DIET AND EPIDEMIOLOGY OF NON-COMMUNICABLE CHRONIC DISEASES

Focusing on dietary and nutrient patterns and bone fragility in adults

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ABSTRACT

Existing evidence supports the increasing consumption of unhealthy diet and associated growing impact on the current burden of non-communicable diseases (NCDs) globally. However, evidence on the extent of diet-related NCD burden remains limited. Firstly, this thesis assesses the trends in diet-related NCDs in Australia from 1990 to 2015 and compares the results with other countries of the Organization for Economic Co-operation and Development (OECD).

Fourteen dietary risk factors (eight food groups, five nutrients and fibre intake) were included in Global Burden of Disease (GBD) 2015. Body mass index, total serum cholesterol, fasting plasma glucose and systolic blood pressure were considered to mediate the relationship between dietary factors and NCDs. The results demonstrated that over the past 25 years, the burden of diet-related NCDs in Australia has declined. However, despite this and improvements in Australia's comparative global standing, the relative contribution of dietary risk factors to NCD burden is still high in Australia. In 2015, nearly one-fifth (19.7%) of NCD deaths in Australia were attributable to dietary risk factors. Young (25–49 years) and middle-age (50–69 years) males had a higher population attributable fraction of diet-related NCD deaths and disability-adjusted life years (DALYs) than their female counterparts. Overall, more than three-quarters (80.5%) of diet-related NCD deaths were caused by cardiovascular disease (CVD) and 42.3% of all CVD deaths were attributable to dietary risks. Diets low in fruits, vegetables (FV), nuts and seeds, and whole grains, and high in sodium were the major contributors to both NCD deaths and DALYs.

The findings above form the basis for the remaining studies presented in this thesis. The

above study did not look at the impact of diet on musculoskeletal diseases, specifically on osteoporosis and fractures. In the subsequent studies, I hypothesize that diet is an important risk factor for osteoporosis and fractures.

Previous studies on the association between dietary patterns and bone mineral density (BMD) have reported inconsistent findings. Data from the North West Adelaide Health Study (NWAHS), a population-based cohort study undertaken in Australia, are used to assess this association among adults aged 50 years and above. Overall, 1182 adults (545 males, 45.9%) had dietary data collected using a food frequency questionnaire (FFQ) and also had BMD measurements taken using Dual-energy X-ray absorptiometry (DXA). Factor analysis using the principal component analysis (PCA) method was applied to ascertain dietary patterns. Two distinct dietary patterns were identified. Pattern 1 ('prudent' pattern) was characterised by high intake of FV, sugar, nut-based milk, fish, legumes and high-fibre bread. In contrast, pattern 2 ('Western' pattern) was characterised by high levels of processed and red meat, snacks, takeaway foods, jam, beer, soft drinks, white bread, poultry, potato with fat, high-fat dairy products and eggs. Compared with the study participants with lowest consumption (first tertile) of the 'prudent' pattern, participants in the third tertile had a lower prevalence of low BMD (prevalence ratio (PR) = 0.52; 95% confidence interval (CI): 0.33, 0.83) after adjusting for sociodemographic, lifestyle and behavioural characteristics, chronic conditions and energy intake. Participants in the third tertile of the 'Western' pattern had a higher prevalence of low BMD (PR = 1.68; 95% CI: 1.02, 2.77) compared with those in tertile 1. In contrast to the 'Western' diet, a dietary pattern characterised by high intake of FV and dairy products is positively associated with BMD.

In addition to dietary patterns, exploring the association between nutrient patterns and

BMD provides further insight into the physiological mechanisms of how dietary patterns impact BMD. There is limited evidence of the link between the overall nutrients intake from diet and BMD. I assess the association between nutrient patterns and BMD among an older Australian population. Participants (n = 1135; males, 45.8%; median age, 62.0 years) with dietary and BMD data in the NWAHS were included. Dietary intake was assessed using a FFQ. BMD was measured using DXA. Nutrient patterns were identified by factor analysis. Linear regression analyses were conducted to assess the association between nutrient patterns and BMD. Multiple imputation and sensitivity analyses were conducted to investigate the effect of missing data on the estimates. Three nutrient patterns (animal-sourced [cholesterol, protein, Vitamin B12 and fat], plant-sourced [fibre, carotene, vitamin C and Lutein] and mixed-source—a combination of both animal- and plant-sourced [potassium, calcium, fibre, retinol and Vitamin B12]) were identified. After adjusting for sociodemographic, lifestyle and behavioural characteristics, chronic conditions and energy intake, animal ($\beta = -4.07$; 95% CI: −11.89, 3.76) and plant-sourced ($\beta = -0.99$; 95% CI: −7.43, 5.45) patterns were not associated with BMD. However, I found that the mixed-source pattern was positively associated with BMD ($\beta = 10.86$; 95% CI: 1.91, 19.80). There were no interactions between the pattern, other covariates and BMD. The multiple imputation and sensitivity analyses including missing data identified similar patterns of association between nutrient patterns and BMD. Whereas animal- and plant-sourced nutrient patterns are not associated with BMD, a mixed-source pattern may prevent a reduction in BMD.

In addition to investigating the association of dietary and nutrient patterns with BMD, the relationship between long-term dietary and nutrient patterns and the ultimate consequence of low BMD (i.e. fracture risk) is pivotal. However, studies on long-term exposure to foods/nutrients and the associations with fracture risk are scarce. Using data from the

China Health and Nutrition Survey, I determine the prospective association of dietary and nutrient patterns with fractures. Data from 15,572 adults aged ≥18 years were analysed. Fracture occurrence was self-reported and dietary intake data were collected using a 24-hour (24-h) recall method for three consecutive days, for each individual across nine waves (1989–2011). I used cumulative and overall mean, recent and baseline dietary and nutrient exposures. Hazard ratios (HR) were used to determine the associations. Two dietary (traditional and modern) and two nutrient (plant- and animal-sourced) patterns were identified. After adjusting for potential confounders, study participants within the highest intake (third tertiles) of the modern dietary and animal-sourced nutrient patterns' cumulative scores had a 34% (HR = 1.34; 95% CI: 1.06–1.71) and 37% (HR = 1.37; 95% CI: 1.08–1.72) increase in fracture risks compared to those in the first tertiles, respectively. While the overall mean factor scores of dietary and nutrient patterns had a similar (or stronger) pattern of association as the cumulative scores, no association between recent and baseline scores and fracture was found. Greater adherence to a modern dietary and/or an animal-sourced nutrient pattern is associated with a higher total fracture risk. This suggests that a modern animal-based diet is related to bone fragility. A repeated three-day 24-h recall dietary assessment provides a stronger association with fracture compared to a recent or baseline exposure.

In the above studies, I used factor analysis with PCA method. However, in addition to this method, there are other common data reduction methods. The relative advantages of these methods, particularly in identifying dietary patterns associated with bone mass, have not been investigated. I evaluated three methods: PCA, partial least-squares (PLS) and reduced-rank regressions (RRR) in determining dietary patterns associated with bone mass. Dietary patterns were constructed using PCA, PLS and RRR and compared based on the performance to identify plausible patterns associated with BMD and bone mineral

content (BMC). PCA, PLS and RRR identified two, four and four dietary patterns, respectively. All methods identified similar patterns for the first two factors (factor 1, 'prudent' and factor 2, 'Western' patterns). Three, one and none of the patterns derived by RRR, PLS and PCA were significantly associated with bone mass, respectively. The 'prudent' and dairy (factor 3) patterns determined by RRR were positively and significantly associated with BMD and BMC. Vegetables and fruit pattern (factor 4) of PLS and RRR was negatively and significantly associated with BMD and BMC, respectively. RRR was found to be more appropriate in identifying more (plausible) dietary patterns that are associated with bone mass than PCA and PLS. Nevertheless, the advantage of RRR over the other two methods (PCA and PLS) should be confirmed in future studies.

The findings from these studies indicate that diet is a leading risk factor for the current burden of disease in Australia and has a significant impact on bone health among adults in Australia and China. In identifying dietary patterns that are associated with bone health, dietary data collection and analysis methods are important factors that potentially bias findings. These analyses have not previously been undertaken and indicate the potential implications of diet on long-term bone health. The findings have significant implications in public health interventions and clinical practices. Future studies should focus on the potential mechanisms and pathways of the associations of diet with osteoporosis and fracture risks. Identification of mediating factors and investigating their roles in the pathways should be the focus of future studies. Further evaluation of statistical methods in the analysis of dietary patterns associated with bone health and other disease outcome is warranted.

DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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Yohannes Adama Melaku

Signature 25/07/2018

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LIST OF PUBLICATIONS

The following list contains publications in peer-reviewed journals in which I was involved as a lead author during my PhD study period (27 July 2015 – 27 July 2018). Of these publications, five (3, 6, 8, 9 and 11) are included in this thesis.

1. **Melaku YA**, Wassie MM, Gill TK, et al: Burden of disease attributable to suboptimal diet, metabolic risks, and low physical activity in Ethiopia and comparison with Eastern sub-Saharan African countries, 1990-2015: findings from the Global Burden of Disease Study 2015: **BMC Public Health** 2018; 18:552.
2. **Melaku YA**, Renzaho A, Gill TK et al: Burden and trend of diet-related non-communicable diseases in Australia and comparison with 34 countries: findings from the Global Burden of Disease Study 2015: **European Journal of Nutrition** 2018. doi: 10.1007/s00394-018-1656-7
3. **Melaku YA**, Gill TK, Taylor AW, Adams R, Shi Z, Worku A: Associations of childhood, maternal and household dietary patterns with childhood stunting in Ethiopia: Proposing an alternative and plausible dietary analysis method to dietary diversity scores: **Nutrition Journal** 2018; 17(1):14.
4. **Melaku YA**, Appleton SL, Gill TK, et al: Incidence, prevalence, mortality, disability-adjusted life years and risk factors of cancer in Australia and comparison with OECD countries, 1990-2015: findings from the Global Burden of Disease Study 2015: **Cancer Epidemiology** 2017; 52: 43-54.
5. **Melaku YA**, Gill TK, Appleton SL, Taylor AW, Adams R, Shi Z: Prospective Associations of Dietary and Nutrient Patterns with Fracture Risk: A 20-Year Follow-Up Study. **Nutrients** 2017; 9(11).

6. **Melaku YA**, Shi Z: Lessons for the Sustainable Development Goals from Ethiopia's success: the case of under-5 mortality: **The Lancet Global Health** 2017; e1060-e1.5 doi:10.1016/S2214-109X(17)30385-6.

7. **Melaku YA**, Gill TK, Taylor AW, Adams R, Shi Z: Association between nutrient patterns and bone mineral density among aging adults. **Clinical Nutrition ESPEN** 2017; doi: 10.1016/ j.clnesp.2017.08.001.

8. **Melaku YA**, Gill TK, Taylor AW, Adams R, Shi Z: A comparison of principal component analysis, partial least-squares and reduced-rank regressions in the identification of dietary patterns associated with bone mass in aging Australians. **European Journal of Nutrition** 2017; DOI: 10.1007/s00394-017-1478-z.

9. **Melaku YA**, Temesgen AM, Deribew A, et al: The impact of dietary risk factors on the burden of non-communicable diseases in Ethiopia: findings from the Global Burden of Disease Study 2013. **International Journal of Behavioural Nutrition and Physical Activity** 2016; 13(1).

10. **Melaku YA**, Gill TK, Adams R, Shi Z: Association between dietary patterns and low bone mineral density among adults aged 50 years and above: findings from the North West Adelaide Health Study (NWAHS). **British Journal of Nutrition** 2016; DOI:10.1017/S0007114516003366.

11. **Melaku YA**, Zello GA, Gill TK, Adams R, Shi Z: Prevalence and factors associated with stunting and thinness among adolescent students in Northern Ethiopia: A comparison to World Health Organization standards. **Archives of Public Health** 2015; 73(1).

RESEARCH PRESENTATIONS

1. **Melaku** YA, Gill T, Taylor A, Adams R, Shi Z (oral presentation) Prospective associations of dietary and nutrient patterns with all-cause mortality: Findings from a 20-year follow-up study in China. **Asia-pacific Conference on Clinical Nutrition–Adelaide, Australia, 26-29 November 2017**
2. **Melaku YA**, Gill T, Taylor A, Adams R, Shi Z. (poster presentation) Prospective associations of dietary and nutrient patterns with fracture risk: a 20-year follow-up study. **World Congress of Epidemiology (The International Epidemiological Association)–Saitama, Japan, 19-22 August 2017**
3. **Melaku YA**, Gill T, Taylor A, Adams R, Shi Z. (poster presentation) Association between nutrient patterns and bone mineral density among aging adults. **Nutrition Society of Australia–Melbourne, Australia, 29 November-2 December 2016**
4. **Melaku YA**, Renzaho A, Gill TK et al. (oral presentation) Burden and trend of diet-related non-communicable diseases in Australia and comparison with 34 countries: findings from the Global Burden of Disease Study 2015. 201. **South Australia Population Health Conference–Adelaide, Australia, 21 October 2017**

ABBREVIATIONS/ACRONYMS

ABD	Australian Burden of Disease
AIC	Akaike's information criterion
BMC	Bone mineral content
BMD	Bone mineral density
BMI	Body mass index
BMR	Basal metabolic rate
CATI	Computer assisted telephone interview
CNFS	China National Fracture Study
CHNS	China Health and Nutrition Survey
CI	Confidence interval
CVD	Cardiovascular disease
DALY	Disability-adjusted life years
DHA	Docosahexaenoic acid
DNA	Deoxyribonucleic acid
DQES	Dietary Questionnaire for Epidemiological Studies
DXA	Dual-energy X-ray absorptiometry
EFA	Explanatory factor analyses
EPA	Eicosapentaenoic acid
EA	Energy intake
FFQ	Food frequency questionnaire
FV	Fruit and vegetables
GBD	Global Burden of Disease
HR	Hazard ratio
KMO	Kaiser–Mayer–Olkin
MET	Metabolic equivalent of task

MSD	Musculoskeletal disease
NCD	Non-communicable disease
NHS	National Health Survey
OECD	Organization for Economic Cooperation and Development
OLS	Ordinary least squares
NWAHS	North West Adelaide Health Study
PAF	Population attributable fraction
PAL	Physical activity level
PCA	Principal component analysis
PLS	Partial least-squares
PR	Prevalence ratio
PUFA	Polyunsaturated fatty acid
RCT	Randomized controlled trials
RRR	Reduced-rank regression
SDG	Sustainable Development Goals
SSB	Sugar-sweetened beverages
ST-GPR	Spatiotemporal Gaussian process regression model
sTOFHLA	Short test of functional health literacy in adults
TMREL	Theoretical minimum risk exposure level
UI	Uncertainty interval
UK	United Kingdom
UN	United Nations
US	United States (of America)
WHO	World Health Organization
YLD	Years lost due to disability
YLL	Years of life lost

CHAPTER 1 INTRODUCTION

1.1 Background

As global life expectancy increases significantly and deaths due to communicable diseases decrease, non-communicable diseases (NCDs) have become the leading causes of death [1-3]. Global crude death and disability-adjusted life years (DALYs) rates due to NCDs in 2016 were 535 and 19,859 per 100,000, respectively. The average crude death and DALYs rates as a result of NCDs in high-income countries were 806 and 22,950 per 100,000, respectively [3]. In 2016, cardiovascular diseases (CVDs) (239 deaths per 100,000 people), neoplasms (121 deaths per 100,000) and chronic respiratory disease (48 deaths per 100,000) were the most common causes of mortality globally. In terms of DALYs, CVDs (4777 DALYs per 100,000) and neoplasms (2884 DALYs per 100,000) were the two highest-ranked NCDs [4]. In addition to these major health problems, musculoskeletal disorders (MSDs) have contributed significantly to the current burden of disease in adults and aging population [5].

MSDs are major contributors to disability, measured by years lived with disability (YLDs) [2]. In 2016, an estimated 89,228 deaths were reported due to MSDs. The crude YLDs rate associated with MSDs were 1865 per 100,000 [4]. The burden is expected to increase as a result of the aging population. MSDs could have an impact on susceptibility of NCDs (e.g. CVDs and neoplasms) by profoundly limiting physical activity [6], an acknowledged risk factor associated with both conditions. Further, impaired musculoskeletal health has a positive association with functionality loss, fragility and independency, leading to personal and community level consequences, and ultimately resulting in multimorbidity and mortality [6-9]. As a result, the health care cost associated with MSDs and its consequences is increasing in developed countries. For instance, in Australia, the cost is already high and will increase by 223% in the year 2033 [10, 11].

Osteoporosis, a condition characterized by a disruption of the balance between bone formation (decreased) and resorption (increased) [12], is potentially preventable or at least manageable MSD. Although the extent of the condition is underestimated, it affects a significant segment of the population globally and in developed countries [13]. It has been estimated that more than 200 million people worldwide had osteoporosis in 2010 [14]. Associated with this condition, the prevalence and consequences of osteoporotic fractures has increased [15, 16]. It has been shown that osteoporosis and other NCDs are likely to coexist [17, 18] with a bidirectional effect on each other. In addition, there are common behavioural risk factors associated with osteoporosis and other NCDs, including diet and physical activity [19, 20]. The extent and influence of these risk factors has increased globally, particularly in developed countries [20].

As a result of the global phenomenon related to an increasing NCD burden and its risk factors, the United Nations (UN) developed and endorsed a political declaration in 2011 [21] and the third Sustainable Development Goals (SDGs) [22] to enable the prevention and control of NCDs. One of the focus areas of the declaration and goals is in reducing risk factors of NCDs at different levels. NCDs are predisposed by various interrelated and correlated risk factors. These risk factors could be modifiable or non-modifiable. Socio-cultural, economic, behavioural, health interventions, environmental/occupational, metabolic, and genetic are alternative broad classifications of risk factors [23, 24]. Of all NCD-related deaths in 2016 globally, 64.4% were attributable to behavioural (43.0%), metabolic (42.9%) and environmental/occupational (16.0%) factors. Dietary risk factors were the leading risks of all-cause and NCD-related deaths globally, contributing 18.8% of all-cause deaths or 26.1% (10.3 million) of the global NCD-related deaths in 2016 [20].

