whilst male participants consumed more fruits (95% CI: 0.06,0.29; p<0.0001), cereal (95% CI: 0.71,1.22; p<0.0001), red and processed meat (95% CI:3.82,4.93; p<0.0001), potatoes (95% CI: 0.10,0.92; p=0.015) and legumes/nuts(95% CI: 0.37,0.92; p<0.0001), alcohol (95% CI: 1.06,1.51; p<0.0001), salt (95% CI: 380.40, 580.13; p<0.0001) and added sugar (95% CI: 7.72,15.41; p<0.0001).

Two major dietary patterns were generated by PCA (n=1037), labelled as *Prudent healthy diet and Western diet* (Supplementary Table 3). A *Prudent healthy diet* was characterised by high consumption of vegetables, nuts, grains and garlic; contrasting *Western diet* with consumption of processed meat, full fat dairy, cakes and biscuits, meat pies and sugar.

Dietary patterns, food components and cognition

Overall adherence to the Mediterranean diet was suboptimal, with mean Mediterranean score approximately half of the highest possible scores for both scoring systems (mean=4.4, SD=1.7 for all, mean value of 4.5 for men and 4.3 for women using 0-9 scoring system; mean=27.7, SD=6.2 for all, with mean value of 27.9 for men and 27.5 for women respectively, using 0-55 scoring system). Similarly, low adherence to the DASH diet was observed. Mean DASH diet scores were 26.7 for men and 27.3 for women, compared to 45 as highest possible DASH score. Details of dietary pattern scores and intake from food groups are presented in Supplementary

Table 6. Those with a higher DASH score were more likely to be female (95% CI: -0.901, -0.379, p=0.016); male participants had higher adherence to Mediterranean diet (95% CI: 0.780,1.374, p<0.0001).

Neither Mediterranean nor DASH dietary scores were significantly associated with overall global cognition, cognitive decline or specific cognition domain scores (Table 2 and Table 3). Results remained non-significant in further exploration on the association between Mediterranean or DASH tertiles as categorical variables and cognitive performance over time, where the lowest tertile indicates lowest and highest tertile represents highest adherence to the diet (Supplementary Table 7-9). Results from a sensitivity analysis for those completed all follow-up cognitive tests were presented in Supplementary Table 10.

Further analysis of the Mediterranean/DASH food groups [29] (Supplementary Table 11 and Table 4) showed that after full adjustment, consumption of the legume and nuts group was associated with better overall performance in global cognition (β=0.091; 95% CI:0.035, 0.146; P=0.001) and multiple cognitive domains, including areas of language (β=0.087; 95% CI:0.029,0.144; P=0.003) and visuospatial (β=0.074; 95% CI:0.032,0.166; P<0.001); as well as slower decline in global cognition over six years (β=-0.016; 95% CI:-0.032, -0.001; P=0.032), suggesting 1 serve increase in daily consumption of legumes and nuts intake, equivalent to 150 grams of legumes or 30 grams of nuts, is associated with 0.016 SD slower cognitive decline and 0.091 SD better overall global cognition over six years. Alcohol intake (Supplementary Table 12) was linked to less global cognition decline (β=-0.021; 95% CI: -0.039, -0.002; P=0.030) and better overall global cognition (β=0.11; 95% CI:0.05,0.171; P<0.001).

Table 2. The association between baseline diet scores and overall cognitive performance over 6 years: Sydney Memory and Aging study (N=1037)

Cognition Domains		Model 1			Model 2		
		β	**95% CI**	***P value***	**β**	**95% CI**	***P value***
Attention	MED (0-55 system)	-0.002	-0.025,0.022	0.882	0.000	-0.023,0.023	0.983
	MED (0-9 system)	-0.036	-0.098,0.027	0.267	-0.024	-0.086,0.038	0.447
	DASH	0.006	-0.020,0.032	0.632	0.008	-0.018,0.034	0.536
Language	MED (0-55 system)	-0.004	-0.029,0.022	0.787	0.001	-0.024,0.026	0.943
	MED (0-9 system)	-0.054	-0.123,0.015	0.123	-0.031	-0.098,0.035	0.353
	DASH	-0.002	-0.031,0.027	0.897	0.000	-0.028,0.028	0.998
Executive	MED (0-55 system)	-0.001	-0.027,0.025	0.940	0.001	-0.025,0.027	0.933
	MED (0-9 system)	-0.019	-0.088,0.050	0.589	-0.014	-0.082,0.055	0.694
	DASH	0.005	-0.025,0.034	0.761	0.006	-0.023,0.036	0.670
Visuo-Spatial	MED (0-55 system)	0.016	-0.001,0.034	0.722	0.017	-0.001,0.035	0.063
	MED (0-9 system)	-0.002	-0.052,0.048	0.941	0.002	-0.048,0.052	0.943
	DASH	0.017	-0.004,0.037	0.134	0.017	-0.003,0.038	0.097
Memory	MED (0-55 system)	-0.003	-0.023,0.018	0.792	0.000	-0.020,0.020	0.932
	MED (0-9 system)	-0.023	-0.078,0.031	0.400	-0.016	-0.071,0.038	0.562
	DASH	0.006	-0.017,0.029	0.560	0.007	-0.015,0.030	0.525
Verbal	MED (0-55 system)	-0.004	-0.023,0.016	0.720	-0.002	-0.022,0.018	0.845
	MED (0-9 system)	-0.025	-0.082,0.033	0.400	-0.019	-0.077,0.039	0.515
	DASH	0.006	-0.016,0.028	0.595	0.007	-0.015,0.029	0.515
Global	MED (0-55 system)	0.002	-0.021,0.024	0.899	0.005	-0.018,0.028	0.690
	MED (0-9 system)	-0.042	-0.110,0.026	0.225	-0.026	-0.093,0.041	0.446
	DASH	0.006	-0.022,0.033	0.684	0.008	-0.019,0.035	0.570

Notes: Values are β (95% CI), n = 1037. β - Coefficients show a 1 score increase in dietary pattern score is associated with better cognitive performance (positive β) or worse cognitive performance (negative β). CI = confidence interval. In model 1 results were adjusted for age, sex, education, in model 2 results were fully adjusted with age, sex, education, as well as non-

English-speaking background, physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype. P value<.05 is significant for global cognition and p <.01 for subdomains.

Table 3. The association between baseline diet scores and slopes of cognitive change over 6 years: Sydney Memory and Aging study (N=1037)

Cognition Domains		Model 1			Model 2		
		β	**95% CI**	***P value***	**β**	**95% CI**	***P value***
Attention	MED (0-55 system)	0.000	-0.007,0.007	0.915	0.001	-0.007,0.008	0.874
	MED (0-9 system)	0.013	-0.007,0.033	0.200	0.006	-0.015,0.027	0.567
	DASH	-0.001	-0.010,0.007	0.767	-0.001	-0.010,0.007	0.758
Language	MED (0-55 system)	0.000	0.007,0.008	0.929	0.001	-0.007,0.008	0.890
	MED (0-9 system)	0.007	-0.014,0.028	0.520	0.012	-0.008,0.033	0.227
	DASH	-0.001	-0.010,0.008	0.791	-0.001	-0.010,0.008	0.788
Executive	MED (0-55 system)	0.002	-0.006,0.011	0.614	0.002	-0.007,0.011	0.630
	MED (0-9 system)	0.010	-0.015,0.035	0.420	0.010	-0.015,0.035	0.427
	DASH	-0.001	-0.010,0.009	0.885	-0.001	-0.010,0.009	0.849
Visuo-Spatial	MED (0-55 system)	-0.002	-0.008,0.003	0.431	-0.002	-0.008,0.003	0.451
	MED (0-9 system)	0.002	-0.01,0.019	0.781	0.002	-0.014,0.018	0.804
	DASH	-0.004	-0.011,0.003	0.231	-0.004	-0.011,0.003	0.222
Memory	MED (0-55 system)	0.002	-0.005,0.008	0.627	0.002	-0.004,0.008	0.468
	MED (0-9 system)	0.008	-0.011,0.027	0.410	0.008	-0.011,0.027	0.430
	DASH	-0.001	-0.008,0.007	0.896	0.000	-0.008,0.007	0.886
Verbal	MED (0-55 system)	0.002	-0.004,0.008	0.498	0.002	-0.004,0.009	0.589
	MED (0-9 system)	0.009	-0.010,0.028	0.354	0.009	-0.010,0.028	0.363
	DASH	-0.001	-0.008,0.006	0.759	-0.001	-0.009,0.006	0.751
Global	MED (0-55 system)	0.001	-0.007,0.008	0.843	0.001	-0.006,0.008	0.791
	MED (0-9 system)	0.011	-0.012,0.034	0.340	0.010	-0.012,0.327	0.374
	DASH	-0.001	-0.010,0.008	0.797	-0.001	-0.010,0.008	0.781

Notes: Values are β (95% CI), n = 1037. β - Coefficients show a 1 score increase in dietary pattern score is associated with less cognitive decline (negative β) or more cognitive decline (positive β). CI = confidence interval. In model 1 results were adjusted for age, sex, education, in model 2 results were fully adjusted with age, sex, education, as well as non-English-speaking background. physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype. P value<.05 is significant for global cognition and p <.01 for subdomains.

Among PCA derived patterns, the *Prudent healthy diet* pattern was linked to better overall performance in global cognition (β=0.108; 95% CI: 0.039, 0.177; P=0.002) and visuospatial function over six years (β=0.79; 95% CI: 0.021, 0.137; P=0.008). A *Western diet* was related to worse overall performance in global cognition (β=-0.096; 95% CI-0.188, 0.005; P=0.038) over six years. However, neither pattern derived by PCA was found to be associated with cognitive decline over 6 years (Supplementary Table 13).

There was no interaction between dietary scores (Mediterranean diet, DASH diet, *Prudent healthy* diet and *Western* diet) with age or education (Supplementary Table 14). Marginally significant Mediterranean diet score (0-55 system) * sex interaction (p interaction=0.033 for global memory, and p interaction=0.039 for verbal memory) (Supplementary Table 14) warranted further analysis using stratification of data by sex, results of which revealed a positive trend (p=0.036) between higher adherence to Mediterranean diet and better overall performance in verbal memory among women, however this did not reach significant level of p<0.01 set for individual cognitive domains when adjust for multiple comparisons in this analysis (Supplementary Table 15-16). There were no significant interactions between other dietary scores (DASH diet, Prudent healthy diet and Western diet) with sex were found (Supplementary Table 14).

Table 4. Association of intake of legumes and nuts with overall cognitive function and change of cognitive performance over 6 years in the Sydney Memory and Aging study (N=1037)

Cognition Domains		Model 1			Model 2		
		β	**95% CI**	***P value***	**β**	**95% CI**	***P value***
Attention	Overall performance	0.051	-0.001,0.103	0.057	0.051	-0.002,0.103	0.058
	cognitive change	-0.014	-0.029,0.002	0.083	-0.013	-0.029,0.003	0.105
Language	Overall performance	0.088	0.029,0.146	**0.003**	0.087	0.029,0.144	**0.003**
	cognitive change	-0.016	-0.032,0.000	0.049	-0.014	-0.030,0.001	0.074
Executive	Overall performance	0.040	-0.018,0.098	0.178	0.043	-0.017,0.103	0.158
	cognitive change	-0.010	-0.029,0.009	0.299	-0.011	-0.030,0.008	0.253
Visuo-Spatial	Overall performance	0.075	0.033,0.118	**<0.001**	**0.074**	0.032,0.116	**<0.001**
	cognitive change	-0.010	-0.022,0.002	0.110	-0.009	-0.022,0.003	0.131
Global Memory	Overall performance	0.038	-0.010,0.086	0.120	0.040	-0.007,0.087	0.099
	cognitive change	-0.003	-0.018,0.011	0.678	-0.003	-0.017,0.011	0.662
Verbal memory	Overall performance	0.034	-0.012,0.079	0.150	0.036	-0.010,0.081	0.123
	cognitive change	-0.003	-0.016,0.010	0.681	-0.002	-0.015,0.011	0.740
Global Cognition	Overall performance	0.092	0.037,0.148	**0.001**	**0.091**	0.035,0.146	**0.001**
	cognitive change	-0.017	-0.033, -0.001	**0.034**	**-0.016**	-0.032, -0.001	**0.032**

Notes: Values are *β* (95% CI), *n* = 1037. *β* - Coefficients show a 1 serve increase in daily consumption of the food group is associated with higher cognitive score (positive *β*) or lower cognitive score (negative *β*); faster cognitive

decline (positive β) and slower cognitive decline (negative β). CI = confidence interval. 1 serve of legumes/nuts group is 150 g legume or 30 g nuts. In model 1, results were adjusted for age, sex, education; in model 2, results were fully adjusted with age, sex, education, as well as non-English speaking background, physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype.

$P < 0.05$ for global cognition or $P<0.01$ for individual cognitive domains, is significant.

DISCUSSION

The impact of dietary factors on age-related changes in cognitive health is important in the context of an ageing population. This study investigated the associations between dietary patterns, food components, and overall cognition as well as cognitive decline over 6 years in the Sydney Memory and Ageing Study. While Mediterranean and DASH dietary patterns were not associated with any cognitive outcomes, specific food groups and PCA derived patterns were. The PCA derived *Prudent healthy diet* was associated with better global cognition and visuospatial function, while the *Western diet* was related to worse global cognition over six years. Higher consumption of the legumes and nuts food group was not only significantly associated with better overall cognitive performance in global and multiple domains, but was also linked to less cognitive decline over a 6-year-peroid. Alcohol intake was associated with less global cognitive decline and better overall global cognition performance.

This prospective study revealed that higher adherence to a *Western diet* which is rich in saturated/trans fatty acids, excessive animal proteins, processed foods and sugars, was associated with poorer overall cognitive performance, similar to findings from systematic reviews [11,60]. Consistent with existing studies, the Westernised diet derived by PCA contained unhealthy categories of food components (full fat dairy, processed meat, pastries and sweets)

[18,61,62]. However, the detrimental effects from a westernised diet may be attenuated by improved intake of healthy foods intake such as vegetables, nuts and wholegrains [19]. Further investigation is needed.

The *Prudent healthy diet* derived by PCA was associated with better overall global and visuospatial function, but not cognitive decline over time. Results of studies of the Prudent diet vary with one study showing no effect [18] and others reporting less MMSE decline and larger left hippocampal volume in those with higher adherence to prudent dietary pattern [19,61] . These discrepancies may be due to the definition of the prudent dietary pattern and food items factor loadings which vary between study populations due to population-specific dietary intake. Although most studies featured fruits and vegetables in a prudent diet, in MAS the *Prudent Healthy diet* was characterised by green leafy vegetables and other vegetables, nuts, grains and garlic; by contrast, prudent dietary patterns found in other studies have been characterised by nuts, fish, potato, low fat dairy, tomato and garlic [18] ; or were represented by cereal, rice/pasta legumes, fish, poultry, water and cooking/dressing oil [19]; or simply were calculated by predefined consumption of fresh fruit, vegetables, salads and grilled fish without using PCA [61]. Thus, it is also important to further investigate food group components in relation to cognitive health.

The report of significant positive associations between legume and nut consumption with better performance in global cognition and multiple cognition domains, and slower cognition decline, was in line with other research [63,64], and consistent with a recently published Australian study that reported association between nut intake and lower incidence of MCI [65]. The Nurses' Health Study found that removing the nuts plus legumes component of the total long-term DASH score attenuated the significant associations between long-term DASH adherence and better

cognitive function [17]. These findings as well as results from this study, suggested that legume and nut intake, may play an important role in preventing cognitive decline and maintaining cognitive health in the elderly population.

The benefits of legumes and nuts may be explained by multiple biochemical mechanisms. Bioactive compounds and plant polyphenols [66] from legumes and nuts may reduce oxidative stress [67], reduce inflammation [67] and contribute to lowering cardiometabolic risk factors [68]. Another possible explanation is via glucose management and insulin metabolism. Legumes and nuts improve insulin sensitivity due to their low glycaemic index properties and richness in mono-/poly- unsaturated fatty acids, and could benefit long-term cognition and slow cognitive decline by stabilizing brain glucose levels [69]. A healthy microbiome may also contribute to improved cognition through the brain-gut-connection. Nuts and legumes are rich in plant based protein, fibre, anti-inflammatory agents such as polyphenols, poly-/mono-unsaturated fatty acids and may impact intestinal microbiota composition, influence permeability of the gut barrier [70], improve anti-inflammatory effects and attenuate neuroinflammation [71], positively affecting cognition [72]. When legume and nut intakes were analysed separately in relation to cognitive decline in MAS population, no significant associations were found, suggesting that it may be the synergy from nutrients of both groups for neuroprotective effects, or need a higher total consumption. MAS population had a relatively low average intake of either legumes (mean 16.9 g per day) and nuts (mean 5.8 g per day), when compared to the levels of consumption for brain health, e.g., more than three servings of legumes (approximately 450g cooked) per week [73], and 30g nuts per day from PREDIMED study [74,75]. While results of this study point to the need to encourage more legumes and nuts to older people in daily eating, future research is needed to investigate how the gut-microbiota acts as a mediator between diet and cognitive health, as well as how the actions of

nutrients can be synergetic.

Although higher adherence to Mediterranean diet and DASH diet were both linked to better baseline visuospatial function in previous cross-sectional analysis of MAS [20], no significance was found between total Mediterranean diet scores or DASH scores, and cognition or cognitive change over time, despite hypothesized protective effects of these diets with their potential antioxidant and anti-inflammatory mechanisms. The results remained non-significant in further analysis comparing higher tertiles with lowest tertile of Mediterranean diet and DASH diet adherence. The findings are consistent with some studies [15,16,76,77], but not others [17,18,78-81] . This may be explained by the relatively lower Mediterranean/DASH scores in the highest tertile in MAS, compared with studies reporting neuroprotective effects [11,14,78,82]. Additionally, only baseline food intake was assessed thus change of dietary habits over time were not captured; the dietary assessment tool only covered limited food items, nor was it designed for assessing adherence to these diets. Furthermore, despite more consistent research outcomes in Mediterranean populations, mixed results have been reported by studies in Western environments, possibly indicating population differences in food supply, lifestyle, attitude towards foods and eating habit that could have impacted significantly on outcomes [11]. The Australian PATH Through Life study reported similar results that Mediterranean diet was not protective of cognitive decline in a younger cohort aged 60-64 years [83], while the AIBL study found higher baseline adherence to Australian-style Mediterranean diet was associated with less decline in executive function after 36 months in APOE ε4 carriers with a mean age at 68.4 years [18]. Future research is warranted to reveal differential effects of diet on cognition, stratified by age groups and APOE ε4 carriage.

Food groups other than legumes and nuts showed no assocations with cognition. Despite

existing studies finding increased fruit and vegetable intake was positively linked to cognitive performance [84,85], findings from this study reported no association. This may be related to low intake of vegetable intake (mean value at 95.9 g daily, ≈1.5 servings), and limited range of vegetables (18 items) and fruits (10 items) covered by the FFQ used. Furthermore, this study did not distinguish between types of fruit, and fruit juice/canned fruit with added sugar/syrup may not be beneficial to cognition due to higher GI properties compared to fresh low GI fruit which improve brain glucose stability [69]. Moreover, the type of fruit may also play a role in cognition, such as those with very low GI and high in phenolic compounds, for example berries [86]. Similarly, despite biological studies suggesting that omega-3 fatty acids from fish may play a role in primary prevention of cognitive decline by improving blood flow, reducing inflammation / amyloid-β pathology [87], no link was observed between fish intake and overall cognitve performance, or cognitive decline over six years in MAS population, consistent with recent existing cohort studies [88] It is also worth noting that although a moderate intake of fish was observed in the MAS population (mean value of 40.6g fish daily), fried fish and tinned fish were included in the total fish consumption, which might lead to a higher level of saturated fat, salt, and energy intake, diminishing expected protective effects on vascular health which related to cognitive health, from unsaturated fatty acids via fish consumption [16,18]. Due to those mixed findings, future research should explore further the relationships between food groups and cognition at older age.

This study has multiple strengths, including that MAS is a large population-based older-aged (70-90 years old at baseline) cohort who underwent comprehensive screening and diagnosis for cognitive impairment according to standard clinical criteria, using comprehensive neurocognitive tests in multiple cognition domains. Participants were followed for 4 waves over 6 years to track cognition and other medical conditions, and change over time. Multiple

imputations to deal with missing data is another advantage of this study, which is a better approach to deal with missing observations in both outcome and independent variables with repeated measures [55]. Furthermore, a validated dietary assessment tool was used and dietary patterns constructed by qualified dietitians, multiple dietary patterns were tested including using two different scoring systems (0-9 system and 0-55 systems) to construct Mediterranean diet scores, DASH diet scores, *Prudent healthy* diet and *Western* diet scores. Other strengths include statistical adjustments for important confounding factors such as non-English-speaking background, cardiovascular risk factors and APOE ε4 genotype, on analysis on both dietary patterns. Association between consumption of key food groups and cognitive health over time was also investigated.

There are limitations. The MAS population is an older Australian cohort and the results may not be generalized to younger or other ethnic groups. Secondly, self-reports of dietary history may introduce bias, even though participants were assisted by interviewers. Thirdly, only baseline dietary data were obtained. Repeated measures across four waves may have been more representative of overall dietary intake during the study period. However, while we are unable to obtain a lifelong dietary history, a British birth cohort study that investigated dietary pattern over the life course reported no significant change of eating pattern among older adults [89]. Fourthly, there were limitations to the dietary assessment methods used. The Dietary Questionnaire for Epidemiological studies (DQES v2) does not assess olive oil intake, an essential component of Mediterranean diet, and a replacement of monounsaturated to saturated fat ratio may not fully compensate. Extra virgin olive oil has identified health benefits as it is rich in monounsaturated fatty acids and poly-phenols [11], and studies show lower plasma inflammatory markers and increased anti-oxidant capacity when compared to other vegetable oils [90]. Fourthly, the PCA approach was limited by the number of derived patterns, rotation

method, and empirically selected factor-loading cut-off value. Fifthly, six years of follow up time may not be adequate to detect long-term cognitive decline. Finally, cognitive activities, and use of medication or oral supplements such as psychotropic, anti-cholinergic and anti-cholesterol medications as well as nutrition supplements were not adjusted for in this study.

CONCLUSION

In conclusion, this study found no significant association of the Mediterranean and DASH diets with cognitive function over six years. Results showed negative associations between *Western diet* and overall performance in global cognition. Higher adherence to *Prudent Healthy diet* was linked to better overall global cognition and visuospatial function over six years. More significantly, legumes and nuts had a positive association with overall cognitive health and intake was linked to less cognitive decline over time among older adults.

Future research is recommended to further investigate and clearly understand underlying mechanisms between the diet-gut-cognition relationships, and large-scale longitudinal studies in diverse samples to test relative effects between diet, food components and synergy between nutrients on cognitive decline among older population.

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Chapter 6: Association of adherence to Australian Dietary Guidelines with cognitive performance and cognitive decline in Sydney Memory and Ageing Study- a longitudinal analysis

6.1 Publication details

This chapter is a formatted for the Journal of Nutritional Science and contains identical text to the prepared manuscript entitled "Association of adherence to Australian Dietary Guidelines with cognitive performance and cognitive decline in Sydney Memory and Ageing Study: a longitudinal analysis".

Supplementary material of this manuscript can be found in Appendix D.

6.2 Author contribution statement

I, Xi Chen (the candidate) designed the research protocol, conducted data analysis, drafted the protocol and report, including creating reference list and tables. Dr Zhixin Liu was responsible for technical support on statistical analysis, interpreting results and providing comments on manuscript. Professor Perminder Sachdev contributed to acquisition of research funds, co-design of research protocol for the Memory and Ageing Study (MAS), supervision of data acquisition and review of manuscript. Dr Nicole Kochan contributed to design of neuropsychology research protocol of MAS, supervision of data acquisition and review of manuscript. Professor Henry Brodaty was responsible for co-designing the research protocol for MAS, interpreting results, critical revision and final approval of report. Dr Fiona O'Leary co-designed the data analysis protocol, supported dietary

pattern score construction, data analysis, interpretation of results, critical revision of manuscript and was responsible for final approval of report. All authors reviewed the final manuscript.

6.3 Introduction to chapter

In chapter 4 and chapter 5, association between dietary patterns, key food components and cognitive performance had been explored both cross-sectionally and longitudinally. However, it remained unknown, if higher adherence to a healthy diet recommended by ADG, which were used widely by health professionals as guidance of food selections for general well-being and chronic disease prevention, would be associated with cognitive performance among older adults. In this chapter, diet quality and adherence to ADG was measured by DGI-2013, and the longitudinal relationship between ADG adherence and cognitive performance was examined and results compared against studies with other dietary guidelines from World Health Organisation, and national peak bodies.

6.4 Manuscript: Association of adherence to Australian Dietary Guidelines with cognitive performance and cognitive decline in Sydney Memory and Ageing Study- a longitudinal analysis

Association of adherence to Australian Dietary Guidelines with cognitive performance and cognitive decline in Sydney Memory and Ageing Study: a longitudinal analysis

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ABSTRACT

We investigated associations of adherence to Australian Dietary Guidelines with cognition and cognitive decline over 6-years. We included 1037 community dwelling non-demented participants aged 70-90 years. Dietary intake was assessed using the Dietary Questionnaire for Epidemiological Studies Version 2 at baseline, with adherence to Australian Dietary Guidelines scored using the Dietary Guideline Index 2013 (DGI-2013). Cognition was assessed using neuropsychological tests in six cognitive domains and global cognition at baseline and 2, 4 and 6 years later. Linear mixed model analyses examined the association between adherence to Australian Dietary Guidelines and cognitive function and cognitive decline over six years. Overall adherence to DGI-2013 was suboptimal (mean score 43.8 with standard deviation of 10.1; median score 44, range 12-73 with interquartile range of 7). Percent of participants attaining recommended serves for the five food groups were 30.2% for fruit, 11.2% for vegetable, 54.6% for cereal, 28.9% for meat and alternatives, and 2.1% for dairy consumption. Adherence to Australian Dietary Guidelines was not associated with overall global cognition over six years (β=0.000; 95% CI: -0.007,0.007; P=0.95). Neither were DGI-2013 scores associated with change of cognitive performance over six years in global cognition (β=0.002; 95% CI: -0.002,0.005; P=0.41) or any individual cognitive domains. In conclusion, adherence to Australian Dietary Guidelines was not associated with cognitive health over time in this longitudinal analysis of an Australian older cohort. Our findings suggested that future research is needed to provide evidence to support specific dietary guidelines for neurocognitive health among Australian older adults.