Bone mass is influenced by modifiable lifestyle factors. Of these factors, the impact of

nutrition on bone mineral density (BMD) is pivotal [19]. A number of studies have shown associations of individual nutrients [19], foods [19, 25] and food patterns [26] with BMD and osteoporosis. In addition, previous studies have also demonstrated associations between nutrients [27], foods [28, 29] and dietary patterns [30, 31] with fracture risks. For instance, although the evidence is limited, a study demonstrated that increased soda intake was positively associated with hip fracture among postmenopausal women [32]. The association of diet with BMD, osteoporosis and fracture risk could be due to a direct effect of nutrients [19, 33, 34] and food groups [19, 35] or indirectly through its effect on inflammation [36] and other NCDs [37, 38].

However, accuracy and precision of dietary data collection and analysis methods have been long-standing major challenges in the area of nutritional epidemiology [39, 40]. In the past two decades, with the increasing development of statistical software and their applications, dietary data collection and analysis methods have been improved [41, 42]. As a result, dietary analysis methods have shifted from an individual food-/nutrient-based approach to a comprehensive analysis of diet and nutrients to reflect the overall intake and an interaction of foods and nutrients. There has been a growing body of evidence that has shown the importance of dietary analysis methods (both *a posterior and a priori*) in identifying dietary patterns associated with health outcomes [43-45]. These methods include principal component analysis (PCA) [46], partial least-squares (PLS) [47] and reduced-rank regressions (RRR) [48]. PCA is purely *a posteriori* method while RRR and PLS are combinations of both *a priori* and *a posteriori* analysis methods. These methods are relatively new and evolving in the field of nutritional epidemiology.

1.2 Rationale for this thesis

Existing evidence supports the increasing consumption of unhealthy diet and associated growing impact on the current burden of NCDs globally [49, 50]. However, it is not known what proportion of the current NCD burden is attributable to dietary habits. In addition, a ranking of countries based on the burden of NCDs attributable to dietary risk factors has not been investigated and there is limited evidence to show which dietary components are the leading contributors to the current burden of disease.

While it is essential to determine the health effect of individual foods and nutrients, acknowledging the interaction of these components is equally important. Foods and nutrients are consumed as a whole, not as single entities and dietary habits may vary across communities due to religious and cultural differences and food availability [51]. Previous studies have not investigated the association between nutrient patterns and BMD and long-term associations of nutrient and dietary patterns with fracture risks have also not been assessed in previous studies. To address this, the application of dietary pattern analysis methods (both *a posterior* and *a priori* methods) has become a common practice in nutritional epidemiology. These methods are important and popular because they are useful approaches in identifying dietary habits, taking the relative contribution of each food items consumed (rather than focusing on a single item) into account, and providing a comprehensive picture of dietary behaviours [51]. However, although there are studies that have evaluated different dietary patterns analysis in association with other outcomes [52, 53], no studies have evaluated these in relation to BMD, bone mineral content (BMC) or osteoporosis.

Therefore, this thesis will fill the aforementioned gaps by adding a body of evidence on diet-related burden of NCDs (particularly in developed countries) and how dietary and

nutrient patterns are associated with BMD, BMC, osteoporosis and fracture risk. By comparing common dietary analysis methods in nutritional epidemiology (PCA, PLS and RRR), the thesis will contribute to this growing field.

1.3 Aims and objectives

This thesis is in three parts. The first aims to assess the impact of dietary risk factors on the overall the burden of common NCDs (CVD, cancer and diabetes mellitus) in Australia and other developed countries using the Global Burden of Disease (GBD) Study. Secondly, the thesis aims to investigate the associations of dietary and nutrient patterns with BMD, osteoporosis and fracture risks among adults using datasets from Australia and China. Finally, the thesis compares common dietary pattern analysis methods in identifying patterns that are associated with BMD and BMC.

The objectives of this thesis are:

- To assess the contribution of dietary risk factors to the current NCD-related disabilities and mortality in Australia
- To examine whether dietary patterns were associated with low BMD in older adults
- To identify nutrient patterns and investigate how the patterns are associated with BMD in aging adults
- To investigate the association of dietary and nutrient patterns with fracture risks in adults
- To compare RRR, PLS and PCA methods in identifying dietary patterns associated with BMD and BMC

1.4 Format and outline of the thesis

The first chapter of this thesis contains an introduction, rationales and objectives. In the second chapter (CHAPTER 2), a detailed review of literature is provided on the burden and risk factors of NCDs. Diet-related burden of disease and the association between diet and bone fragility are the main focuses of this chapter. CHAPTER 3 provides an overview of method for all studies in the thesis. CHAPTER 4 contains a published paper which focuses on the overall burden of NCDs associated with dietary risk factors in Australia and compares with other 34 members of Organization for Economic Cooperation and Development (OECD). CHAPTER 5 assesses the association between dietary patterns and osteoporosis. The subsequent chapter (CHAPTER 6) identifies nutrient patterns associated with BMD/BMC. CHAPTER 7 focuses on the associations of dietary and nutrient patterns with fracture risks among adults and, CHAPTER 8 focuses on the evaluation of common dietary analysis methods (RRR, PLS and PCA) in association with BMD. The last chapter contains discussions of the overall findings, future directions and conclusions (Figure 1.1).

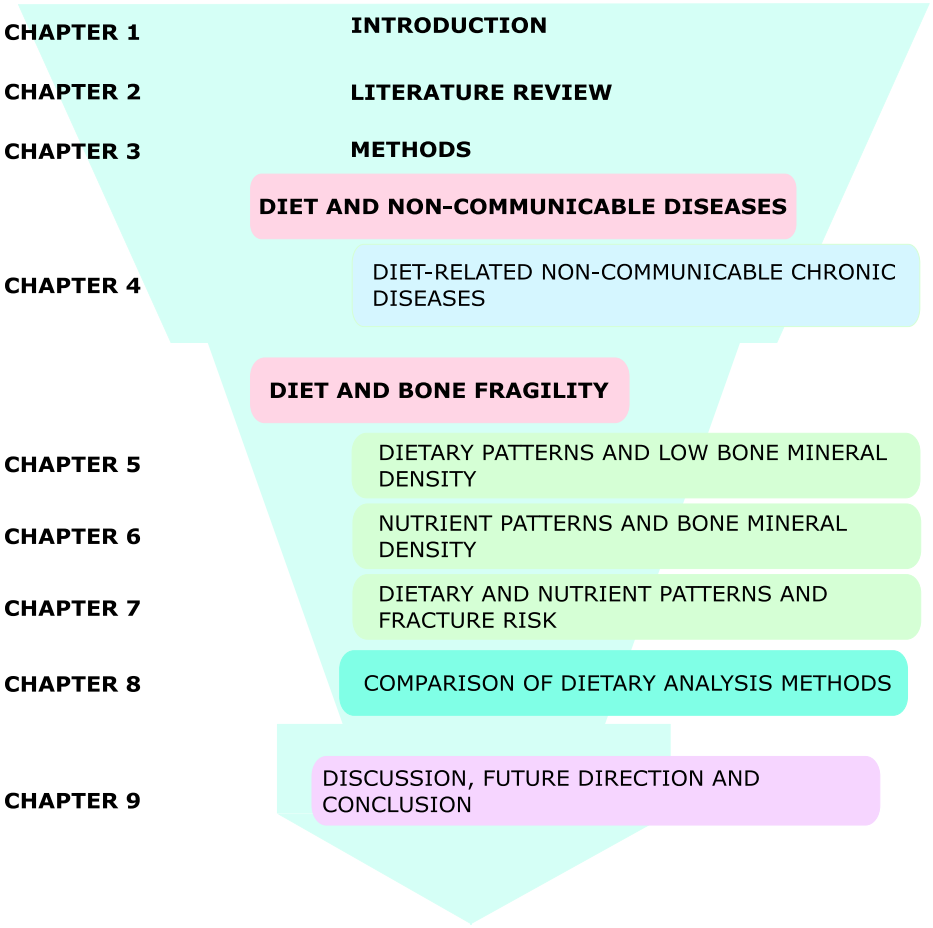

Figure 1.1 Format and outline of the thesis

CHAPTER 2 LITERATURE REVIEW

2.1 Burden of non-communicable chronic diseases

NCDs impose a major burden on health worldwide. Globally, 38 million (68%) deaths each year are due to NCDs. Of these, 16 million (more than 40%) are premature deaths (deaths that occur between 30 and 70 years of age). By 2030, NCD deaths are projected to be 53 million [54]. In 2016, with 17.7 million deaths, CVDs were the leading causes of deaths, followed by cancer (8.9 million), chronic respiratory diseases (3.5 million) and diabetes/urology/blood and endocrinology disorders (3.2 million) [4]. Although MSDs are often neglected chronic diseases [55], the health and economic impact of the disorders have been already high and increasing [2]. In 2016, an estimated 140 million DALYs were due to MSDs [4].

2.2 Burden of musculoskeletal disorders

MSDs are a group of disorders that include osteoporosis, fractures, low back pain, neck pain, osteoarthritis, rheumatoid arthritis and gout. These conditions affect the muscles, bones, soft tissue and joints, and spine and all age groups. In 2016, 1.3 billion (17.8%) people had MSDs worldwide. In the same year, an estimated 652 million new cases of MSDs were reported [4]. Of the MSDs, osteoporosis and fractures are associated with significant disability, mortality, social and economic burden and the conditions are increasing in societies which warrant a due attention by clinicians and public health practitioners.

2.2.1 Osteoporosis

Pathophysiology, definition and measurements of osteoporosis

Bone is a dynamic tissue comprising of cellular, organic, and inorganic components with

a complex internal structure. This structure is maintained by bone modelling and remodelling. It is constantly formed and resorbed throughout life as the result of the opposing activities of two major cell groups—osteoblasts and osteoclasts. Osteoblasts have a building role (formation of bone tissues) as opposed to osteoclasts which resorb bone [56]. However, disruption of the balance between bone formation and resorption due to excessive production of osteoclasts or inadequate presence of osteoblasts leads to bone loss and hence osteoporosis (bad bone) [12].

Objective definitions and measurements of osteoporosis vary by age, sex, race, skeletal site measured, the technology used, and even by country of residence [57-61]. However, generally, it can be defined as a condition of compromised bone quantity (BMD) and quality (architecture) which can consequently lead to low-trauma fracture [59]. Based on predisposing factors, there are two major categories of osteoporosis—primary and secondary. Primary osteoporosis can occur in both sexes and at any age but it is more common among menopausal women or very elderly men, whereas, secondary osteoporosis is predisposed by specific conditions, like diseases, such as chronic liver diseases [18] and medications, for instance, glucocorticoids [62].

Osteoporosis can be diagnosed by history, physical examination, biochemical samples, radiography and bone densitometry (e.g. Dual-energy X-ray Absorptiometry (DXA)) [58, 63]. Screening survey tools have also been developed, tested and used to identify osteoporosis risk at community level [64, 65]. These methods have different levels of sensitivity and specificity. Currently, the gold-standard method is DXA. Values of the measurements of DXA can be expressed in grams, grams/centimeter^2 and Z- or T-score. A T-score indicates how much bone mass is higher or lower than the bone mass of a healthy 30-year old person [58, 59]. The most accepted definition is that, according to the

World Health Organization (WHO), individuals with T-scores ≤ -2.5, between -2.5 and -1, and ≥ -1 are classified as osteoporotic, osteopenic and normal, respectively [58].

Burden of osteoporosis

The burden of osteoporosis continues to be high at a global level [14]. In developed countries, varying and increasing prevalence estimates have been reported. In the year 2010, 53.6 million adults were diagnosed with low BMD in the United States of America (US). It was also projected that this number will be increased to 64.6 and 71.4 million by the years 2020 and 2030, respectively [66]. In Europe, 27.5 million (22 and 5.5 million women and men, respectively) residents were diagnosed with osteoporosis in 2010. This figure was predicted to increase [67] and varies significantly by country. The highest (33 million) and lowest (152, 000) absolute numbers of osteoporosis were reported in Germany and Malta respectively [68]. Common to all developed nations including Australia, the prevalence and incidence of osteoporosis among older people and particularly women is higher [66, 68-70].

Although national and state-level estimates in Australia are largely based on self-reported prevalence of osteoporosis, there is a documented evidence of epidemiological studies which have objective measurements [71-74]. According to an Australian Bureau of Statistics report, 6% of men and 23% of women aged 50 years and above had osteoporosis in 2006. In 2012, 3.3% (5.3% and 1.2% in men and women, respectively) of the general Australian population had osteoporosis which is double the 2000 estimate (1.6%). This figure was higher among those aged 50 and above (15% and 3% in women and men, respectively) [71]. Another report in 2012 revealed that 1.04 and 3.70 million Australians over 50 years of age (66% of people over 50) had osteoporosis and osteopenia, respectively. By 2022, a total of 6.2 million Australians over the age of 50 will live with

osteoporosis or osteopenia which is a 31% increase from 2012 [11].

However, all the above estimates are based on self-reported surveys, hence these figures may lead to bias by underestimating the magnitude of the problem [75] because a person with osteoporosis does not know that they have the condition until there is fracture, particularly as a result of low-trauma. Some more recent epidemiological studies have used objective measurements (DXA) of osteoporosis. For instance, the recent estimate from the Geelong Osteoporosis Study was 23% and 6% among women and men aged 50 years and older, respectively [76]. The Concord Health and Ageing in Men Project (CHAMP) has reported that a quarter of men has osteoporosis [74].

The Australian National Health Survey (NHS) findings for South Australia reported a prevalence of 4.0% for osteoporosis which is higher than the national average and well above each of other states of Australia [71]. Trend analysis in the South Australian population has demonstrated a significant increase in osteoporosis prevalence over the past years [77, 78]. For instance, Gill et al. noted that between 1995 and 2006 there was a significant increase of osteoporosis in the general population and elderly people. In these years, 3.7% and 6.9% of the South Australian population were diagnosed with osteoporosis using self-report. This report added that the risk of osteoporosis was higher in older people and women. It also stressed underestimations in reports of osteoporosis epidemiology in South Australia [78].

The North West Adelaide Health Survey (NWAHS) is one of the few longitudinal epidemiological studies in Australia which examines the prevalence and incidence of osteoporosis. This study has collected both self-reported and DXA measured prevalence of osteoporosis. In the study, the prevalence of DXA measured low BMD among 50 years and over was 18.6%, of which 3.6% and 15.0% were osteoporotic and osteopenic,

respectively [73, 75].

Consequences of osteoporosis

Available evidence suggests that the burden of osteoporosis is high and increasing significantly. Low-trauma fracture, increased risk of mortality, dependency, decreased life quality and psychological impact are major consequences of osteoporosis [13, 79-81]. Globally, a third of fall-related deaths were attributed to reduced BMD [13]. These consequences bring additional economic pressure at individual and community levels by increasing health care, medication and other indirect costs [79-82].

In terms of disability burden, the relative impact of low BMD is also increasing (Figure 2.1). In 2016, there were 12 million DALYs and 5.6 million YLDs associated with low BMD at a global level. In the same year, 441, 226 deaths were associated with the condition [83].

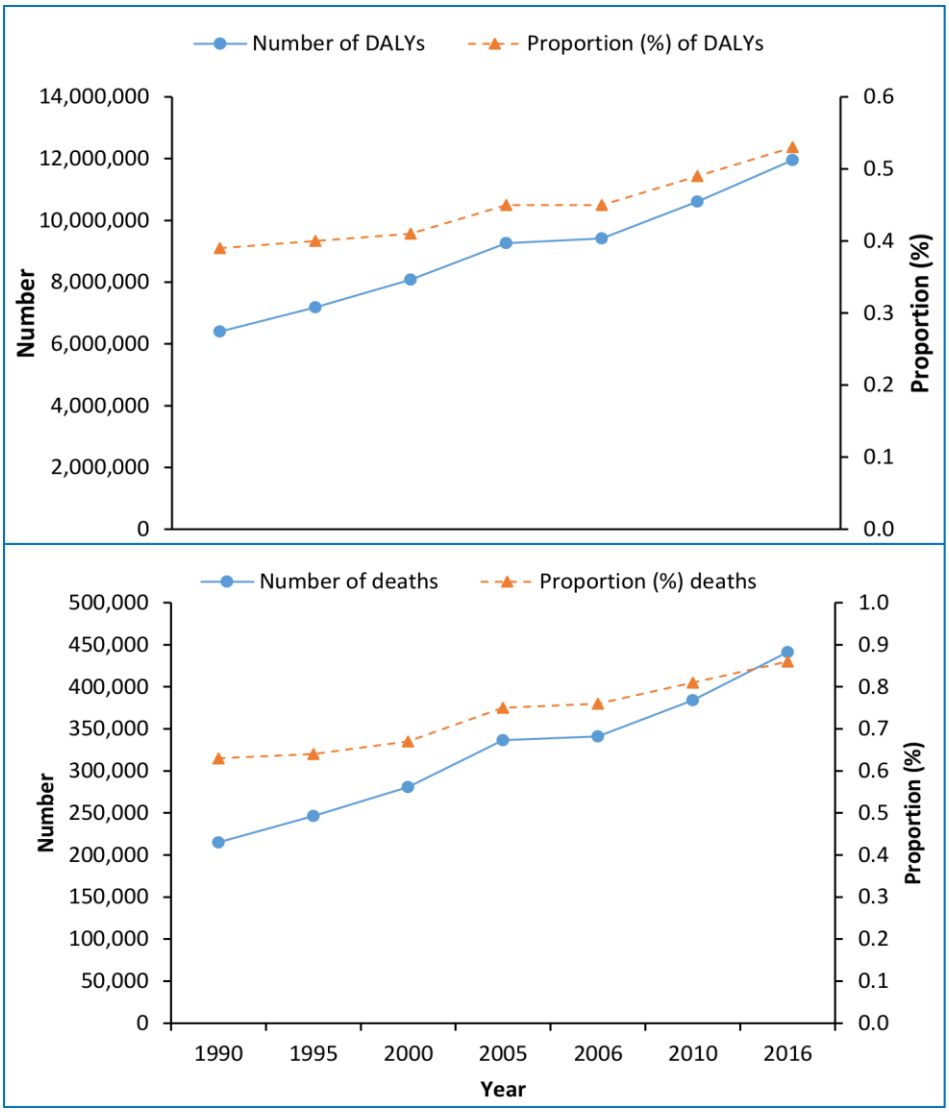

Figure 2.1 Number and age-standardized proportion of all-cause disability-adjusted life years (DALYs) and deaths attributable to low bone mineral density, 1990-2016 [83]

An increasing effect of osteoporotic fractures in terms of cost, DALYs, YLD, death and years of life lost (YLLs) due to premature mortality has been observed in high-income countries [13, 68, 80, 82, 84]. In these countries, the risk of death due to low BMD is higher than the global average. In 2016, it was estimated that 9.1 deaths per 100,000 population (age-standardized rate) in these countries were due to low BMD which is a 16.0% increase from 1990's estimate. Almost 1.5 million YLD and 2.4 million DALYs due to low BMD were observed in the same year [83].