Keywords: Cognitive health, Nutrition epidemiology, Diet quality, Food consumption, Dietary Guide Index

INTRODUCTION

Increasing numbers of people are living with Mild Cognitive Impairment (MCI) or dementia worldwide[1-3] against the background of increased longevity. Diet is recognised as one of several possible modifiable factors to prevent or delay the onset of cognitive decline in older adults[4-10]. Studies have reported positive effects on cognitive health in association with higher adherence to the Mediterranean diet, the Dietary Approach to Stop Hypertension (DASH) diet, the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet and Prudent healthy diet derived by statistical dimension reduction approaches[11]. A recent systematic review concluded that higher adherence to a dietary pattern that is plant-based, rich in poly-/ mono-unsaturated fatty acids and low in processed foods is likely to be beneficial to long term cognitive performance among older adults[11].

Healthy diets recommended by dietary guidelines of national peak bodies and the World Health Organisation (WHO), have also attracted research attention. Mixed cognitive outcomes were reported from cohort studies using the WHO's Healthy Diet Indicator (HDI)[12] or American dietary guidelines indexes including modified Alternative Healthy Eating Index (mAHEI), Healthy Eating Index(HEI)-2005, HEI 2010 and HEI-2015[11].

The Australian Dietary Guidelines (ADG), released by the Australian National Health and Medical Research Council, were developed to guide food selection for general well-

being and chronic disease prevention, with evidenced-based recommendations to both public and health professionals[13]. Higher adherence to the ADG , measured by the Dietary Guideline Index (DGI-2013), has been associated with lower risk of hypertension, obesity and type 2 diabetes [14-16], health behaviours and body mass index[16]. However, there is very little research as to whether greater adherence to the ADG is related to cognitive performance among older Australians[11,17]. One cross-sectional Australian study reported no significant association between DGI-2013 and cognition or brain MRI[17]; there has been no longitudinal analysis.

Our study has two aims: firstly, to examine the associations of adherence to ADG with cognitive performance and cognitive decline in an Australian older cohort over six years; and secondly, to explore diet quality and consumption of food groups recommended by ADG among older adults and investigate effects of food components on overall cognition and cognitive decline.

METHODS

Participants

Participants were from the community-based Sydney Memory and Ageing Study (MAS)[18] which comprised 1037 individuals aged 70-90 years without dementia recruited between 2005 and 2007 through the electoral roll following a random approach from two local government areas of Sydney, New South Wales, Australia. Exclusion criteria for study entry were insufficient English to complete assessments; Mini-Mental State Examination score < 24 after adjustment for age, education and non-English speaking background (NESB); psychotic symptoms or a diagnosis of schizophrenia or bipolar

disorder, multiple sclerosis, motor neuron disease, developmental disability; progressive malignancy (active cancer or receiving treatment for cancer, other than prostate – non-metastasised, and skin cancer); implausible energy intake (<500 kcal or >4000 kcal per day)[19]; or other medical or psychological conditions that may prevent assessment[18]. Participants provided demographic data, completed a detailed interview reporting medical conditions, current medications and years of education. At baseline and after two, four and six years they underwent neuropsychological and medical assessments and donated blood samples for clinical chemistry and genomics. Informants (relatives or close friends of participants) were interviewed by phone or in person and completed questionnaires by mail, over the 6-year period.

Ethics statement

The Sydney Memory and Ageing study was approved by the Ethics Committees of the University of New South Wales and the South Eastern Sydney and Illawarra Area Health Service. Written informed consent was obtained from all participants.

Dietary assessment

Participants' dietary intake was assessed at baseline via completion of the Dietary Questionnaire for Epidemiological Studies Version 2 (DQES v2). DQES v2 is a validated food frequency questionnaire (FFQ) for assessing food and nutrient intake of adults in epidemiological studies, including seventy-four food items and six alcoholic beverages as a modification of FFQ developed by the Cancer Council of Victoria for use in an ethnically diverse Australian population[20-22]. Using DQES v2, participants report intake of foods and alcoholic beverages over the past 12 months using 10 response options ranging from "never" to "3 or more times per day", with a series of photographs in the

FFQ for elucidating usual portion sizes, as well as a section covering intake of 6 types of alcoholic beverage with 10 frequency response options ranging from 'never' to 'every day'. Food intake (g) was adjusted for total energy intake[23]. Nutrient intakes were calculated by the Cancer Epidemiology Centre of the Cancer Council in Victoria using an Australian food composition NUTTAB database[24].

Adherence to ADG was measured by DGI-2013, an updated tool composed of eight components to assess quality of diet and reflect compliance with recommendations of the 2013 Australian Dietary Guidelines[16] (see Supplementary Table 1). Scoring criteria, all based on daily consumption, consisted of the following: diet variety; the five food groups including daily intake of fruit (servings), vegetables/ legumes (servings), cereals (frequency of cereal intake and proportion of whole-grain cereal), meat and alternatives (servings lean meat and alternatives such as tofu, eggs, nuts, seeds and legumes), dairy and alternatives (all dairy products including low-fat dairy); fat intake (poly-/mono-unsaturated fat to total fat ratio); and consumption of energy-dense foods/fluids (total intake of serves of discretionary foods/drinks)[16]. Scores ranged between 0 indicating poorest adherence and 90 indicating maximum adherence which occurred when participants met age-/sex-specific recommendations. Detrimental factors including discretionary foods (energy dense foods/drinks) intake received reverse scoring, while diet variety and consumptions of foods from the five food groups received positive scoring. The components for water intake or non-alcoholic beverages were not scored as they were not included in DQES v2.

The DGI-2013 scoring criteria and serving sizes for the five food groups recommended

by ADG 2013 are listed in Supplemental Table 1 and 2 respectively. The higher DGI-2013 scores suggest higher overall adherence to ADG 2013. DGI-2013 total scores were also categorized into quintiles subsequently, representing groups of very low, low, moderate, high, very high adherence to ADG 2013.

The reporting of this work is compliant with STROBE-nut guidelines (STrengthening the Reporting of OBservational studies in Epidemiology- Nutritional Epidemiology)[25] (Supplementary Material).

Cognitive Assessment

Cognitive assessments were conducted at baseline (wave 1), 2-year (wave 2), 4-year (wave 3) and 6-year (wave 4) follow-up. Trained psychology graduates administered a comprehensive neuropsychological battery according to standard protocols, covering six cognitive domains: attention/processing speed (comprising Digit Symbol-Coding[26] and Trail Making Test (TMT) A[27]), language (the Boston Naming Test[28] and Semantic Fluency (Animals)[27]), executive function (Controlled Oral Word Association Test[27] and Trail Making Test (TMT) B[27]), visuospatial function (the Block Design test[29]), verbal memory (using Logical Memory Story A delayed recall[30], Rey Auditory Verbal Learning Test (RAVLT)[27]) and global memory (verbal tests as above, and additional visual memory test using Benton Visual Retention Test recognition[31]). Raw cognitive scores were converted to z-scores using the baseline mean and standard deviation (SD) values for a reference group (selected from 504 MAS participants who were fluent in English by 10 years of age and classified as cognitive normal at baseline). If necessary, the signs of the z-scores were reversed so that higher scores reflected better performance. Domain

scores were calculated by averaging z-scores of the component tests with the exception of the visuo-spatial domain which is represented by a single test. Global cognition scores were calculated by averaging the domain scores. All domain and global cognition scores were standardised so that reference group had means of 0 and SDs of 1[18,32].

Other Measurements

Participants were interviewed at baseline and each following wave about their medical history including cardiovascular diseases and related risk factors (including hypertension, hypercholesterolemia, diabetes, atrial fibrillation, smoking, obesity, stroke or transient ischemic attack etc[18]), mental health issues and current medications. Physical examinations were conducted by trained research assistants who measured height and weight, and seated blood pressure. Apolipoprotein E (APOE) genotyping was determined by peripheral blood or saliva deoxyribonucleic acid (Taqman assays, Applied Biosystems Inc., Foster City, CA); genetic susceptibility was defined as ε4 carriage[18].

Hypertension was defined as self-reported previous diagnosis, current treatment, or either systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥ 90 mmHg. History of stroke or transient ischaemic attack (TIA) was defined by previous diagnosis. Diabetes was recognized by either having a previous diagnosis or a fasting blood glucose ≥ 7.0 mmol/L. History of depression was defined as self-reported previous diagnosis and treatment due to one or more depressive episodes that required attention from a general practitioner, psychologist or psychiatrist. Assessment of physical activities was conducted using self-report questionnaires developed by the MAS[32], and total physical activity scores calculated, based on the sum of metabolic equivalent minutes per week[33]

of participation across listed activities including walking, gardening, yoga, gym work, bowls, golf, tennis, swimming, dancing, bicycling, dancing, aerobics and other sports. Body mass index (BMI=weight in kg/height in m^2) was determined by measured weight and height. Mild cognitive impairment[34] and dementia[35] were diagnosed according to international diagnostic criteria at consensus meetings of experienced clinicians comprising psychogeriatricians, neuropsychiatrists and clinical and research neuropsychologists[32]. The severity of dementia was measured by the Clinical Dementia Rating (CDR) scale[36]. All measurements were conducted at each wave.

Statistical Analysis

Statistical analyses were performed using R version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria). Linear mixed effects models were used to examine the associations between adherence to ADG measured by DGI-2013 scores and food components at baseline, with cognitive decline over time, as primary outcome. As secondary exploration, association between diet and overall cognitive performance across four waves was investigated, in answering the question about the association between diet and average cognition over six years. Overall cognitive performance is representative of average cognitive performance over years, which attenuates variability in each single cognitive assessment, and may be helpful when cognition is measured over a relatively short follow-up in community-dwelling and non-demented participants[37,38]. Individual domains were analyzed in separate models. The interaction of dietary intake by time is included to examine the impact of dietary intake on the trend of cognitive change over time. Model 1 adjusted for age, sex and education (basic model), and model 2 as the final model, additionally adjusted for NESB, physical activity, BMI, hypertension,

diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression, ethnicity and APOE ε4 genotype (fully adjusted model). A sensitivity ananlysis was conducted excluding participants whose baseline global cognition were below the 10th percentile, to explore the role of reverse causalty. Further exploration was also conducted to investigate each DGI-2013 quintile (analysed as categorical variables) and cognition in the final model, with the lowest quintile as reference group.

Significance level of 0.05 was set for global cognition, and a level of 0.01 was set for multiple secondary outcomes including individual cognitive domains to adjust for multiple tests. Means, standard deviations and percentages are provided for characteristics of the Sydney Memory and Ageing study cohort as well as stratified by sex. Independent t tests (for continuous variables) and chi-square tests (for categorical variables) were used to compare group differences in clinical characteristics, dietary intake, and cognitive functions, between female and male participants.

Missing values in the dataset were dealt with using multiple imputation by the chained equation (MICE) appoach under assumption of missing at random (MAR)[39,40] (details of mising data as in Supplementary Table 3). The multilevel imputation (MI) model was used and 100 imputed data sets were generated. The parameter estimates for the linear mixed effects model from the imputed datasets were combined to form a single inferrence following Rubin's rule[41]. Variables used in the imputation model included age, sex, education, NESB, BMI, physical activity, CVD risk factors (hypertention, diabetes and hypercholestromia), history of depression, history of stroke, history of TIA, ethnicity and

APOE ε4. In addition to listed covariates, global cognition and scores in each cognitve domains were included in the MI process. The MI was conducted using R-package MICE[42-44].

The interaction of DGI-2013 scores by sex, age and education were also tested in this study. Further analyses were planned to repeat following stratification by sex, if there was evidence of a dietary score and sex interaction, using dietary score * sex as an interaction term (p interaction < 0.05).

RESULTS

The cohort of 1037 participants (55.2% female, n=572) had an average age of 78.8 years, a mean education level of 11.6 years (11.0 years for women; 12.3 years for men) and a mean BMI of 25.7 kg/m^2 (25.3 kg/m^2 for women; 26.1 kg/m^2 for men) at baseline; 15.8% were from non-English speaking backgrounds. About 21.4% of participants were carriers of the APOE ε4 allele (genotypes ε2/4, ε3/4 or ε4/4) (Table 1).

Overall male participants were more likely to perform better in visuo-spatial function tests while females scored better in memory tests at all waves (Table 2). As expected, all mean cognitive composite domain scores gradually declined over time. Approximately 9.5% of participants developed dementia during the 6-year follow-up. For 6.9% (n = 63 incomplete and n=9 with implausible energy intake) dietary data were missing, global cognition data were missing for 0.5% (n = 5) at baseline and increased to 38.9% (n = 403) at wave 4 (Supplementary Table 3).

DGI-2013 scores and food components

In general, adherence to ADG was poor, with the mean DGI-2013 score of 43.8 out of a maximum 90 points (Table 3). Men consumed more fruit, cereal, protein, and women consumed more low-fat dairy foods, and less discretionary foods.

Among the five food groups, more than half of the participants (54.6%, n=566 total; 60.0 % n=343 for women; 48.0% n=223 for men) consumed a satisfactory amount of cereal recommended for the 70 years and older age group. However, daily fruit and vegetable intakes were limited when compared to ADG 2013 recommendations, with only 1.2% (n=12) of all participants (1.2%, n=7 women; 1.1%, n=5 men) meeting the daily vegetable (including legumes) recommendations and 30.2 % participants (n=313 total; 25.3%, n=145 women and 36.1%, n=168 men) meeting the daily fruit recommendations. Most participants (71.1%, n=737) failed to satisfy requirements from the meat and alternatives food group, which excludes high fat and sodium sources, with only 25.5 % (n=146) women and 33.1% (n=154) of men meeting ADG daily recommendations. Low intakes of dairy products were also observed; only 22 participants (2.1%) met daily requirements; including eight women (1.4%) and 14 men (3.0%). Overall, there was limited ADG adherence and low consumption of all of the five food groups (Table 3 and 4).

Association between DGI-2013 and cognitive function

DGI-2013 scores were neither associated with overall performance in global cognition over the six years nor cognitive decline over six years. No significant associations were found with overall performance or decline in any individual cognitive domains over six years. In sensitivity analysis excluding participants with the lowest 10 percentile of

cognitive performance at baseline, results remained non-significant (Supplementary Table 7). There was no interaction between DGI-2013 scores with age, sex or education (Supplementary Table 8).

Results remained non-significant in further analysis on the association between DGI-2013 quintiles as categorical variables and cognitive performance over time, where the lowest quintile indicates lowest and highest quintile represents highest adherence to DGI-2013 (Supplementary Table 4). Trajectories of cognitive decline by DGI-2013 quintiles are demonstrated (Supplementary Figure 1 and 2). Further analysis of the DGI-2013 food groups[45] (Supplementary Table 5 and 6) showed that individual food components were not associated with overall cognitive performance or cognitive decline over time.

DISCUSSION

To our knowledge, this is the first longitudinal study to investigate associations between adherence to the Australian Dietary Guidelines, cognitive performance and age-related changes in cognitive health in older adults. Overall adherence to the ADG was suboptimal among older adults with limited consumption from each of the five food groups and especially poor for vegetables. We observed no associations between DGI-2013 scores measuring ADG adherence, and overall cognition or cognitive decline over 6 years in the Sydney Memory and Ageing Study. No food groups scored by DGI-2013 were related to cognitive health.

Our report of no associations between an index assessing adherence to national dietary guidelines with cognition in ageing populations, confirms previous research on adherence to Dietary Guidelines for Americans (measured by HEI)[46,47] and the World Health

Organisation's recommendations (measured by HDI)[12], and is consistent with an Australian cross-sectional study that reported no significant findings between ADG adherence and cognition or brain MRI measures, in a slightly younger cohort with average age of 70 years[17]. By contrast, a lower risk of cognitive decline as measured by MMSE, was found among those with the highest dietary quality from the Dietary Guidelines for Americans measured by the modified Alternative HEI (mAHEI)[48], when compared with poorest compliance. Mixed results may be due to study power, different cognitive outcome measurements using various tools and cohort characteristics including food consumption patterns, food supply and lifestyle. Discrepancies between dietary guidelines and dietary index tools may also play a role in explaining these mixed results, such as recommended serving sizes and whether or not brain-healthy foods[49] are scored separately. For example, nuts and soy protein as well as the ratio of fish to meat and eggs were individually scored components of the mAHEI[48]; while adherence to the ADG by the DGI-2013 scored legumes and fish with the meat and alternatives category, and therefore may be less able to discriminate dietary pattern differences.

Importantly, the Australian Dietary Guidelines are based on evidence for the prevention of wide range of chronic disease such as cardiovascular disease, diabetes and obesity, and not specifically designed for cognitive health or the prevention of cognitive decline among older adults. By contrast, higher adherence to the Mediterranean and DASH diets, have been associated with better cognitive function in visuospatial domains in a cross-sectional analysis arising from this MAS cohort [50]. Furthermore, dietary patterns currently considered protective against cognitive decline, are plant based, rich in poly-and mono-unsaturated fatty acids with anti-oxidant, anti-inflammatory, and anti-diabetic

properties[11]. Details of comparison between diet recommended by ADG and major dietary patterns associated with better cognitive health from existing studies, were presented in Supplementary Table 9. For example, although the ADG encourages such foods including fruits, vegetables and whole grains, the mono-/poly- unsaturated fats including olive oil have only a small recommended allowance (approximately 20 g spread or 14g oil at maximum)[16], much lower than the level of daily consumption reported to be beneficial for cognitive health among older adults. By contrast, in the PREDIMED study one litre/week extra virgin olive oil was provided for participants on a Mediterranean diet[51]. On the other hand, ADG recommends limiting discretionary foods, salt, and added sugar and is consistent with diets benefiting cognition. However, some detrimental factors as specified by brain-healthy diets, such as red meat, are counted positively as an essential protein source in the DGI-2013, while foods linked to better brain health such as legumes[52] and nuts[53] are included within food groups but without specific recommendations on daily servings or individual scoring in the DGI-2013. Other foods that may benefit cardiovascular health[54] and cognition during ageing could be emphasised. For example, berries[55,56], a key component of the MIND diet, has been reported to link to better cognitive health [49,57-59] , and diet with low GI ranking and high phenolic content, could also be encouraged. This suggests that more specific dietary guidelines for cognition may be needed for education and policy around better cognitive health for older adults, with clearer messaging on beneficial and detrimental components to guide food selection and eating behaviour.

Our study provided insight into the diet quality of older Australians, and health implications for this aging population, although we acknowledge that patterns may have

changed since baseline[60]. Despite the majority of participants (Tables 3 and 4) scoring well on food group intakes for whole grain cereals (72.4% meeting requirements), consumption of other food groups was low, especially for vegetables (1.2% meeting requirements), dairy products (2.1% meeting requirements) and protein group (28.9% meeting requirements for lean meats and alternatives). This raised concerns as prolonged low intakes may be associated with deficiencies in vitamins, minerals and beneficial bio-active molecules and negatively affect quality of life and the ageing process[61-63]. However, it is worth noting that the baseline dietary data in MAS was collected between 2005 to 2007[64], while dietary intake of the older Australian population has changed over time. An analysis based on 1995 & 2011/12 national surveys showed a significant increase in protein intake (g/kg body weight), and of particular concern a decline in vegetable consumption and higher alcohol intake[60]. Continued monitoring of dietary intake is needed to reveal food quantity, quality and trends of dietary intake among older Australians.

We found no sex differences in revised DGI scores reflecting overall adherence to the Australian Dietary Guidelines. However, when we compared food group consumption, men consumed a larger number of serves of some foods including fruits, cereal, protein foods; while women appeared to be more health-conscious in food selection, as they consumed more low-fat dairy products, and performed better in limiting intakes in discretionary foods that were high in salt, sugar and saturated fat. This is consistent with previous studies showing that older women made healthier food choices than men, possibly due to differences in capacity and interest to obtain nutritional knowledge, and

translating this knowledge into actions, self-monitoring, and level of capacity in cooking, and preparing nutritious meals and snacks[65,66].

Our study has multiple strengths, including that MAS is a large population-based older-aged (70-90 years old at baseline) cohort who underwent comprehensive screening and diagnosis for cognitive impairment according to standard clinical criteria, using comprehensive neurocognitive tests in multiple cognition domains. Participants were followed for 4 waves over 6 years to track cognition and other medical conditions, and the change over time. Multiple imputations to deal with missing data is a better approach to deal with missing observations in both outcome and independent variables with repeated measures[42]. Statistical adjustments were made for multiple important confounding factors such as NESB, cardiovascular risk factors, depression, smoking status, physical activity and APOE ε4 genotype.

There are limitations. The MAS population is an older Australian cohort (98% White, see table 1 for details of ethnicity) and the results may not be generalized to younger groups or other ethnic groups. The dietary assessment tool DQES v2 has limited items (for example, 18 vegetables and 10 fruits). As DQES v2 under-reports snacks foods, and does not assess consumption of water and non-alcoholic beverages including sugary drinks or soft drinks, accurate data on miscellaneous foods, total fluid intake and total sugar intake (from both food and beverages) were not obtained. Nor does DQES v2 capture specific brain-healthy items of interest, such as varieties of berries and olive oil intake[11,37]. A FFQ with a more extensive food and beverage list, may be needed to accurately capture food groups and nutrients, ideally with reference to nutrient biomarkers that reflect dietary

habits [67,68]. This would enable detailed comparison of dietary patterns from groups with different rates of cognitive decline, within the Australian ageing cohort. Only baseline dietary data were obtained. Repeated measures across four waves may have been more representative of overall dietary intake during the study period, and follow-up dietary data could have enabled investigation of dietary changes with age. We were unable to obtain a lifelong dietary history, due to the nature of nutrition research and difficulty in tracking dietary intake over a lifetime, especially for older populations. However, a British birth cohort study that investigated dietary patterns over the life course reported no significant changes of eating patterns among older adults when dietary intake was assessed at 36, 43, 53, 60-64 years old[69]. This may not apply in Australia, where diet and food consumption have been increasingly impacted by multiculturalism, with influences from Asian and European countries[70,71]. Other factors that may play a role in change of an individual's eating patterns are complex, including changes of health status such as a new diagnosis of diabetes, changes in geographic or living environments, and significant life events such as death of a spouse or socioeconomic changes[72-74]. Future research with long-term follow up is needed, to investigate and compare the differences between dietary patterns and eating habits of people who developed dementia, and those who remained cognitively intact at older age.

CONCLUSION

This is the first longitudinal analysis to investigate associations between adherence to Australian Dietary Guidelines and cognitive function over time among older adults. No significance was found in global cognition or any cognitive domains over six years' follow-up. Our results provided insight into the diet quality of this well characterised Australian ageing population. Future guidelines for better cognitive health and dementia

prevention in older adults require further research with large-scale longitudinal studies to investigate life course dietary intake, and underlying mechanisms between diet, nutrition and cognition.

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CONFLICT OF INTEREST

Henry Brodaty is an Advisory Board member for Nutricia Australia. None declared by other authors.

AUTHORSHIP DECLARATION

XC designed the research protocol, conducted data analysis, drafted the protocol and report, including creating reference list and tables. ZXL was responsible for technical support on statistical analysis, interpreting results and providing comments on manuscript. PS contributed to acquisition of research funds, design of research protocol, supervision of data acquisition and review of manuscript. NAK contributed to design of research protocol, supervision of data acquisition and review of manuscript. HB was responsible for designing the research protocol, interpreting results, critical revision and final approval of report. FOL supervised the data analysis protocol, dietary pattern score construction, data analysis, interpretation of results, critical revision of manuscript and was responsible for final approval of report. All authors reviewed the final draft.

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Table 1. Baseline demographic and clinical characteristics of participants from the Sydney Memory and Ageing study (N=1037)

Variables	All (n=1037)		Females(n=572)		Males(n=465)		P value for between sex differences
	Mean / N (%)	SD	Mean / N (%)	SD	Mean / N (%)	SD	
Age (year)	78.8	4.8	78.9	4.9	78.8	4.7	0.659
Years of education	11.6	3.5	11.03	3.1	12.3	3.8	<0.001
BMI, kg/m2 [a]	25.7	4.4	25.3	4.7	26.1	4.0	0.011
Total cholesterol (mmol/L)	4.7	1.0	5	1.0	4.4	0.9	<0.001
Triglyceride (mmol/L)	1.1	0.5	1.1	0.5	1.1	0.6	0.900
HDL-chol (mmol/L) [b]	1.4	0.4	1.6	0.4	1.3	0.4	<0.001
LDL-chol (mmol/L) [c]	2.8	0.9	2.9	0.9	2.7	0.8	<0.001
Total energy intake (KJ/day)	6888.0	2234.2	6086.6	1860.9	7904.0	2256.5	<0.001
History of hypertension, N (%)	629(60.7%)	n/a	359(62.8%)	n/a	270(58.1%)	n/a	0.121
History of diabetes, N (%)	126(12.2%)	n/a	48(8.4%)	n/a	78(16.7%)	n/a	<0.001
History of hyperlipidaemia, N (%)	623(60.1%)	n/a	344(60.1)	n/a	279(60.1%)	n/a	0.976
History of depression, N (%)	163(15.7%)	n/a	102(17.8%)	n/a	61(13.1%)	n/a	0.036
History of stroke, N (%)	41(4.0%)	n/a	14(2.4%)	n/a	27(5.8%)	n/a	0.005
History of TIA, N (%)	69(6.7%)	n/a	40(7.0%)	n/a	29(6.2%)	n/a	0.608
Current smoker, N (%)	381(36.7%)	n/a	172(30.1%)	n/a	209(54.9%)	n/a	0.060
Sum of physical activity [d]	1.6	1.1	1.5	1.1	1.7	1.1	0.003
APOE4 genotype, N (%)	222(21.4%)	n/a	118(20.6%)	n/a	104(22.4%)	n/a	<0.001
Ethnicity							0.025
White	1016(98.0%)	n/a	566(99.0%)	n/a	450(96.8%)	n/a	
Asian	10(1.0%)	n/a	3(0.5%)	n/a	7(1.5%)	n/a	
Other [e]	11(1.1%)	n/a	3(0.5%)	n/a	8(1.7%)	n/a	

Notes: Abbreviations: SD, Standard Deviation. n/a, not applicable.

a. BMI, body mass index, calculated by BMI= kg/m2 where kg is weight in kilograms and m2 is height in metres squared

b. HDL chol, High-density-lipoprotein cholesterol

c. LDL chol, Low-density-lipoprotein cholesterol

d. Physical activity scores were calculated by minutes of each physical activity variable (time spent per week for that activity) multiplied the metabolic equivalent value assigned to each physical activity. Level of intensity: physical activity score < 3, light; physical activity score ≥ 3 and <6, moderate; physical activity score ≥ 6, vigorous.

e. Indigenous Australian Torres Strait Islander, Pacific Islander and African.

Table 2. Cognitive performance expressed as z scores over 6 years: the Sydney Memory and Aging study

Cognition Domains	All (n=1032)		Female (n=569)		Male (n=463)		P value*
Wave 1	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Attention/Processing Speed	-0.42	1.22	-0.39	1.22	-0.45	1.22	0.41
Language	-0.74	1.53	-0.80	1.50	-0.68	1.58	0.22
Executive	-0.46	1.27	-0.48	1.26	-0.44	1.28	0.63
Visuo-Spatial	-0.34	1.09	-0.48	1.03	-0.16	1.14	<0.001*
Global Memory	-0.52	1.21	-0.29	1.20	-0.81	1.15	<0.001*
Verbal Memory	-0.47	1.18	-0.20	1.17	-0.80	1.11	<0.001*
Global Cognition	-0.72	1.38	-0.71	1.34	-0.74	1.41	0.75
Wave 2	**All (n=862)**		**Female (n=463)**		**Male (n=399)**		
Attention/Processing Speed	-0.50	1.44	-0.45	1.29	-0.57	1.59	0.22
Language	-0.88	1.55	-0.92	1.52	-0.84	1.58	0.49
Executive	-0.64	1.54	-0.58	1.48	-0.71	1.61	0.27
Visuo-Spatial	-0.35	1.16	-0.49	1.15	-0.17	1.15	<0.001*
Global Memory	-0.60	1.28	-0.31	1.26	-0.96	1.22	<0.001*
Verbal Memory	-0.59	1.24	-0.25	1.22	-0.99	1.15	<0.001*
Global Cognition	-0.86	1.53	-0.79	1.45	-0.94	1.62	0.17
Wave 3	**All (n=734)**		**Female (n=394)**		**Male (n=340)**		
Attention/Processing Speed	-0.68	1.46	-0.60	1.49	-0.78	1.43	0.09
Language	-0.94	1.62	-0.98	1.64	-0.89	1.60	0.44
Executive	-0.68	1.39	-0.69	1.44	-0.66	1.35	0.80
Visuo-Spatial	-0.33	1.15	-0.45	1.16	-0.19	1.13	0.002*
Global Memory	-0.57	1.35	-0.29	1.37	-0.90	1.25	<0.001*

Verbal Memory	-0.55	1.30	-0.22	1.30	-0.94	1.19	<0.0001*
Global Cognition	-0.89	1.51	-0.86	1.57	-0.93	1.43	0.563
Wave 4	**All (n=634)**		**Female (n=348)**		**Male (n=286)**		
Attention/Processing Speed	-0.89	1.51	-0.83	1.50	-0.96	1.53	0.286
Language	-1.03	1.68	-1.08	1.72	-0.97	1.64	0.278
Executive	-1.04	1.98	-1.03	1.84	-1.05	2.15	0.897
Visuo-Spatial	-0.54	1.22	-0.65	1.19	-0.41	1.24	0.013
Global Memory	-0.71	1.41	-0.41	1.42	-1.07	1.33	<0.0001*
Verbal Memory	-0.67	1.37	-0.32	1.37	-1.08	1.27	<0.0001*
Global Cognition	-1.22	1.75	-1.14	1.68	-1.32	1.84	0.221

Notes: statistical significance by gender using independent t test. If necessary, the signs of the z-scores were reversed so that higher scores reflect better performance. Domain scores were calculated by averaging z-scores of the component tests with the exception of the visuo-spatial domain represented by a single test. Global cognition scores were calculated by averaging the domain scores. All domain and global cognition scores were standardised. *P < 0.05 for global cognition or P<0.01 for individual cognitive domains, is significant.

Table 3. Consumption of food groups from Australian Dietary Guidelines 2013 and food group differences by sex at baseline: the Sydney Memory and Aging study (N=1037)

Dietary pattern	Mean DGI-2013 Score/ serves of Food groups/day (Recommendation of daily serves for older adults ≥70 years old)	All (N=1037)		Female (N=572)		Male (N=465)		Mean Differences (95% CI)	P value*
		Mean	SD	Mean	SD	Mean	SD		
DGI 2013 (score range 0-90)	**DGI-2013 score**	43.8	10.1	44.3	10.2	43.2	10.0	-1.11 (-2.39,0.18)	0.09
Food group serves/day	Fruits (≥2 serves/day)	1.7	0.9	1.6	0.8	1.8	1.0	0.18(0.06, 0.29)	0.003*
	Vegetables (≥5 serves/day)	1.9	1.0	1.9	1.0	2.0	1.1	-0.26(-0.71, 0.19)	0.37
	Grains and cereals (M ≥ 4.5, F ≥ 3 serves/day)	4.2	2.1	3.8	2.2	4.8	1.9	0.97(0.71, 1.22)	<0.001*
	Whole Grains (mostly whole grain)	2.6	1.6	2.4	1.5	2.8	1.7	0.35(0.15, 0.55)	0.001*
	Lean meats or alternatives (M ≥ 2.5, F ≥ 2 serves/day)	2.0	1.6	1.7	1.2	2.4	1.9	0.73(0.53, 0.93)	<0.001*
	Dairy products or alternatives (M ≥ 3.5, F ≥ 4 serves/day)	1.7	0.8	1.7	0.8	1.7	0.8	-0.08(-0.18, 0.03)	0.14
	Low fat dairy (mostly choose low fat)	0.9	0.8	1.0	0.8	0.8	0.8	-0.15(-0.25, -0.04)	0.008*

	Saturated fats (g) (trim fat from meat and choose low fat dairy)	40.6	479.6	22.4	10.4	63.3	718.1	40.95(-19.70, 101.59)	0.19
	Unsaturated fats (g) (M ≤ 2, F ≤ 2 serves/day)	31.7	13.0	28.2	11.4	36.1	13.6	7.91(6.32, 9.49)	<0.001*
	Discretionary foods serves/day (M ≤ 3, F ≤ 2.5 serves/day)	3.6	2.5	2.9	1.8	4.6	2.8	1.72(1.42, 2.01)	<0.001*

Notes: Statistical significance by sex using two sample t test. Abbreviations- M, male; F, female; CI, Confidence Interval. *P < 0.05 is significant.

Table 4. Dietary Guideline Index 2013 component scores and percentage meeting dietary guidelines: the Sydney Memory and Aging study (N=1037)

DGI-2013 component scores (score range)	All (n=1037)			Females(n=572)			Males(n=465)		
	Mean	SD	% meeting requirement	Mean	SD	% meeting requirement	Mean	SD	% meeting requirement
Food Variety (0-10)	7.9	2.1	35.9%	7.9	2.2	35.8%	8.0	2.0	35.9%
Fruits (0-10)	6.3	3.5	30.2%	6.1	3.4	25.3%	6.5	3.6	36.1%
Vegetables (0-10)	4.6	2.9	1.2%	4.5	2.9	1.2%	4.6	3.0	1.1%
Cereal foods									
a. Total quantity (0-5)	3.7	1.7	54.6%	3.9	1.7	60.0%	3.5	1.8	48%
b. Whole grains ratio (0-5)	2.0	1.4	72.4%	2.2	1.5	75%	1.8	1.4	69.1%
Meat and alternatives (0-10)	6.1	3.6	28.9%	5.9	3.6	25.5%	6.4	3.6	33.1%
Dairy and alternatives									
a. Total dairy/alternatives (0-5)	2.1	1.5	2.1%	2.0	1.4	1.4%	2.1	1.5	3%
b. Low fat dairy ratio (0-5)	1.7	1.6	61.9%	1.8	1.5	65.7%	1.6	1.6	57.1%
Limit saturated fat and small allowance of unsaturated fat									
a. Unsaturated fat ratio (0-10)	5.5	2.9	61.2%	5.4	2.9	58.8%	5.6	2.8	64.1%
Discretionary foods (0-20)	3.3	5.1	37.7%	4.1	5.4	45.5%	2.3	4.6	28.2%

Notes: Abbreviations: DGI, Dietary guideline index; SD, Standard deviation. Fruit intake ≥ 2 serves and vegetable intake ≥ 5 serves considered as satisfactory. Cereal food intake ≥4.5 serves for men and ≥3 serves for women were considered satisfactory. Total protein intake ≥2.5 serves for men and ≥2 serves for women were satisfactory. Dairy intake ≥ 3.5 serves for men and ≥ 4 serves for women were satisfactory. Whole grain consumption equal to or more than half of total cereal intake serves, and low fat dairy equal to or more than half of total dairy intake serves was considered meeting requirements here. Unsaturated fats/oils ratio ≥ 0.5 considered meeting requirements. Discretionary foods: ≤ 3 serves for men and ≤ 2.5 serves for women were considered as satisfactory.

Table 5. Association of the Dietary Guideline Index 2013 scores with overall cognitive function and change of cognitive performance over 6 years in the Sydney Memory and Aging study (N=1037)

Cognition Domains		Model 1			Model 2		
		β	95% CI	*P value*	β	95% CI	*P value**
Attention	Overall cognitive performance	-0.001	-0.008,0.006	0.78	0.001	-0.006,0.007	0.86
	cognitive change	0.001	-0.003,0.004	0.74	0.001	-0.003,0.004	0.75
Language	Overall cognitive performance	-0.003	-0.011,0.005	0.43	0.000	-0.007,0.007	0.96
	cognitive change	0.003	-0.000,0.007	0.09	0.003	-0.000,0.007	0.09
Executive	Overall cognitive performance	-0.001	-0.008,0.006	0.78	-0.000	-0.007,0.007	0.96
	cognitive change	0.001	-0.003,0.004	0.75	0.000	-0.003,0.004	0.80
Visuo-Spatial	Overall cognitive performance	0.002	-0.004,0.007	0.52	0.002	-0.003,0.008	0.40
	cognitive change	-0.001	-0.004,0.002	0.52	-0.001	-0.004,0.002	0.51
Memory	Overall cognitive performance	-0.002	-0.009,0.004	0.46	-0.001	-0.015,0.003	0.68
	cognitive change	0.002	-0.001,0.005	0.24	0.002	-0.007,0.005	0.24
Verbal	Overall cognitive performance	-0.002	-0.008,0.004	0.47	-0.001	-0.007,0.005	0.67
	cognitive change	0.002	-0.001,0.005	0.21	0.002	-0.001,0.005	0.22
Global	Overall cognitive performance	-0.003	-0.010,0.005	0.48	0.000	-0.007,0.007	0.95
	cognitive change	0.002	-0.002,0.005	0.41	0.002	-0.002,0.005	0.41

Notes: Abbreviations: CI, confidence interval. Values are *β* (95% CI), *n* = 1037. In overall cognitive performance, *β* Coefficients show a 1 score increase measured by Dietary Guideline Index-2013 is associated with higher cognitive score (positive *β*) or lower cognitive score (negative *β*)); in slope of cognitive change over six years, *β* Coefficients show a 1 score increase measured by Dietary Guideline Index-2013 is associated with faster cognitive decline (positive *β*) or slower cognitive decline (negative *β*). Results were adjusted for age, sex, education for model 1; and fully adjusted with age, sex, education, as

well as non-English speaking background, physical activity, BMI, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), smoking, depression and APOE ε4 genotype for model 2.

*P < 0.05 for global cognition or P<0.01 for individual cognitive domains, is significant.

Chapter 7: Thesis conclusion

7.1 Introduction to Chapter

My aim was to examine the association between dietary patterns and cognition in older Australians. I led a number of studies exploring this and testing hypotheses. I hypothesised that greater adherence to healthy dietary patterns would be associated with better cognitive function in one or multiple domains, and less cognitive decline among older Australians, after adjusting for multiple confounding factors; and these associations may differ according to the diet type.

This chapter summarises the key evidence arising from the body of research presented from Chapter 3 to Chapter 6, outlines future implications, and suggests future research to provide further evidence supporting dietary changes for better neurocognitive health among older adults.

7.2 Key research findings in this thesis

1. *Introduction (Chapter 1)*

The key research findings in this thesis are listed below, corresponding to research questions, aims and hypotheses that were presented in Chapter 1.

2. *Methods (Chapter 2)*

Research methods included details of data source, data collection and measures from the Sydney Memory and Ageing study, as well as statistical analysis methods for cross-sectional and longitudinal analysis. Approval by institutional Ethics was documented.

3. *To search and review literature on existing evidence of the relationship between dietary pattern and cognitive health among older adults (Chapter 3)*

A comprehensive systematic review of the literature was conducted to understand current evidence regarding the association between dietary patterns, cognitive performance and cognitive decline with ageing among older population (1). The literature search returned six RCTs and 31 prospective cohort studies, covering a variety of dietary patterns: the Mediterranean diet, Dietary Approach to Stop Hypertension (DASH) diet, Mediterranean-DASH diet Intervention for Neurodegenerative Delay (MIND) diet, Anti-inflammatory diet, Healthy diets recommended by dietary guidelines assessed via a dietary index, and Prudent healthy diets generated via statistical approaches.

From a total of 37 studies, the Mediterranean diet was the most investigated. Stronger evidence supporting protection against cognitive decline among older adults came from Mediterranean countries where the majority of research was conducted; mixed results were reported from studies in Western environments.

Evidence from other dietary patterns such as the MIND, DASH, Anti-inflammatory, and Prudent healthy diets was more limited but showed promising results, especially for those at risk of cardiovascular disease. By contrast, long term detrimental cognitive effects were reported, with higher adherence to the Westernised diet which is rich in saturated/trans fatty acids, excessive animal proteins, processed foods, fried foods and sugars. Chapter 3 reported that although not yet conclusive, most research supported potentially positive relationships between dietary patterns which are plant-based, rich in poly/monounsaturated fatty acids with reduced consumption of processed foods and cognitive health in older adults (1).

Chapter 3 also noted the inconsistent results and the need for future research to investigate effectiveness of food components as well as diet-cognition relationships, and to consider and adjust for multiple covariates including physical activity, obesity, smoking, and cardiovascular risk factors such as diabetes, hypertension and hyperlipemia.

4. *To investigate cross-sectional relationships between dietary patterns, food components with cognitive function among older adults in an Australian Ageing cohort (Chapter 4)*

The cross-sectional relationships between dietary patterns, key food components and cognitive health were investigated in a well-characterised Australian Ageing cohort from the Sydney Memory and Ageing Study. Participants in this study were selected from 1037 non-demented community-dwelling individuals aged 70-90 years recruited from two local government areas of Sydney, following a random approach to 8914 individuals on the electoral roll. For this study, only participants from an English-speaking background (n= 819) were selected to reduce confounding of neuropsychological assessments. The Cancer Council of Victoria Food Frequency Questionnaire was used to assess dietary intake. Dietary patterns were constructed for the Mediterranean diet, Dietary Approaches to Stop Hypertension (DASH) diet and the Dietary Guidelines Index (DGI 2013), a statistically (using Principal Component Analysis) derived Prudent healthy and a Western dietary pattern. Neuropsychological tests were used to assess global cognition and six cognitive domains (attention processing speed, language, executive, visuo-spatial, visual and verbal memory). Multivariate linear modelling assessed the relationship between dietary patterns, key food components and cognitive domain scores using IBM SPSS statistics 23.0 software.

Overall, higher adherence to the Mediterranean diet, DASH diet, Prudent healthy diet and greater consumption of legumes and nuts was associated with better cognition among older adults. The Mediterranean and DASH diets were both positively linked to the domain of visuospatial cognition (β=0.045; 95% CI:0.017, 0.072; P=0.002 and β=0.053; 95% CI:0.023, 0.083; P=0.001 respectively) only. Higher intake of legumes and nuts was related to better performance in global cognition (β=0.117; 95% CI:0.052, 0.181; P<0.001), language (β=0.113; 95% CI:0.038, 0.189; P=0.003) and visuospatial cognitive domains (β=0.105; 95% CI:0.047, 0.163; P<0.001). The Prudent healthy diet was associated with better global cognition (β=0.307; 95% CI: 0.053, 0.562; P=0.019) in women; and a Western diet was related to poorer global function (β=-0.242; 95% CI: -0.451, -0.034; P=0.023) and executive function (β=-0.325; 95% CI: -0.552, -0.099; P=0.005) in men. No association was found between adherence to Australian Dietary Guidelines (ADG) measured by DGI-2013, and cognitive function.

In summary, Chapter 4 highlighted the link between higher legume and nut intake and better cognition in multiple domains. Results also confirmed cross-sectional associations between healthy diets with anti-inflammatory/anti-oxidant/cardiovascular-protective properties and cognitive health among older adults, especially in the domain of visuospatial function, which appeared to be more susceptible to dietary influence in this population (2, 3). The need for longitudinal analysis to further investigate the relationship of diet and cognition change over time among older adults was discussed.

5. *To examine the longitudinal associations between dietary patterns, food components with overall cognitive performance over time and cognitive decline with ageing among older adults in Sydney Memory and Ageing Study (Chapter 5)*

Longitudinal relationships between dietary patterns, food components and cognitive

performance and cognitive decline with ageing, were examined in the Sydney Memory and Ageing study. As described above, 1037 participants, who were non-demented, community dwelling and aged 70-90 years at baseline, were recruited between 2005 and 2007. They had neuropsychological tests at baseline and 2, 4 and 6 years later. Linear mixed model analyses were conducted to examine the relationship between dietary scores, food components with cognitive change over six years. As secondary exploration, association between diet and overall cognitive performance across four waves was investigated, in answering the question about the association between diet and average cognition over a certain time frame, which is six years for this study. Overall cognitive performance is representative of average cognitive performance over years, which attenuates variability in each single cognitive assessment, and may be helpful when cognition is measured over a relatively short follow-up in community-dwelling and non-demented participants (4, 5). A novel approach using multiple imputation (MI) by chained equation (MICE) was applied to handle missing data in the analyses, under assumption of data being "missing at random" (MAR) (6, 7), using R version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria). Additional exploration was also conducted to investigate each tertile of Mediterranean diet and DASH diet (analysed as categorical variables) and cognition in the fully adjusted model, with the lowest tertile as reference group.

No significant associations were found between Mediterranean or DASH dietary scores with cognitive decline or overall cognition over six years among older adults. The *Prudent healthy* diet derived by PCA was associated with better overall global function (β=0.108; 95% CI: 0.039, 0.177; P=0.002) and visuospatial function (β=0.079; 95% CI: 0.021, 0.137; P=0.008), while the other PCA based pattern of *Western* diet was related to worse scores in overall global cognition (β=-0.096; 95% CI-0.188, 0.005; P=0.038) over six years. This prospective study

confirmed findings from systematic reviews (1,5) in demonstrating long term detrimental cognitive effects among those who adhered more to the Westernised diet which is rich in saturated/trans fatty acids, excessive animal proteins, processed foods and sugars.

Chapter 5 also reported findings on the association between consumption of key food components with cognitive performance and cognitive decline over time. In this longitudinal analysis over six years, higher intake of legumes and nuts was positively related to less decline in global cognition (β=-0.016; 95% CI: -0.032, -0.001; P=0.032); and to better overall performance in global cognition (β=0.091; 95% CI:0.035, 0.146; P=0.001) and individual cognitive domains of visuospatial and language across four waves. These results were similar/consistent with cross-sectional results described in chapter 4. Possible underlying mechanisms discussed include low glycaemic index (GI) properties of legumes and nuts which may improve insulin sensitivity and benefit cognition by stabilizing brain glucose levels (8). The brain-gut-microbiota connection and interplay between food and gut microbiota may be another mechanism (9), as gut microbiota has been associated with the presence and progression of cognitive impairment and Alzheimer's disease (10). Nuts and legumes are rich in plant-based protein, fibre, anti-inflammatory agents such as polyphenols, poly-/mono-unsaturated fatty acids and thus may improve intestinal microbiota composition (11) and attenuate neuroinflammation (12), positively affecting cognition (9).

6. *To investigate diet quality and food consumption among older adults in the researched population, with regard to recommendations from the Australia Dietary Guidelines; and to examine the longitudinal association between a diet quality index, recommended food groups and cognitive health among older adults in Sydney Memory and Ageing Study (Chapter 6)*

Diet quality and food group consumption were reported, with reference to the Australian Dietary Guidelines investigated using the Dietary Guideline Index-2013 (score range from 0 to 90). Among Sydney Memory and Ageing study participants, overall adherence to the DGI-2013 was suboptimal (mean score 43.8, standard deviation of 10.1). Percent of participants attaining recommended serves for the five food groups were 54.6% for cereal, 30.2% for fruit, 28.9% for meat and alternatives, 11.2% for vegetables, and 2.1% for dairy consumption. These results raised concerns as intake of fruit, vegetables and legumes were associated with reduced risk of cardiovascular disease, cancer and all-cause mortality (13-15); and prolonged low intakes of all essential food groups may be associated with deficiencies in multiple macro- and micro-nutrients, which are associated with increased risk in a range of chronic conditions and malnutrition, negatively affect quality of life and the ageing process (16-18). However, the dietary intake of the older Australian population may have changed since the baseline dietary data in Sydney Memory and Ageing Study were collected between 2005 to 2007 (19). An analysis based on 1995 & 2011/12 national surveys showed a significant increase in protein intake (g/kg body weight) but, of particular concern, a decline in vegetable consumption and higher alcohol intake (20, 21). Continued monitoring of dietary intake is essential to reveal food quantity, quality and dietary trends among older Australians.

Gender differences were observed and indicated that men consumed more fruit, cereal, and protein rich foods from the meat and alternative group, contrasting women who appeared to be more health-conscious in food selection (22, 23), and consumed more low-fat dairy foods, and less discretionary foods that were high in salt, sugar and saturated fat. This is possibly due to differences in capacity and interest to obtain nutritional knowledge, and translating this knowledge into actions, self-monitoring, and level of capacity in cooking, and preparing nutritious meals (22, 24).

This is the first longitudinal analysis of the association of the Dietary Guideline Index-2013 scores, serves from essential food groups as defined by the Australian Dietary Guidelines, with cognitive decline and cognitive performance over time. Adherence to the Australian Dietary Guidelines as assessed by the DGI-2013 was not associated with cognitive decline over six years in global cognition (β=0.002; 95% CI: -0.002,0.005; P=0.41) or any individual cognitive domains. Neither were DGI-2013 scores associated with overall global cognition over six years (β=0.000; 95% CI: -0.007,0.007; P=0.95). Results remained non-significant in further analysis on the association of DGI-2013 quintiles as categorical variables with cognitive performance over time, where the lowest quintile indicates lowest and highest quintile represents highest adherence to the DGI-2013.

Findings from the Sydney Memory and Ageing study were contrasted with studies that examined association of adherence to diets recommended by World Health Organization or national peak bodies such as American Dietary guidelines and Australian Dietary Guidelines, with cognition in ageing populations. Our results were in line with research that reported adherence to Dietary Guidelines for Americans measured by Healthy Eating Index (HEI) (25, 26), and the World Health Organisation's recommendations measured by Healthy Diet Indicator (HDI) (27) were not associated with cognitive outcomes among older adults. Furthermore, a cross-sectional analysis from the Cognition and Diabetes in Older Tasmanians (CDOT) Study in Australia also reported no significant findings between adherence to Australian Dietary Guidelines measured by DGI-2013 and cognition or brain MRI measures (28). By contrast, our results were inconsistent with studies that reported significant associations between higher adherence to healthy diets recommended by national guidelines and cognitive performance in older populations (29). Among participants enrolled in two international parallel trials - the ONTARGET (Ongoing Telmisartan Alone and in Combination

with Ramipril Global Endpoint Trial) and TRANSCEND (Telmisartan Randomised Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease), lower risk of cognitive decline as measured by the MMSE was observed among those with the highest dietary quality from the Dietary Guidelines for Americans measured by the modified Alternative HEI (mAHEI) (29). These mixed results may be due to study power, different cognitive outcome measurements using different tools and cohort characteristics including food consumption patterns, food supply and lifestyle. Importantly, discrepancies between dietary guidelines and dietary index tools may also play a role in explaining these mixed results, such as recommended serving sizes and whether or not brain-healthy foods (30) are scored separately. For example, nuts and soy protein as well as the ratio of fish to meat and eggs were individually scored components of the mAHEI (29); while adherence to the ADG by the DGI-2013 scored legumes and fish with the meat and alternatives category, and therefore may be less able to discriminate dietary pattern differences.

Furthermore, the Australian Dietary Guidelines have been developed for public health promotion and prevention of chronic diseases such as diabetes and obesity; they were not designed specifically for cognitive health or the prevention of cognitive decline among older adults. Although the ADG encourages foods linked to better cognitive health including fruits, vegetables and whole grains; the mono-/poly- unsaturated fats including olive oil have only a small recommended allowance (approximately 20 g spread or 14g oil at maximum) (31), much lower than the level of daily consumption reported to be beneficial for cognitive health among older adults (32). Dietary intake of mono-/poly- unsaturated fatty acids has been positively linked to cognitive performance (33, 34). The reason may be due to the human brain's requirement for fatty acids as it consists of approximately 60% fat, and essential fatty acids play a vital role in the brain's integrity and are required for maintaining cognitive health (35,

36). Other foods related to better brain health such as legumes (37), nuts (38) and berries (39, 40) are included within essential food groups but without specific recommendations on daily servings or individual scoring in the DGI-2013. Moreover, some factors considered detrimental by brain-healthy diets, such as red meat, are counted as an essential lean protein source in the DGI-2013, but without clear upper limits on servings per day. On the other hand, ADG recommendations of limiting discretionary foods, salt and added sugar are consistent with diets benefiting cognition. Chapter 6 recommends that more specific dietary guidelines for cognition are needed for education and policy around better cognitive health for older adults, with clearer messaging on beneficial and detrimental components to guide food selection and eating behaviour.

7.3 Implications for dementia prevention

This thesis revealed that in the Sydney Memory and Ageing Study, greater adherence to healthy dietary patterns were proven to be cross-sectionally associated with better cognition: Mediterranean diet and DASH diet were both positively linked to visuospatial cognition. Longitudinally, no association was found between adherence to Mediterranean diet or DASH diet and cognitive performance over time; however, the *Prudent Healthy diet* was linked to better overall global cognition over six years whilst higher adherence to the *Western diet* was associated with worse cognitive performance over time. Intake of legumes and nuts were positively linked to better performance and less decline in multiple cognition domains and global cognition both cross-sectionally and longitudinally. The findings emphasise the importance of brain-healthy diets especially legume and nut intake. Modification to eating patterns and dietary habits appear to be promising strategies to maintain better cognitive health and prevent cognitive impairment and dementia among older adults. Improving legume and nut intake may also be a simple strategy to less cognitive decline over years, as indicated by

findings of this thesis. However, effects from other lifestyle factors were not measured in this research, including physical activity, mental activity and social activity.

Dementia prevention is complex, and a multidisciplinary team approach is highly recommended (41). As brain healthy diets and foods are promising approaches for better cognitive health, dietetics intervention and nutrition education may play an important role for promoting diet quality, as well as for prevention of dementia and cognitive impairment among older adults. For long term benefits, preventative approaches for dementia are recommended at several levels: 1) individual, intervention with personalised dietary advice; 2) household, involving family members in educational programmes; 3) community work with local authorities to develop initiatives and interventions; and 4) at a population level for whole of country approach including national guidelines (41). In preventative programmes, traditional methods such as use of visual aids in education and validated questionnaires for evaluation; should be supplemented by close cooperation and interaction between theoretical knowledge and behavioural science. Modern digital technology may assist, for example using computer-based software and smartphone apps for monitoring and evaluating behavioural changes (42).