Low BMD was a risk for 0.8% of all Australian deaths in 2016. The age-standardized proportion of deaths was increased by 61.0% from 1990's estimate. Similarly, almost 26,994 YLDs and 45,277 DALYs were caused by low BMD. The age-standardized DALYs rate was increased by 22.2% between 1990 and 2016. These effects were larger among elderly people and males [83]. An increasing burden of low BMD could be partially accounted for a better life expectancy resulting in an increased proportion of elderly people [3].

In terms of death and other outcomes, osteoporosis creates a significant burden on the Australian population. In 2012, of all fractures in Australia, 140,882 (2765 fractures) per week were due to low BMD. This number is estimated to increase to 3521 per week in the year 2022. It is also estimated that 1.6 million fractures will occur among Australians between 2012 and 2022. Females share 70% of all low BMD burden in the country [11].

The impact of osteoporosis in terms of financial costs is the other feature which has been observed in the Australian health care system [11, 85]. It is believed that Australia lost 171 million dollars due to osteoporosis in 2008/2009 [85]. It is also predicted that the cost as a result of osteoporosis, osteopenia and fractures will be $A33.6 billion between 2013 and 2022 with gradual increase over time [11].

2.2.2 Bone fracture

Fracture rates are high both in developed and developing countries [86, 87]. In the China National Fracture Study (CNFS), a nationally representative study from eight provinces, 24 urban cities and 24 rural counties that involved 512,187 participants, the incidence of fracture in 2014 was around 3.2 per 1000. This study indicated that fracture is a major public health issue in the country with various lifestyle and behavioural risk factors, including deprivation of sleep and high alcohol consumption [88]. However, nutrition

was not considered in the analysis.

BMD is an important predictor of fracture [89]. Osteoporosis causes more than 8.9 million fractures per year [87]. Thirty percent of women and 20% of men aged 50 years and above will have osteoporotic fractures in their lifetime [90, 91]. Excess mortality and disability as a result of osteoporotic fracture cause high health and social burdens [68]. An increased life expectancy and the growing proportion of aging population result in the increased incidence of osteoporotic fracture. Other factors, such as previous fracture history [92], comorbidities [93], and diet (nutrients) [30, 94] are also associated with fracture risks.

2.3 Risk factors of osteoporosis and fracture

In order to prevent or to delay the onset of osteoporosis and associated fractures and to maintain bone strength through the lifespan, achieving optimal bone mass is crucial [95, 96]. However, there are many factors which prevent this from happening. Like other NCDs, determinants of osteoporosis are multifaceted and interlinked. Genetic, lifestyle, nutritional, medical disorders, medications, and metabolic (biological) risk are identified as major contributors to the development of osteoporosis [97]. These risk factors are both non-modifiable and modifiable. Determinants of low BMD and their relationship to each other are summarized in Figure 2.2.

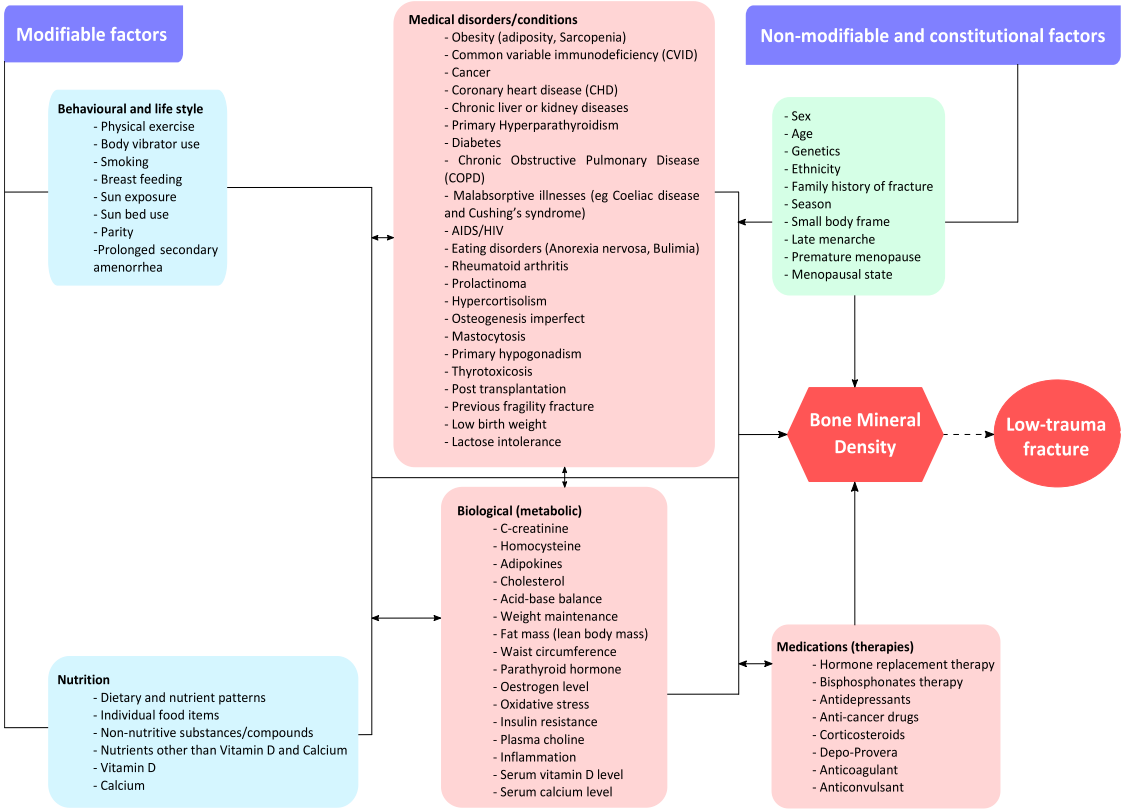

Figure 2.2 Summary of factors associated with bone mineral density and low-trauma fracture

Non-modifiable risk factors include female sex [98-102], ethnicity [102, 103], age [98, 102, 104], genetics [97, 105-107], family history of fracture [97, 108], season [109-113], small body frame [97], late menarche [97, 114], premature menopause [97, 115], and menopausal state [115]. The risk of osteoporotic fracture in females is reported to be one in three compared to one in five in males. This is primarily due to late bone mass gain during adolescence and faster bone loss later in life. Old age also increases the risk of osteoporosis by two to fourfold [103].

Another interesting feature of osteoporosis is that it is associated with other chronic conditions which may suggest the risk of comorbidity could be higher among those with osteoporosis. Obesity [116], rheumatoid arthritis [117], CVD [17], type 2 diabetes [118], asthma [119], chronic liver diseases [118], gastrointestinal malabsorption [97] and

endocrine disorders [115] have been found to influence BMD negatively.

In addition, metabolic (biological) risk factors have been reported in various studies. Studies have shown that cholesterol level is inversely associated with BMD [120]. It is also reported that adipokines [121], homocysteine [122], and oestrogen levels in the blood have a negative association with BMD [123]. Other biological factors that could affect BMD are atherosclerosis [124] and serum acid-base balance [125]. Studies have also observed the impact of proportion of fat to lean mass on BMD, with fat mass negatively associated with BMD as opposed to lean (muscle and bone) mass [126, 127]. A study on waist circumference has found an inverse relationship with BMD [116].

Some drugs used for treatment of chronic conditions are also risks for bone loss. For instance, anti-cancer drugs [95], corticosteroids [95, 128], Depo-Provera [129, 130], anticoagulants [131, 132] and anticonvulsant, anxiolytics, sedatives, antidepressants and neuroleptics [133] have been associated with the risk of developing osteoporosis.

There are treatment options which could help to regain bone loss, especially in elderly people. These include hormone replacement therapy [95] and bisphosphonates [134]. But, modifiable risk factors can be used as an intervention targets to reverse, delay or prevent the progression and onset of osteoporosis. These factors could be behavioural, lifestyle and nutrition-related [135-142]. Nutrition, known for its major and central role to build and maintain BMD, is becoming the focus area of interventions against osteoporosis [143-145].

2.4 Nutrition and non-communicable chronic diseases

Poor dietary quality, such as high salt, unsaturated fat and sugar intake and low fruit and vegetables (FV) intake, and low physical activity are important factors associated with

NCDs and mortality and disability. Diet is a leading risk factor for mortality at the global level, causing one in five deaths in 2016 [20]. Reducing salt intake to 6 g/day could prevent 2.5 million deaths globally every year [146].

In 2016, a diet low in whole grains accounted for the largest number of deaths (4.6% [3.0–6.4]), followed by a diet low in fruits (4.3% [2.7–6.3]) and a diet high in sodium (4.2% [1.2–8.3]). In the GBD risk factors study, it has been reported that most of the NCD deaths and DALYs are related to low intake of a healthy diet rather than a high intake of unhealthy foods [20]. It has been indicated that more than half of diet-related deaths (51.5% [44.2–59.2]) and DALYs (54.1% [47.1–61.5]) were caused by CVDs. Despite the available evidence on the importance of diet in predicting NCD risk, studies comparing developed countries in relation to diet-related burden of diseases are limited.

2.5 Nutrition and musculoskeletal disorders

2.5.1 Individual nutrients and bone fragility

Macronutrients

Half of the volume of bone and a third of its mass is made up of protein [147]. Protein intake can affect bone health in several ways. It forms bone matrix, increases insulin growth factor-1, urinary calcium retention and intestinal calcium absorption [148]. The effect of protein on bone depends on the level of protein in the diet, the protein source, calcium intake, acid/base balance of the diet and weight maintenance status.

The overwhelming majority of studies report a benefit of protein for bone health. However, these studies note that protein intake should be balanced with calcium intake. Intake of high soy protein among postmenopausal women [149] and higher animal to plant protein ratio [150] have shown a positive effect on bone mass. Other studies have

shown similar results [151, 152], a modest positive effect of protein on bone mass [34, 153] and an importance of adequate protein in maintaining bone mass and prevention of osteoporosis [154] among elderly people.

Carbohydrates, like oligosaccharides, are receiving more attention for their role in bone health. Two reviews in 2002 and 2006 revealed the positive impact of non-digestible carbohydrates on calcium absorption [155, 156]. However, simple sugars and energy-dense foods were found to be harmful to bone health [157].

The effect of fat on bone health has been investigated in recent years. However, these studies have reported contrasting results. A study by Weiss et al. reported that a higher ratio of polyunsaturated fatty acid (PUFA)-6 and -3 negatively impacted BMD in both men and women [158]. Bone loss was increased by the intake of PUFA among 891 women (aged 50 to 59 years) in the Aberdeen Prospective Osteoporosis Screening Study [159]. A systematic review of animal (13 studies) and human (11 studies) studies in 2008 examining the impact of PUFA-3 on osteoporosis claimed that it was difficult to reach a conclusion as to the effect of PUFA, as very heterogeneous results were reported [160].

The Framingham Osteoporosis Study has reported the importance of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in maintaining bone mineral when combined with arachnoid acid [161]. Other studies also reported the benefit of PUFAs on bone health in adults [162, 163]. In 2013, a study on genistein, PUFA and vitamin D and K_1 found a positive effect of these fatty acids on bone health [164]. A review in the same year reported the benefit of PUFA, especially PUFA-3 [165] which was in line with another study among postmenopausal women [166]. The contradictory findings of these studies could be partially due to not being able to account for potential interactions between fat and other nutrients.

Vitamins

All fat-soluble vitamins and some water-soluble ones are known to be involved in bone metabolism. Vitamins A, B complex, C, D, E and K [167] have been confirmed to have a role in bone metabolism. The role and effect of these vitamins on bone health and findings of observational and interventional studies are discussed briefly below.

Vitamin A is a generic term which includes retinol and provitamin A (beta-carotene). Various vitamin A families have been shown to show different effects on bone health in vivo. For instance, retinol and retinoic acid have been reported to have an inhibitory effect on osteoblasts [168], whereas lycopene, which is a carotenoid, had an opposite effect by inhibiting basal and parathyroid hormone-stimulated osteoporosis in rat bone [169]. Epidemiological studies reported contradicting findings on the association of vitamin A intake, serum retinole level and osteoporosis and osteoporotic fracture [170-172].

Alternatively, studies on vitamins with anti-oxidant characteristics, like vitamin C and E, have a positive effect on bone health [173-176]. Vitamin K has also been found to be associated with bone mass in epidemiological studies [177-180] though this association was not reported with risk of fractures [181]. With regards to B vitamins, particularly folate and B_{12}, studies reported unclear and contradicting findings [182-185] suggesting further investigations. It is also imperative to study how the interaction of vitamins among themselves and other nutrients affects BMD and the risk of fracture.

Vitamin D

Vitamin D is a steroid hormone. There are two main forms of vitamin D—vitamin D_3 (cholecalciferol) which is produced by the skin after sunlight exposure and D_2 (ergocalciferol) which is available in food. The active metabolite of vitamin D is 1, 25-

dihydroxyvitamin D_3 (1, 25$(OH)_2$ D) which is produced by a process involving the liver and kidney. The vitamin is important in facilitating calcium absorption in the body by forming calcium-binding proteins in intestinal cells [186]. These proteins help to maintain the calcium in the serum and the bone by continuously supplying calcium for the process of bone modelling and remodelling. According to the Australian guidelines, an adequate intake for adults ranges from 5.0 to 15.0 μg /day and should be increase with age [187].

The evidence regarding the importance of vitamin D for bone health is well documented, particularly among older people [188]. However, existing evidence focuses on the individual effect of vitamin D intake on BMD and fracture risk. So far, no studies have examined the role of vitamin D as part of the whole picture of nutrients intake (nutrient patterns) in predicting BMD or fracture risk.

Minerals

Minerals like phosphorus, magnesium, potassium, copper, zinc, fluoride and sodium have a significant role in maintaining bone health [189]. A high calcium/phosphorus ratio was positively associated with bone mass in the general population and postmenopausal women [190, 191]. On the contrary, recent cross-sectional and prospective studies in Asia reported an absence of an association between phosphorous intake and bone mass among adult women and men [192, 193]. The effect of dietary phosphorus on bone health remains to be clarified particularly focusing on the amount for maintaining bone mass in elderly people.

A study among Turkish postmenopausal women by Okyay et al. reported a positive association between serum levels of zinc, copper, iron and magnesium and osteoporosis but not potassium and sodium [194]. Similarly, in other studies, dietary potassium intake was negatively correlated with BMD among postmenopausal women [195] and dietary

intake of sodium was not associated with BMD in elderly people [192]. Supplementary zinc, but not copper intake, has also been positively associated with BMD in postmenopausal women [196]. Studies have provided contradictory results among various population groups for fluoride intake [197-199].

Although these minerals have varying levels of involvement in bone metabolism, available evidence generally suggests that a high mineral intake results in a negative effect on bone mass. This could be due to high intake of plant-based diet. Investigations of different intake levels and the effect on bone mass are important to provide appropriate recommendations for people who are at risk of developing osteoporosis. The relative intake of these minerals and their associations can be assessed using contemporary statistical approaches, such as PCA.

Calcium

Bone, intestine, and kidney are the three major organs that are important in calcium movement. Calcium is vital for normal growth and function of the skeletal system, and more than 99% of the calcium in the body is found in bone [200]. Bone is also a storehouse of calcium in the body and calcium is vital for normal growth and function of the skeleton system. The calcium in the bone also helps to maintain serum calcium levels [201]. The importance of calcium in bone health is well-established from epidemiological studies [202, 203]. Australian nutrient reference guidelines recommend that the adult population consumes 1,000 to 1,300 mg/day of calcium with a higher intake required in advanced ages [187].

The interactions of nutrients between themselves and non-nutritive substances in the body are inevitable. Thus, nutrients do not act individually in cells and tissues. Therefore, the existing evidence with regard to individual nutrients should be interpreted carefully

because these studies have assessed the effect of specific nutrients on bone health without considering the interactions. In addition, these studies do not consider the correlation of nutrient quantity. It is imperative to understand how these influence bone health rather than studying the individual effects of nutrients. Further detailed research with robust designs is necessary to fill this gap by clearly indicating the relative impact of nutrients, as part of the whole nutrient analysis, on bone health. One of the potential approaches to investigate this interaction is constructing nutrient patterns and assessing the association with BMD and fracture risk. This approach provides an insight into the relative contribution of nutrient intake to bone health.

2.5.2 Nutrient patterns and bone fragility

Most of the previous studies have focused on the association between dietary patterns and osteoporosis/fracture risk [30, 204]. However, there are limited studies that have investigated the association between nutrient patterns and BMD or fracture risk. A study by Samieri et al. have found that a high intake of calcium, phosphorous, vitamin B_{12}, protein and unsaturated fats lowered the risk of wrist and hip fracture among ageing adults [94]. Another study among postmenopausal women showed a positive association between a nutrient pattern characterized by a high intake of folate, total fibre, vitamins B_6, C, K and A, potassium and magnesium, copper and manganese and BMD [205]. However, these studies have limitations. These include inadequate sample size, cross-sectional study design, or the samples were limited to specific population groups. In addition, none of these studies have dietary data collected using a repeated 3-day 24-hour (24-h) recall method which can reflect the habitual intake of diets.

2.5.3 Individual foods and bone fragility

Dairy products

Dairy products are a good source of protein and calcium. Furthermore, per calorie of dairy food, the yield of protein, calcium, magnesium, potassium, zinc, and phosphorus is higher than any other food [25, 206]. Hence dairy sources can be as efficacious as calcium supplements in some instances.

A review in 2011 by Caroli and et al. confirmed the importance of dairy products in maintaining bone health [25]. Several studies including randomized controlled trials (RCTs) showed the importance of dairy products in maintaining bone mass and preventing osteoporosis in elderly people across different communities [207-210]. Epidemiological studies have also demonstrated the effect of dairy products in maintaining bone health among elderly people [211, 212]. Currently, the evidence on the positive effect of dairy products and bone mass is much stronger and well established, unlike some other food entities.