To enhance positive changes towards better cognitive health from multiple perspectives, a multi-disciplinary team involving doctors, nurses, dietitians, physiotherapists/exercise physiologists, psychologists, occupational therapists and social workers, should receive specialised training in dementia prevention and work collaboratively to provide multidomain interventions including dietary education, physical exercise, cognitive activities, social activities, structured screening for cognitive performance, monitoring and encouraging behavioural change, and vascular risk monitoring and treatment (43, 44). Furthermore, as an established framework for healthy eating among the public, national dietary guidelines have

played an important role in nutrition education and are widely used by health professionals, policy makers, educators, food manufacturers, and researchers. Thus, as Chapter 6 has pointed out, there appears to be a gap between a healthy diet as defined by the current dietary guidelines and specific brain healthy diets. Specific dietary guidelines for neurocognitive health for Australian older adults, may be an option for investigation as the evidence base with more supportive evidence emerges from future research.

It is never too early to start dementia prevention including dietary intervention as an important approach, as many types of dementia may start to develop in middle life (45). For example, Alzheimer's disease pathology - amyloid beta (Aβ) plaques and neurofibrillary tangle formation - started to accumulate in the brain two or three decades before emergence of clinical symptoms of dementia (46, 47). Mid-life cardiovascular risk factors such as elevated levels of blood pressure, cholesterol and glucose, are associated with higher risk for not only late-life cognitive impairment (45) and vascular dementia, but also Alzheimer's disease (48). Obesity in midlife has been reported to increase the risk of dementia (49). Lifestyle intervention and dietary modifications with improvement in dietary knowledge, attitude, and practices, are effective management approaches for these conditions (50-52), and so may protect against cognitive decline via improving vascular health and reducing risk factors from midlife (1).

Even at older ages, dietary changes are beneficial. Recent research reported that among those aged 60 years or older with mean age at 70.6 years, cognitive decline associated with a Westernised dietary pattern was attenuated if people also incorporated prudent healthy food choices with fruits, vegetables, legumes, nuts, fish and whole grains (53). Thus, importance of nutrition education and encouraging positive dietary changes for better brain health even among older population, should be emphasised, rather than overlooked.

7.4 Future studies on the effect of dietary pattern on cognition

For future prospective studies on the association between dietary patterns and cognitive health, a validated dietary assessment tool that covers a wide range of both commonly consumed food and beverage items and that adequately captures potentially brain healthy foods inclusive of berries, legumes, nuts, olive oils are recommended (1, 4). This should be administered more than once so any change in intake can be determined. An accurate dietary assessment optimally including dietary history in midlife or even at earlier life stage is preferrable, to investigate long term dietary intake and habits and its influences on cognitive health at older ages (54); and if possible, including data from dietary checks as part of a standard health assessment on a regular basis, which may become feasible in the future with digital health (55, 56). Complex factors that may play a role in changing an individual's eating patterns should be taken into consideration during investigation and analysis, including changes of health status such as a new diagnosis of diabetes, changes in geographic or living environments, and significant life events such as death of a spouse or socioeconomic changes (57-59). Adjustments for medications are needed for data analysis as older adults are increasingly likely to be on multiple medications (60, 61). Other factors that have been linked to cognitive decline and should be considered are education, cognitive activity, physical activity, socialisation, alcohol intake, hearing, history of head injury and exposure to air pollution (62). Furthermore, selection of Mediterranean scoring system should be carefully considered. As discussed in Chapter 4, the 0-55 system uses pre-defined cut-offs based on frequency of consumption of foods relative to recommended amounts from the Mediterranean diet pyramid, so is more characteristic of a Mediterranean dietary pattern; while the 0-9 system uses population sex-specific cut-offs around the median, and provides a relative ranking only within a given study population. Future research also needs to investigate further on how to evaluate adherence to the Mediterranean diet. On one hand, the scoring system should be appropriate for the culture, lifestyles, eating

habits, and characteristics of the specific study cohort; further adaptation may be needed to construct a "Mediterranean-like diet score" (63). For example, the use of olive oil in countries where it is not the main source of culinary oil in the diet, the component of olive oil intake may be replaced by a monounsaturated fat: saturated fat ratio (64). On the other hand, efforts are needed to better characterize elements in the definition of a Mediterranean diet dietary pattern component, such as, whether or not potato intake/ poultry intake should be counted as independent components (63, 65); to decide the weights of each component in the scoring system (66), and the evaluation on how the cutting points of the scoring system could be established to categorize the population into levels of adherence to the Mediterranean diet (65).

This thesis has predominately focused on the association between dietary patterns, key food groups and cognitive health in older adults., Nutrition approaches for dementia prevention using oral supplementations have been investigated. According to WHO guidelines, vitamins B and E, polyunsaturated fatty acids and multi-complex supplementation should not be recommended for risk reduction of cognitive decline or dementia, (67); however, effects of nutrients from dietary sources on cognition need further investigation. The association between vitamin D and cognition is complex. Low vitamin D levels have been linked to poor cognition, but there is no evidence from interventional studies that vitamin D supplementation has a beneficial effect on cognition (68). Furthermore, generally among research on nutrition and cognition, methodological qualities of existing RCTs were generally low with small sample sizes. Future high-quality and larger-scale RCTs with longer durations are warranted; and it may be worth differentiating between well-nourished participants and participants with nutritional deficiencies, as the effects differ (69).

The mechanisms underpinning the link between the brain-healthy diet and cognition are

important. The Mediterranean diet, which is naturally lower in glycaemic load and rich in poly-/mono- unsaturated fat, was beneficial for cardiovascular risk reduction, thus benefiting cognition among older adults who are at high cardiovascular risk (70, 71). Similarly, the DASH diet is effective in managing hypertension (72), which may confer greater benefit in older people at higher cardiovascular risk, showing a significant association with better cognition (73). Another mechanism may be linked to anti-inflammatory effects from healthy diets or from the consumption of legumes and nuts; this needs further exploration (1). Long-term inflammation might damage the blood-brain barrier leading to cognitive impairment; higher levels of circulating inflammatory markers are associated with greater cognitive decline (74, 75). Importantly, for future research novel research methods should be applied as various diets may show different associations with cognition, depending on the type of dementia due to the varied underlying pathology.

For future mechanism study, association of diet with cognitive health, with respect to hallmark AD biomarkers (tau, amyloid) in cerebrospinal fluid (CSF), in blood, and in brain, should be further investigated. The core CSF biomarkers of neurodegeneration (such as total tau, phosphorylated tau, and the 42-aminoacid form of Aβ), CSF Neurofilament light protein (NFL), and plasma total tau were reported to be strongly associated with Alzheimer's disease (76, 77). Although limited, current research examined the effects of dietary intervention on plasma and CSF AD biomarkers, support that diet and nutrition may play important roles for nonpharmacological AD prevention (78-80). For future research on the underlying mechanisms and early effects of diets on AD pathogenesis, a biomarker-based selection of participants and long follow up are highly recommended (81, 82). Furthermore, using brain imaging techniques, healthier diets have been associated with brain volume and cortical thickness among older adults (82-84). For future studies, a variety of brain imaging modalities

could be effectively applied such as magnetic resonance imaging (MRI) and positron emission tomography (PET). These would assist in the investigation of the relationship between diet and pathological age-related brain changes (85), and facilitate development of effective disease-modifying therapies and preventative dietary strategies (86).

The brain-healthy diet from the gut-brain-axis perspective appears to be a promising area of research for dementia prevention (87). Imbalance in the gut microbiota composition, referred as dysbiosis, has been associated with several medical conditions, in the gastroenteric and other systems (88). During ageing, gut microbiota composition reduces in species richness, and age-related cognitive decline has been associated with dysbiosis (89, 90). The increased permeability of the gut and blood-brain barrier induced by microbiota dysbiosis may affect Alzheimer's disease pathogenesis (91). Moreover, gut-microbiota are a mediating factor between diet and physiology linked to cardiovascular risk factors which are associated with the development of dementia (92, 93). The gut–brain axis also mediates the neuroinflammatory response after a vascular injury and may be involved in vascular cognitive impairment (94). Dietary intervention, as one approach to modulate the gut microbiota, may prevent or delay cognitive impairment and dementia. Despite research findings supporting the gut–brain regulation of cognition from studies based on animal models of Alzheimer's disease and few preliminary human studies with small sample sizes (87, 90), the existing evidence is inadequate for making any clinical recommendations. Future research is needed both from observational and intervention studies to establish a rigorous link between ageing, gut microbiota and cognition (87).

Behavioural change studies are urgently needed, against a background of suboptimal intake of fruits and vegetables and increased alcohol intake according to the 1995 & 2011/12 Australian

national nutrition surveys (20, 21). Studies monitoring and analysing dietary intake are needed to reveal food quantity, quality and trends of dietary intake among older Australians. It is important to develop approaches to deal with feasibility and practicality issues for those groups with habitual Westernised diets and provide strategies to change to a more prudent or Mediterranean-like diet with higher legume and nut intakes (95). Behaviour change studies should investigate not only techniques such as self-monitoring, goal-setting, motivational interviewing and personalised dietary advice; but also broaden the scope of utilising information technologies, for example, smartphone applications to assist with monitoring and modifying health behaviours, and big data research to identify risk factors and promote changes for early dementia prevention (96, 97). Dietitians and researchers also need to collaborate to provide practical nutrition interventions, enhancing healthy changes towards better cognitive health. Moreover, research needs to take into consideration food availability and access, as well as financial, psychological and socio-cultural factors, using larger-scale dietary intervention trials to help establish feasible and longer-term approaches for cognitive health among older adults in Australia (95, 98). As multiple-behaviour interventions are suggested to have a greater impact than single behaviour intervention (99), incorporating other lifestyle modification such as physical activity and cognitive activity are also important; and correlations between diet, physical activity and cognitive activities need to be further explored in future studies.

7.5 Conclusion to chapters and thesis

This research has shown that healthy dietary patterns are a promising approach for prevention of dementia and maintaining cognitive health and recommends future specific guidelines for better cognitive health in older adults. Continuing research including large-scale longitudinal studies and RCTs to investigate brain healthy diets and foods have been recommended, to consolidate research and elucidate the underlying mechanisms between diet, nutrition and

cognition.

In future, to promote cognitive health and slow down age-related cognitive decline, higher quality research on dietary patterns and nutrients, as well as underlying mechanisms of brain healthy diets are required. Behavioural change research is needed to determine best practice methods to enhance uptake of healthy diets. Dietitians and researchers need to collaborate for practical nutrition interventions to enhance healthy changes towards better cognitive health. A multidisciplinary team approach involving dietitians is highly recommended for dementia prevention. A specific dietary guide should be established for improving cognitive function and dementia prevention among Australian adults, based on best available evidence. Earlier preventative interventions are highly recommended.

7.6 References

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Appendix A. Supplementary material of manuscript "Dietary Patterns and Cognitive Health in Older Adults: A Systematic Review"

Supplementary Table 1. Quality assessment of cohort studies included in the review (SIGN50)

	Journal Article	**Journal Article**	**Journal Article**
Sign 50 Checklist	Feart et al. (2009) [1]	Trichopoulou et al. (2015) [2]	Galbete et al. (2015) [3]
1.1 Research question clearly defined and stated?	Yes	Yes	Yes
1.2 Source populations are described and comparable?	Yes	Yes	Yes
1.3 Are participation rates recorded?	Yes	Yes	Yes
1.4 Evaluates if study outcomes were present at the time of enrolment?	Can't Say	Yes	Yes
1.5 What was the dropout rate?	24%	50.9%	24%
1.6 Comparison between full participants and those lost to follow-up by exposure	Can't Say	No	No
1.7 The outcomes are clearly defined?	Yes	Yes	Yes
1.8 Is assessment of outcome made blind to exposure status?	Can't Say	Can't say	Can't say
1.9 Recognised limitations of non-blinding?	N/A	Can't say	No
1.10 The method of assessment of exposure is reliable?	Yes	Yes	N/A
1.11 The method of outcome assessment is valid and reliable?	Yes	Yes	No
1.12 Exposure level is assessed more than once?	No	No	No
1.13 The main confounders are identified?	Yes	Can't say	Yes
1.14 Have confidence intervals been provided?	Yes	Yes	Yes
2.1 How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)	Acceptable (+)	Acceptable (+)

	Journal Article	**Journal Article**	**Journal Article**	**Journal Article**
Sign 50 Checklist	Kesse-Guyot et al. (2013) [4]	Vecambre et al. (2012) [5]	Samieri et al. (2013) [6]	Cherbuin et al. (2012) [7]
1.1 Research question clearly defined and stated?	Yes	Yes	Yes	Yes
1.2 Source populations are described and comparable?	Yes	Yes	Yes	Yes
1.3 Are participation rates recorded?	Yes	Yes	Yes	Yes
1.4 Evaluates if study outcomes were present at the time of enrolment?	Can't Say	No	Can't Say	Yes
1.5 What was the dropout rate?	54.9%	17.0%	18.0%	40.1%
1.6 Comparison between full participants and those lost to follow-up by exposure	Can't Say	No	No	No
1.7 The outcomes are clearly defined?	Yes	Yes	Yes	Yes
1.8 Is assessment of outcome made blind to exposure status?	Can't Say	Can't Say	No	Yes
1.9 Recognised limitations of non-blinding?	Can't Say	Can't Say	No	N/A
1.10 The method of assessment of exposure is reliable?	Yes	Yes	Yes	No
1.11 The method of outcome assessment is valid and reliable?	Yes	Yes	Yes	Yes
1.12 Exposure level is assessed more than once?	Yes	No	Yes	Yes
1.13 The main confounders are identified?	Yes	Yes	Yes	Yes
1.14 Have confidence intervals been provided?	Yes	Yes	Yes	Yes
2.1 How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)	Acceptable (+)	High Quality (++)	High Quality (++)

	Journal Article	**Journal Article**	**Journal Article**	**Journal Article**
Sign 50 Checklist	Olsson et al. (2015) [8]	Haring et al. (2016) [9]	Tangney et al. (2011) [10]	Koyama et al. (2015) [11]
1.1 Research question clearly defined and stated?	Yes	Yes	Yes	Yes
1.2 Source populations are described and comparable?	Yes	Yes	Yes	Yes
1.3 Are participation rates recorded?	Yes	Yes	Yes	Yes
1.4 Evaluates if study outcomes were present at the time of enrolment?	Can't say	Yes	Yes	Can't say
1.5 What was the dropout rate?	38%	3%	51.4%	14.9%
1.6 Comparison between full participants and those lost to follow-up by exposure	Can't say	Yes	No	No
1.7 The outcomes are clearly defined?	Yes	Yes	Yes	Yes
1.8 Is assessment of outcome made blind to exposure status?	Can't say	Can't say	Can't Say	Can't say
1.9 Recognised limitations of non-blinding?	Can't say	Can't say	N/A	Can't say
1.10 The method of assessment of exposure is reliable?	Yes	Yes	No	Yes
1.11 The method of outcome assessment is valid and reliable?	Can't say	Yes	Yes	Yes
1.12 Exposure level is assessed more than once?	No	No	Yes	No
1.13 The main confounders are identified?	Yes	Can't say	No	Yes
1.14 Have confidence intervals been provided?	Yes	Yes	Yes	Yes
2.1 How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)	High Quality (++)	Acceptable (+)	Acceptable (+)

	Journal Article	**Journal Article**	**Journal Article**	**Journal Article**
Sign 50 Checklist	Gardener et al. (2015) [12]	Bhushan et al. (2017) [13]	Scarmeas et al. (2006) [14]	Scarmeas et al. (2009) [15]
1.1 Research question clearly defined and stated?	Yes	Yes	Yes	Yes
1.2 Source populations are described and comparable?	Yes	Yes	Yes	Yes
1.3 Are participation rates recorded?	Yes	Yes	Yes	Yes
1.4 Evaluates if study outcomes were present at the time of enrolment?	Yes	No	Yes	Yes
1.5 What was the dropout rate?	Can't say	9.9 %	45.8%	20.7%
1.6 Comparison between full participants and those lost to follow-up by exposure	Can't say	No	Yes	Can't Say
1.7 The outcomes are clearly defined?	Yes	Yes	Yes	Yes
1.8 Is assessment of outcome made blind to exposure status?	Can't say	Can't say	Yes	No
1.9 Recognised limitations of non-blinding?	No	No	N/A	No
1.10 The method of assessment of exposure is reliable?	Yes	Yes	No	Yes
1.11 The method of outcome assessment is valid and reliable?	Yes	Can't say	Yes	Yes
1.12 Exposure level is assessed more than once?	No	Yes	Can't Say	Can't Say
1.13 The main confounders are identified?	Yes	Yes	Yes	Yes
1.14 Have confidence intervals been provided?	No	Yes	Yes	Yes
2.1 How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)	Acceptable (+)	High Quality (++)	High Quality (++)

	Journal Article	**Journal Article**	**Journal Article**	**Journal Article**
Sign 50 Checklist	Gu et al. (2010a) [16]	Tsivgoulis et al. (2013) [17]	Morris et al. (2015a) [18]	Qin et al. (2015) [19]
1.1 Research question clearly defined and stated?	Yes	Yes	Yes	Yes
1.2 Source populations are described and comparable?	Yes	Yes	Yes	Yes
1.3 Are participation rates recorded?	Yes	Yes	Yes	Yes
1.4 Evaluates if study outcomes were present at the time of enrolment?	Yes	Yes	Yes	Yes
1.5 What was the dropout rate?	49%	42%	29 %	31.5 %
1.6 Comparison between full participants and those lost to follow-up by	No	Yes	No	No
1.7 The outcomes are clearly defined?	Yes	Yes	Yes	Yes
1.8 Is assessment of outcome made blind to exposure status?	Can't Say	Yes	Can't say	Can't say
1.9 Recognised limitations of non-blinding?	No	N/A	Can't say	No
1.10 The method of assessment of exposure is reliable?	Yes	No	Yes	Can't say
1.11 The method of outcome assessment is valid and reliable?	Yes	Yes	Yes	Yes
1.12 Exposure level is assessed more than once?	No	Can't Say	No	No
1.13 The main confounders are identified?	Yes	Yes	Yes	Yes
1.14 Have confidence intervals been provided?	Yes	Yes	Yes	Yes
2.1 How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)	High Quality (++)	High Quality (++)	Acceptable (+)

	Journal Article	**Journal Article**	**Journal Article**	**Journal Article**
Sign 50 Checklist	Brendenson et al. (2017a) [20]	Morris et al. (2015b) [21]	Brendenson et al. (2017b) [22]	Ozawa et al. (2017) [23]
1.1 Research question clearly defined and stated?	Yes	Yes	Yes	Yes
1.2 Source populations are described and comparable?	Yes	Yes	Yes	Yes
1.3 Are participation rates recorded?	Yes	Yes	Yes	Yes
1.4 Evaluates if study outcomes were present at the time of enrolment?	No	Yes	No	Yes
1.5 What was the dropout rate?	16.8%	29%	17.3 %	35.4%
1.6 Comparison between full participants and those lost to follow-up by exposure	No	No	No	Can't Say
1.7 The outcomes are clearly defined?	Yes	Yes	Yes	Yes
1.8 Is assessment of outcome made blind to exposure status?	Can't Say	Can't say	Can't Say	No
1.9 Recognised limitations of non-blinding?	Can't Say	Can't say	Can't Say	No
1.10 The method of assessment of exposure is reliable?	Can't say	Yes	Yes	Yes
1.11 The method of outcome assessment is valid and reliable?	Yes	Yes	Yes	Yes
1.12 Exposure level is assessed more than once?	Yes	No	Yes	Yes
1.13 The main confounders are identified?	Yes	Yes	Yes	Yes
1.14 Have confidence intervals been provided?	Yes	Yes	Yes	Yes
2.1 How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)	High Quality (++)	High Quality (++)	High Quality (++)

	Journal Article	**Journal Article**	**Journal Article**	**Journal Article**
Sign 50 Checklist	Hayden et al. (2017) [24]	Wengreen et al. (2009) [25]	Symth et al. (2015) [26]	Shakersain et al. (2016) [27]
1.1 Research question clearly defined and stated?	Yes	Yes	Yes	Yes
1.2 Source populations are described and comparable?	Yes	Yes	Yes	Yes
1.3 Are participation rates recorded?	Can't say	Yes	Yes	Yes
1.4 Evaluates if study outcomes were present at the time of enrolment?	Yes	Yes	Yes	Yes
1.5 What was the dropout rate?	5.3%	23.3%	10%	14.6%
1.6 Comparison between full participants and those lost to follow-up by exposure	No	Can't Say	No	Yes
1.7 The outcomes are clearly defined?	Yes	Yes	Yes	Yes
1.8 Is assessment of outcome made blind to exposure status?	Can't say	No	Can't say	Can't say
1.9 Recognised limitations of non-blinding?	No	No	Can't say	Can't say
1.10 The method of assessment of exposure is reliable?	Yes	Yes	Can't say	Yes
1.11 The method of outcome assessment is valid and reliable?	Yes	Yes	Yes	Yes
1.12 Exposure level is assessed more than once?	No	Yes	No	No
1.13 The main confounders are identified?	Yes	Yes	Yes	Yes
1.14 Have confidence intervals been provided?	Yes	No	Yes	Yes
2.1 How well was the study done to minimise the risk of bias or confounding?	Acceptable (+)	High Quality (++)	Acceptable(+)	High Quality (++)

	Journal Article	**Journal Article**	**Journal Article**	**Journal Article**
Sign 50 Checklist	Jacka et al. (2015) [28]	Gu et al. (2010b) [29]	Granic et al. (2016) [30]	Chen et al. (2017) [31]
1.1 Research question clearly defined and stated?	Yes	Yes	Yes	Yes
1.2 Source populations are described and comparable?	Yes	Yes	Yes	Yes
1.3 Are participation rates recorded?	Yes	Yes	Yes	Yes
1.4 Evaluates if study outcomes were present at the time of enrolment?	Yes	Yes	Yes	Yes
1.5 What was the dropout rate?	30.7%	37.5%	41.7% 3rd /58.5% 5th	21.5%
1.6 Comparison between full participants and those lost to follow-up by exposure	No	No	No	No
1.7 The outcomes are clearly defined?	Yes	Yes	Yes	Yes
1.8 Is assessment of outcome made blind to exposure status?	Yes	Can't Say	No	Can't say
1.9 Recognised limitations of non-blinding?	N/A	No	Can't say	Can't say
1.10 The method of assessment of exposure is reliable?	Yes	Yes	Yes	Yes
1.11 The method of outcome assessment is valid and reliable?	Yes	Yes	Yes	Yes
1.12 Exposure level is assessed more than once?	No	No	No	No
1.13 The main confounders are identified?	Yes	Yes	Yes	Yes
1.14 Have confidence intervals been provided?	Yes	Yes	Yes	Yes
2.1 How well was the study done to minimise the risk of bias or confounding?	High Quality (++)	Acceptable (+)	Acceptable (+)	Acceptable (+)

Supplementary Table 2. Food Components in Dietary Patterns

Dietary Pattern	Food components and frequency
Mediterranean diet [32]	High consumption of plant-based foods- fruits (3 serves per day or more) and nuts (3 serves per week or more), vegetables (2 serves per day or more), legumes (3 serves per day or more) and minimally processed cereals Moderate-to-high consumption of fish (3 serves per week or more) and seafood (2 serves per week or more) Low consumption of butter or other dairy products and meat or meat products (1 serve per day or less) Regular but moderate intake of alcohol, preferentially red wine during meals Use of olive oil as main culinary fat (4 TBS or more per day)
Modified Mediterranean diet (Chinese) [19]	High consumption of plant-based foods, tofu, peas, beans, peanuts; vegetables e.g. Chinese cabbage, bok choy, celery, spinach, Chinese chive, lettuce, radish High consumption of fibre-rich grains, corn grain, yellow corn flour, corn grits, barley grain, buckwheat Limited cooking oil from animal source including Lard, butter, sheep fat, beef tallow Moderate consumption of alcohol including beer, rice wine, grape wine, liquor
MIND diet [22]	Higher intake of green leafy vegetables (spinach, lettuce, kale), other vegetables (7 serves vegetables or more per week), berries (blueberries, strawberries) (2 serves or more per week), nuts (5 serves or more per week), whole grains (3 serves or more per day), fish (1 serve or more per week), beans (3 serves or more per week), poultry (2 serves or more per week), limited intake of wine (red and white wine, 1 serve or less per day), and use of olive oil as primary source of fat; lower intakes of butter and margarine, cheese, red meat and products, fast fried foods (less than 1 serve per week), and pastries and sweets (less than 5 serves per week)
Prudent healthy diet [27]	Frequent intake of fruits, vegetables, cooking oil/dressing oil, cereals and legumes, whole grains, rice, pasta, fish, low fat dairy, poultry and water
Western diet [27, 30]	Frequent intake of processed meat, saturated/trans-fat, refined grains, sugar, beer and spirits
Inflammatory Diet [33, 34]	High intake of red meat, processed meat, peas and legumes, and fried food Low intake of whole grains
DASH diet [20, 35]	High consumption of fruits (4-5 serves per day), vegetables (4-5 serves per day), whole grains, poultry, fish, nuts, low fat dairy (2-3 serves per day)

	Low consumption of fats, red meat, processed meat, sugar sweetened beverage and desserts. Low added salt (2300 mg or less per day)
Low GI diet [36]	Glycaemic index <55 low GI food items include whole grains, legumes, non-starchy vegetables, most fruits (except for watermelon, rockmelon, lychee), dairy foods
Healthy Eating Index (HEI)/Healthy diet indicator (HDI) [9, 37]	High consumption of fruits, vegetables, whole grains, low fat dairy, fish and lean meats

Supplementary Table 3. Summary of recent systematic reviews (2015-2017)

Author Year	Title	Dietary patterns discussed	Type of studies	Key findings
Aridi et al. 2017 [32]	The Association between the Mediterranean Diet and Cognitive Health: A Systematic Review	Mediterranean diet	7 Cross-sectional 22 Cohort 2 RCT	Cohort studies in the Mediterranean region and RCTs showed consistent beneficial effects of the Mediterranean Diet on cognitive function
Loughrey et al. 2017 [38]	The Impact of the Mediterranean Diet on the cognitive functioning of healthy older adults: a systematic review and meta-analysis	Mediterranean diet In healthy older adults	15 Cohort 2 RCT	The strongest evidence suggests a beneficial effect of the Mediterranean Diet on older adults' global cognition.
Berendsen et al. 2017 [39]	Association of adherence to a Healthy diet with cognitive decline in European and American older adults: a meta-analysis within	Healthy diet Indicator (HDI)	3 Cohort From the CHANCES Consortium	A higher HDI score was not related to reduced rates of cognitive decline in European and American older adults
Yusufov et al. 2017 [40]	Alzheimer's disease and diet: a systematic review	Mediterranean diet Multi-nutrient	9 Cross-sectional 6 Case-control 46 Cohort 2 retrospective 1 RCT	Inconsistent findings with respect to sample size, AD diagnosis and food measures.
Masana et al. 2017 [41]	N-3 fatty acids, Mediterranean diet and cognition in normal	Mediterranean diet	3 Cross-sectional 15 cohort 5 RCT	Adherence to Mediterranean Diet significantly associated with better cognitive performance and less cognitive decline.