Soy

Soybeans are an important food staple in Asian countries and are used globally as a source of protein. Soybeans contain protein, oil, carbohydrate and ash. Vitamins, flavonoids and polysaccharides are also constitutes of soybeans and they are also an excellent source of calcium [213]. In addition, it had been postulated that flavonoids in soybeans, particularly, isoflavones mimic estrogenic activity which could be effective in maintaining bone health and in preventing osteoporosis in elderly women [214]

Some epidemiological studies on soy support the positive effect of soy protein on bone mass, conflicting results have been reported in other studies. Studies were undertaken to

assess the effect of soy on bone formation and resorption identified no effect among postmenopausal women [215, 216]. In contrast to previous reviews [217, 218], a recent review reported the absence of strong evidence to support the importance of soy food (as a result isoflavone content) in preventing bone loss in postmenopausal women [219]. However, this review did not do a pooled analysis of included studies. Several other studies found the clear importance of soy foods in maintaining bone health [220, 221]. Contradictory results could be due to variation in the design of the studies, setting and sample size. In addition, these studies also did not consider the confounding effect of other food items.

Seafood

In line with animal experimental studies [222-224], epidemiological studies consistently support the importance of seafood in building and maintaining bone mass. Consumption of fish was associated with BMD but not with hip fracture in a large prospective cohort of older adults [225]. Another well-known study, the Framingham Osteoporosis Study, confirmed the benefit of fish consumption in building BMD longitudinally; however, this benefit was dependent on the interaction between EPA and DHA, and arachidonic acid [161]. Three Chinese cross-sectional studies among adults found a significant positive association between increased seafood intake and BMD [192, 226, 227].

Beverages (alcohol, soft and hot drinks)

Alcohol

Alcohol intake has been linked to bone mass especially in men. Alcohol intake impairs Deoxyribonucleic acid (DNA) synthesis and cell proliferation resulting in a reduction in osteoblasts [228] leading to an imbalance in bone remodelling due to decreasing bone

formation [229]. Alcohol also interferes in the metabolic pathways of bone metabolism [229, 230]. However, moderate intake of alcohol consumption was inversely associated with hip fracture in an epidemiological study [231]. In addition to the alcoholic component of ethanol, wine contains grape-derived phenolics, known for their potent antioxidant effect in the body [232] and this might be important in bone health although a clear mechanism of action is not so far well understood [233].

A longitudinal study by Macdonald et al. reported that a unit increase (in quartile) intake of alcohol was positively associated with a higher lumbar BMD among peri-menopausal women [159]. A review on alcohol and bone health in 2012 revealed that the effect of alcohol is dependent on the amount and duration of alcohol intake, age, sex and hormonal status. One glass for women and two glasses per day for men is an optimal level of alcohol consumption to provide a positive effect on bone health [229] and the relationship between alcohol and skeletal health is reported to be "J" shaped curve [234]. The benefits of alcohol intake including wine on bone health were also reported by other studies among various communities with different study designs [231, 234-238]. Thus, it is possible to conclude that moderate intake of alcohol is beneficial for bone health.

Soft drink

Soft drink production and consumption have rapidly increased globally. Soft drink intake is associated with metabolism of bone in the body [239]. The effect of soft drink on bone health depends on the amount and duration of intake [240]. It has been postulated that the presence of phosphoric acid [241] and carbonates and, the replacement of nutrient-dense foods by these drinks may have a major role in this effect [242, 243].

Early studies reported the absence of associations between soft drink consumption and BMD and bone fracture [240, 244, 245]. Recently, two cross-sectional studies have also

shown a non-significant association between soft drink consumption and BMD/osteoporosis among postmenopausal women and among the general adult population [246, 247]. However, the majority of studies have reported the presence of a negative association between soft drink intake and bone mass [241, 248] and an increased risk of fracture among elderly people [32, 249]. A clear association between soft drink consumption and osteoporosis is still not established and further studies are required to fill this gap.

Coffee and tea

Coffee contains a stimulant called caffeine which could affect bone metabolism by interacting with calcium metabolism pathways [250]. Although tea contains caffeine, it also has other important components like flavonoids that coffee does not have. Phytoestrogens, polyphenols and fluoride are also found in tea.

Although the majority of studies support the negative effect of caffeine intake on bone mass [251-254], some others have claimed an absence of this effect as long as an adequate amount of calcium is served [250, 255]. But, in spite of the caffeine content, studies have reported a positive association between tea consumption and bone mass [256] and a reduction in fracture risk [29]. However, a systematic review (both in animal and human studies) on the association between tea consumption and BMD reported that the benefit in humans is inconclusive and putative [257]. In addition, these inconsistent findings with regard to the association of coffee and tea consumption with bone health could be partially accounted for the methodological differences, such as study design and population, incomplete adjustment of confounders and tea categories (black, oolong, green, etc.), in the studies. Similarly, because coffee and tea are confectionary foods and are not part of main dishes, an assessment of these food items could be subjected to an inaccurate report

because people may not consider the food items as their important daily food components resulting in measurement bias. In addition, the association of coffee and tea consumption with bone health could be due to other dietary factors which are highly correlated with intake of these foods. Therefore, assessment of associations of coffee and tea intake with bone health should not be independent of other dietary factors.

2.5.4 Development of dietary patterns and association with bone fragility

Studying the association of individual food items with BMD and fracture risk has a potential risk of bias as a result of not controlling for the effect of other dietary components and correlations among diets. For instance, people who eat seafood are more likely to eat other healthy diets such as FV and less likely to consume unhealthy food items, such as soft drinks [258]. Therefore, studies investigating the effect of seafood, without considering other diets, on bone health will give a spurious association. In addition, quantifying the consumption of a single diet does not mirror the dietary behaviour of study participants. Therefore, alternative methods which consider these limitations are important. In this regard, statisticians have developed alternative approaches (such as a statistical approach that reduces the dimensionality of dietary data) to reflect the relative intake of individual food items within the whole pattern of dietary consumption. It has been demonstrated that these methods are useful in characterizing the dietary behaviour of individuals and population groups [45, 259].

Recent epidemiological studies have focused on the analysis of food patterns [45, 259] rather than individual nutrients or food constitutes to investigate the effect of nutrition on diseases. A dietary pattern shows the totality of diet with multiple dimensions, but also interdependency in dietary components in predicting a disease outcome. Disease outcomes could be the results of this interdependency instead rather than a single

constitute of diet. Therefore, an increasing number of studies are focusing on dietary patterns rather than a single diet [40].

Fruit and vegetables patterns

FV are constituted with components which are important in the metabolism of bone. These components include nutrients (minerals and vitamins) and non-nutritive (bioactive) compounds (antioxidants and phytochemicals). Vitamin C, K, magnesium, potassium, calcium, polyphenols and phytoestrogens are among these components [260-264]. Vitamins K and C, and magnesium are important nutrients for building bone matrix [182, 265]. In addition, the alkaline effect of FV in the body as a result of a high content of potassium and magnesium can help in maintaining bone mass by preventing calcium resorption [266, 267] and by buffering metabolic acidosis in the body [268, 269].

Evidence shows that a dietary pattern based on FV intake is vital for the overall [270] and bone health. Across Asian population, consistent results have been reported on the benefit of FV consumption for bone health. A study in Korea reported that high fruit intake is positively associated with BMD [271]. A case-control study among postmenopausal women in China has found that recommended level intake of FV was associated with decrease forearm fracture [272]. By the same token, two cross-sectional studies among Chinese postmenopausal women found that greater FV intake was independently associated with better BMD [273, 274].

A prospective cohort study in Dutch elderly people (Rotterdam Study) and Scotland reported that a dietary pattern characterized by high FV intake was positively associated with BMD [159, 275]. Cross-sectional studies in the United Kingdom and Scotland have found similar findings [276, 277]. The Framingham Study in the US found that a higher intake of FV among men was protective for low BMD [143]. A higher adherence to a

healthy dietary pattern characterized by a higher intake of FV was found to be protective against hip fractures among women in the Swedish Mammography Cohort [30].

However, some other studies have reported none or weak associations between FV intake and bone health. A systematic review of 8 studies among women aged 45 and above revealed that the benefit of FV in maintaining BMD found to be inconclusive [35]. In addition, two clinical trials among postmenopausal women found that increased consumption of FV was not associated with bone turnover [278] or BMD [279]. Further, in the US, a follow-up study among women and men aged 50 years and above reported that a dietary pattern characterized by a higher FV intake has no association with hip fracture risk [280].

These inconsistent findings on the benefit of FV to bone health could be due to differences in study designs and dietary data collection methods. In addition, since RCTs are only for a short period of time, they may not be an appropriate design to see the intended outcome (in this case bone mass and fracture risk) of a given dietary exposure. Further studies with better observational study designs, such as long-term follow-up studies and a repeated measurement of dietary intake, will be important to settle the arguments over the importance of FV for bone health.

Other dietary patterns

In addition to FV based dietary patterns, studies have reported a variety of other patterns which are associated with BMD. These food patterns are derived from four groups alone or in combination with FV. These are grains, dairy, protein foods, and other foods such as snacks and sweets. Table 2.1 summarizes some of the studies on dietary patterns and their associations with musculoskeletal outcomes.

Table 2.1 Summary of studies on dietary pattern and musculoskeletal outcome

Author; year; country	Study design; sample size; sex of participants	Dietary data collection and analysis method	Musculoskeletal outcome	Identified dietary pattern – food components	Adjusted variables	Association with the musculoskeletal outcome
Langsetmo L, et a [281]; 2011; Canada	Cohort; 5188; postmenopausal Women and men (>50 years)	FFQ; factor analysis	Low-trauma fracture	• Nutrient dense – fruit, vegetables and whole grain • Energy dense – soft drink, potato chips, French fries, meat and desert	• For all: BMI, bone mineral density, falls, prior fracture, comorbidities, smoking, milk consumption, and supplements (vitamin D and calcium) • For women only: diagnosis of osteoporosis, antiresorptive use, education, alcohol use, physical activity, and sedentary hours	Nutrient dense dietary pattern is negatively associated with fracture
Fung TT, et al [280]; 2015; The United States	Cohort; 74,540; postmenopausal women and men (>50 years)	FFQ; PCA	Hip fracture	• Prudent – whole grains, fruits and vegetables • Western - higher intakes of red/processed meats and refined grains	Age, energy intake, BMI, smoking, physical activity, postmenopausal hormone use (women), thiazides, lasix, anti-inflammatory steroids, calcium supplements, and multivitamin supplements	No associations
França N, et al [254]; 2015; Brazil	Cross sectional; 156; postmenopausal women (>45 years)	A 3-day food diary; PCA	BMD (DXA)	• Healthy • Red meat and refined cereals • Low-fat dairy • Sweet foods, coffee and tea and • Western	Energy intake, calcium intake, lean mass, height and postmenopausal time’	Sweet foods, coffee and tea pattern was inversely associated

Author; year; country	Study design; sample size; sex of participants	Dietary data collection and analysis method	Musculoskeletal outcome	Identified dietary pattern – food components	Adjusted variables	Association with the musculoskeletal outcome
Benetou V, et al [282]; 2012; Europe	Cohort; 188,795; (48,814 men and 139,981 women); mean age=48.6 years	FFQ; *a priori* dietary index	Hip fracture	Mediterranean diet	Age, sex, education, smoking status, body mass index, height, physical activity, total energy intake from calibrated data , history of diabetes, history of cardiovascular disease, history of cancer, history of fracture, and menopausal status (for women)	Negatively associated
Fairweather-Tait SJ et al [237]; 2011; The United Kingdom	Co-twin controlled study; 2000; Postmenopausal women	FFQ; PCA	BMD (DXA)	• Fruit and vegetable pattern score • High-alcohol pattern score • Traditional English pattern score • Low-meat pattern score	Age, age squared, BMI, smoking, and physical activity	Traditional English pattern (fried fish, fried potatoes, legumes, red and processed meats, savoury pies, and cruciferous vegetables) was negatively associated
Lemming EW, et al [30]; 2017; Sweden	Cohort; 56,736; Women (median age=52 years)	FFQ; PCA	Hip fracture	• Healthy – fruit, vegetable, cereals, whole meal bread, fish and milk • Western – potato, white bread, meat, offal's, soda and egg	Height, educational level, living alone, calcium-supplement, Multivitamin/mineral-use, physical activity, previous fractures, postmenopausal-status, Charlson's comorbidity index, total energy, body mass index and smoking status	• Healthy pattern was negatively associated • Western pattern was positively associated

Author; year; country	Study design; sample size; sex of participants	Dietary data collection and analysis method	Musculoskeletal outcome	Identified dietary pattern – food components	Adjusted variables	Association with the musculoskeletal outcome
Whittle CR, et al [283]; 2012; Ireland	Cohort; 489; both sexes (20–25 years)	Dietary history; a dietary index and PCA	Bone mass (DXA)	• Healthy – fruit, vegetables, brown bread, breakfast cereal and milk • Traditional – white bread, fats, potatoes, poultry and hot drinks • Refined – white bread, chips, soft drinks, chocolate, confectionary and condiments • Social – vegetables, fruit, rice and pasta, eggs, white fish, alcohol and cheese • Nuts and meat pattern – red meat, poultry, vegetables and nuts	Age, BMI, smoking, physical activity father's social class and energy intake	• Nuts and meat pattern was positively associated • refined pattern was negatively associated
Jonge E, et al [275]; 2015; Netherlands	Cohort; 5144; males and females of 55 years and olde	FFQ; dietary index	BMD (DXA)	• High-BMD – fruit, vegetables, fish, whole grains, legumes/beans and dairy • Low-BMD – meat and confectionary	Age, sex, total energy intake, body weight, height, education, household income, smoking behaviour, physical activity, use of lipid lowering drugs, use of any dietary supplement, alcohol intake, calcium intake	High-BMD pattern was positively associated
Kontogianni MD, et al [284]; 2009; Greek	Cross-sectional; 220; women (mean age=48)	3-day food records; dietary index	BMD (DXA)	• Mediterranean • Fish and olive oil and low red meat intake based	BMI, smoking status, physical activity level, and low energy reporting	• No association with Mediterranean diet • The Fish and olive oil and low red meat based pattern was positively associated with BMD

Author; year; country	Study design; sample size; sex of participants	Dietary data collection and analysis method	Musculoskeletal outcome	Identified dietary pattern – food components	Adjusted variables	Association with the musculoskeletal outcome
Okubo H, et al [285]; 2006; Japan	Cohort; 291; postmenopausal women (40 – 55 years)	Diet history questionnaire; factor analysis	BMD (DXA)	• Healthy - green and dark yellow vegetables, mushrooms, fish and shellfish, fruit, and processed fish; • Western - fats and oils, meat, and processed meat	age, BMI, grasping power, current smoking, fracture history, the use of hormone replacement therapy, age at menarche, parity, calcium and multivitamin supplements	• Healthy pattern was positively associated • Western pattern was negatively associated
Shin S, et al [286]; 2015; Korea	Cohort; 1828; men and women (≥30 years)	A 3-day food record; factor analysis	BMD (DXA)	• Rice and kimchi • Eggs, meat and flour • Fruit, milk and whole grains • Fast food and soda	Age, body size (weight and height adjusted for weight residual) , energy intake, smoking, alcohol consumption, and physical activity, and for women, menopausal status	Fruit, milk and whole grains pattern was positively associated
Park SJ, et al [287]; 2012; Korea	Cohort; 1725; Korean postmenopausal women (40 – 69 years)	FFQ; factor analysis	Osteoporosis [yes/no] quantitative ultrasound	• Traditional - rice, kimchi, and vegetables), • Dairy - milk, dairy products, and green tea), and • Western - sugar, fat, and bread)	Age, residual area, exercise, and passive smoking	Dairy pattern was positively associated
Shin S, et al [288]; 2013; Korea	Cross-sectional; 3735; postmenopausal women (mean age=64.1 years)	A 24-hour recall method; factor analysis	Osteoporosis [yes/no] (DXA)	• Meat, alcohol and sugar • Vegetables and soya sauce • White rice, kimchi and seaweed • Dairy and fruit	Age, BMI, energy intake, parathyroid hormone and serum 25-hydroxyvitamin D, smoking, alcohol intake, moderate physical activity, supplement use and oral contraceptive use	• Dairy and fruit was positively associated • White rice, kimchi and seaweed was negatively associated

Author; year; country	Study design; sample size; sex of participants	Dietary data collection and analysis method	Musculoskeletal outcome	Identified dietary pattern – food components	Adjusted variables	Association with the musculoskeletal outcome
McNaughton SA, et al [157]; 2011; Australia	Cross-sectional; 527; Women (18 – 65 years)	A 4-day diary; factor analysis	BMC (DXA)	• Pattern 1 - processed cereals: white bread, sandwiches, other cereals, soft drinks • Pattern 2 – potatoes, carrot, peas, cabbage, cauliflower • Pattern 3 – leafy vegetables, tomato, diary, fruit, and cheese • Pattern 4 – legumes, seafood, seeds, nuts, wine and rice • Pattern 5 – chocolate, confectionary, and added sugar	Age and height, energy intake, smoking, sport, walking, and education, and calcium intake	• Pattern 1 was negatively associated • Pattern 4 was positively associated
Wu F, et al [289]; 2017; Australia	Cross-sectional; 347; Women (36 – 57 years)	FFQ; factor analysis	BMD (DXA)	• Healthy (plant-based diet) – vegetables, legumes, fruit, tomatoes, nuts, snacks, garlic, whole grains • High protein, high fat - red meats, poultry, processed meats, potatoes, cruciferous and dark-yellow vegetables, fish, chips, spirits and high-fat dairy products • Processed foods - meat pies, hamburgers, beer, sweets, fruit juice, processed meats, snacks, spirits, pizza	Weight, height, strenuous physical activity, smoking, total energy intake, Ca and vitamin D supplement and menopausal status	A processed food pattern was negatively associated

BMC – bone mineral content; BMD – bone mineral density; BMI – body mass index; DXA – dual-energy x-ray absorptiometry; FFQ – food frequency questionnaire; PCA –principal component analysis

2.5.5 Summary on dietary patterns and bone fragility

In general, it can be concluded that, whereas a dietary pattern containing high FV, dairy products and whole grains are beneficial for bone health, a dietary pattern characterized by high intake of soft drinks, meat, processed foods and confectionaries are detrimental to bone. However, this conclusion is not consistent across all studies (Table 2.1).