	aging: A systematic review			Better cognitive performance in men compared to women.
Milte et al. 2016 [42]	Dietary patterns and successful aging: a systematic review	Whole-diet approach Mediterranean diet Healthy diet Fruit and vegetable rich diet/DASH diet Western diet High processed food	11 Cross-sectional 23 Cohort	Although dietary pattern and outcome assessment methods varied, most studies reported positive association between a healthier diet and better health outcomes.
Knight et al. 2016 [43]	Is the Mediterranean diet a feasible approach to preserving cognitive function and reducing risk of dementia for older adults in western countries? New insights and future directions	Mediterranean diet vs. Western diet	3 Cross-sectional 9 Cohort 2 RCT	Demonstrated evidence the Mediterranean Diet as a potential strategy to reduce cognitive decline while the Western diet may play a role in the aetiology of cognitive decline. However, intrinsic Western socio-cultural values and traditions may impact the feasibility.
Knight et al. 2017 [44]	The Mediterranean diet and age-related cognitive functioning: A systematic review of study findings and neuropsychological assessment methodology	Mediterranean diet	4 Cross-sectional 11 Cohort	Conflicting results of Mediterranean Diet efficacy found. Clear study differences in neuropsychological assessments are probable contributor to the lack of consistency
Petersson et al. 2016 [45]	Mediterranean diet, cognitive function, and dementia: a systematic review of the evidence	Mediterranean diet	21 Cross-sectional 6 Cohort 5 RCT	Adherence to the Mediterranean Diet is associated with better cognitive performance. However, the

				majority of findings come from epidemiologic studies that provide evidence not for a cause-and-effect relation.
Hardman et al. 2016 [46]	Adherence to a Mediterranean-style diet and effects on cognition in adults: a qualitative evaluation and systematic review of longitudinal and prospective trials	Mediterranean diet	4 RCT 13 Cohort	Higher adherence to a Mediterranean Diet is associated with slower cognitive decline, reduced conversion to AD, and improvements in cognitive function. Domains were memory, executive function, and visual constructs.
Cao et al. 2015 [47]	Dietary patterns and risk of dementia: a systematic review and meta-analysis of cohort studies	Mediterranean diet, fish, unsaturated fat, antioxidants, B vitamins, vitamin D, drinking, smoking, vegetable and fruit, and aluminium	43 cohort	Mediterranean Diet and higher consumption of unsaturated fatty acids, antioxidants, and B vitamins decrease the risk of dementia while smoking and higher consumption of aluminium increase the risk.
Solfrizzi et al. 2017 [48]	Relationships of dietary patterns, foods, and micro- and macronutrients with Alzheimer's disease and late-life cognitive disorders: a systematic review	Mediterranean diet DASH diet MIND diet Food groups	15 Cross-sectional 32 Cohort	Mediterranean/DASH/MIND diet was associated with decreased cognitive decline. Negative correlation of cognitive functions with saturated fatty acids and a protective effect against cognitive decline of elevated fish consumption, high intake of MUFA/PUFA

Supplementary Table 4: PRISMA 2009 Checklist [49]

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3-7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7-8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7-8
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	9-10
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7-8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8-10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	37-55
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8-10

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8-9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8-9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10-25
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	11-12
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11-24
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	37-55
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	11-12
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	25-31
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	25-31
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	32
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

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Appendix B. Supplementary material of manuscript "Dietary Patterns and Cognitive Health in Older Adults: Findings from the Sydney Memory and Ageing Study"

Supplementary table 1. Comparisons between Mediterranean score construction system

	0-9 system by Trichopoulou[1]	0-55 system by Panagiotakos[2]
All food groups	**9 Food groups** Non-refined cereals/grains Fruits and nuts Vegetables Legumes Fish Red and processed meat Dairy products Mono-unsaturated : saturated fat ratio Alcohol	**11 Food groups** Non-refined cereals/grains Potatoes Fruits Vegetables Legumes and nuts Fish Red and processed meat Poultry Full fat dairy products Mono-unsaturated : Saturated fat ratio Alcohol
Detrimental factors	Dairy foods, Red and Processed meat Alcohol intake (Little or excessive)	Full fat Dairy foods, Red and Processed meat, Poultry, Alcohol intake
Scoring strategy	Value of one is given if consumption of a beneficial group is at or above sex-specific median, or if consumption of a detrimental group is below sex-specific median, or if alcohol intake is mild to moderate.	Value from 0 to 5 in ascending order with increased consumption of a beneficial food group, reverse scoring for detrimental food groups [1].
Food Measurements	gram/day	servings/day

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Supplementary table 2. Scoring criteria according to Dietary Guidelines Index (DGI) -2013 for Australian Healthy Eating Guideline adherence using DQES[1-3]

Dietary Guideline	Indicator and description	Criteria for Maximum Score	Minimum Score	Maximum score
Enjoy a wide variety of nutritious foods	Food variety: 2 points awarded for each of the five food groups when at least one serving was consumed per day of that group.	Consumption of at least one serve from each food group	0	10
Eat plenty of vegetables and fruits	Servings of vegetables and legumes per day: (tomato, capsicum, lettuce, cucumber, celery, beetroot, carrot, cabbage, cauliflower, broccoli, spinach, green beans, bean sprouts, pumpkin, onion, garlic, mushroom, zucchini, avocado, potato, peas, baked beans, tofu, other beans)	>70 year: M ≥5, F ≥ 5 serves/day	0	10
	Servings of fruits per day (including tinned fruit, fruit juice, orange, apple, pear, banana, melon, pineapple, strawberry, apricot, peach, mango)	>=2 serves/day	0	10
Eat plenty of cereals (including breads, rice, pasta, and noodles), preferably whole-grain	Consumption of breads and cereals per day (All-Bran, bran flakes, weetbix, cornflakes, porridge, muesli, rice, pasta, and bread including high fibre white bread, white bread, wholemeal bread, rye bread, multi-grain bread)	>70 year: M ≥4.5, F ≥3 serves/day	0	5
	Proportion of whole grain/high fibre cereal consumed relative to total cereal.	100%	0	5
Include lean meat, fish, poultry, and/or alternatives (including tofu,	Consumption of meats and alternatives per day (beef, veal, chicken, lamb, pork, fish, eggs, baked beans,	>70 year: M ≥2.5, F ≥ 2 serves/day	0	10

egg, nuts and seeds, legumes)	soybean/tofu, other beans, peas, nuts, peanut butter)			
Include milks, yoghurts, cheeses, and/or alternatives Reduced-fat varieties should be chosen, where possible	Consumption of dairy products per day, including cheese (hard cheese, firm cheese, soft cheese, ricotta cheese, cottage cheese, cream cheese, low-fat cheese), yoghurt, milk (full cream, reduced fat milk, skim milk, and soya milk).	>70 year: M ≥ 3.5, F ≥ 4 serves/day	0	5
	Low-fat/reduced-fat dairy to total dairy ratio	100%	0	5
Limit saturated fat and moderate total fat intake, small allowance of unsaturated oils, fats or spreads	Total poly and mono unsaturated fat intake to total fat ratio	100%	0	10
Prevent weight gain: eat according to your energy needs, limit discretionary foods containing saturated fat, alcohol, added salt, and added sugars	Consumption of total Energy-dense foods/fluids that are not essential for nutrient requirements and contain too much fat, sugar, and salt. Such as soft drinks, cordials, fruit juice drinks, mayonnaise and dressing, chips, jam, confectionery, chocolate, hamburgers, hot chips, meat pies, pizza, cakes and muffins, pies and pastries, puddings, ice cream, cream, biscuits, and all alcoholic beverages	>70 year: M = 0, F = 0 serves/day	0 for M ≥3 0 for F ≥2.5	20

Notes: M, male; F, female.

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Supplementary Table 3. Food group composition for Principle Component Analysis(PCA)

Whole grains	**Refined grains**	**Red meat**	**Processed meat**	**Cakes and biscuits**
high fiber white-bread wholemeal bread rye bread multigrain bread all bran/sultana bran bran flakes muesli/ or with fibre Weetbix/ porridge Vitabrits/Weeties	white bread crackers crispbread/crisps dry biscuits cornflakes special k rice pasta noodles	beef veal lamb pork	bacon ham sausage salami	cakes sweet biscuits
Fresh Fruit	**Yellow vegetables**	**Green leafy vegetables**	**Cruciferous vegetables**	**Other vegetables**
apple pear banana melon pineapple strawberry apricot peach mango orange	carrots pumpkin	lettuce spinach	broccoli cauliflower cabbage	capsicum celery beetroot cucumber green beans bean sprouts zucchini onion mushroom
Legumes	**Low fat dairy**	**Margarine**	**Butter**	**Nuts**
baked beans peas other beans	low fat cheese skim milk reduced fat milk cottage cheese ricotta cheese	margarine poly-/mono-unsaturated fat margarine	butter	nuts peanut butter
Poultry - chicken	**Meat pies**	**Pizza**	**Hamburger**	**Chocolate**
Eggs	**Flavoured milk**	**Fish**	**Fried fish**	**Tinned fish**
Tofu	**Fruit juice**	**Tinned fruit**	**Chips**	**Potatoes**
Garlic	**Avocado**	**Tomato sauce**	**Tomato**	**Soy milk**
Vegemite	**Jam**	**Added sugar**	**Butter and margarine blend**	

Supplementary Table 4. Dietary pattern scores and food group characteristics (Mean±SD): Sydney Memory and Ageing Study (N=819)

Dietary pattern	Score/ Food groups	All (N=819) Mean±SD	Female(N=459) Mean±SD	Male(N=360) Mean±SD	P value*
Mediterranean diet (score range 0-9)	**MED score**	4.3±1.7	4.3±1.7	4.4±1.7	0.292
Food group grams/day	Fruits/Nuts	310.2±173.1	284.1±152.3	343.5±191.7	<0.001*
	Vegetables	98.6±51.9	102.0±52.4	94.4±50.9	0.036*
	Legume	17.7±16.9	15.8±15.3	20.1±18.5	<0.001*
	Cereal	188.4±110.1	167.8±98.4	214.7±118.3	<0.001*
	Dairy foods	362.8±193.7	371.3±187.6	352.0±201.0	0.159
	Red / Processed meat	75.3±76.7	58.1±54.1	97.3±94.0	<0.001*
	Fish	39.2±57.5	34.1±60.9	45.7±52.2	0.004*
	Alcohol	16.2±19.9	9.8±12.9	22.4±23.8	<0.001*
	MUFA:SFA	0.9±0.2	0.9±0.2	0.9±0.2	0.339
Mediterranean diet (score range 0-55)	**MED score**	30.9±4.6	27.5±6.2	27.9±6.3	0.351
Panagiotakos Food group grams/day	Fruits	304.4±171.4	279.1±150.6	336.9±190.2	<0.001*
	Vegetables	98.6±51.9	102.0±52.4	94.4±50.9	0.036*
	Legume/ Nuts	23.4±19.9	20.8±18.4	26.7±21.1	<0.001*
	Potato	34.1±35.0	31.4±32.4	37.4±37.8	0.014*
	Whole Grain	118.2±92.9	111.6±87.0	126.6±99.5	0.024*
	Full fat Dairy	162.5±182.3	156.3±174.7	170.4±201.8	0.187

	Red / Processed meat	75.3±76.7	58.1±54.1	97.3±94.0	<0.001*
	Poultry	21.1±24.9	20.4±29.1	22.0±18.3	0.359
	Fish	39.2±57.5	34.1±60.9	45.7±52.2	0.004*
	Alcohol	16.2±19.9	9.8±12.9	22.4±23.8	<0.001*
	MUFA:SFA	0.9±0.2	0.9±0.2	0.9±0.2	0.339
DASH diet (score range 9-45)	**DASH score**	27.0±4.1	27.3±4.0	26.6±4.2	0.014*
Food group grams/day	Fruits	304.4±171.4	279.1±150.6	336.9±190.2	<0.001*
	Vegetables	98.6±51.9	102.0±52.4	94.4±50.9	0.036*
	Legume/ Nuts	23.4±19.9	20.8±18.4	26.7±21.1	<0.001*
	Whole Grain	118.2±92.9	111.6±87.0	126.6±99.5	0.024*
	Low fat Dairy	200.3±206.2	215.0±202.7	181.6±209.5	0.021*
	Red / Processed meat	75.3±76.7	58.1±54.1	97.3±94.0	<0.001*
	MUFA+PUFA	31.7±12.9	28.1±11.2	36.4±13.6	<0.001*
	Sugar	82.9±31.7	77.6±28.7	89.7±34.0	<0.001*
	Sodium (mg)	1989.4±833.5	1774.5±739.6	2266.5±866.5	<0.001*
DGI 2013 (score range 0-90)	**DGI score**	43.4±10.0	44.1±10.2	42.5±9.7	0.029*
Food group serves/day	Fruits	1.6±0.9	1.5±0.8	1.7±1.0	0.028*
	Vegetables	2.0±1.0	2.0±1.0	2.0±1.1	0.633
	Grains and cereals	4.1±1.8	2.4±1.5	4.7±1.8	<0.001*
	Dairy products or alternatives	1.7±0.8	1.8±0.8	1.7±0.8	0.183
	Lean meats or alternatives	2.0±1.5	1.7±1.3	2.4±1.6	<0.001*
	Discretionary foods	3.8±2.5	2.9±1.8	4.9±2.8	

Notes: MED, Mediterrean diet; DASH, Dietary approaches to stop hyptertension; DGI, Dietary guideline index; MUFA, Mono-unsaturated fatty acids; PUFA, Poly-unsaturated fatty acids; SFA, Saturated fatty acids. SD, Standard deviation. Statistical significance by gender using independent sample t test. *P < 0.05 is significant.

Supplementary table 5. Alcohol consumption among male and female participants: Sydney Memory and Ageing Study (N=819)

Alcohol intake	**All(N=819)** gram per day	**Female(N=459)** gram per day	**Male(N=360)** gram per day
Mean±SD	16.2±19.9	9.8±12.9	24.4±23.8
1st quartile	0-1.0	0-0.5	0-4.3
2nd quartile	1.0-9.2	0.5-4.8	4.3-18.9
3rd quartile	9.2-24.3	4.8-14.3	18.9-35.9
4th quartile	24.3-109.0	14.3-12.9	35.9-109.0

Notes: SD, Standard deviation.

Supplementary Table 6. Associations of dietary scores with cognition in a basic model: Sydney Memory and Ageing Study (N=819)

Cognition Domains-model1	Dietary Scores	β	95% CI		*P value*
Global Cognition	Mediterranean score (0-55 system)	0.003	0.015	0.020	0.767
	Mediterranean score (0-9 system)	-0.027	-0.074	0.021	0.273
	DASH score	0.001	-0.018	0.021	0.905
	DGI score	-0.001	-0.009	0.007	0.867
Attention/Processing speed	Mediterranean score (0-55 system)	-0.003	-0.019	0.014	0.734
	Mediterranean score (0-9 system)	-0.038	-0.085	-0.007	0.104
	DASH score	-0.005	-0.024	0.014	0.600
	DGI score	0.000	-0.007	0.008	0.989
Language	Mediterranean score (0-55 system)	-0.001	-0.020	0.019	0.945
	Mediterranean score (0-9 system)	0.010	-0.064	0.044	0.719
	DASH score	-0.003	-0.025	0.019	0.787
	DGI score	-0.002	-0.010	0.007	0.724
Executive	Mediterranean score (0-55 system)	0.001	-0.017	0.018	0.951
	Mediterranean score (0-9 system)	-0.017	-0.067	0.033	0.505
	DASH score	0.001	-0.019	0.021	0.922
	DGI score	0.000	-0.008	0.008	0.986
Visuospatial	Mediterranean score (0-55 system)	0.013	-0.002	0.028	0.091
	Mediterranean score (0-9 system)	-0.005	-0.047	0.037	0.808
	DASH score	0.003	-0.014	0.020	0.699
	DGI score	0.005	-0.002	0.012	0.177
Memory	Mediterranean score (0-55 system)	-0.005	-0.021	0.011	0.536
	Mediterranean score (0-9 system)	-0.022	-0.067	0.024	0.347
	DASH score	0.002	-0.017	0.020	0.842
	DGI score	-0.006	-0.014	0.001	0.106
Verbal memory	Mediterranean score (0-55 system)	-0.006	-0.022	0.010	0.454
	Mediterranean score (0-9 system)	-0.027	-0.073	0.018	0.238
	DASH score	0.004	-0.014	0.022	0.679
	DGI score	-0.006	-0.014	0.001	0.094

Notes: DASH,Dietary approaches to stop hyptertension; DGI, Dietary guideline index; CI, Confidence Interval.

Values are *β*(95% CI), *n* = 819. *P value<.05 is significant for global cognition and p <.01 for subdomains. *β* - Coefficients show a 1 score increase in dietary pattern adherence score is associated with higher cognitive score (positive *β*) or lower cognitive score (negative *β*). CI=Confidence Interval.

Results were based on a basic model with adjustment for age, gender and education.

Supplementary Table 7. Associations of dietary pattern scores and cognition at baseline after full adjustment: Sydney Memory and Ageing Study (N=819)

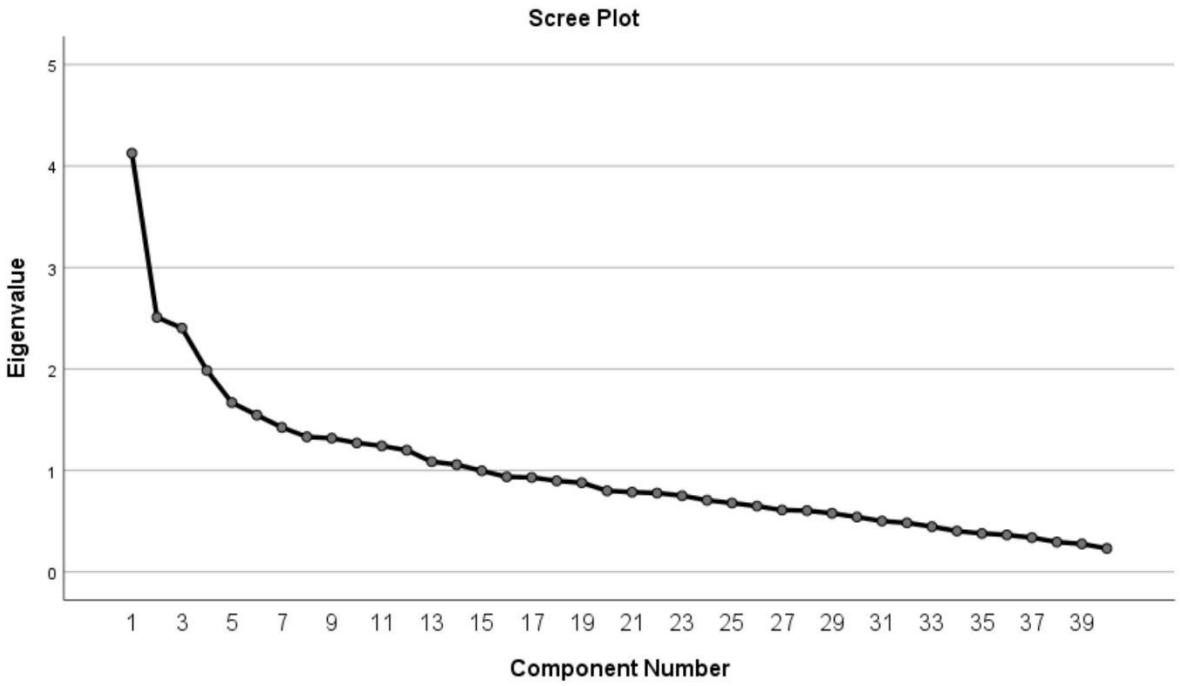
Cognition Domains-model2	Dietary Scores	β	95% CI		*P value*
Global Cognition	Mediterranean score (0-55 system)	0.030	-0.004	0.064	0.084
	Mediterranean score (0-9 system)	-0.005	-0.098	0.088	0.918
	DASH score	0.013	-0.024	0.050	0.481
	DGI score	-0.003	-0.018	0.013	0.757
Attention/Processing speed	Mediterranean score (0-55 system)	0.017	-0.017	0.052	0.316
	Mediterranean score (0-9 system)	-0.046	-0.138	-0.046	0.328
	DASH score	0.000	-0.037	0.036	0.985
	DGI score	0.001	-0.015	0.017	0.914
Language	Mediterranean score (0-55 system)	0.016	-0.024	0.056	0.431
	Mediterranean score (0-9 system)	0.003	-0.105	0.111	0.958
	DASH score	-0.002	-0.046	0.043	0.942
	DGI score	-0.012	-0.031	0.006	0.190
Executive	Mediterranean score (0-55 system)	0.015	-0.021	0.052	0.415
	Mediterranean score (0-9 system)	-0.010	-0.109	0.088	0.837
	DASH score	0.015	-0.024	0.053	0.455
	DGI score	-0.003	-0.019	0.014	0.759
Visuospatial	Mediterranean score (0-55 system)	0.045	0.017	0.072	**0.002***
	Mediterranean score (0-9 system)	0.086	0.008	0.164	0.030
	DASH score	0.053	0.023	0.083	**0.001***
	DGI score	0.011	-0.003	0.025	0.110
Memory	Mediterranean score (0-55 system)	0.007	-0.028	0.041	0.694
	Mediterranean score (0-9 system)	-0.037	-0.124	0.050	0.405
	DASH score	-0.007	-0.044	0.031	0.728
	DGI score	-0.007	-0.023	0.009	0.412
Verbal memory	Mediterranean score (0-55 system)	0.009	-0.026	0.045	0.596
	Mediterranean score (0-9 system)	-0.041	-0.128	0.045	0.348
	DASH score	-0.005	-0.042	0.033	0.810
	DGI score	-0.005	-0.021	0.011	0.558

Notes: CI, Confidence Interval. Values are *β*(95% CI), *n* = 819. *β* - Coefficients show a 1 unit score increase in dietary pattern adherence score is associated with higher cognitive score (positive *β*) or lower cognitive score (negative *β*). Results were fully adjusted with age, gender, education, as well as physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype. *P value<.05 is significant for global cognition and p <.01 for subdomains.

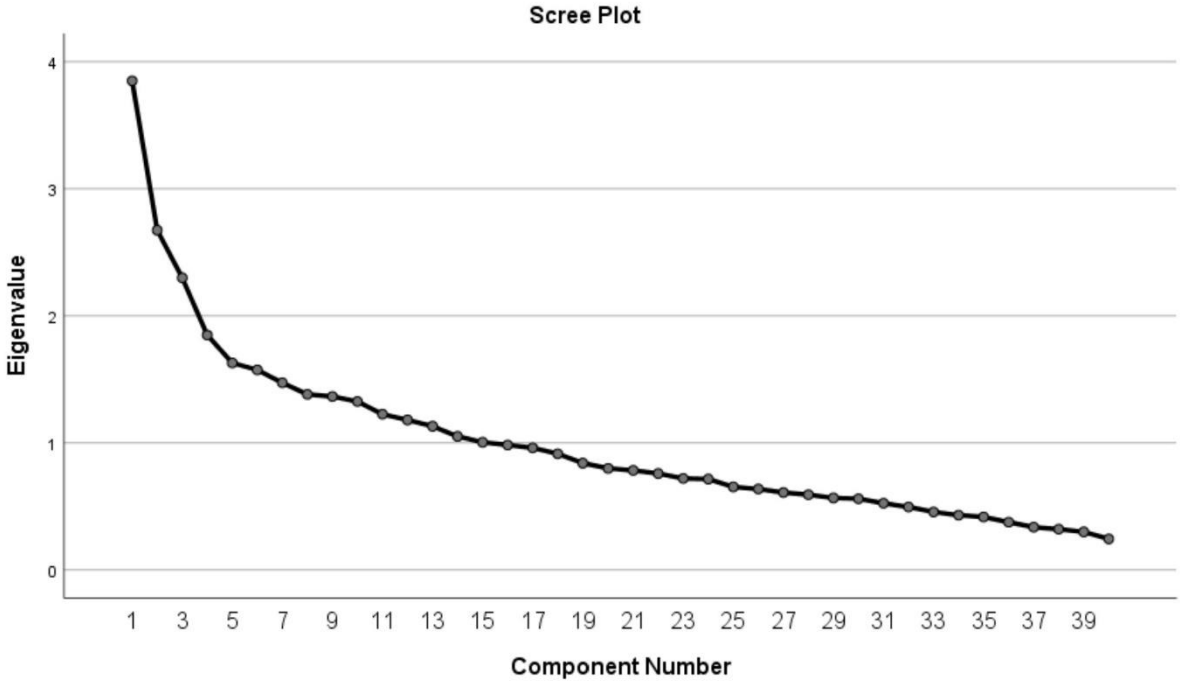
Supplementary table 8. Alcohol intake and cognition at baseline: Sydney Memory and Ageing Study (N=819)

	Basic model		Fully adjusted model	
Cognition Domains	**P value**	**β (95% CI)**	**P value**	**β (95% CI)**
Global Cognition	0.000*	0.009 (0.004-0.013)	0.17	0.006 (-0.003 - 0.014)
Attention Processing Speed	0.008*	0.005 (0.001-0.009)	0.257	0.004 (-0.003 - 0.012)
Language	0.000*	0.010 (0.005-0.015)	0.136	0.010 (-0.003 - 0.022)
Executive	0.007*	0.006 (0.002-0.010)	0.560	0.003 (-0.006 - 0.011)
Visuospatial	0.660	0.001 (-0.003-0.004)	0.851	-0.001 (-0.008 - 0.006)
Memory	0.008*	0.005 (0.001-0.009)	0.109	0.007 (-0.002 - 0.015)
Verbal Memory	0.009*	0.005 (0.001-0.009)	0.170	0.006 (-0.002 - 0.014)

Notes: CI, Confidence interval. Values are *β* (95% CI), *n* = 819. P value<.05 is significant for global cognition and p <.01 for subdomains. *β* - Coefficients show a 1 serve increase in alcohol intake is associated with higher cognitive score (positive *β*) or lower cognitive score (negative *β*). Results were based on a basic model with adjustment for age, gender and education; and a fully adjusted model with covariates including age, gender, education, as well as physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype.