The inconsistency of findings on the associations of dietary patterns, as presented in Table 2.1, with bone fragility could be partly due to differences in study population and the available and commonly consumed food. Thus, a food pattern which is associated with a musculoskeletal outcome in a specific community might not apply in a different community and tailored dietary pattern optimal for bone health could be necessary.

Furthermore, the inconsistencies can be attributable to differences in dietary data collection methods and statistical approaches used in constructing dietary patterns. Although considering the totality of food items and looking at the contribution of the specific dietary components in a dietary pattern have become a recent focus in nutritional epidemiology, related methodological deficits have been important discussion points. These include lack of standardization and absence of a conceptual framework in defining dietary patterns, particularly in data-driven approaches, which have contributed in compromising comparison of results from different studies. In addition to other methodological differences of studies, limitations in these dietary pattern analysis methods have been responsible for inconsistent findings in the literature. Further, studies that evaluate dietary pattern analysis methods in relation to bone health are limited.

2.6 Methods in nutritional epidemiology

Methodological advancements in nutritional epidemiology have been growing rapidly,

particularly in the last two decades. Most of the evidence in nutrition comes from population-based observational studies which apply the principles of both epidemiology and nutrition. However, critics of study designs investigating diet-health relationships have grown at the same time. For instance, Ioannidis [290] argued that findings from observational studies have been incorrectly reporting diet-health relations and many of these observational studies are implausible. He concluded that RCTs are the only option to establish plausible diet-health relations.

However, although RCTs are top in the hierarchy of evidence, it is inappropriate or unfeasible to conduct trials to answer all nutritional epidemiologic questions, making them the least preferred study designs in nutritional epidemiology. There are several reasons for this, including: (1) assessing the exposure of interest (dietary intake) is complex, given the interaction of different dietary items which can be hard to study using RCTs; (2) RCTs last a relatively short time period eventually creating difficulties in observing the effect of long-term impact of diet on a disease outcome, particularly on NCDs; (3) ethical challenges are also major issues in studying diet-disease relations in RCTs; (4) methodological issues such as blinding and high compliance are difficult in diet intention trials [291]. Therefore, observational studies with large sample sizes, long follow-up periods and better dietary intake assessment and analysis methods are alternatives for the above challenges. Sensitivity analysis of findings from observational studies are also an important approach to further validate findings related to diet-disease relations.

Studies in nutritional epidemiology have focused on dietary data collection and analysis methods, which are also potentially the criticism of these studies because of implausible findings resulting from random and systematic errors [40]. Figure 2.3 summarizes

common study designs, data collection and analysis methods in nutritional epidemiology.

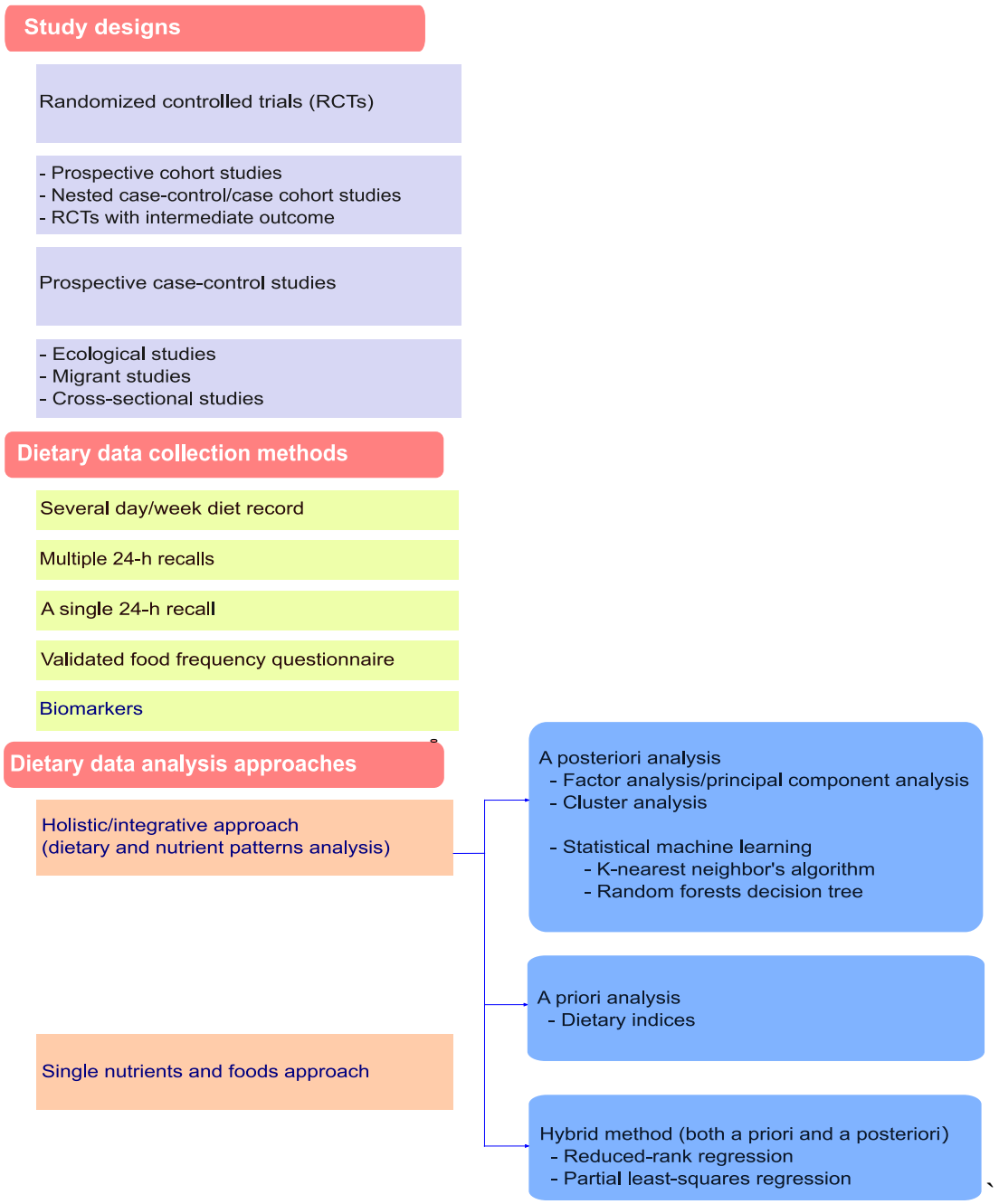

Figure 2.3 Common study designs, dietary data collection and analysis methods in nutritional epidemiology

2.6.1 Dietary data collection

Diet is the most complex lifestyle factor to measure because of its multidimensionality and dynamicity. Variations by time (such as, differences in intake levels during weekdays

and weekends and different seasons) and complexity (such as, the presence of a number of dietary components and cultural and ecological aspects) of dietary intake, have been major challenges in nutritional epidemiology. Due to these inherent characteristics of diet, random and measurement errors are the major issues in investigating diet-disease relations. Advancements in dietary data collection have been made to mitigate these, by modifying the collection methods. Although there are many modified versions of dietary data collection methods, there are three core types: food record, 24-h recall and food frequency questionnaire (FFQ) (Figure 2.3). Even though the utilization of biomarkers are expensive and invasive, these methods can be also used to objectively measure nutritional status of individuals and populations [39].

Food record, which is the "gold-standard" method, provides accurate and detailed dietary data with minimal systematic errors [292]. Although there are short-term recall and portion size errors, 24-h recall method also provides an accurate dietary intake level. These two methods are particularly useful in evaluating FFQ and measuring the usual intake if they are applied for several different days, seasons and years [40]. However, there is limited evidence with regard to the impact of using a single 24-h record and repeated 24-h records on the estimate of diet-disease associations, particularly estimates of associations between diet and fracture risk.

FFQ is the most commonly used dietary assessment method in large-scale epidemiological studies. Utilization of a validated FFQ is an inexpensive method of measuring a usual food intake. However, the semi-quantitative nature of the method, recall error and potential omission of foods are major limitations of this tool [40].

To enhance the performance of dietary data collection methods, the incorporation of innovative technologies in the methods has been an important step forward in reducing

cost, error and lowering the burden of assessment. For instance, the Automated Self-Administered 24-h Recall was developed to measure dietary intake of populations with low cost and a relatively high quality [293]. Focus has also been given to dietary data analysis methods.

2.6.2 Dietary data analysis

Dietary data analysis and presentation techniques have been developing over the past years. Consideration of dietary data analysis ranges from data cleaning and how to use the collected dietary data to adjustment for random and measurement errors. Dietary data have four components: food items, nutrients, non-nutritive substances and contaminants. Each of these, and the combination have an impact on health. Therefore, analyses that consider these components are crucial in investigating the true diet-disease relations.

There are two major approaches in dietary data analysis methods to investigating diet-disease associations. Historically, considering single foods or nutrients in predicting disease outcomes was a common approach. Although this approach helps in understanding the biological mechanisms, the dimensionality of dietary intake and the correlation among foods and nutrients are ignored [40]. Foods and nutrients are not consumed in isolation. Therefore, methods that look food as a whole and consider the totality of diet are important to assess the combined effect of foods and nutrients.

The second approach considers the totality and multiple components of diet and nutrients simultaneously as a dietary pattern. This approach acknowledges and considers the importance of the relative contribution of each dietary component within the entirety of the diet consumed. In this approach, the interaction and correlation of foods and nutrients are accounted for. Dietary pattern analysis is also pivotal in controlling for diet (as a confounding factor) in assessing the association of a predictor and disease outcomes.

However, in the presence of an association between a dietary pattern and a disease outcome, lack of specificity of this association is an issue, which may lead to an unclear understanding of the role of each food and nutrient.

There are three major categories of dietary pattern analysis approach—*a priori*, *a psoteriori* and hybrid methods (Figure 2.3). *A priori* methods use an existing evidence to construct a dietary pattern. Methods, such as the Healthy Eating Index and Mediterranean diet, are classified under this group. *A posteriori* methods are data-driven approaches. Factor analysis/PCA [294], and cluster analyses are classified under this method. RRR [48] and PLS regressions [47] combine both *a priori* and *a posteriori* approaches (i.e. hybrid methods). These methods are relatively new and further evaluation, improvement and understanding of the methods are needed.

Previous studies have evaluated the relative importance of dietary pattern analysis methods in identifying eating patterns associated with health outcomes, such as myocardial infarction [53] and diabetes [295]. However, to the best of my knowledge, no study has evaluated the comparative advantage of common dietary pattern analysis methods in constructing patterns that are associated with BMD and BMC.

2.7 Literature summary and gaps

All in all, although a body of evidence has been generated on the association between diet and NCDs, particularly the impact of diet on BMD, BMC and fracture risk, an evidence gap that limits the understanding of the aforementioned issue still exists.

The following is known evidence in the literature:

- Suboptimal diet is a pivotal risk factor of NCDs.

- Fracture, a condition mostly caused by low BMD, is a public health problem at globally.
- Some foods (such as milk) and nutrients (such as calcium and vitamin D) are the important dietary factors associated with BMD and fracture.
- Compared to single foods and nutrients, dietary and nutrient patterns are better approaches in reflecting the dietary behaviours of individuals and in assessing interactions among diet components and nutrients in identifying diet-disease relations.

However, the following are not clear:

- The burden of diet-related disease in developed countries and their comparative ranks in terms of the burden; and

Specifically,

- The association between dietary patterns and osteoporosis in aging adults
- The association between nutrient patterns and BMD/BMC
- The associations of long-term dietary and nutrient patterns with fracture risks in adults
- The comparative advantage and impact of using a baseline, recent, overall and cumulative means of dietary exposure on association estimates of dietary pattern and fracture
- Comparative advantages of dietary pattern analysis methods in identifying dietary patterns associated with BMD and BMC

CHAPTER 3 METHODS

3.1 Overview of datasets

For each of the studies, detailed methods are provided in CHAPTER 4, CHAPTER 5, CHAPTER 6, CHAPTER 7 and CHAPTER 8. However, a brief description of the databases from which data were used for the studies in this thesis is given below.

3.1.1 Global Burden of Disease (GBD)

GBD Study is a comprehensive research project that investigates the burden of disease, including disability and mortality from diseases, injuries and risk factors, at a global level, and at the level of 7 super-regions, 21 regions and 195 countries. The GBD Study began in 1990 at Harvard University in collaboration with WHO. Currently, the project is coordinated at the Institute of Health Metrics and Evaluation, University of Washington. More than 3,000 researchers in over 130 countries are involved in the GBD project. The GBD has produced scientific publications and reports every year since 2015 [296].

The purpose of GBD Study is to discover noble global health assessment tools and provide estimates of global health loss from diseases, injuries and risk factors, with an ultimate goal of improving global health and minimizing health disparities. The GBD data incorporate premature death and disability from more than 300 diseases and injuries and 79 risk factors in 195 countries, by age and sex, from 1990 to the present, with comparisons over time, across age groups, and among countries [297].

The GBD 2015 risk factors study has provided an up-to-date analysis of the evidence for 79 behavioural, environmental /occupational and metabolic risk factors between 1990 and 2015. A comparative risk assessment approach was used to estimate attributable deaths, DALYs and trends in exposure by age group, sex, year and geography for 79 risk factors organized in four causal risk factor hierarchies. The first hierarchy included behavioural,

environmental/occupational and metabolic risks. The second hierarchy contained 17 clusters or granular risk factors. The third and fourth levels of the causal hierarchy included cluster and granular risk factors [297].

The GBD 2015 risk factors study incorporated 388 risk-outcome pairs that met the World Cancer Research Fund criteria. Relative risks were extracted from RCTs, cohorts, pooled cohorts, household surveys, census data, satellite data, and other sources. In estimating the attributable deaths and DALYs, biases were adjusted and covariates were included. A counterfactual approach, called theoretical minimum risk exposure level (TMREL), was used. TMREL is the level of risk exposure that reduces risk at the population level.

Under behavioural risk factors, seven factors (child and maternal malnutrition, dietary risk, tobacco, alcohol and drug use, unsafe sex, low physical activity and sexual abuse and violence) were included. Under dietary risk factors, 14 dietary components (diet low in FV, whole grains, nuts and seeds, fibre, seafood omega-3 fatty acids, polyunsaturated fatty acids, calcium; and diets high in red meat, processed meat, sugar-sweetened beverages, *trans* fatty acids, and sodium) were included. Figure 3.1 depicts the process of dietary risk estimation in the GBD 2015 risk factors study. Detailed methods in estimating dietary risk factors are described in the GBD study [297] and the study in this thesis which is presented in CHAPTER 4 (Burden of Diet-related NCDs).

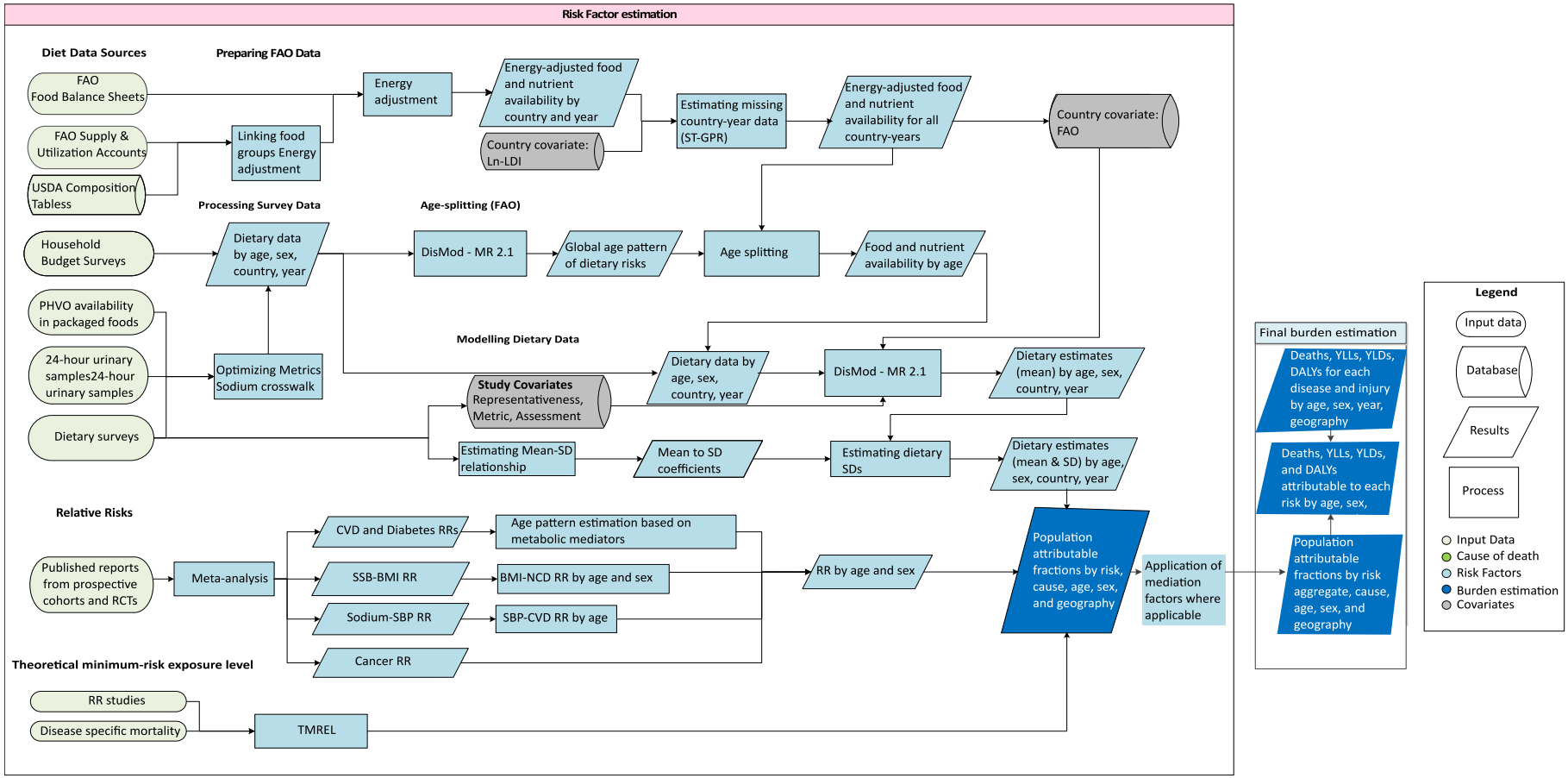

Figure 3.1 Flow chart of dietary risk factors estimation process, the Global Burden of Disease 2015 [297]

BMI – body mass index; CVD – cardiovascular diseases; DALY – disability-adjusted life years; FAO – Food and Agriculture organization; NCD – non-communicable diseases; PHVO – partially hydrogenated vegetable oil; RCT – randomized controlled trail; RR – relative risk; SBP – systolic blood pressure; SD – standard deviation; SSB – sugar-sweetened beverage; ST-GPR – spatiotemporal Gaussian process regression model; TMREL – theoretical minimum risk exposure level; USDA – United States Department of Agriculture; YLD – years lost due to disability; YLL – Years of Life Lost

3.1.2 North West Adelaide Health Study (NWAHS)

In developed countries, including Australia, the majority of disabilities and deaths are caused by NCDs [1]. However, in Australia, most data in relation to NCDs and their risk factors are from cross-sectional studies and/or medical records. The NWAHS was established to provide self-reported and measured longitudinal data of NCDs and their risk factors. Randomly selected participants aged 18 years and above were recruited from the north-west suburbs of Adelaide, South Australia. Questionnaires, phone interviews and clinical assessments were used to collect data. The study covers chronic diseases including CVD, diabetes, cancer, asthma, arthritis, osteoporosis and their risk factors. A number of sub-studies have also been conducted in the cohort [73].

The NWAHS commenced in 1999 in collaboration with The University of Adelaide, The Queen Elizabeth Hospital and South Australian Government Department of Health. The study involves multidisciplinary investigators including epidemiologists, clinicians and social scientists.

Three main stages of data collection were conducted between 1999 and 2010. At the first stage (1999-2003) 4056 participants aged 18 years and over had clinical assessments. At Stage 2 (2004-2006), 3564 participants completed interview and 3205 had clinical assessments. In the third major follow-up (2008-2010), 2871 participants were involved, of which 2487 attended a clinic for assessment [73]. At Stage 2, participants aged 50 years and over were invited to have BMD/BMC (DXA) measurements and 1588 of them had the measurement. In the third stage, 2500 study participants had dietary data. Combining these two datasets, 1182 participants for the studies in CHAPTER 5 and CHAPTER 8 and 1135 for the study in CHAPTER 6 had complete data on diet and bone mass measurements. Data from NWAHS were used for three studies (CHAPTER 5,

CHAPTER 6 and CHAPTER 8) in the thesis (Figure 3.2). Detailed sampling and sample size for each of the studies are provided in the respective studies the chapters.

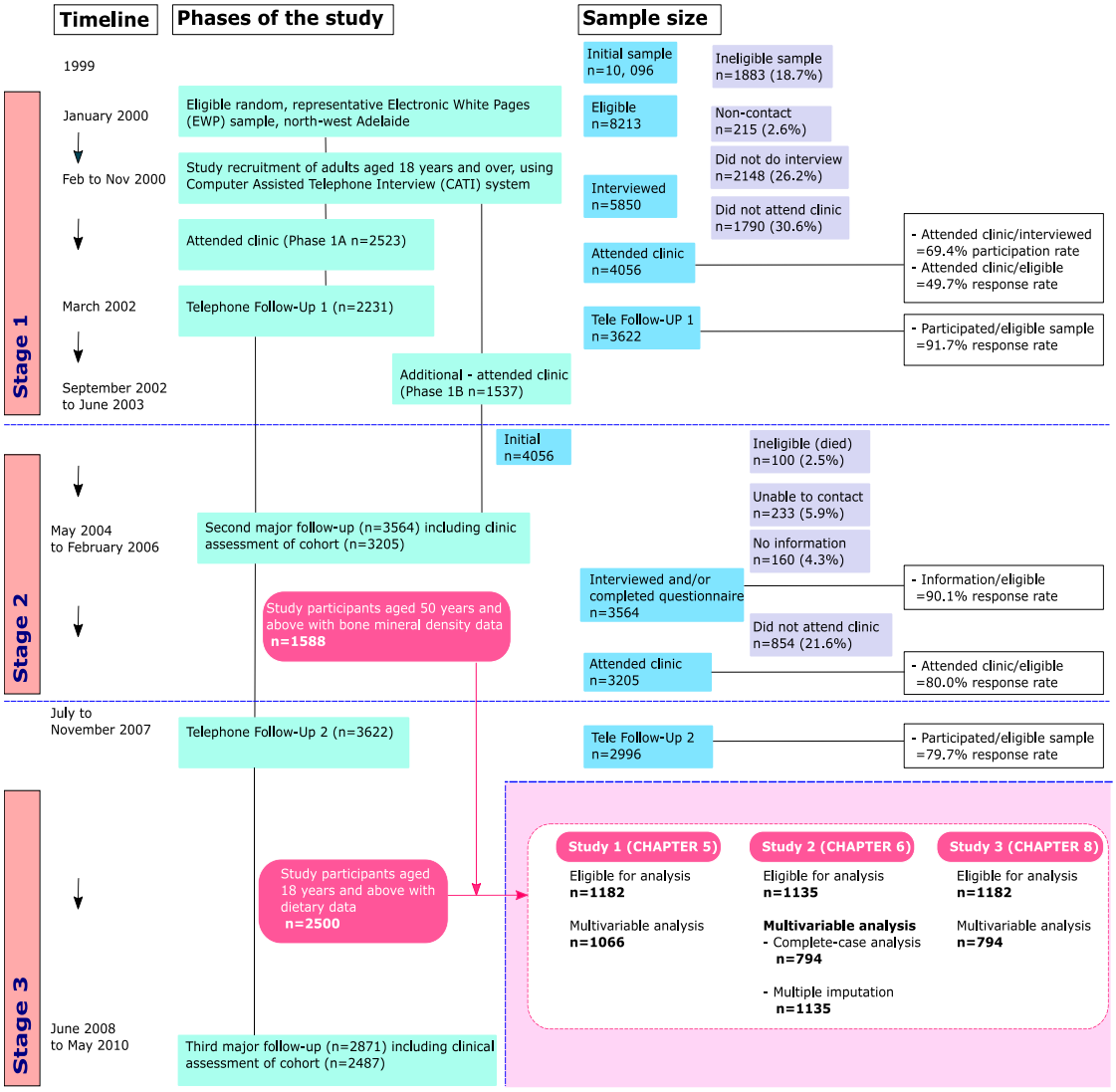

Figure 3.2 Study timeline, phases and sample size of the North West Adelaide Health Study (South Australia) [73] and subsamples used for studies (CHAPTER 5, CHAPTER 6 and CHAPTER 8) in this thesis

Study population and measurements

In this thesis, those who were 50 years and over were included because the invitation for DXA measurements was provided for participants of this age group. Data that were collected at each stage are presented in Table 3.1. Dietary data were collected using Cancer Council Victoria Diet Questionnaire for Epidemiological Studies (DQES-V3.1).

Details of the measurement of variables included in the three studies (CHAPTER 5, CHAPTER 6 and CHAPTER 8) based on NWAHS are described in each study.

Table 3.1 Variables collected in three stages of North West Adelaide Health Study (1999-2010), South Australia

Phase	Computer Assisted Telephone Interview (CATI)	Questionnaire	Clinic
Stage 1 (Ph1A 2000 & Ph1B 2002/03)	**Chronic Health conditions** – doctor diagnosed diabetes, asthma, bronchitis, emphysema, heart attack, stroke, angina **Smoking** - current and ever smoked regularly **High cholesterol** – doctor diagnose ever or current **High blood pressure** (Ph 1B only) – doctor/nurse diagnosed; ever and current **Height & weight** (Ph 1B only) **Mental Health conditions** (doctor diagnose last 12 months) – anxiety, depression, stress-related, other; still current **Demographics** – age, sex, work done for most of life, no of people 18+ in household, number of children <18 in household	**36-Item Short Form Survey (SF-36)** (v1) **Physical activity** (National Health Survey) **Health care utilisation** (last year) **Family history** – diabetes, heart disease, stroke **Diabetes** – doctor diagnose ever, gestational, high blood sugar ever and now, type when first told (Ph 1B only) **Asthma** – ever, confirmed by doctor, current; when first told, severity (Ph 1B only) **Bronchitis** **Emphysema** **Lung function** – Chronic Lung Disease Index **Alcohol** – frequency and amount **Smoking** – current, amount, ever smoked regularly, cigs per day, age when last gave up smoking **Demographics** – age when left school, trade or higher qualifications, annual gross household income, country of birth, year of arrival in Australia, Aboriginal and Torres Strait Islander status, marital status, work status, pension/benefit status, age, postcode	**Appointment information** – date, time, date of birth, age, sex, location of clinic, location of blood sample, reimbursement status **Clinic administration** – fasting, hospital patient, consent forms, general practice & secondary contacts, Medicare consent **Blood pressure** - systolic and diastolic, medication for hypertension **Height & weight** **Waist & hip circumference** **Blood tests** – triglycerides, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, glucose, HbA1c; currently on cholesterol medication, taken in last 24 hours **Spirometry**

Phase	Computer Assisted Telephone Interview (CATI)	Questionnaire	Clinic
Stage 2 2004-06	**Chronic Health conditions** (doctor diagnosed ever) – heart attack, stroke, angina, TIA/ mini-stroke, osteoporosis, arthritis (including type) **Health care utilisation** (last year) **Low Back** – pain, aching or chronic stiffness in last month **Hips** – serious sprain/strain, operation, hip joint replacement, pain, aching or chronic stiffness in last month, reason **Knees** – serious sprain/strain, operation, knee replacement, pain, aching or chronic stiffness in last month, reason, WOMAC **Feet** – pain, aching or stiffness, degree of severity and time for each foot **Shoulders** – pain, aching or chronic stiffness in last month, SPADI **Hands** – pain, aching or chronic stiffness in last month **Injury** – falls, fractures **Menopause** – status, length of time **Mental Health conditions** (Doctor diagnosed in the 12 months) – anxiety, depression, stress-related, other Depression (CES-D)	**SF36** (v1) **Physical activity** (National Health Survey) **Family history** – diabetes, heart disease, stroke, osteoporosis **Osteoporosis** – fall, trauma or fracture in last 5 years **Sunlight** – direct sunlight exposure - weekdays and weekends - summer and winter; tendency to burn **Diabetes** **Asthma** **Bronchitis (chronic)** **Emphysema** **Alcohol** **Smoking** **Mental health & wellbeing (GHQ12)** **Demographics** – family structure, highest education qualifications, annual gross household income, marital status, work status, pension/benefit status, age, postcode	**Appointment information** – date, time, date of birth, age, sex, location of clinic, location of blood sample, reimbursement status **Clinic administration** – fasting, urine sample, consent forms, general practitioner & secondary contacts, Medicare consent **Blood pressure** – systolic and diastolic, medication for hypertension, currently on HBP medication, taken in last 24 hours **Height & weight** **Waist & hip circumference** **Blood tests** – triglycerides, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, glucose, HbA1c; currently on cholesterol medication, taken in last 24 hours **Arthritis** – photo of both hands, flexion, abduction, external rotation & hand behind back; both hands grip strength, feet pain, aching or stiffness location **Spirometry** **Dual-energy x-ray absorptiometry (DXA)** (for those 50+ years) – body composition and total body scan (osteoporosis)

Phase	Computer Assisted Telephone Interview (CATI)	Questionnaire	Clinic
Stage 3 2008 – 2010	**Health conditions** (doctor diagnose ever) – heart attack, stroke, angina, mini-stroke, heart procedures (bypass, angiogram, stent), osteoporosis, gout, arthritis; **Mental Health** (doctor diagnosis in last 12 months) – anxiety, depression, stress-related, other **Injury** – falls, fractures **Shoulders** – pain, aching or chronic stiffness in last month **Health care utilisation** (last year) **Physical activity** (Active Australia) **Quality of life** (AQOL) **Cardiovascular knowledge** **Self-reported body measures** (height, weight, waist) **Household food habits** – cost and quality of fruit & veg; soft drink & milk consumption; frequency of home-cooked & fast foods purchase **Household environment** – no of television sets, computer game consoles, bicycles, smoke-free household, number and type of pets and indoor habitation **Household** – age, sex & relationship of household members **Early learning** – kindergarten in SA, residential suburb at age 4 **Demographics** (marital, work, education, income, family structure, housing, pension, money situation)	**SF36** (v2) **Carers** – long-term care, effect on health **Family history** – diabetes, heart disease, stroke, osteoporosis, high blood pressure, asthma, body type (size) of mother & father **Diabetes** – doctor diagnosis ever, gestational, type, vision affected, laser therapy on eyes, cataract surgery, tingling etc of feet & toes **Asthma** **Lung function** **Alcohol consumption** **Smoking** **Sleep** **Depression** (CES-D) **Mastery and control** – problem-solving, control **Low Back** – pain, aching or chronic stiffness in last month **Hips** – hip joint replacement, pain, aching or chronic stiffness in last month **Feet** – pain, aching or stiffness, degree of severity and duration for each foot **Knees** – serious sprain/strain, operation, knee replacement, pain, aching or chronic stiffness in last month, reason, knee arthritis **Hands** – pain, aching or chronic stiffness in last month, hand arthritis **Major health event(s) in last 5 years** **Feedback from participants** **Cardiovascular knowledge** **Food Frequency Questionnaire** (Cancer Council Victoria)	**Appointment information** – date, time, date of birth, age, sex, location of clinic, location of blood sample, reimbursement status **Clinic administration** – fasting, consent forms, general practitioner & secondary contacts, Medicare & DNA consents **Blood pressure** **Height & weight** **Waist & hip circumference** **Urine specimen** – sodium, potassium, creatinine, albumin, phosphate, micro-albuminaria, iodine & sodium **Blood tests** **Arthritis** – both hands grip strength **Spirometry** **Health Literacy** – Short-Test of Functional Health Literacy in Adults (S-TOFHLA)

Ph – Phone follow-up

3.1.3 China Health and Nutrition Survey (CHNS)

The CHNS is a community-based longitudinal open cohort started in 1989. It is a collaborative project between University of North Carolina (UNC) and the Chinese Centre for Disease Control and Prevention (CCDC) to examine economic, sociological, demographic and health conditions at individual, household and community levels. The data are collected every two to three years. The CHNS data are open access (http://www.cpc.unc.edu/projects/china) that cover nine waves over 22 years (1989-2011). A multistage random-cluster sampling method is used to select households in both urban and rural areas and all members of the selected households are invited to participate in the study [298].

Between 1989 and 2011, 35,703 study participants were involved in at least one study wave. However, we included 15,572 participants in the current study because others were either less than 18 years of age, participated only in one wave, had missing dietary data and/or fracture history or had extremely high or low energy intake. The response rate based on those who participated in previous waves staying in the subsequent survey was around 88%. However, the response rate among the participants included at baseline (1989) and remained in 2006 was more than 60%. The dataset contains self-reported fracture history and dietary data along with other sociodemographic characteristics, behavioural risk factors and chronic conditions [298].

Dietary data were collected using a repeated 3-day 24-h recall method and a household inventory by trained health workers at each wave of the study. The three days were randomly allocated in the week and weekdays. All the food available in the household were measured using weighing scales [298, 299]. CHAPTER 7 explores the longitudinal associations of dietary and nutrient patterns and self-reported fracture among adults aged

18 years and over using data from 15,572 participants between 1991 and 2011. Data of the 1989 survey were excluded because dietary data were available only for middle-aged adults. Detailed methods, including a description of variable measurements, are presented in the study presented in CHAPTER 7.

3.2 Statistical analysis

3.2.1 Analysis methods in the GBD Study

For GBD 2015 risk factors study, definitions of the 14 dietary components were is provided in Supplementary Table 3.1. For example, a diet low in fruits is defined as average daily intake of less than 250 grams per day. Different data input sources, including nationally and sub-nationally representative nutrition surveys, household budget surveys, and UN Food and Agricultural Organization (FAO) Food Balance Sheets and Supply Utilization Accounts were used to determine the exposure levels of the dietary components. DisMod-MR 2.1 was used to estimate the intake of components by age, sex, and year in each country. DisMod-MR 2.1 is a Bayesian meta-regression tool that models exposure levels and it corrects for bias associated with variations of studies that are used as data sources. With joint application of DisMod-MR 2.1 and a spatiotemporal Gaussian process regression model (ST-GPR), data from different sources can be integrated by controlling and adjusting for potential bias. Further, additional important covariates, such as country and study level factors, can be included in the estimation. These two models also allow borrowing information across age, time, and geography to get unified estimates [297].

Disease burden attributable to each dietary component if the dietary exposure was maintained at the level (TMREL) that is associated with the lowest disease risk was

calculated [297]. In the analysis, metabolic mediators were considered. Details of the statistical approaches, including formulas, used in estimating dietary data exposure levels and attributable burden of NCDs are provided in CHAPTER 4 and an extra description was also provided the GBD risk factors study [297].

3.2.2 Dietary data analysis methods in NWAHS and CHNS

Exploratory factor analysis using PCA method was used to analyse dietary data from NWAHS and CHNS. Factor analysis is important to investigate the relationships of complex variables by extracting virtual factors that cannot be measured directly. It is a data-driven reduction approach that collapses multidimensional data into a few factors that reflect the original variables. The concept behind factor analysis is that multidimensional observed variables have similar patterns that are related to unmeasured (latent) factors [294]. The relationship between the observed variables and a latent variable can be conceptually represented in Figure 3.3.