Supplementary Figure 1. Scree plot: *a-posterori* patterns derived by PCA (female)
Notes: PCA- Principal Component Analysis



Supplementary Figure 2. Scree plot: *a-posterori* patterns derived by PCA (male)
Notes: PCA- Principal Component Analysis

Supplementary material: secondary dietary patterns derived by PCA

A. Factor loading for secondary dietary patterns derived by PCA with sex stratification: *High carbohydrate Diet (female)* and *fruit/vegetable Diet (male)* in Sydney Memory and Aging study (N=819)

High carbohydrate Diet (female)		***Fruit and vegetable Diet (male)***	
Food items	Factor Loading	Food items	Factor Loading
Cakes and biscuits	0.537	Whole grains	0.159
Red meat	0.288	Yellow vegetable	0.253
Processed meat	0.333	Green leafy vegetable	0.463
Legume	0.360	Fresh fruit	0.474
Potatoes	0.288	Cruciferous vegetable	0.387
Chips	0.287	Other vegetable	0.445
Tinned fruit	0.246	Low fat dairy	0.299
Fruit juice	0.311	Potatoes	0.230
Sugar	0.400	Avocado	0.271
Jam	0.425	Tomato	0.298
Garlic	-0.300	Tofu	0.279
Tomato	-0.185	Soy milk	0.292
Avocado	-0.388	Garlic	0.133
Low fat dairy	-0.256	Sugar	-0.437
Green leafy vegetable	-0.248	Egg	-0.329
Other vegetable	-0.201	Meat pies	-0.326
Fish	-0.337	Full fat dairy	-0.390
Tinned fish	-0.273	Processed meat	-0.373

B. Results of linear regression model analyses examining the association between secondary patterns derived by PCA stratified by sex and baseline cognition: the Sydney Memory and Aging study (N=819)

Cognition Domains	DP derived by PCA	β	95% CI	*P value*[*]
Attention	*High carbohydrate (female)*	0.133	-0.108, 0.374	0.276
	Fruit and vegetable Diet(male)	0.259	0.061, 0.457	0.011
Language	*High carbohydrate (female)*	0.284	0.009, 0.559	0.043
	Fruit and vegetable Diet(male)	-0.008	-0.238, 0.221	0.943
Executive	*High carbohydrate (female)*	0.064	-0.190, 0.319	0.617
	Fruit and vegetable Diet(male)	0.043	-0.165, 0.250	0.685
Visuospatial	*High carbohydrate (female)*	0.093	-0.117, 0.303	0.382
	Fruit and vegetable Diet(male)	0.138	-0.020, 0.297	0.087
Memory	*High carbohydrate (female)*	0.090	-0.173,0.352	0.499
	Fruit and vegetable Diet(male)	0.012	-0.167, 0.192	0.892
Verbal Memory	*High carbohydrate (female)*	0.104	-0.149, 0.357	0.416
	Fruit and vegetable Diet(male)	0.023	-0.160, 0.207	0.802
Global cognition	*High carbohydrate (female)*	0.195	-0.067, 0.457	0.143
	Fruit and vegetable Diet(male)	0.100	-0.099, 0.299	0.320

Notes: Results were fully adjusted with age, sex, education, as well as non-English speaking background, physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype.

*P < 0.05 for global cognition or P<0.01 for individual cognitive domains, is significant.

Appendix C. Supplementary material of manuscript "Association of dietary patterns with cognitive function and cognitive decline in Sydney Memory and Ageing Study: a longitudinal analysis"

Supplementary Table 1. Comparisons between Mediterranean score construction system

	0-9 system by Trichopoulou[13,28]	**0-55 system by Panagiotakos[29]**
All food groups	**9 Food groups** Non-refined cereals/grains Fruits and nuts Vegetables Legumes Fish Red and processed meat Dairy products Mono-unsaturated: saturated fat ratio Alcohol	**11 Food groups** Non-refined cereals/grains Potatoes Fruits Vegetables Legumes and nuts Fish Red and processed meat Poultry Full fat dairy products Mono-unsaturated: Saturated fat ratio Alcohol
Detrimental factors	Dairy foods, Red and Processed meat Alcohol intake (Little or excessive)	Full fat Dairy foods, Red and Processed meat, Poultry, Alcohol intake
Scoring strategy	Value of one is given if consumption of a beneficial group is at or above sex-specific median, or if consumption of a detrimental group is below sex-specific median, or if alcohol intake is mild to moderate.	Value from 0 to 5 in ascending order with increased consumption of a beneficial food group, reverse scoring for detrimental food groups.
Food Measurements	gram/day	servings/week

Supplementary Table 2. Food group composition for Principle Component Analysis in Sydney Memory and Ageing study

Whole grains	**Refined grains**	**Red meat**	**Processed meat**	**Cakes and biscuits**
High fiber white-bread Wholemeal bread rye bread multigrain bread all bran/sultana bran bran flakes muesli/ or with fibre Weetbix/ porridge Vitabrits/Weeties	white bread crackers crispbread/crisps dry biscuits cornflakes special k rice pasta noodles	beef veal lamb pork	bacon ham sausage salami	cakes sweet biscuits
Fresh Fruit	**Yellow vegetables**	**Green leafy vegetables**	**Cruciferous vegetables**	**Other vegetables**
apple pear banana melon pineapple strawberry apricot peach mango orange	carrots pumpkin	lettuce spinach	broccoli cauliflower cabbage	capsicum celery beetroot cucumber green beans bean sprouts zucchini onion mushroom
Legumes	**Low fat dairy**	**Margarine**	**Butter**	**Nuts**
baked beans peas other beans	low fat cheese skim milk reduced fat milk cottage cheese ricotta cheese	margarine poly-/mono-unsaturated fat margarine	butter	nuts peanut butter
Poultry - chicken	**Meat pies**	**Pizza**	**Hamburger**	**Chocolate**
Eggs	**Flavoured milk**	**Fish**	**Fried fish**	**Tinned fish**
Tofu	**Fruit juice**	**Tinned fruit**	**Chips**	**Potatoes**
Garlic	**Avocado**	**Tomato sauce**	**Tomato**	**Soy milk**
Vegemite	**Jam**	**Added sugar**	**Butter and margarine blend**	

Supplementary Table 3. Factor loading for two major dietary patterns derived by PCA: *Prudent Healthy Diet* and *Western Diet* in Sydney Memory and Aging study (N=1037)

Prudent Healthy Diet		*Western Diet*	
Food items	Factor Loading	Food items	Factor Loading
grains	0.583	processed meat	0.462
yellow vegetable	0.179	red meat	0.279
green leafy vegetables	0.360	full fat dairy	0.428
nuts	0.373	cakes and biscuits	0.372
fresh fruit	0.274	butter	0.122
other vegetables	0.448	meat pies	0.351
fish (not fried or tinned)	0.202	pizza	0.216
poultry	-0.501	fried fish	0.104
legume	0.151	chips	0.328
tomato	0.150	fruit juice	0.246
tofu	0.236	egg	0.187
egg	0.154	sugar	0.386
soy milk	0.108	low fat dairy	-0.320
vegemite	0.160	other vegetables	-0.463
Fried fish	-0.378	cruciferous vegetable	-0.325
garlic	0.697	fresh fruit	-0.359
potatoes	0.181	tomato	-0.288
chips	-0.101	green leafy vegetable	-0.442
tinned fruit	-0.107	yellow vegetable	-0.224
sugar	-0.127	fish (not fried or tinned)	-0.168

Supplementary Table 4. Cognitive performance expressed as z scores and raw scores over 6 years: the Sydney Memory and Aging study (N=1037)

Cognition Domains	Z scores	Raw scores
Wave 1	**Mean± SD**	**Mean± SD**
Attention/Processing Speed	-0.42±1.22	94.70±14.13
Language	-0.74±1.53	39.84±7.26
Executive	-0.46±1.27	157.62±51.25
Visuo-Spatial	-0.34±1.09	21.33±8.22
Global Memory	-0.52±1.21	76.96±18.41
Verbal Memory	-0.47±1.18	65.15±17.80
Global Cognition	-0.72±1.38	76.26±9.38
Wave 2		
Attention/Processing Speed	-0.50±1.44	95.37±17.81
Language	-0.88±1.55	38.95±7.28
Executive	-0.64±1.54	158.41±69.58
Visuo-Spatial	-0.35±1.16	21.26±8.74
Global Memory	-0.60±1.28	75.10±19.62
Verbal Memory	-0.59±1.24	63.09±18.85
Global Cognition	-0.86±1.53	75.76±11.96
Wave 3		
Attention/Processing Speed	-0.68±1.46	95.54±18.01
Language	-0.94±1.62	38.62±7.60
Executive	-0.68±1.39	156.21±61.51
Visuo-Spatial	-0.33±1.15	21.38±8.63
Global Memory	-0.57±1.35	75.76±20.70
Verbal Memory	-0.55±1.30	63.65±19.76
Global Cognition	-0.89±1.51	74.63±10.91
Wave 4		
Attention/Processing Speed	-0.89±1.51	95.87±19.36
Language	-1.03±1.68	38.06±7.89
Executive	-1.04±1.98	153.11±94.84
Visuo-Spatial	-0.54±1.22	19.78±9.14
Global Memory	-0.71±1.41	73.85±21.71
Verbal Memory	-0.67±1.37	61.90±21.00
Global Cognition	-1.22±1.75	74.07±14.10

Notes: SD, Standard Deviation. Wave 1- at baseline; wave 2- at 2 year follow up; wave 3- at 4 year follow up; wave 4- at 6 year follow up. If necessary, the signs of the z-scores were reversed so that higher scores reflect better performance. Domain scores were calculated by averaging z-scores of the component tests with the exception of the visuo-spatial domain represented by a single test. Global cognition scores were calculated by averaging the domain scores.

Supplementary Table 5. Missing data at each wave during 6 year follow up in Sydney Memory and Aging Study (N=1037)

Missing data	Global cognition	Attention Processing speed	Language	Executive	Visuo-spatial	Memory	Verbal Memory	Dietary data	Reason of missing data
Wave 1	5 (0.48%)	16 (1.54%)	7 (0.68%)	87 (8.39%)	3 (0.29%)	11 (1.06%)	13 (1.25%)	63 (6.08%)	Not assessed or incomplete data at wave 1
Wave 2	175 (16.9%)	197 (19.0%)	165 (15.9%)	247 (23.8%)	172 (16.6%)	184 (17.7%)	190 (18.3%)	N/A	N=43 deceased; N=6 loss of follow-up; N=76 withdrawn; other (not assessed or incomplete data at wave 2)
Wave 3	303 (29.2%)	318 (30.7%)	285 (27.5%)	368 (35.5%)	302 (29.1%)	312 (30.1%)	313 (30.2%)	N/A	N=86 deceased; N=10 loss of follow-up; N=125 withdrawn; other (not assessed or incomplete data at wave 3)
Wave 4	403 (38.9%)	428 (41.3%)	387 (37.3%)	457 (44.1%)	414 (39.9%)	428 (41.2%)	428 (41.2%)	N/A	N=136 deceased; N=11 loss of follow-up; N=164 withdrawn; other (not assessed or incomplete data at wave 4)

Notes: Wave 1- at baseline; wave 2- 2 year follow up; wave 3- 4 year follow up; wave 4- 6 year follow up.

Supplementary Table 6. Nutrient and food groups assessment of participants from Sydney Memory and Aging Study (N=1037)

Dietary pattern	Score/ Food groups	All (n=1037) Mean±SD	Female(n=572) Mean±SD	Male(n=465) Mean±SD	P value for differences between sexes
Mediterranean diet (0-9)	**MED score**	4.4±1.7	4.3±1.7	4.5±1.7	0.172
Food group grams/day	Fruits/Nuts	321.0±180.2	292.6±154.1	356.3±202.8	<0.0001
	Vegetables	95.9±52.3	98.3±52.7	92.9±51.7	0.105
	Legume	16.9±16.8	14.8±14.9	19.5±18.6	<0.0001
	Cereal	196.3±132.5	176.3±136.7	221.2±122.9	<0.0001
	Dairy foods	371.4±187.3	377.8±183.0	363.4±192.3	0.237
	Red/Processed Meat	74.5±84.5	56.4±51.4	97.0±108.9	<0.0001
	Fish	40.6±57.0	35.0±58.7	47.6±53.9	0.001
	Alcohol	14.8±19.0	9.1±12.3	22.0±23.0	<0.0001
	MUFA:SFA	0.9±0.2	0.9±0.2	0.9±0.2	0.093
Mediterranean diet (0-55) Panagiotakos	**MED score**	27.7±6.2	27.5±6.2	27.9±6.3	<0.0001
Food group grams/day	Fruits	315.2±178.4	287.6±152.5	349.5±201.1	<0.0001
	Vegetables	95.9±52.3	98.3±52.7	92.9±51.7	0.105
	Legume/ Nuts	22.7±19.7	19.8±18.1	26.3±21.1	<0.001
	Potato	31.8±34.7	29.3±31.8	34.8±37.9	0.015
	Whole Grain	121.3±93.4	114.3±86.9	130.1±100.4	0.009
	Full fat Dairy	159.3±167.4	151.8±157.5	168.7±178.7	0.117
	Red / Processed meat	74.5±84.5	56.4±51.4	97.0±108.9	<0.0001
	Poultry	21.8±25.1	20.7±27.5	23.3±21.7	0.106
	Fish	40.6±57.0	35.0±58.7	47.6±53.9	0.001
	Alcohol	14.8±19.0	9.1±12.3	22.0±23.0	<0.0001
	MUFA:SFA	0.9±0.2	0.9±0.2	0.9±0.2	0.093

DASH diet (9-45)	**DASH score**	27.0±4.1	27.3±3.9	26.7±4.3	0.016
Food group grams/day	Fruits	315.2±178.4	287.6±152.5	349.5±201.1	<0.0001
	Vegetables	95.9±52.3	98.3±52.7	92.9±51.7	0.105
	Legume/ Nuts	22.7±19.7	19.8±18.1	26.3±21.1	<0.0001
	Whole Grain	121.3±93.4	114.3±86.9	130.1±100.4	0.009
	Low fat Dairy	193.8±199.2	209.3±197.2	174.5±200.3	0.008
	Red / Processed meat	74.5±84.5	56.4±51.4	97.0±108.9	<0.0001
	MUFA+PUFA	31.7±13.0	28.2±11.4	36.1±13.6	<0.0001
	Sugar	82.1±30.8	77.0±28.0	88.56±32.8	<0.0001
	Sodium (mg)	1989.5±819.4	1777.1±734.2	2257.3±843.3	<0.0001

Notes: Abbreviations: DASH, Dietary Approaches to Stop Hyptertension; MUFA, Mono-unsaturated fatty acids; PUFA, Poly-unsaturated fatty acids; SFA, Saturated fatty acids. SD, Standard Deviation

Supplementary Table 7. Association between adherence to Mediterranean diet (0-9 system) with overall cognitive function and change of cognitive performance over 6 years by tertiles (tertile 1–3, corresponding to low to high adherence) of Mediterranean diet measured by 0-9 system: the Sydney Memory and Ageing study (N=1037)

Cognition Domains	Tertile of Mediterranean diet (0-9)	Overall performance			Slope of cognitive change		
		β	95% CI	*P value*	β	95% CI	*P value**
Attention	**Tertile 1 (0-3)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (4-5)	0.011	-0.142, 0.164	0.886	0.061	-0.021, 0.143	0.145
	Tertile 3 (6-9)	-0.049	-0.209, 0.130	0.644	0.015	-0.077, 0.106	0.753
Language	**Tertile 1 (0-3)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (4-5)	0.041	-0.149, 0.232	0.669	0.001	-0.087, 0.089	0.980
	Tertile 3 (6-9)	-0.062	-0.272, 0.148	0.563	0.015	-0.085, 0.114	0.772
Executive	**Tertile 1 (0-3)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (4-5)	-0.041	-0.218, 0.136	0.648	0.100	0.011, 0.189	0.027
	Tertile 3 (6-9)	0.042	-0.154, 0.237	0.677	0.045	-0.062, 0.153	0.406
Visuospatial	**Tertile 1 (0-3)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (4-5)	0.003	-0.126, 0.131	0.968	0.022	-0.041, 0.085	0.501
	Tertile 3 (6-9)	0.018	-0.131, 0.167	0.809	0.008	-0.063 0.079	0.822
Memory	**Tertile 1 (0-3)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (4-5)	0.008	-0.137, 0.153	0.910	0.044	-0.032, 0.120	0.256
	Tertile 3 (6-9)	0.023	-0.138, 0.184	0.782	0.025	-0.057, 0.108	0.546
Verbal	**Tertile 1 (0-3)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (4-5)	0.010	-0.137, 0.157	0.897	0.041	-0.030, 0.112	0.257
	Tertile 3 (6-9)	0.016	-0.151, 0.182	0.855	0.026	-0.051, 0.104	0.503
Global	**Tertile 1 (0-3)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (4-5)	-0.019	-0.186, 0.148	0.821	0.049	-0.035, 0.133	0.254
	Tertile 3 (6-9)	-0.029	-0.219, 0.161	0.764	0.024	-0.072, 0.121	0.621

Notes:

CI, confidence interval.

Values are β (95% CI), n = 1037. In overall cognitive performance, β Coefficients show individual tertile by Mediterranean diet 0-9 scoring system, is associated with higher cognitive score (positive β) or lower cognitive score (negative β) with reference to tertile 1; in slope of cognitive change over six years, β Coefficients show individual tertile measured by Mediterranean diet 0-9 scoring system, is associated with faster cognitive decline (positive β) or slower cognitive decline (negative β) with reference to tertile 1.

Results were fully adjusted with age, sex, education, as well as non-English speaking background, BMI, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype.

$P < 0.05$ for global cognition or $P<0.01$ for individual cognitive domains, is significant.

Supplementary Table 8. Association between adherence to Mediterranean diet (0-55 system) with overall cognitive function and change of cognitive performance over 6 years by tertiles (tertile 1–3, corresponding to low to high adherence) of Mediterranean diet measured by 0-55 system: the Sydney Memory and Ageing study (N=1037)

Cognition Domains	Tertile of Mediterranean diet (0-55)	Overall performance			Slope of cognitive change		
		β	95% CI	*P value*	β	95% CI	*P value**
Attention	**Tertile 1 (0-29)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (30-33)	-0.068	-0.317, 0.181	0.594	0.047	-0.210, 0.303	0.722
	Tertile 3 (34-55)	0.001	-0.260, 0.261	0.990	0.077	-0.188, 0.343	0.568
Language	**Tertile 1 (0-29)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (30-33)	0.016	-0.241, 0.273	0.904	0.048	-0.039, .135	0.277
	Tertile 3 (34-55)	0.003	-0.279, 0.286	0.982	0.024	-0.064, 0.111	0.591
Executive	**Tertile 1 (0-29)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (30-33)	0.015	-0.277, 0.306	0.922	0.031	-0.067, 0.130	0.529
	Tertile 3 (34-55)	0.044	-0.259, 0.347	0.776	0.010	-0.093, 0.113	0.850
Visuospatial	**Tertile 1 (0-29)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (30-33)	0.168	-0.031, 0.369	0.098	-0.015	-0.081, 0.050	0.649
	Tertile 3 (34-55)	0.196	-0.006, 0.398	0.057	-0.030	-0.095, 0.035	0.368
Memory	**Tertile 1 (0-29)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (30-33)	-0.039	-0.258, 0.180	0.727	0.046	-0.026, 0.118	0.213
	Tertile 3 (34-55)	-0.010	-0.251, 0.232	0.936	0.036	-0.039, 0.111	0.349
Verbal	**Tertile 1 (0-29)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (30-33)	-0.039	-0.258, 0.181	0.729	0.050	-0.018, 0.118	0.148
	Tertile 3 (34-55)	-0.022	-0.243, 0.199	0.845	0.038	-0.034, 0.110	0.296
Global	**Tertile 1 (0-29)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (30-33)	0.047	-0.210, 0.303	0.722	0.037	-0.045, 0.118	0.376
	Tertile 3 (34-55)	0.077	-0.188, 0.343	0.568	0.011	-0.075, 0.097	0.807

Notes:

CI, confidence interval.

Values are β (95% CI), n = 1037. In overall cognitive performance, β Coefficients show individual tertile by Mediterranean diet 0-55 scoring system, is associated with higher cognitive score (positive β) or lower cognitive score (negative β) with reference to tertile 1; in slope of cognitive change over six years, β Coefficients show individual tertile measured by Mediterranean diet 0-55 scoring system, is associated with faster cognitive decline (positive β) or slower cognitive decline (negative β) with reference to tertile 1.

Results were fully adjusted with age, sex, education, as well as non-English speaking background, BMI, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype.

$P < 0.05$ for global cognition or $P<0.01$ for individual cognitive domains, is significant.

Supplementary Table 9. Association between adherence to DASH diet with overall cognitive function and change of cognitive performance over 6 years by tertiles (tertile 1–3, corresponding to low to high adherence) of DASH diet: the Sydney Memory and Ageing study (N=1037)

Cognition Domains	Tertile of DASH diet (9-45)	Overall performance			Slope of cognitive change		
		β	95% CI	*P value*	β	95% CI	*P value**
Attention	**Tertile 1 (9-25)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (26-29)	0.125	-0.120,0.369	0.317	-0.023	-0.105, 0.058	0.571
	Tertile 3 (30-45)	0.048	-0.213,0.309	0.719	-0.006	-0.099, 0.087	0.895
Language	**Tertile 1 (9-25)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (26-29)	0.047	-0.212, 0.306	0.721	-0.006	-0.093, 0.081	0.896
	Tertile 3 (30-45)	0.026	-0.255,0.307	0.855	-0.013	-0.099, 0.073	0.764
Executive	**Tertile 1 (9-25)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (26-29)	0.024	-0.263,0.312	0.867	0.000	-0.092, 0.092	0.994
	Tertile 3 (30-45)	-0.034	-0.326, 0.258	0.817	0.019	-0.082, 0.120	0.713
Visuospatial	**Tertile 1 (9-25)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (26-29)	0.076	-0.116,0.267	0.439	-0.017	-0.077, 0.043	0.576
	Tertile 3 (30-45)	0.125	-0.084, 0.334	0.240	-0.034	-0.099, 0.031	0.310
Memory	**Tertile 1 (9-25)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (26-29)	0.066	-0.154, 0.286	0.556	-0.012	-0.085, 0.062	0.754
	Tertile 3 (30-45)	0.005	-0.228, 0.238	0.965	0.004	-0.071, 0.079	0.907
Verbal	**Tertile 1 (9-25)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (26-29)	0.068	-0.145, 0.281	0.530	-0.010	-0.080, 0.060	0.778
	Tertile 3 (30-45)	-0.016	-0.247, 0.215	0.892	0.012	-0.065, 0..088	0.763
Global	**Tertile 1 (9-25)**	Reference	Reference	Reference	Reference	Reference	Reference
	Tertile 2 (26-29)	0.091	-0.155, 0.337	0.467	-0.015	-0.100, 0.069	0.727
	Tertile 3 (30-45)	0.029	-0.249, 0.308	0.835	-0.010	-0.099, 0.078	0.817

Notes:

CI, confidence interval.

Values are β (95% CI), n = 1037. In overall cognitive performance, β Coefficients show individual tertile by DASH diet, is associated with higher cognitive score (positive β) or lower cognitive score (negative β) with reference to tertile 1; in slope of cognitive change over six years, β Coefficients show individual tertile measured by DASH diet, is associated with faster cognitive decline (positive β) or slower cognitive decline (negative β) with reference to tertile 1.

Results were fully adjusted with age, sex, education, as well as non-English speaking background, BMI, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype.

$P < 0.05$ for global cognition or $P<0.01$ for individual cognitive domains, is significant.

Supplementary Table 10. Sensitivity analyses examining the association between baseline dietary scores and overall cognitive performance and slope of cognitive change over 6 years: participants with complete cognitive testing scores over 4 waves only (N=484) in Sydney Memory and Aging study

Cognition Domains		Overall performance			Slope of cognitive change		
		β	95% CI	*P value*	β	95% CI	*P value*
Attention	MED (0-55 system)	-0.027	-0.063, 0.009	0.161	-0.002	-0.026, 0.021	0.884
	MED (0-9 system)	-0.073	-0.167, 0.022	0.153	-0.049	-0.123, 0.022	0.191
	DASH	-0.020	-0.056, 0.017	0.321	-0.001	-0.024, 0.025	0.968
Language	MED (0-55 system)	0.021	-0.028, 0.069	0.427	-0.005	-0.033, 0.023	0.712
	MED (0-9 system)	0.014	-0.112, 0.696	0.841	-0.016	-0.081, 0.048	0.630
	DASH	0.009	-0.040, 0.058	0.725	-0.010	-0.004, 0.025	0.174
Executive	MED (0-55 system)	0.001	-0.041, 0.043	0.984	0.002	-0.039, 0.040	0.937
	MED (0-9 system)	-0.015	-0.127, 0.096	0.802	-0.093	-0.193, 0.005	0.070
	DASH	0.018	-0.025, 0.061	0.437	-0.038	-0.078, 0.003	0.078
Visuo-Spatial	MED (0-55 system)	0.048	0.007, 0.091	0.034	0.006	-0.020, 0.032	0.670
	MED (0-9 system)	0.053	-0.059, 0.165	0.382	-0.061	-0.120, -0.004	0.041
	DASH	0.027	-0.015, 0.070	0.237	-0.012	-0.039, 0.015	0.395
Memory	MED (0-55 system)	-0.004	-0.046, 0.039	0.870	-0.001	-0.027, 0.026	0.926
	MED (0-9 system)	0.008	-0.103, 0.119	0.894	-0.048	-0.113, 0.018	0.157
	DASH	0.012	-0.029, 0.054	0.580	-0.004	-0.030, 0.025	0.800
Verbal	MED (0-55 system)	-0.012	-0.054, 0.030	0.598	0.001	-0.023, 0.025	0.952
	MED (0-9 system)	-0.010	-0.121, 0.101	0.866	-0.035	-0.096, 0.027	0.270
	DASH	0.005	-0.928, 0.299	0.833	-0.002	-0.026, 0.024	0.874
Global	MED (0-55 system)	0.012	-0.029, 0.054	0.585	0.003	-0.024, 0.029	0.840
	MED (0-9 system)	0.000	-0.109, 0.109	0.999	-0.075	-0.142, -0.009	0.052
	DASH	0.013	-0.029, 0.056	0.562	-0.021	-0.048, 0.007	0.143

Notes: Values are β (95% CI), n = 1037. β - Coefficients show a 1 score increase in dietary pattern score is associated with better cognitive performance (positive β) or worse cognitive performance (negative β); or associated with less cognitive decline (negative β) or more cognitive decline (positive β). CI = confidence interval. Results were adjusted for age, sex, education, as well as non-English-speaking background. physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype. P value<.05 is significant for global cognition and p <.01 for subdomains.