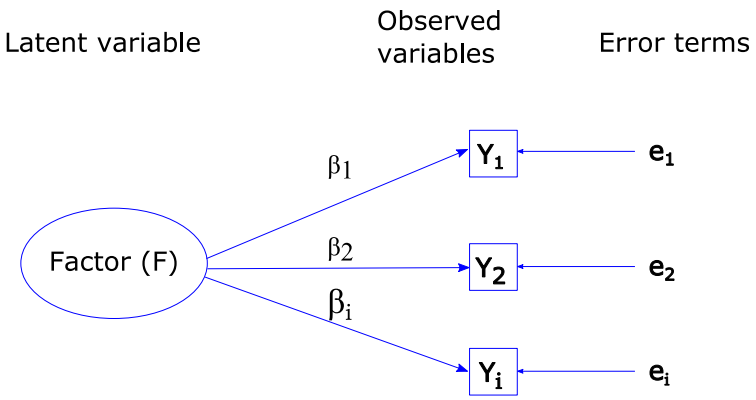

Figure 3.3 Relationship of observed and latent variables in factor analysis

Factor analysis assumes a number of variables (in this case, intakes of food and nutrients in unit per day), $\boldsymbol{Y_1, Y_2, \ldots. Y_i}$, are linearly related to a reduced number of hidden factors

(in this case, dietary and nutrient patterns), $\boldsymbol{F_1 . F_2 \ldots\ldots F_i}$, and can be expressed with the following equation:

$$Y_i = \beta_{i0} + \beta_{i1}F_1 + \beta_{i2}F_2 + \ldots \beta_{ik}F_i + e_i, \qquad i=1, 2, 3 \ldots .. I \quad \textbf{Equation 3.1}$$

where $\boldsymbol{e_i}$ is an error term, $\boldsymbol{\beta_{i0}}$ represents intercept of factors, and $\boldsymbol{\beta_{i1}}$, $\boldsymbol{\beta_{i2}}$, $\boldsymbol{\ldots.\beta_{ik}}$ are correlation coefficients (factor loadings) of variables, $\boldsymbol{Y_1, Y_2, \ldots.. Y_i}$, on factors $\boldsymbol{F_1 . F_2 \ldots\ldots F_k}$. A higher factor loading indicates a greater correlation with a specific pattern.

In factor analysis, there are similar number of factors as there are variables. Therefore, selecting the optimal number of factors to be included in the final iteration should be determined as it is not always possible to include all factors. There are three commonly used approaches: 1) using an eigenvalue which is a measure of how much of the variance of observed variables a factor explains. If an eigenvalue of a factor is greater than one or 1.5, then the factor explains more variance than a single observed value; 2) using a scree plot; 3) interpretability of factors. Consequently, the decision on the number of factors is subjective.

Each factor contains the amount of variance in the observed variables and can be explained in percentage. To enhance interpretability of, and minimize, the correlation between factors, rotation of factor scores are used [294, 300].

Factor analysis and PCA are similar analysis methods—both are data reduction techniques that allow variances in a smaller number of variables with weighted correlation. However, whereas PCA is a linear combination of a number of observed variables to create components, factor analysis is a measurement model of factors. PCA is counter-intuitive to factor analysis [300]. PCA can be summarized with the following conceptual diagram and equation (Figure 3.4):

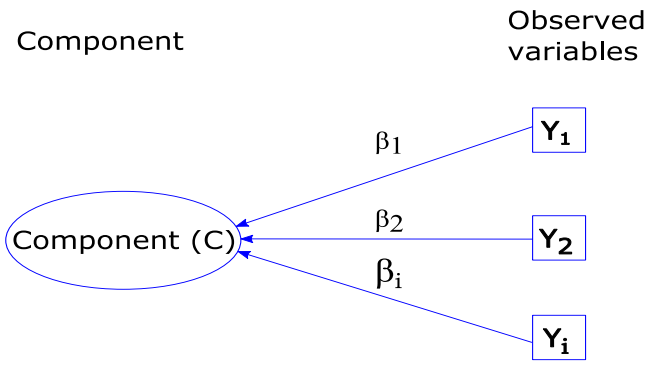

Figure 3.4 Relationship of observed and component variables in principal component analysis

$$C_i = \beta_{i0} + \beta_{i1}Y_1 + \beta_{i2}Y_2 + \ldots \beta_{ii}Y_i, \qquad i=1, 2, 3\ldots.. I \qquad \textbf{Equation 3.2}$$

where $\boldsymbol{\beta_{i1}}$, $\boldsymbol{\beta_{i2}}$, ….$\boldsymbol{\beta_{ik}}$ are correlation coefficients (component loadings) of variables, $\boldsymbol{Y_1}$, $\boldsymbol{Y_2}$, ,….. $\boldsymbol{Y_i}$ on components $\boldsymbol{C_1}$, $\boldsymbol{C_2}$…….$\boldsymbol{C_i}$. Like factor analysis, a higher factor loading indicates a greater weighted correlation with a specific pattern.

Four studies (CHAPTER 4, CHAPTER 6, CHAPTER 7 and CHAPTER 8) of this thesis used factor analysis with PCA to construct dietary and nutrient patterns. In STATA, this analysis was performed using "*factor* Y_1 Y_2…..Y_i, *pcf factor (n)*" command, where *Y* are observed variables (intake of foods and nutrients) and *n* is the number of factors (components) needed to be retained. Detailed dietary analysis approaches are described in each study.

One study evaluates three common dietary analysis methods (PCS, PLS and RRR) in the thesis (CHAPTER 8). PLS and RRR are *a priori* and *a posteriori* methods (hybrid approaches). These methods are extensions of a linear regression analysis that specifies the linear correlation between a response (dependent) variable (Y) and a set of predictor variables (X_s).

The three methods (PCA, PLS and RRR) are similar in their mathematical fundamentals and technique of deriving factors. In addition, they are extensions of a linear regression method and the assumption behind these methods is that the extracted factors (components) are uncorrelated. However, in contrast to PCA, RRR identifies factors that explain as much response variation as possible. PLS moderates the two—explains predictor and response variation simultaneously. Assuming there are two predictors, X_1 and X_2, one response variable, Y; Figure 3.5 depicts how each of the three methods explains predictor (X_s) and response (Y) variations.

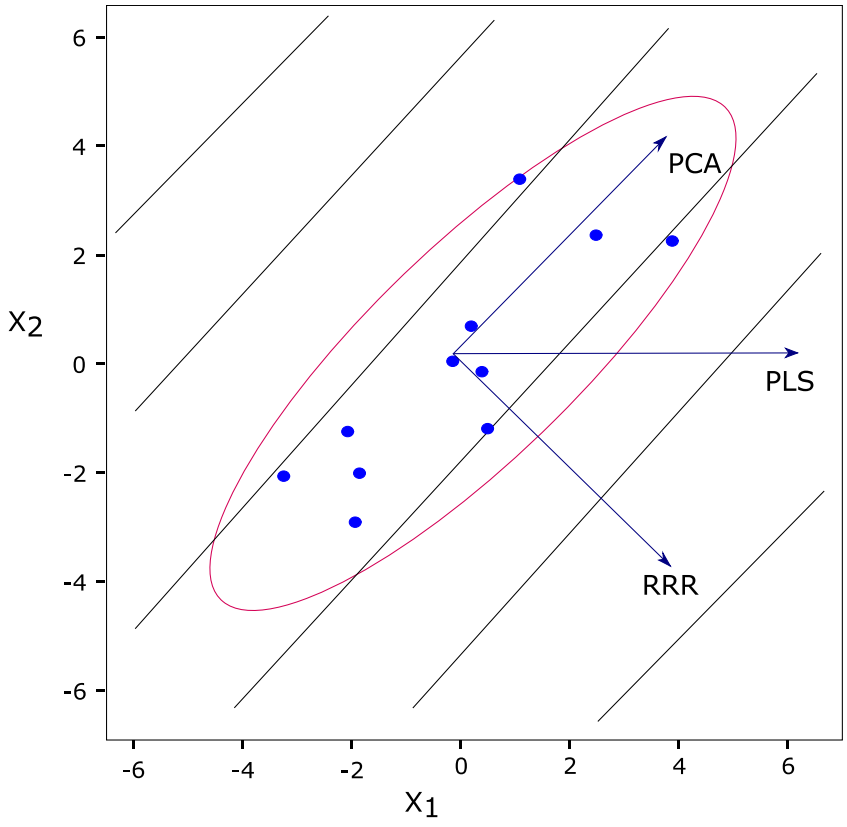

Figure 3.5 Comparison of predictor and response variations in three data reduction methods (Principal component analysis [PCA], partial least-squares [PLS] and reduced-rank regression [RRR]) [301]

From Figure 3.5, one can understand that the response (Y) varies orthogonally when the predictors vary most in the X_1=X_2 direction. This phenomena explains why PCA

effectively ignores response data and explains as much predictor variation as possible and RRR ignores predictors and explains as much response variation as possible. PLS balances the two and extracts one factor at a time.

RRR constructs the factors to account for the maximum predicted responses by ignoring the predictors. Assume $\boldsymbol{Y}$ is a centred response ($\boldsymbol{n} \times \boldsymbol{q}$) variable which is dependent on centred predictors $\boldsymbol{X}$ ($\boldsymbol{n} \times \boldsymbol{p}$). The $\boldsymbol{X}$ scores are the projections of the $\boldsymbol{Y}$ scores ($\boldsymbol{Y_{qi}}$) onto the $\boldsymbol{X}$ space. The $\boldsymbol{Y}$ weighted ($\boldsymbol{Y_{qi}}$) are the vectors of covariance matrix $\hat{\mathrm{Y}}'_{\boldsymbol{OLS}}\hat{\mathrm{Y}}_{\boldsymbol{OLS}}$ of the responses predicted by ordinary least squares (OLS) regression. The OLS can be expressed as [48]:

$$\mathrm{L} = \| \mathrm{Y} - \Pi \mathrm{X} \|^2 \qquad \textbf{Equation 3.3}$$

where $\boldsymbol{\Pi}$ is a ($\boldsymbol{p} \times \boldsymbol{q}$) matrix of regression weights. It can be expressed as [48]:

$$\Pi_{\mathrm{OLS}} = (\mathrm{X}^{\top}\mathrm{X})^{-1}\mathrm{X}^{\top}\mathrm{Y} \qquad \textbf{Equation 3.4}$$

RRR maximizes $\boldsymbol{\Pi}$ to constraint rank $(\boldsymbol{\Pi}) \leq \boldsymbol{r}$, where $\boldsymbol{0 \leq r < min(p, q)}$. Therefore, a RRR model can be given as:

$$\mathrm{Y_i} = \Pi \mathrm{X}_i + \Psi \mathrm{Z}_i + \varepsilon_i, \qquad i=1, 2, 3\ldots.. I \qquad \textbf{Equation 3.5}$$

where Z_i is the latent variable that needs to be estimated.

Or

$$Y_i = \alpha\beta' X_i + \Psi Z_i + \varepsilon_i, \qquad i=1, 2, 3\ldots.. I \qquad \textbf{Equation 3.6}$$

where $\Pi = \alpha\beta'$ and $\boldsymbol{\alpha}$ and $\boldsymbol{\beta}$ have dimensions $\boldsymbol{p} \times \boldsymbol{r}$ and $\boldsymbol{p} \times \boldsymbol{r}$, respectively [48].

Unlike PCA and RRR, PLS model considers both predictors and responses simultaneously. Assume $\boldsymbol{X}=\boldsymbol{X_0}$ and $\boldsymbol{Y}=\boldsymbol{Y_0}$ are the centred and scaled matrix of predictors and responses, respectively. Let $\boldsymbol{t}=\boldsymbol{X_0 w}$, where $\boldsymbol{t}$ is a score vector and $\boldsymbol{w}$ is associated weight vector. In general, the PLS method uses regression to predict $\boldsymbol{X_0}$ and $\boldsymbol{Y_0}$ on $\boldsymbol{t}$ [47, 301]:

$$\hat{X}_0 = tp' \text{ , where } p = (t't)^{-1}t'X_0 \qquad \textbf{Equation 3.7}$$

$$\hat{Y}_0 = tc' \text{ , where } c = (t't)^{-1}t'Y_0 \qquad \textbf{Equation 3.8}$$

The vector $\boldsymbol{p}$ and $\boldsymbol{c}$ are the $\boldsymbol{X}$ (predictor) and $\boldsymbol{Y}$ (response) loadings, respectively [47, 301].

In my study (CHAPTER 8), the performance of the three methods (PCA, PLS and RRR) in constructing plausible dietary patterns associated with BMD and BMC was evaluated. PLS and RRR analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, North Carolina) using "*proc pls <options> method = ;*" [301] command and defining the methods (*rrr* or *pls*).

3.2.3 Model building in the NWAHS and CHNS data

In each study, models using statistical approaches that were appropriate for the data in NWAHS and CHNS were developed. Linear, Poisson and Cox proportional hazard regressions were used. Table 3.2 summarizes model building process and statistical approaches used.

Table 3.2 Summary of predictors, outcome and confounding variables and statistical approaches used in the studies of this thesis (CHAPTER 5, CHAPTER 6, CHAPTER 7 and CHAPTER 8)

Study (Chapter)	Predictor and outcome variables	Model	Covariates (adjusted for)	Statistical approaches	Additional analyses
Study 1 (CHAPTER 5)	• Predictor: dietary patterns (tertiles of factor scores) • Outcome: low BMD (T-score<-2.5)	Crude	None	Poisson regression	
		Model 1	Sex and age		
		Model 2	Model 1 + socio-economic and lifestyle factors (smoking status, alcohol intake (no risk, low risk, medium/very high risk), marital status, income, health literacy, leisure-time and job-related physical activity levels)		
		Model 3	Model 2 + chronic conditions (diabetes mellitus, family history of osteoporosis and BMI (continuous)		
		Model 4	Model 3 + energy intake (continuous)		• Subgroup analysis • Interaction of covariates with the predictor variable • Sensitivity analysis • Trend analysis
Study 2 (CHAPTER 6)	• Predictor: nutrient patterns (factor scores) • Outcome: BMD (mg/cm^2)	Crude	None	Linear regression	
		Model 1	Sex and age		
		Model 2	Model 1 + socio-economic and lifestyle factors [smoking, alcohol intake (no/low risk, medium/very high risk), marital status, income, health literacy (limited, adequate), leisure time and job-related physical activity levels (low, moderate/high)]		
		Model 3	Model 2 + chronic conditions [diabetes mellitus, family history of osteoporosis and body mass index (continuous)]		
		Model 4	Model 3 + energy intake (continuous)		• Subgroup analysis • Interaction of covariates with the predictor variables • Sensitivity analysis • Multiple imputations • Trend analysis

Study (Chapter)	Predictor and outcome variables	Model	Covariates (adjusted for)	Statistical approaches	Additional analyses
Study 3 (CHAPTER 7)	• Predictors: dietary and nutrient patterns (tertiles of factor scores) • Outcome: self-reported Fracture	Model 1	Sex, age (continuous) and energy intake (continuous)	Cox proportional hazard regression	
		Model 2	Model 1 + educational status (low, medium and high), income (low, medium and high), alcohol consumption (none, <1, 1–2, 3–4 per week and daily), smoking (non-smoker and current/ex-smoker), residency (rural and urban) and physical activity level (metabolic equivalent task-hours/week, continuous)		
		Model 3	Model 2 + body-mass index (continuous) and high blood pressure (yes/no)		• Subgroup analysis • Interaction of covariates with the predictor variable • Sensitivity analysis • Evaluation of different dietary exposure measurement approaches • Trend analysis
Study 4 (CHAPTER 8)	• Predictor: dietary patterns (tertiles of factor scores) derived using principal component analysis, partial least-squares and reduced-rank regression • Outcome: BMD (mg/cm^2) and BMC (g)	Model 1	Sex and age	Linear regression	
		Model 2	Model 1 + socio-economic and lifestyle factors (income, marital status, smoking, alcohol risk, health literacy, leisure time and job-related physical activity levels), chronic conditions (diabetes mellitus, family history of osteoporosis and body mass index) Model 2 of bone mineral content (BMC) was additionally adjusted for height (cm).		
		Model 3	Model 2 + total energy intake Model 3 of bone mineral content (BMC) was additionally adjusted for height (cm).		• Subgroup analysis • Sensitivity analysis • Trend analysis

BMC – bone mineral content; BMD – bone mineral density

CHAPTER 4 BURDEN OF DIET–RELATED NON-COMMUNICABLE CHRONIC DISEASES

4.1 Publication

Melaku YA, Renzaho A, Gill TK et al: Burden and trend of diet-related non-communicable diseases in Australia and comparison with 34 countries: findings from the Global Burden of Disease Study 2015: Eur J Nutr 2018. https://doi.org/10.1007/s00394-018-1656-7.

Statement of Authorship

Title of Paper	Burden and trend of diet-related non-communicable diseases in Australia and comparison with 34 countries: findings from the Global Burden of Disease Study 2015: Eur J Nutr 2018. https://doi.org/10.1007/s00394-018-1656-7
Publication Status	☑ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted work written in manuscript style
Publication Details	Melaku YA, Renzaho A, Gill TK, Taylor AW, Dal Grande E, de Courten B, Baye B, Gonzalez-Chica D, Hyppönen E, Shi Z, Riley M, Adams R, Kinfu K: Burden and trend of diet-related non-communicable diseases in Australia and comparison with 34 countries: findings from the Global Burden of Disease Study 2015: Eur J Nutr 2018. https://doi.org/10.1007/s00394-018-1656-7

Principal Author

Name of Principal Author (Candidate)	Yohannes Adama Melaku		
Contribution to the Paper	Conception and design, organization and interpretation of data, manuscript preparation, contribution to the materials/analysis tools and critical revision and editing of the manuscript		
Overall percentage (%)	50%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	23/07/2018

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Andre Renzaho		
Contribution to the Paper	Conception and design, interpretation of results, critical manuscript evaluation and editing and contribution to the materials/analysis tools		
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Contribution to the Paper	Conception and design, interpretation of results and critical manuscript evaluation and editing		
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Burden and trend of diet-related non-communicable diseases in Australia and comparison with 34 OECD countries, 1990-2015: findings from the Global Burden of Disease Study 2015

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Abstract

Background: Diet is a major determining factor for many non-communicable chronic diseases (NCDs). However, evidence on diet-related NCD burden remains limited. We assessed the trends in diet-related NCDs in Australia from 1990 to 2015 and compared the results with other countries of the Organization for Economic Co-operation and Development (OECD).

Methods: We used data and methods from the Global Burden of Disease (GBD) 2015 study to estimate the NCD mortality and disability-adjusted life years (DALYs) attributable to 14 dietary risk factors in Australia and 34 OECD nations. Countries were further ranked from the lowest (first) to highest (35^{th}) burden using an age-standardized population attributable fraction (PAF).

Results: In 2015, the estimated number of deaths attributable to dietary risks was 29,414 deaths (95% uncertainty interval [UI] 24,697-34,058 or 19.7% of NCD deaths) and 443,385 DALYs (95% UI 377,680- 511,388 or 9.5% of NCD DALYs) in Australia. Young (25-49 years) and middle-age (50-69 years) male adults had a higher PAF of diet-related NCD deaths and DALYs than their female counterparts. Diets low in FV, nuts and seeds and whole grains, but high in sodium, were the major contributors to both NCD deaths and DALYs. Overall, 42.3% of CVD deaths were attributable to dietary risk factors. The age-standardized PAF of diet-related NCD mortality and DALYs decreased over the study period by 28.2% (from 27.0% in 1990 to 19.4% in 2015) and 41.0% (from 14.3% in 1990 to 8.4% in 2015), respectively. In 2015, Australia ranked 12^{th} of 35 examined countries in diet-related mortality. A small improvement of rank was recorded compared to the previous 25 years.