Supplementary Table 11. Association of consumption of key food components with overall global cognition and change of global cognition over 6 years in the Sydney Memory and Aging study (N=1037)

Food components (serves/day)	Global cognition	Model 1			Model 2		
		β	95% CI	*P value*	β	95% CI	*P value*
Fruits	Overall performance	-0.011	-0.025,0.002	0.098	-0.003	-0.016,0.010	0.671
	Cognitive change	0.004	-0.001,0.010	0.129	0.005	-0.001,0.010	0.126
Vegetables	Overall performance	0.005	-0.013,0.023	0.559	-0.004	-0.022,0.014	0.653
	Cognitive change	-0.002	-0.010,0.006	0.618	-0.002	-0.010,0.005	0.559
Legumes/ nuts	Overall performance	0.092	0.037,0.148	**0.001**	0.091	0.035,0.146	**0.001**
	Cognitive change	-0.017	-0.033,-0.001	**0.034**	-0.016	-0.032,0.001	**0.032**
potatoes	Overall performance	0.002	-0.023,0.027	0.886	-0.006	-0.031,0.018	0.616
	Cognitive change	-0.003	-0.014,0.008	0.587	-0.004	-0.016,0.007	0.462
Grains	Overall performance	0.001	-0.006,0.009	0.731	0.003	-0.004,0.010	0.384
	Cognitive change	0.001	-0.002,0.005	0.360	0.002	-0.002,0.005	0.344
Dairy products	Overall performance	0.003	-0.012,0.018	0.696	0.002	-0.013,0.017	0.778
	Cognitive change	-0.002	-0.009,0.006	0.688	-0.002	-0.009,0.006	0.689
Red/processed meat	Overall performance	0.009	-0.005,0.024	0.209	0.004	-0.011,0.019	0.691
	Cognitive change	-0.002	-0.007,0.004	0.575	-0.002	-0.007,0.004	0.575
Poultry	Overall performance	0.006	-0.045,0.058	0.804	0.018	-0.032,0.067	0.480
	Cognitive change	-0.001	-0.023,0.021	0.932	0.000	-0.021,0.021	0.999
Fish	Overall performance	-0.020	-0.051,0.011	0.210	-0.011	-0.042,0.019	0.465
	Cognitive change	-0.000	-0.014,0.013	0.961	0.002	-0.012,0.015	0.805
Alcohol	Overall performance	0.11	0.050,0.171	**<0.001**	0.11	0.050,0.171	**<0.001**
	Cognitive change	-0.021	-0.039,-0.002	**0.028**	-0.021	-0.039,-0.002	**0.030***
Unsaturated fats	Overall performance	-0.005	-0.019,0.008	0.430	-0.003	-0.016,0.009	0.581
	Cognitive change	-0.002	-0.006,0.002	0.263	-0.002	-0.006,0.002	0.293

Notes: CI, confidence interval. Values are β (95% CI), n = 1037. In overall cognitive performance, β Coefficients show a 1 serve/unit increase in daily consumption of food component is associated with higher cognitive score (positive β) or lower cognitive score (negative β)); in slope of cognitive change over six years, β Coefficients show a 1 serve/unit increase in daily consumption of food components is associated with faster cognitive decline (positive β) or slower cognitive decline (negative β). In model 1 results were adjusted for age, sex, education, in model 2 results were fully adjusted with age, sex, education, as well as non-English-speaking background. physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype. $P < 0.05$ for global cognition or $P<0.01$ for individual cognitive domains, is significant.

Supplementary Table 12. Association of alcohol consumption with overall cognitive function and change of cognitive performance over 6 years in the Sydney Memory and Aging study (N=1037)

Cognition Domains		Model 1			Model 2		
		β	**95% CI**	***P value****	**β**	**95% CI**	***P value****
Attention	Overall performance	0.075	0.019,0.132	**0.009**	0.075	0.018,0.131	**0.009**
	cognitive change	-0.012	-0.030,0.006	0.189	-0.012	-0.030,0.006	0.199
Language	Overall performance	0.128	0.065,0.192	**<0.001**	0.128	0.065,0.191	**<0.001**
	cognitive change	-0.022	-0.040,-0.003	0.023	-0.021	-0.040,-0.003	0.022
Executive	Overall performance	0.074	0.009,0.140	0.026	0.072	0.007,0.137	0.031
	cognitive change	-0.010	-0.033,0.012	0.369	-0.010	-0.032,0.013	0.400
Visuo-Spatial	Overall performance	0.030	-0.016,0.076	0.199	0.030	-0.016,0.076	0.202
	cognitive change	-0.014	-0.028,0.001	0.067	-0.014	-0.028,0.001	0.067
Memory	Overall performance	0.057	0.006,0.109	0.027	0.058	0.007,0.110	0.026
	cognitive change	-0.008	-0.024,0.007	0.298	-0.008	-0.024,0.007	0.308
Verbal	Overall performance	0.051	0.001,0.102	0.046	0.052	0.001,0.102	0.044
	cognitive change	-0.008	-0.024,0.007	0.297	-0.008	-0.024,0.007	0.308
Global	Overall performance	0.11	0.050,0.171	**<0.001**	0.11	0.050,0.171	**<0.001**
	cognitive change	-0.021	-0.039,-0.002	**0.028**	-0.021	-0.039,-0.002	**0.030**

Notes: Values are β (95% CI), n = 1037. β Coefficients show a 1 standard drink increase in daily consumption is associated with higher cognitive score (positive β) or lower cognitive score (negative β). CI = confidence interval. Results were fully adjusted with age, sex, education, as well as physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype.

P < 0.05 for global cognition or P<0.01 for individual cognitive domains, is significant.

Supplementary Table 13. The association between major dietary patterns derived by PCA with overall cognitive performance and cognitive decline over 6 years: Sydney Memory and Aging study (N=1037)

Cognition Domains		Overall performance			Cognitive change		
		β	**95% CI**	***P value***	**β**	**95% CI**	***P value***
Attention	Prudent healthy diet	0.059	-0.012, 0.131	0.104	0.005	-0.033, 0.044	0.790
	Western diet	-0.054	-0.141, 0.033	0.222	0.018	-0.018,0.053	0.327
Language	Prudent healthy diet	0.092	0.014, 0.170	0.021	0.018	-0.019, 0.055	0.339
	Western diet	-0.105	-0.207, -0.004	0.041	-0.016	-0.055,0.022	0.404
Executive	Prudent healthy diet	0.069	-0.003, 0.142	0.061	-0.010	-0.054, 0.034	0.657
	Western diet	-0.052	-0.143, 0.040	0.266	0.020	-0.023, 0.062	0.369
Visuo-Spatial	Prudent healthy diet	0.079	0.021, 0.137	**0.008**	-0.012	-0.040, 0.016	0.391
	Western diet	-0.031	-0.106, 0.043	0.410	-0.017	0.043, 0.010	0.219
Memory	Prudent healthy diet	0.079	0.015,0.143	0.015	-0.002	-0.033,0.030	0.925
	Western diet	-0.064	-0.147, 0.019	0.132	0.000	-0.033,0.033	0.987
Verbal	Prudent healthy diet	0.070	0.008,0.133	0.027	-0.005	-0.036, 0.027	0.774
	Western diet	-0.057	-0.140, 0.026	0.177	0.000	-0.029, 0.030	0.979
Global	Prudent healthy diet	0.108	0.039,0.177	**0.002**	0.009	-0.028,0.045	0.647
	Western diet	-0.096	-0.188, 0.005	**0.038**	0.001	-0.033, 0.036	0.945

Notes: Values are β (95% CI), n = 1037. β - Coefficients show a 1 score increase in dietary pattern score is associated with better cognitive performance (positive β) or worse cognitive performance (negative β); faster cognitive decline (positive β) and slower cognitive decline (negative β). CI = confidence interval. In this analysis, results were fully adjusted with age, sex, education, as well as non-English-speaking background, physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype. P value<.05 is significant for global cognition and p <.01 for subdomains.

Supplementary Table 14. Interactions between dietary scores and age, sex and education (indicated by p values) in Sydney Memory and Aging Study (N=1037)

Cognition Domains	Dietary Pattern	Age	Sex	*Education*
Attention	*Mediterranean Diet (0-9)*	0.423	0.711	0.062
	Mediterranean Diet (0-55)	0.671	0.300	0.659
	DASH diet (9-45)	0.378	0.630	0.223
	Prudent healthy Diet	0.338	0.623	0.124
	Western Diet	0.968	0.292	0.522
Language	*Mediterranean Diet (0-9)*	0.931	0.106	0.172
	Mediterranean Diet (0-55)	0.711	0.318	0.700
	DASH diet (9-45)	0.699	0.208	0.790
	Prudent healthy Diet	0.818	0.525	0.328
	Western Diet	0.625	0.834	0.774
Executive	*Mediterranean Diet (0-9)*	0.944	0.226	0.542
	Mediterranean Diet (0-55)	0.560	0.106	0.490
	DASH diet (9-45)	0.309	0.359	0.372
	Prudent healthy Diet	0.845	0.799	0.922
	Western Diet	0.408	0.750	0.532
Visuospatial	*Mediterranean Diet (0-9)*	0.654	0.692	0.723
	Mediterranean Diet (0-55)	0.231	0.385	0.958
	DASH diet (9-45)	0.225	0.738	0.809
	Prudent healthy Diet	0.836	0.948	0.076
	Western Diet	0.349	0.807	0.318
Memory	*Mediterranean Diet (0-9)*	0.900	0.128	0.180
	Mediterranean Diet (0-55)	0.424	**0.033**	0.480
	DASH diet (9-45)	0.275	0.239	0.264
	Prudent healthy Diet	0.799	0.239	0.326
	Western Diet	0.776	0.591	0.435
Verbal Memory	*Mediterranean Diet (0-9)*	0.928	0.145	0.294
	Mediterranean Diet (0-55)	0.585	**0.039**	0.534
	DASH diet (9-45)	0.388	0.214	0.264
	Prudent healthy Diet	0.561	0.299	0.459
	Western Diet	0.746	0.449	0.197
Global cognition	*Mediterranean Diet (0-9)*	0.679	0.120	0.084
	Mediterranean Diet (0-55)	0.298	0.103	0.824
	DASH diet (9-45)	0.228	0.548	0.617
	Prudent healthy Diet	0.467	0.364	0.065
	Western Diet	0.951	0.765	0.840

Note: p values<0.05 is significant

Supplementary Table 15. The association between baseline diet scores and overall cognitive performance over 6 years: Stratified by sex

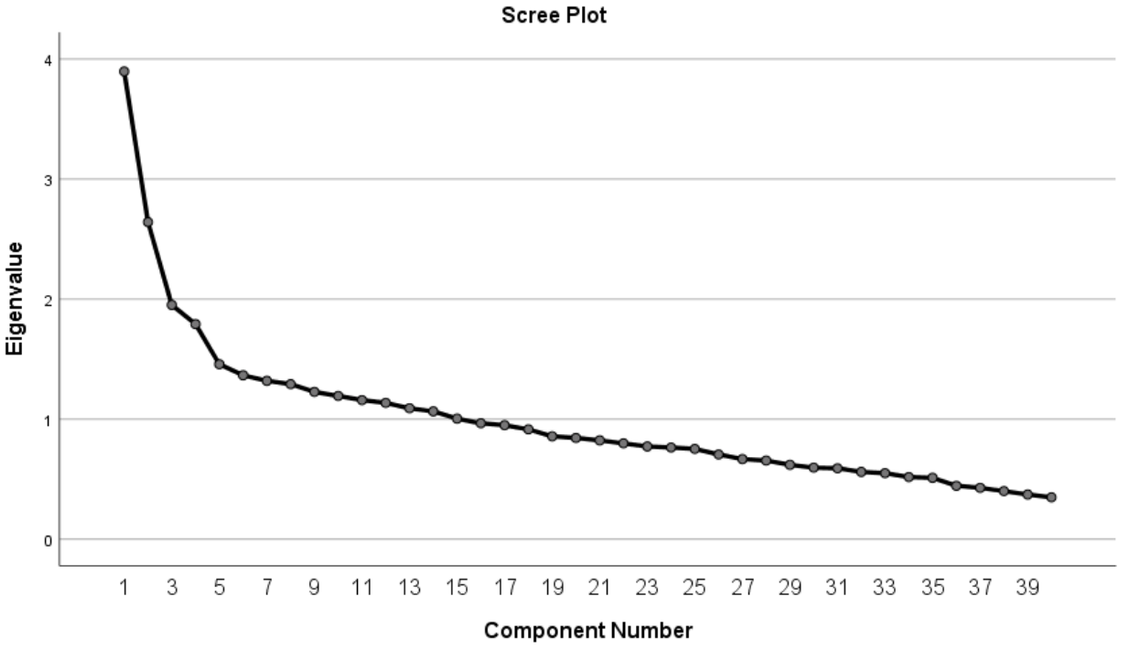
Cognition Domains		Female			Male		
		β	**95% CI**	***P value***	**β**	**95% CI**	***P value***
Attention	MED (0-9 system)	-0.031	-0.112, 0.050	0.450	-0.019	-0.114, 0.076	0.693
	MED (0-55 system)	0.027	-0.008, 0.063	0.133	0.019	-0.023, 0.062	0.373
Language	MED (0-9 system)	-0.015	-0.105, 0.075	0.744	-0.039	-0.136, 0.058	0.427
	MED (0-55 system)	0.014	-0.030, 0.058	0.523	0.004	-0.044, 0.051	0.884
Executive	MED (0-9 system)	0.011	-0.077, 0.101	0.795	-0.054	-0.163, 0.055	0.332
	MED (0-55 system)	0.027	-0.012, 0.067	0.174	0.011	-0.037, 0.058	0.652
Visuo-Spatial	MED (0-9 system)	0.006	-0.060, 0.073	0.852	-0.009	-0.086, 0.068	0.811
	MED (0-55 system)	0.029	0.008, 0.066	0.125	0.005	-0.032, 0.041	0.809
Memory	MED (0-9 system)	0.031	-0.047, 0.108	0.439	-0.059	-0.137, 0.020	0.142
	MED (0-55 system)	0.029	-0.000, 0.058	0.053	0.005	-0.033, 0.043	0.806
Verbal	MED (0-9 system)	0.027	-0.051, 0.104	0.500	-0.066	-0.140, 0.007	0.075
	MED (0-55 system)	0.031	0.002, 0.060	**0.036**	0.000	-0.037, 0.037	0.999
Global	MED (0-9 system)	0.001	-0.084, 0.0885	0.986	-0.063	-0.161, 0.034	0.204
	MED (0-55 system)	0.037	-0.005, 0.080	0.083	0.014	-0.033, 0.061	0.550

Notes: Values are β (95% CI), n = 1037. β - Coefficients show a 1 score increase in dietary pattern score is associated with better cognitive performance (positive β) or worse cognitive performance (negative β). CI = confidence interval. Results were adjusted for age, sex, education, as well as non-English-speaking background. physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype. P value<.05 is significant for global cognition and p <.01 for subdomains.

Supplementary Table 16. The association between baseline diet scores and slopes of cognitive decline over 6 years: Stratified by sex

Cognition Domains		Female			Male		
		β	**95% CI**	***P value***	**β**	**95% CI**	***P value***
Attention	MED (0-9 system)	0.011	-0.018, 0.040	0.463	0.003	-0.029, 0.035	0.831
	MED (0-55 system)	0.003	-0.007, 0.013	0.526	-0.002	-0.013, 0.010	0.750
Language	MED (0-9 system)	0.019	-0.010, 0.048	0.196	0.002	-0.029, 0.032	0.920
	MED (0-55 system)	0.004	-0.007, 0.015	0.481	-0.002	-0.012, 0.007	0.618
Executive	MED (0-9 system)	0.009	-0.021, 0.038	0.568	0.013	-0.026, 0.051	0.513
	MED (0-55 system)	0.003	-0.009, 0.015	0.615	0.002	-0.011, 0.014	0.802
Visuo-Spatial	MED (0-9 system)	0.003	-0.018, 0.025	0.762	0.003	-0.022, 0.027	0.829
	MED (0-55 system)	-0.003	-0.007, 0.006	0.528	-0.001	-0.009, 0.007	0.814
Memory	MED (0-9 system)	-0.002	-0.027, 0.024	0.904	0.015	-0.010, 0.041	0.242
	MED (0-55 system)	-0.002	-0.012, 0.007	0.654	0.004	-0.005, 0.013	0.347
Verbal	MED (0-9 system)	-0.001	-0.027, 0.024	0.917	0.018	-0.006, 0.041	0.139
	MED (0-55 system)	-0.001	-0.010, 0.008	0.817	0.003	-0.005, 0.012	0.423
Global	MED (0-9 system)	0.011	-0.017, 0.038	0.449	0.014	-0.018, 0.045	0.390
	MED (0-55 system)	0.002	-0.008, 0.012	0.703	0.001	-0.105, 0.012	0.870

Notes: Values are β (95% CI), n = 1037. β - Coefficients show a 1 score increase in dietary pattern score is associated with less cognitive decline (negative β) or more cognitive decline (positive β). CI = confidence interval. Results were adjusted for age, sex, education, as well as non-English-speaking background. physical activity, BMI, metabolic syndrome, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype. P value<.05 is significant for global cognition and p <.01 for subdomains.



Supplementary Figure 1. Scree plot: *a-posterori* patterns derived by PCA in Sydney Memory and Aging Study

Notes: PCA- Principal Component Analysis

Supplementary Figure 2. Global cognition over 6 years in the Sydney Memory and Aging Study (4 waves: at baseline and two, four, six year follow-up over six years; N=1037)

Appendix D. Supplementary material of manuscript "Association of adherence to Australian Dietary Guidelines with cognitive performance and cognitive decline in Sydney Memory and Ageing Study: a longitudinal analysis"

Supplementary Table 1. Scoring criteria according to Dietary Guidelines Index (DGI) -2013 for Australian Healthy Eating Guideline adherence using DQES[1-3]

Dietary Guideline	Indicator and description	Criteria for Maximum Score	Minimum Score	Maximum score
Enjoy a wide variety of nutritious foods	Food variety: 2 points awarded for each of the five food groups when at least one serving was consumed per day of that group.	Consumption of at least one serve from each food group	0	10
Eat plenty of vegetables and fruits	Servings of vegetables and legumes per day: (tomato, capsicum, lettuce, cucumber, celery, beetroot, carrot, cabbage, cauliflower, broccoli, spinach, green beans, bean sprouts, pumpkin, onion, garlic, mushrooms, zucchini, avocado, potato, peas, baked beans, tofu, other beans)	>70 year: M ≥5, F ≥ 5 serves/day	0	10
	Servings of fruits per day (including tinned fruit, fruit juice, orange, apple, pear, banana, melon, pineapple, strawberry, apricot, peach, mango)	>=2 serves/day	0	10
Eat plenty of cereals (including breads, rice, pasta, and noodles), preferably whole-grain	Consumption of breads and cereals per day (All-Bran, bran flakes, weetbix, cornflakes, porridge, muesli, rice, pasta, and bread including high fiber white bread, white bread, wholemeal bread, rye bread, multi-grain bread)	>70 year: M ≥4.5, F ≥3 serves/day	0	5

	Proportion of whole grain/high fiber cereal consumed relative to total cereal.	100%	0	5
Include lean meat, fish, poultry, and/or alternatives (including tofu, egg, nuts and seeds, legumes)	Consumption of meats and alternatives per day (Beef, veal, chicken, lamb, pork, fish, eggs, baked beans, soybean/tofu, other beans, peas, nuts, peanut butter)	>70 year: M ≥2.5, F ≥ 2 serves/day	0	10
Include milks, yoghurts, cheeses, and/or alternatives, reduced fat varieties should be chosen, where possible	Consumption of dairy products per day, including cheese (hard cheese, firm cheese, soft cheese, ricotta cheese, cottage cheese, cream cheese, low-fat cheese), yoghurt, milk (Full cream, reduced fat milk, skim milk, and soya milk).	>70 year: M ≥ 3.5, F ≥ 4 serves/day	0	5
	Low-fat/reduced-fat dairy to total dairy ratio	100%	0	5
Limit saturated fat and moderate total fat intake, small allowance of unsaturated oils, fats or spreads	Total Poly and Mono unsaturated fat intake to total fat ratio	100%	0	10
Prevent weight gain: eat according to your energy needs, limit discretionary foods containing saturated fat, alcohol, added salt, and added sugars	Consumption of total Energy-dense foods/fluids that are not essential for nutrient requirements and contain too much fat, sugar, and salt. Such as soft drinks, cordials, fruit juice drinks, mayonnaise and dressing, chips, jam, confectionery, chocolate, hamburgers, hot chips, meat pies, pizza, cakes and muffins, pies and pastries, puddings, ice cream, cream, biscuits, and all alcoholic beverages	>70 year: M = 0, F = 0 serves/day	0 M ≥ 3, F ≥ 2.5	20

Notes: M, Male; F, Female.

References

1. Thorpe, M.G., et al., A Revised Australian Dietary Guideline Index and Its Association with Key Sociodemographic Factors, Health Behaviors and Body Mass Index in Peri-Retirement Aged Adults. Nutrients, 2016. 8(3): p. 160.
2. McNaughton, S.A., et al., An Index of Diet and Eating Patterns Is a Valid Measure of Diet Quality in an Australian Population. The Journal of Nutrition, 2008. 138(1): p. 86-93.
3. National Health and Medical Research Council (2013) Australian Dietary Guidelines Educator Guide. Canberra: National Health and Medical Research Council.

Supplementary Table 2. Five food groups and recommended daily servings for older adults (≥70 years old): Australian Dietary Guidelines

Essential food groups	Female (serves per day)	Male (serves per day)	Size of a serve
Vegetables	5	5	A serve of vegetables is approximately 75g: • ½ cup of cooked green or orange vegetables (for example broccoli, spinach, carrots or pumpkin) • ½ cup cooked, dried or canned beans, peas or lentils (preferably with no added salt) • 1 cup of green leafy or raw salad vegetables • ½ cup of sweetcorn • ½ medium potato other starchy vegetables (for example sweet potato, taro or cassava) • 1 medium tomato
Fruits	2	2	A serve of fruit is about 150g: • 1 medium apple, banana, orange or pear • 2 small apricots, kiwi fruits or plums • 1 cup diced or canned fruit (with no added sugar) • or occasionally as a substitute for other foods in the group • ½ cup (125ml) 100% fruit juice (no added sugar) • 30g dried fruit (for example 4 dried apricot halves or 1½ tablespoons of sultanas)
Cereals	3	4.5	• 1 slice of bread (40g) • ½ medium roll or flat bread (40g) • ½ cup cooked rice, pasta, noodles, barley, buckwheat, semolina, polenta, bulgur or quinoa (75–120g) • ½ cup cooked porridge (about 120g) • 2/3 cup wheat cereal flakes (30g) • ¼ cup muesli (30g) • 3 crispbreads (35g) • 1 crumpet (60g) or a small English muffin/ plain scone (35g).
Meat and alternatives	2	2.5	• 65g cooked lean meat (about 90–100g raw weight of beef, veal, lamb, pork, kangaroo or goat) • 80g cooked poultry (about 100g raw weight of skinless chicken or turkey) • 100g cooked fish fillet (about 115g raw weight) or small can of fish • 2 large eggs (120g) • 1 cup (150g) cooked or canned legumes/beans such as lentils, chick peas or split peas (preferably with no added salt) • 170g tofu • 30g nuts, seeds or peanut or almond butter or tahini or other nut or seed paste (no added salt)
Dairy and alternatives	4	3.5	• 1 cup (250ml) fresh, UHT long-life or reconstituted powdered milk or buttermilk • ½ cup (120ml) evaporated milk • 2 slices, or 4x3x2cm piece (40g) hard cheese • ½ cup (120g) ricotta cheese • ¾ cup (200g tub) yoghurt • 1 cup (250ml) soy beverage

References: National Health and Medical Research Council (2013) Australian Dietary Guidelines Educator Guide. Canberra: National Health and Medical Research Council.

Supplementary Table 3. Missing data (Mean±SD): Sydney Memory and Aging Study (N=1037)

Missing data	Global cognition	Attention Processing speed	Language	Executive	Visuospatial	Memory	Verbal Memory	Dietary data	Reason of missing data
Wave 1	5 (0.48%)	16 (1.54%)	7 (0.68%)	87 (8.39%)	3 (0.29%)	11 (1.06%)	13 (1.25%)	72 (6.9%)	N=63 not assessed and N=9 not valid (misreported with implausible energy intake)
Wave 2	175 (16.9%)	197 (19.0%)	165 (15.9%)	247 (23.8%)	172 (16.6%)	184 (17.7%)	190 (18.3%)	N/A	N=43 deceased; N=6 loss of follow-up; N=76 withdrawn; other (not assessed)
Wave 3	303 (29.2%)	318 (30.7%)	285 (27.5%)	368 (35.5%)	302 (29.1%)	312 (30.1%)	313 (30.2%)	N/A	N=86 deceased; N=10 loss of follow-up; N=125 withdrawn; other (not assessed)
Wave 4	403 (38.9%)	428 (41.3%)	387 (37.3%)	457 (44.1%)	414 (39.9%)	428 (41.2%)	428 (41.2%)	N/A	N=136 deceased; N=11 loss of follow-up; N=164 withdrawn; other (not assessed)

Notes: SD, standard deviation. Wave 1- at baseline; wave 2- 2 year follow up; wave 3- 4 year follow up; wave 4- 6 year follow up.

Supplementary Table 4. Association between adherence to Australian Dietary Guidelines with overall cognitive function and change of cognitive performance over 6 years by quintiles (quintile 1–5, corresponding to very low to very high adherence) of Dietary Guideline Index-2013: the Sydney Memory and Ageing study (N=1037)

Cognition Domains	Quintile DGI-2013	Overall cognitive performance in 6 years			Slope of cognitive change over 6 years		
		β	95% CI	*P value*	β	95% CI	*P value**
Attention	**Quintile 1 (0-35)**	Reference	Reference	Reference	Reference	Reference	Reference
	Quintile 2 (36-42)	0.06	-0.13,0.26	0.53	0.08	-0.03,0.19	0.15
	Quintile 3 (43-47)	0.03	-0.18,0.24	0.77	0.07	-0.04,0.18	0.24
	Quintile 4 (48-52)	-0.01	-0.22,0.20	0.93	0.03	-0.09,0.15	0.59
	Quintile 5 (53-90)	0.05	-0.15,0.26	0.62	0.04	-0.07,0.15	0.48
Language	**Quintile 1 (0-35)**	Reference	Reference	Reference	Reference	Reference	Reference
	Quintile 2 (36-42)	0.12	-0.11,0.36	0.31	0.02	-0.09,0.14	0.67
	Quintile 3 (43-47)	0.11	-0.13,0.35	0.35	0.06	-0.05,0.18	0.30
	Quintile 4 (48-52)	0.07	-0.16,0.30	0.56	0.10	-0.02,0.22	0.10
	Quintile 5 (53-90)	-0.00	-0.24,0.23	0.99	0.07	-0.05,0.18	0.28
Executive	**Quintile 1 (0-35)**	Reference	Reference	Reference	Reference	Reference	Reference
	Quintile 2 (36-42)	0.03	-0.18,0.24	0.80	-0.05	-0.17,0.08	0.46
	Quintile 3 (43-47)	0.05	-0.18,0.27	0.68	0.06	-0.07,0.19	0.40
	Quintile 4 (48-52)	-0.02	-0.26,0.21	0.84	-0.05	-0.18,0.08	0.47
	Quintile 5 (53-90)	0.03	-0.20,0.25	0.82	-0.01	-0.13,0.12	0.93
Visuo-Spatial	**Quintile 1 (0-35)**	Reference	Reference	Reference	Reference	Reference	Reference
	Quintile 2 (36-42)	0.15	-0.01,0.31	0.07	-0.02	-0.10,0.07	0.70
	Quintile 3 (43-47)	0.15	-0.02,0.33	0.08	-0.02	-0.10,0.07	0.70
	Quintile 4 (48-52)	0.02	-0.17,0.20	0.87	-0.02	-0.10,0.07	0.69
	Quintile 5 (53-90)	0.11	-0.06,0.28	0.20	-0.03	-0.12,0.06	0.54
Memory	**Quintile 1 (0-35)**	Reference	Reference	Reference	Reference	Reference	Reference
	Quintile 2 (36-42)	0.12	-0.06,0.31	0.19	0.04	-0.04,0.13	0.33
	Quintile 3 (43-47)	0.00	-0.20,0.21	0.99	0.08	-0.02,0.18	0.12

	Quintile 4 (48-52)	0.04	-0.16,0.24	0.70	0.05	-0.05,0.15	0.32
	Quintile 5 (53-90)	-0.03	-0.22,0.16	0.79	0.04	-0.06,0.14	0.40
Verbal	**Quintile 1 (0-35)**	Reference	Reference	Reference	Reference	Reference	Reference
	Quintile 2 (36-42)	0.11	-0.08,0.30	0.26	0.05	-0.04,0.14	0.25
	Quintile 3 (43-47)	-0.00	-0.20,0.19	0.97	0.07	-0.01,0.16	0.10
	Quintile 4 (48-52)	0.04	-0.16,0.24	0.68	0.04	-0.05,0.13	0.37
	Quintile 5 (53-90)	-0.03	-0.22,0.15	0.72	0.04	-0.04,0.13	0.33
Global	**Quintile 1 (0-35)**	Reference	Reference	Reference	Reference	Reference	Reference
	Quintile 2 (36-42)	0.16	-0.05,0.38	0.14	0.03	-0.08,0.14	0.65
	Quintile 3 (43-47)	0.09	-0.12,0.31	0.40	0.06	-0.06,0.17	0.32
	Quintile 4 (48-52)	0.03	-0.20,0.26	0.82	0.03	-0.08,0.14	0.62
	Quintile 5 (53-90)	0.03	-0.19,0.25	0.76	0.04	-0.08,0.16	0.51

Notes:

CI, confidence interval.

Values are β (95% CI), n = 1037. In overall cognitive performance, β Coefficients show individual quintile by Dietary Guideline Index-2013 is associated with higher cognitive score (positive β) or lower cognitive score (negative β) with reference to quintile 1; in slope of cognitive change over six years, β Coefficients show individual quintile measured by Dietary Guideline Index-2013 is associated with faster cognitive decline (positive β) or slower cognitive decline (negative β) with reference to quintile 1.

Results were fully adjusted with age, sex, education, as well as non-English speaking background, BMI, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression and APOE ε4 genotype.

*P < 0.05 for global cognition or P<0.01 for individual cognitive domains, is significant.

Supplementary Table 5: Consumption of food components by Dietary Guideline Index 2013 quintiles: the Sydney Memory and Aging study (N=1037)

DGI-2013 /food group (serves/day)	**Quintile 1 (0-35)**		**Quintile 2** (35-42)		**Quintile 3** (42-47)		**Quintile 4** (47-52)		**Quintile 5** (52-73)	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
DGI score	29.6	5.0	39.3	2.1	45.2	1.4	49.8	1.4	57.9	4.6
Fruits (serves/day)	0.9	0.5	1.4	0.8	1.8	0.9	2.1	0.7	2.3	0.8
Vegetables (serves/day)	1.3	0.7	1.7	0.8	2.0	1.0	2.2	0.9	2.6	1.2
Grains and cereals (serves/day)	3.4	1.5	4.1	1.8	4.5	1.9	4.6	1.7	4.7	3.0
Whole Grains (serves/day)	1.6	1.4	2.4	1.6	2.8	1.5	3.1	1.3	3.3	1.5
Lean meats or alternatives (serves/day)	1.3	0.7	2.0	1.5	2.1	1.6	2.3	1.3	2.4	2.1
Dairy products or alternatives (serves/day)	1.4	0.8	1.6	0.8	1.7	0.7	1.9	0.8	2.0	0.9
Low fat dairy (serves/day)	0.4	0.6	0.7	0.7	1.0	0.7	1.2	0.8	1.5	0.8
Saturated fat (g)	24.6	9.4	28.0	13.8	26.8	15.2	26.1	12.9	21.0	11.4

Unsaturated fat (g)	26.3	9.2	33.8	15.3	34.9	16.1	35.9	15.3	33.2	16.4
Discretionary foods (serves/day)	4.0	1.6	4.2	2.7	4.1	3.0	3.8	2.4	2.0	1.7

Notes: DGI, Dietary Guideline Index; SD, standard deviation.

Supplementary Table 6. Linear mixed model analyses: Association of consumption of DGI-2013 food components with overall global cognition and change of global cognition over 6 years in the Sydney Memory and Aging study (N=1037)

Food components (serves/day)	Overall global cognition			Change in global cognition		
	β	95% CI	*P value*	β	95% CI	*P value**
Fruits	-0.09	-0.22,0.03	0.14	0.02	-0.02,0.06	0.25
Vegetables	0.01	-0.10,0.13	0.85	-0.01	-0.05,0.02	0.45
Grains and Cereals	0.01	-0.06,0.08	0.81	0.01	-0.01,0.03	0.54
Whole grains	-0.03	-0.11,0.05	0.40	0.01	-0.02,0.03	0.49
Lean meat and alternatives	0.01	-0.06,0.09	0.77	-0.01	-0.03,0.02	0.75
Dairy products and alternatives	0.00	-0.14,0.14	0.97	0.00	-0.04,0.04	0.90
Low fat dairy	0.01	-0.14,0.16	0.94	0.00	-0.04,0.04	0.84
Saturated fats (g/day)	0.00	0.00,0.00	0.57	0.00	0.00,0.00	0.67
Unsaturated fats (g/day)	0.01	0.00,0.02	0.27	0.00	0.00,0.00	0.34
Discretionary foods	-0.01	-0.07,0.05	0.81	0.00	-0.02,0.02	0.96

Notes: DGI, Dietary Guideline Index; CI, confidence interval. Values are β (95% CI), n = 1037. In overall cognitive performance, β Coefficients show a 1 serve/unit increase in daily consumption of food component is associated with higher cognitive score (positive β) or lower cognitive score (negative β)); in slope of cognitive change over six years, β Coefficients show a 1 serve/unit increase in daily consumption of food components is associated with faster cognitive decline (positive β) or slower cognitive decline (negative β). Results were fully adjusted with age, sex, education, as well as non-English speaking background, BMI, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), physical activity, smoking, depression, ethnicity and APOE ε4 genotype.

*P < 0.05 for global cognition or P<0.01 for individual cognitive domains, is significant.

Supplementary Table 7. A sensitivity analysis excluding participants with baseline cognition below 10th percentile: Association of the Dietary Guideline Index 2013 scores with overall cognitive function and change of cognitive performance over 6 years in the Sydney Memory and Aging study (N=929)

Cognition Domains		Model 1			Model 2		
		β	95% CI	*P value*	β	95% CI	*P value**
Attention	Overall cognitive performance	0.000	-0.006, 0.006	0.912	0.001	-0.005, 0.007	0.713
	cognitive change	0.000	-0.003, 0.003	0.933	0.000	-0.003, 0.003	0.966
Language	Overall cognitive performance	-0.002	-0.010, 0.006	0.693	0.000	-0.007, 0.007	0.973
	cognitive change	0.002	-0.002, 0.005	0.301	0.002	-0.001, 0.005	0.313
Executive	Overall cognitive performance	-0.001	-0.008, 0.006	0.791	0.000	-0.006, 0.006	0.919
	cognitive change	0.001	-0.003, 0.005	0.634	0.001	-0.003, 0.004	0.685
Visuo-Spatial	Overall cognitive performance	0.001	-0.004, 0.007	0.607	0.002	-0.004, 0.007	0.538
	cognitive change	-0.001	-0.004, 0.002	0.472	-0.001	-0.004, 0.002	0.447
Memory	Overall cognitive performance	-0.001	-0.007, 0.006	0.838	0.000	-0.006, 0.006	0.945
	cognitive change	0.002	-0.001, 0.005	0.292	0.002	-0.001, 0.005	0.303
Verbal	Overall cognitive performance	-0.001	-0.007, 0.005	0.691	-0.001	-0.007, 0.005	0.793
	cognitive change	0.002	-0.001, 0.005	0.240	0.002	-0.001, 0.005	0.251
Global	Overall cognitive performance	0.000	-0.006, 0.006	0.924	0.001	-0.006, 0.008	0.812
	cognitive change	0.000	-0.002, 0.002	0.547	0.000	-0.002, 0.002	0.593

Notes: Abbreviations: CI, confidence interval. Values are β (95% CI), n = 929. In overall cognitive performance, β Coefficients show a 1 score increase measured by Dietary Guideline Index-2013 is associated with higher cognitive score (positive β) or lower cognitive score (negative β)); in slope of cognitive change over six years, β Coefficients show a 1 score increase measured by Dietary Guideline Index-2013 is associated with faster cognitive decline (positive β) or slower cognitive decline

(negative β). Results were adjusted for age, sex, education for model 1; and fully adjusted with age, sex, education, as well as non-English speaking background, physical activity, BMI, hypertension, diabetes, hypercholesterolemia, history of stroke/ transient ischaemic attack (TIA), smoking, depression and APOE ε4 genotype for model 2.

*P < 0.05 for global cognition or P<0.01 for individual cognitive domains, is significant.

Table 8. Interactions between DGI-2013 scores and age, sex and education (indicated by p values) in Sydney Memory and Aging Study (N=1037)

Cognition	Interaction with DGI-2013	β	95% CI	*P value*
Attention	Age	0.000	-0.001, 0.000	0.576
	Sex	0.000	-0.007, 0.008	0.899
	Education	0.000	-0.001, 0.001	0.697
Language	Age	0.000	-0.001, 0.000	0.396
	Sex	0.000	-0.008, 0.007	0.946
	Education	-0.001	-0.002, 0.001	0.324
Executive	Age	0.000	-0.001, 0.001	0.861
	Sex	-0.003	-0.001, 0.005	0.428
	Education	0.000	-0.001, 0.011	0.681
Visuospatial	Age	0.000	-0.000, 0.001	0.578
	Sex	0.000	-0.006, 0.005	0.898
	Education	0.000	-0.001, 0.001	0.724
Memory	Age	0.000	-0.001, 0.001	0.894
	Sex	-0.001	-0.007, 0.006	0.786
	Education	0.000	-0.001, 0.001	0.964
Verbal Memory	Age	0.000	-0.001, 0.001	0.983
	Sex	-0.001	-0.007, 0.005	0.770
	Education	0.000	-0.001, 0.001	0.945
Global cognition	Age	0.000	-0.001, 0.000	0.796
	Sex	-0.003	-0.010, 0.005	0.498
	Education	0.000	-0.001, 0.001	0.776

Note: p values<0.05 is significant

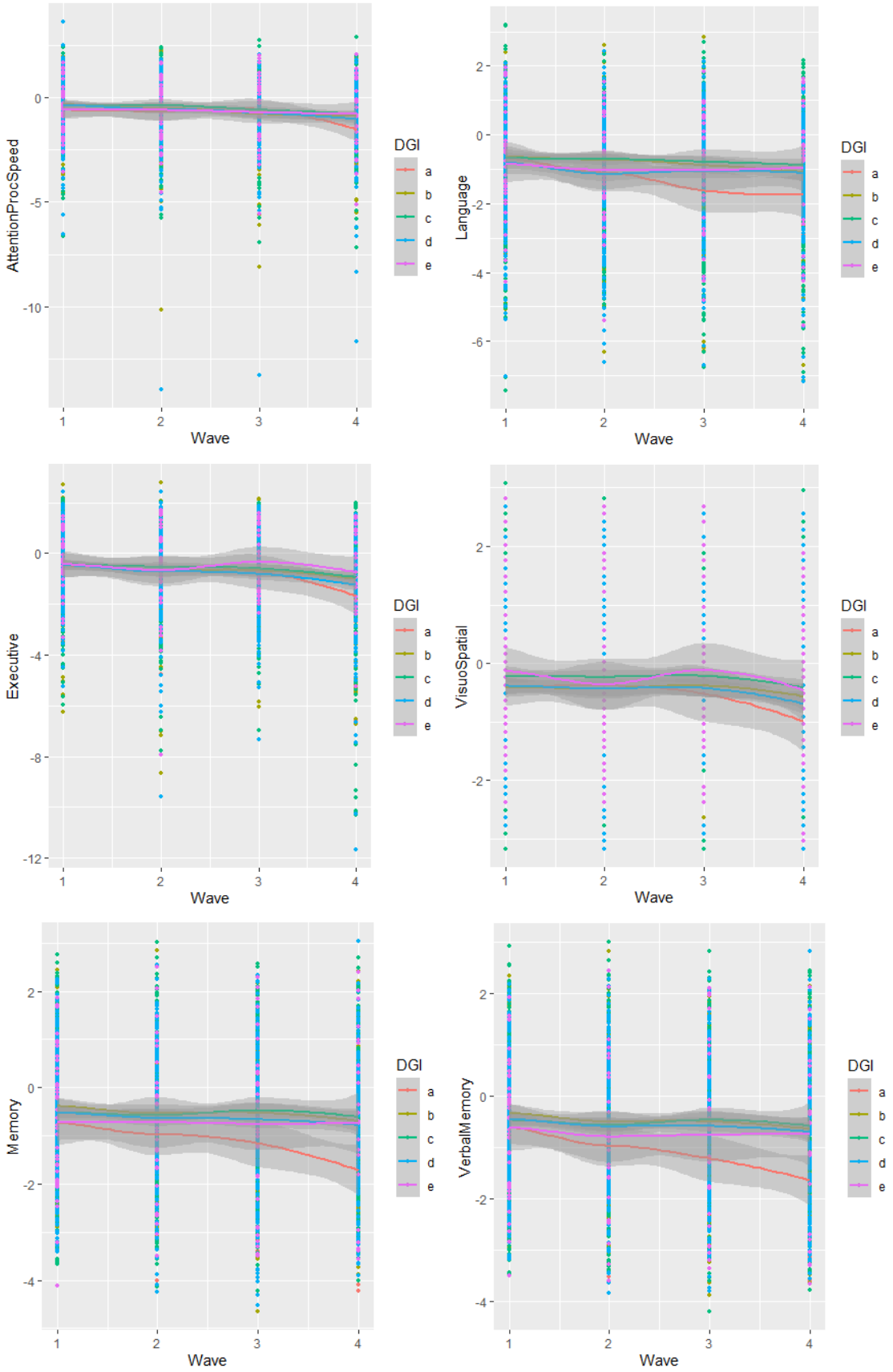
Supplementary Table 9. Food Components in Dietary Patterns: a comparison between healthy diet recommended by Australian Dietary Guidelines and Diets associated with better cognitive health

Diet	Fruits	Vegetables	Cereals	Nuts and legumes	Fish, poultry	Berries	Olive oil	Red and processed meat	Dairy food	Alcohol
Australian Dietary Guide	Encourage ≥2 serves/d	Encourage M ≥5, F ≥ 5 serves /d	Encourage wholegrain, M ≥4.5, F ≥3 serves /d	Not specified, counted as protein food	Not specified, counted as protein food	Not specified, counted as fruits	Small allowance	Counted as protein food limit processed meat	Encourage Low fat dairy M ≥ 3.5, F ≥ 4 serves /d	Limit as discretionary food
Mediterranean diet [(1)]	High consumption ≥3 serves /d	High consumption ≥4 serves /d	Non-refined cereals (whole grain bread, pasta, rice) ≥32 serves/week	Nuts: ≥3 serves/ week Legumes: ≥6 serves/ week	Fish: ≥6 serves/week Poultry: 3 or less serves/week	Not specified, counted as fruits	Use of olive oil as main culinary fat	1 serve / week or less	1 serve/ d or less	moderate intake of alcohol, preferentially red wine during meal
DASH diet [(2)]	Encourage 4-5 serves /d	Encourage 4-5 serves/d	Encourage 2-3 serves/d	Encourage ≥2 serves/d	Encourage fish as source of unsaturated fats	Not specified, counted as fruits	Encourage as source of mono-unsaturated fats	Limit intake	low fat dairy 2-3 serves/d	Not specified, limit sweetened beverages
MIND diet [(3)]	Not specified total fruits, Focused on berries	High consumption ≥ 7 serves/ week, Encourage green leafy vegetables	Wholegrain ≥3 serves /d	Nuts: ≥5 serves/ week Beans: ≥3 serves/ week	Fish: ≥1 serve/ week Poultry: ≥2 serves/ week	≥ 2 serves/ week	Use of olive oil as primary source of fat	Limit intake	Limit intakes of butter and margarine, cheese	limited intake of wine (red and white wine, 1 serve or less per day)

Note: serves /d, serves per day. M, male; F, female. DASH diet, the Dietary Approach to Stop Hypertension diet. MIND diet, the Mediterranean-DASH Intervention for Neurodegenerative Delay diet.

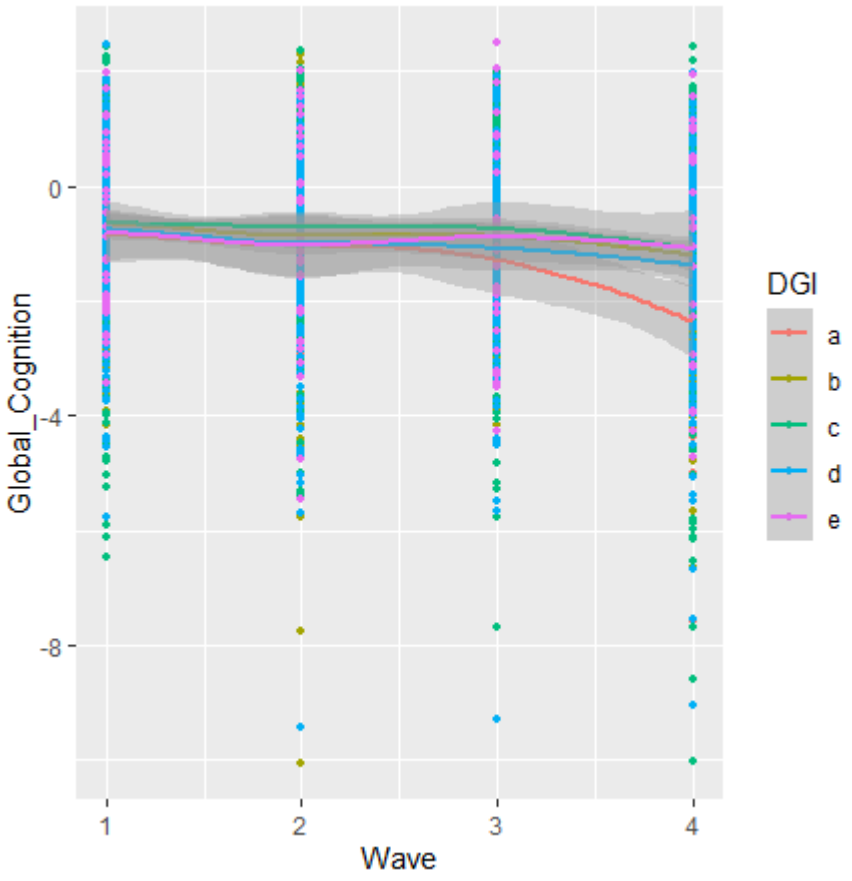
References:

1. Panagiotakos DB, Pitsavos C, Arvaniti F, Stefanadis C. Adherence to the Mediterranean food pattern predicts the prevalence of hypertension, hypercholesterolemia, diabetes and obesity, among healthy adults; the accuracy of the MedDietScore. Prev Med. 2007;44(4):335-40.
2. Berendsen AAM, Kang JH, van de Rest O, Feskens EJM, de Groot L, Grodstein F. The Dietary Approaches to Stop Hypertension Diet, Cognitive Function, and Cognitive Decline in American Older Women. J Am Med Dir Assoc. 2017;18(5):427-32.
3. Berendsen A, Kang JH, Feskens EJM, de Groot CPGM, Grodstein F, van de Rest O. Association of long-term adherence to the mind diet with cognitive function and cognitive decline in American women. The journal of nutrition, health & aging. 2017;22(2):222-9.



Supplementary Figure 1. Trajectories of cognitive decline in individual domains by DGI-2013 quintiles

Note: a, b, c, d, e are quintiles of DGI-2013, representing very low, low, moderate, high, very high adherence to Australian Dietary Guidelines



Supplementary Figure 2. Trajectories of cognitive decline in global cognition by DGI-2013 quintiles

Note: a, b, c, d, e are quintiles of DGI-2013, representing very low, low, moderate, high, very higher adherence to Australian Dietary Guidelines

Supplementary Material: STROBE-nut Statement—Checklist of items for nutritional epidemiological cohort studies

	Item No	Recommendation	STROBE-nut	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	**nut-1** State the dietary/nutritional assessment method(s) used in the title, abstract, or keywords.	Title p.1 and abstract p.2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found		Abstract p.2
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported		Introduction p.3
Objectives	3	State specific objectives, including any prespecified hypotheses		Introduction p.3
Methods				
Study design	4	Present key elements of study design early in the paper		Methods p.4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	**nut-5** Describe any characteristics of the study settings that might affect the dietary intake or nutritional status of the participants, if applicable.	Method p4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	**nut-6** Report particular dietary, physiological or nutritional characteristics that were considered when selecting the target population	Method p4-5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed		

Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	**nut-7.1** Clearly define foods, food groups, nutrients, or other food components. **nut-7.2** When using dietary patterns or indices, describe the methods to obtain them and their nutritional properties.	Method p4-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	**nut-8.1** Describe the dietary assessment method(s), e.g., portion size estimation, number of days and items recorded, how it was developed and administered, and how quality was assured. Report if and how supplement intake was assessed. **nut-8.2** Describe and justify food composition data used. Explain the procedure to match food composition with consumption data. Describe the use of conversion factors, if applicable. **nut-8.3** Describe the nutrient requirements, recommendations, or dietary guidelines and the evaluation approach used to compare intake with the dietary reference values, if applicable.	Method (dietary assessment methods, FFQ used, method to construct dietary pattern scores, Australian Dietary Guide and Dietary Guide Index-2013 used to compare intake with dietary reference values, assessment of non-dietary data, validity of dietary assessment tool) p4-6 Supplementary table 1-2

			nut-8.4 When using nutritional biomarkers, additionally use the STROBE Extension for Molecular Epidemiology (STROBE-ME). Report the type of biomarkers used and their usefulness as dietary exposure markers.	
			nut-8.5 Describe the assessment of nondietary data (e.g., nutritional status and influencing factors) and timing of the assessment of these variables in relation to dietary assessment.	
			nut-8.6 Report on the validity of the dietary or nutritional assessment methods and any internal or external validation used in the study, if applicable.	
Bias	9	Describe any efforts to address potential sources of bias	**nut-9** Report how bias in dietary or nutritional assessment was addressed, e.g. misreporting, changes in habits as a result of being measured, or data imputation from other sources.	Method p4-6 Statistical analysis p.8-9
Study size	10	Explain how the study size was arrived at		Method p4

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	**nut-11** Explain categorization of dietary/nutritional data (e.g., use of N-tiles and handling of nonconsumers) and the choice of reference category, if applicable.	Method p4-7 Statistical analysis p.8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	**nut-12.1** Describe any statistical method used to combine dietary or nutritional data, if applicable. **nut-12.2** Describe and justify the method for energy adjustments, intake modeling, and use of weighting factors, if applicable. **nut-12.3** Report any adjustments for measurement error, i.e,. from a validity or calibration study.	Statistical analysis p.8-9
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	**nut-13** Report the number of individuals excluded based on missing, incomplete or implausible dietary/nutritional data.	Methods p.4 Supplementary material table 3(number of participants, missing data and reasons of missing data)
		(b) Give reasons for non-participation at each stage		Supplementary material table 3

				(number of participants, missing data and reasons of missing data)
		(c) Consider use of a flow diagram		
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	**nut-14** Give the distribution of participant characteristics across the exposure variables if applicable. Specify if food consumption of total population or consumers only were used to obtain results.	Results p.9-11 Table 1-4 Statistical analysis p.8-9 (demographics and characteristics of study participants and information on exposures and potential confounders as covariates in analysis)
		(b) Indicate number of participants with missing data for each variable of interest		Results p.10 Supplementary material table 3
		(c) Summarise follow-up time (eg, average and total amount)		Methods p.5-7
Outcome data	15*	Report numbers of outcome events or summary measures over time		Methods p.4-7 Results p.9-11 Statistical analysis p.8-9

				(outcome events and covariates/models)
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	**nut-16** Specify if nutrient intakes are reported with or without inclusion of dietary supplement intake, if applicable.	Statistical analysis p.8-9 Results p.9-11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	**nut-17** Report any sensitivity analysis (e.g., exclusion of misreporters or outliers) and data imputation, if applicable.	Statistical analysis p.8-9
Discussion				
Key results	18	Summarise key results with reference to study objectives		Results p.9-11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	**nut-19** Describe the main limitations of the data sources and assessment methods used and implications for the interpretation of the findings.	Discussion p.14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	**nut-20** Report the nutritional relevance of the findings, given the complexity of diet or nutrition as an exposure.	Discussion p.11-14

Generalisability	21	Discuss the generalisability (external validity) of the study results		Discussion p.12-14
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	**nut-22.1** Describe the procedure for consent and study approval from ethics committee(s). **nut-22.2** Provide data collection tools and data as online material or explain how they can be accessed.	Methods p.5 Funding and author contribution p.15