Conclusions: Despite a reduction in diet-related NCD burden over 25 years, dietary risks are still the major contributors to a high burden of NCDs in Australia. Interventions targeting NCDs should focus on dietary behaviours of individuals and population groups.

Keywords: dietary risk factors, non-communicable diseases, burden of disease, Australia, OECD countries

Introduction

Dietary risk factors are major contributors to mortality and morbidity from NCDs [302-304]. Despite this finding, food consumption in developed nations is dominated by the intake of an unhealthy diet [50]. Considering this growing global problem, the UN, through the Decade of Action on Nutrition, aims to improve human nutrition by involving stakeholders [305]. Nutrition is also at the centre of the global development agenda and is associated with 12 of the 17 SDGs. Specifically, the third goal ("*Ensure healthy lives and promote well-being for all at all ages*") recognizes NCD as a major global challenge and aims to target a one-third reduction of associated premature deaths by 2030 [306]. However, information on the contribution of dietary risk factors to the burden of NCDs is limited.

In 2011, the Australian Burden of Disease (ABD) study, for the first time, evaluated the effect of 13 dietary risk factors on NCD DALYs [307]. Estimates from the 2015 GBD study also provides similar results for Australia and other countries. However, the approach used by the ABD study and the GBD study are slightly different from each other [297, 307]. For instance, compared to the GBD estimates, the ABD study used more data sources and, therefore, it was less dependent on statistical modelling [307]. On the other hand, the GBD study is based on the most recent high-quality evidence from a range of different data sources (national and international including the FAO database) that can help to obtain better and complete estimates than those based on only local data. The GBD study also provides estimates for 14, rather than 13, dietary risk factors to estimate their effect on the burden of NCDs [297]. Moreover, unlike the ABD study, GBD provides updated effect sizes (relative risks) and exposure levels of dietary risks, as well as an aggregate burden of NCDs, for all dietary risk factors [297, 307]. The study uses

consistent methods and data sources, which indicate that the results from the GBD study provide a better platform than the ABD study to compare the burden of disease and risk factors across countries over time.

The approach developed for the GBD also provides a capacity to specifically report and compare estimates and 95% uncertainty intervals (UIs) of diet-related burden (mortalities and DALYs) of NCDs for all nations worldwide [297]. In this study, using data from the 2015 version of the GBD data, we compiled data on diet-related mortalities and DALYs for Australia between 1990 and 2015 and compared these data with 34 other members of OECD.

Methods

Overview

The GBD 2015 risk factors study captures 79 behavioural, environmental and occupational, and metabolic risks over a 25-year period 1990 to 2015 for 195 countries [297]. All countries were nested under seven super-regions and 21 regions. Using the results from this study, the diet-related burden of NCDs in Australia was determined and compared with other 34 OECD countries (namely, Austria, Belgium, Canada, Chile, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Japan, Luxembourg, Mexico, the Netherlands, New Zealand, Norway, Poland, Portugal, Singapore, Slovakia, Slovenia, South Korea, Spain, Sweden, Switzerland, Turkey, the United Kingdom (UK) and the US, as well as with four GBD groupings: the global average (195 countries) and averages for European (42 countries), OECD (35 countries) and high-income countries (34 countries). Ranking of the countries was from the lowest (first) to the highest (35^{th}) burden based on population

attributable fraction (PAF).

Selection of dietary risk factors

Overall, 14 dietary risk factors (eight food groups, five nutrients and fibre intake) were included in GBD 2015. These included diets low in FV, whole grains, nuts and seeds, milk, fibre, calcium, seafood omega-3, and polyunsaturated fatty acids, as well as diets high in red and processed meat, sugar-sweetened beverages (SSBs), *trans* fatty acids, and sodium [297, 308]. The GBD 2015 selected dietary risks based on the strength of epidemiological evidence for causality and generalizability, significance (or relative contribution) to the burden of disease and availability of sufficient and reliable data [297]. The World Cancer Research Fund evidence assessment tool [297, 309] was used to evaluate the strength of the epidemiological evidence on the causal relationship between each dietary risk factor and a disease outcome. Convincing or probable evidence of diet-disease pairs were included in the study. A more detailed description of the GBD 2015 study has been published elsewhere [297]. The list of studies that support the evidence is shown in Supplementary Table 4.1. The process of dietary factors selection and estimation of the attributable burden of disease is depicted in Figure 4.1. The optimal levels of intake of the dietary risk factors are given in Supplementary Table 3.1.

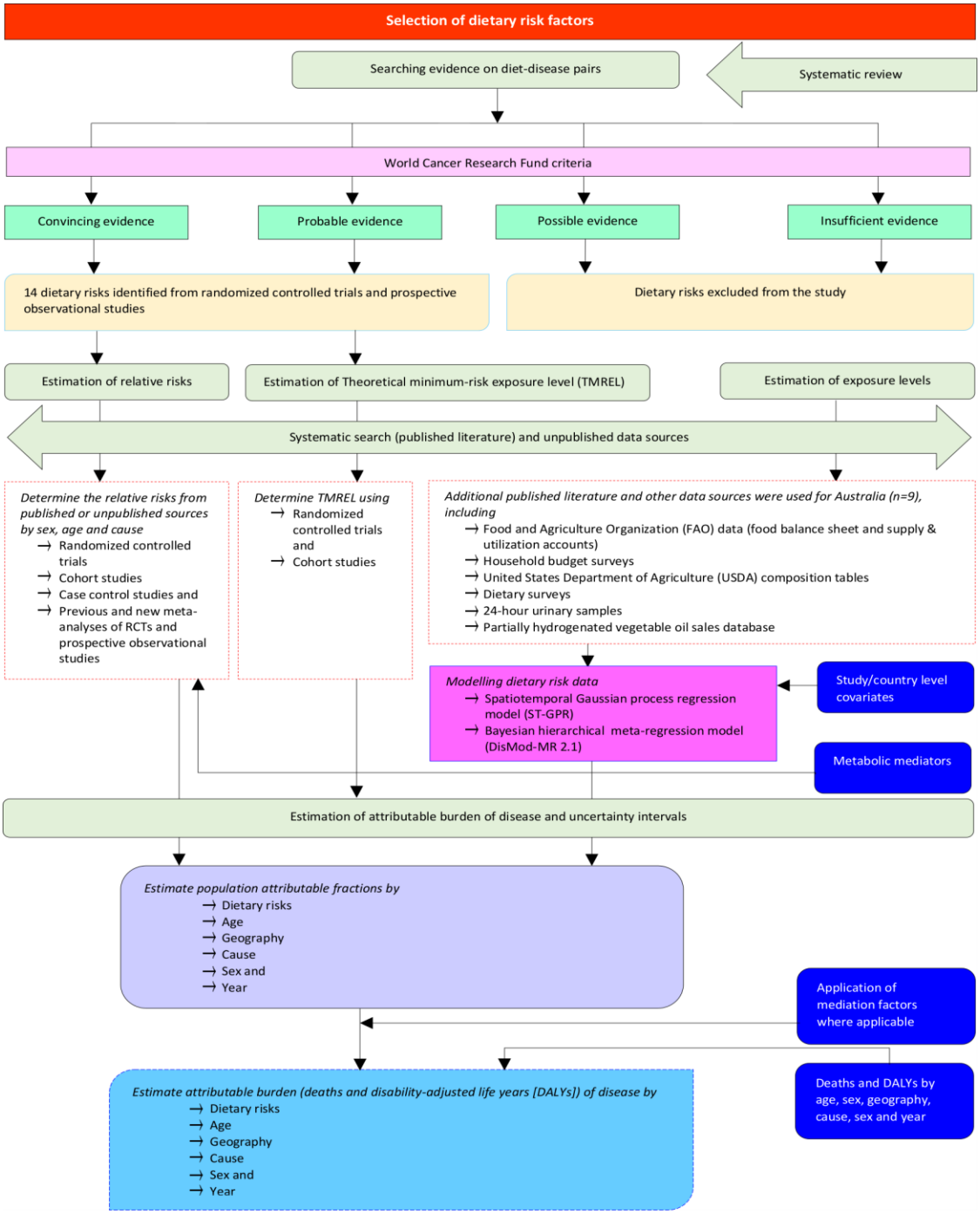

Figure 4.1 Flow diagram depicting an overview of dietary data search, processing, and estimation of relative risks, Theoretical minimum-risk exposure level (TMREL) and burden of non-communicable diseases

[Adapted from the Global Burden of Disease (GBD) 2015 Risk Factors Study. This figure depicts a summary of dietary risk methods. Methods that are more detailed can be accessed from the GBD 2015 Risk Factors Study.]

Data sources and estimating exposure levels

For each dietary risk factor, the literature was searched for nationally or sub-nationally representative nutrition surveys. Data from food balance sheets and supply utilization accounts of the FAO of the UN were also used. For *trans* fatty acids, the availability of partially hydrogenated vegetable oil packaged foods was used. The list of data sources used for Australia is provided in Supplementary Table 4.2. Data sources used for all countries included in GBD can be accessed on the Global Health Data Exchange (http://ghdx.healthdata.org/). All dietary data (other than SSBs and urinary sodium) were standardized to 2000 kcal/day [297].

For FAO data, after adjustments were made for energy intake, the missing country-year data were estimated using spatiotemporal Gaussian process regression (ST-GPR), and age split of the data was then applied to transform to GBD age groups. A Bayesian hierarchical meta-regression method (DisMod-MR 2.1) was used to estimate the intake of each dietary factor by age, sex, country, and year from all data sources. DisMod-MR 2.1 has two important components: a mixed effect meta-regression analysis using sex and country level covariates, and the second component is a cascade repeating the above model by limiting data to one year-sex. If country-specific data were available, the model was mostly informed using these data. Specifically, the relationship between the standard deviation and mean intake of dietary factors and the associated standard deviations observed in nationally representative nutrition surveys were modelled by applying a log-normal distribution on 24-h diet recalls data to characterize the dispersion of the risk factors. A detailed approach and formula are provided in the GBD 2015 risk factor paper [297]. Covariates included in the model are given in Supplementary Table 4.3.

Estimating effect sizes

For each diet-outcome pair, the relative risk for incidence or mortality per unit change in intake was obtained from the most recent dose-response meta-analysis of prospective observational studies [297]. Due to very limited and inconclusive evidence, the relative risks of sodium and SSBs were determined by a two-stage indirect approach using systolic blood pressure and body mass index (BMI), respectively [297, 310, 311]. In this approach, the associations of 24-h sodium excretion with systolic blood pressure and of SSBs with BMI were first determined. Next, the effects of systolic blood pressure and BMI on the risk of disease outcomes were calculated. BMI, total serum cholesterol, fasting plasma glucose and systolic blood pressure were considered to mediate the relationship between dietary factors and NCDs. These mediators were used to estimate the age-specific relative risks of diet and CVD and diabetes mellitus [297]. A complete list of mediators used in the study is shown in Supplementary Table 4.3.

Estimating attributable disease burden and uncertainties

For each dietary risk factor, the proportion of disease burden that could have been prevented if the exposure level had been sustained at the level associated with the lowest risk was quantified. The level of exposure that is associated with the lowest risk is termed as the TMREL. Two steps were used to determine the TMREL. First, the level of intake associated with the lowest risk of each disease endpoint was determined from prospective observational studies. Next, the weighted average of disease-specific optimal intakes was used to determine TMREL (weight: number of deaths due to each outcome divided by the total number of deaths from all the outcomes related to the exposure at the global level). A 20% uncertainty range below and above the weighted mean was applied [297].

To estimate the burden of diseases attributable to dietary risks, the population attributable

fraction (PAF) was first estimated using the following equation [297]:

$$PAF_{joasgt} = \frac{\int_{x=l}^{u} RR_{joasg}(x)P_{jasgt}(x)dx - RR_{joasg}(TMREL)}{\int_{x=l}^{u} RR_{joasg}(x)P_{jasgt}(x)dx} \quad \textbf{Equation 4.1}$$

where PAF_{joasgt} is a population attributable fraction for a risk factor j attributed to cause o for age group a, sex s, geography g, and year t. $RR_{joasg}(x)$ is the relative risk as a function of exposure level x for a risk factor j attributed to cause o, age group a, sex s, and geography g with the lowest level of observed exposure as l and the highest as u; $P_{jasgt}(x)$ is the distribution of exposure at x for age group a, sex s, geography g, and year t; TMREL $_{jas}$ is the TMREL for risk factor j, age group a, and sex s.

Next, the attributable burden was determined using the number of burden (number of deaths and DALYs) and PAF [297].

$$Total\ attributable\ burden_{jasgt} = \sum_{o=1}^{w} Burden_{joasgt}\, PAF_{joasgt} \quad \textbf{Equation 4.2}$$

Data on DALYs and deaths were obtained from the other GBD 2015 studies [312-314].

The overall proportion of disease burden attributable to all dietary risk factors was calculated using the following formula [297]:

$$PAF_{ioasgt} = 1 - \prod_{i=1}^{J}(1 - PAF_{ioasgt}) \quad \textbf{Equation 4.3}$$

where i is a set of risk factors for the aggregation; PAF_{ioasgt} is PAF for risk i for age group a, sex s, geography g, year t and cause o. For those dietary risk factors with mediators, a modified version of this formula was used and can be accessed in the GBD 2015 risk factors study [297].

Using the Monte Carlo approach, the uncertainty of parameters for exposure, relative risk and attributable burden of disease was estimated. All computations were repeated 1000 times using one draw of each parameter at each iteration. The mean and UIs were calculated for the final estimates as per the final 1000 draws [297]. UIs include uncertainty from each relevant component, consisting of exposure, relative risks, TMREL, and burden rates. Where percentage change is reported (with 95% UIs), we calculated it on the basis of the point estimates being compared.

To compute age-standardized estimates, the GBD world population standard was used [315]. Estimates are presented with 95% UIs in parentheses. Rates are reported per 100,000 person-years.

Results

Diet-related NCD burden in Australia for 2015

In 2015, an estimated 29,414 deaths (24,697-34,058) or 19.7% (16.6-22.8) of NCD deaths and 443,385 DALYs (377,680-511,388 or 9.5% of NCD DALYs) were attributable to dietary risks. The proportion of NCD deaths related to dietary factors was higher among 70 years or older (20.1%; 16.8-23.6) than 25-49 years (16.5%; 14.7-18.3) and 50-69 years (19.3%; 16.6-21.9). The proportion of NCD deaths attributed to dietary risk factors was similar among males (20.8% of NCD deaths; 17.6-24.0) and females (18.6%; 15.6-21.7) for all ages; however, deaths were higher in males in the age strata of 25-49 years (19.8% of NCD deaths; 17.6-22.2 compared to 11.5%; 10.0-13.1 in females) and 50-69 years (22.8%; 19.7-25.8 in males and 13.7%; 11.6-15.8 in females). A similar pattern was observed for NCD DALYs related to dietary risk factors. Diet-related NCD DALYs were 276,566 DALYs (235,578-316,856) for males and 166,819 DALYs (141,554-195,842)

for females. The attributable proportion of NCD burden for males was higher in middle and late adulthood, while in females the highest burden occurred at older ages (Table 4.1 and Figure 4.2).

Table 4.1 Diet-related burden of non-communicable diseases (deaths and disability-adjusted life years) by age and sex in Australia, 2015

Age category	Metrics	Deaths (95% UI)			DALYs (95% UI)		
		Male	Female	Both	Male	Female	Both
25-49 years	Number	709 (630-794)	278 (239-317)	987 (877-1106)	39,494 (34,715-44,809)	19,788 (16,499-23,819)	59,283 (51,685-68,137)
	Crude rate per 100,000	12 (10-13)	5 (4-5)	8 (7-9)	644 (566-731)	332 (277-399)	490 (427-563)
	Crude proportion (%) (NCDs)	19.8% (17.6-22.2)	11.5% (10.0-13.1)	16.5% (14.7-18.3)	5.5% (4.7-6.7)	2.6% (2.1-3.1)	4.0% (3.4-4.8)
50-69 years	Number	3824 (3293-4340)	1449 (1224-1678)	5273 (4532-6016)	122,215 (104,691-140,332)	53,747 (44,980-64,142)	175,962 (150,646-204,410)
	Crude rate per 100,000	140 (120-159)	52 (44-60)	95 (82-108)	4470 (3829-5133)	1910 (1599-2280)	3172 (2715-3684)
	Crude proportion (%) (NCDs)	22.8% (19.7-25.8)	13.7% (11.6-15.8)	19.3% (16.6-21.9)	4.7% (12.4-17.0)	7.5% (6.3-8.9)	11.4% (9.6-13.3)
70+ years	Number	11,447 (9498-13,475)	11,706 (9766-13,775)	23,153 (19,278-27,185)	114,857 (95,902-134,426)	93,283 (77,976-110,184)	208,140 (173,907-244,204)
	Crude rate per 100,000	1100 (913-1295)	917 (765-1079)	999 (832-1173)	11,042 (9219-12,923)	7305 (6106-8628)	8982 (7505-10,538)
	Crude proportion (%) (NCDs)	20.4% (17.0-23.9)	19.9% (16.6-23.4)	20.1% (16.8-23.6)	15.6% (12.9-18.3)	13.3% (11.1-15.8)	14.5% (12.0-17.0)
All Ages	Number	15,980 (13,439-18,477)	13,433 (11,255-15,690)	29,414 (24,697-34,058)	276,566 (235,578-316,856)	166,819 (141,554-195,842)	443,385 (377,680-511,388)
	Crude rate per 100,000	132 (111-152)	110 (92-129)	121 (102-140)	2277 (1940-2609)	1370 (1163-1608)	1823 (1553-2103)
	Crude proportion (%) (NCDs)	20.8% (17.6-24.0)	18.6% (15.6-21.7)	19.7% (16.6-22.8)	11.6% (9.7-13.6)	7.3% (6.1-8.8)	9.5% (7.9-11.2)

DALYs – disability-adjusted life years; UI – uncertainty interval; Proportions were calculated out of all NCD-related deaths/DALYs.

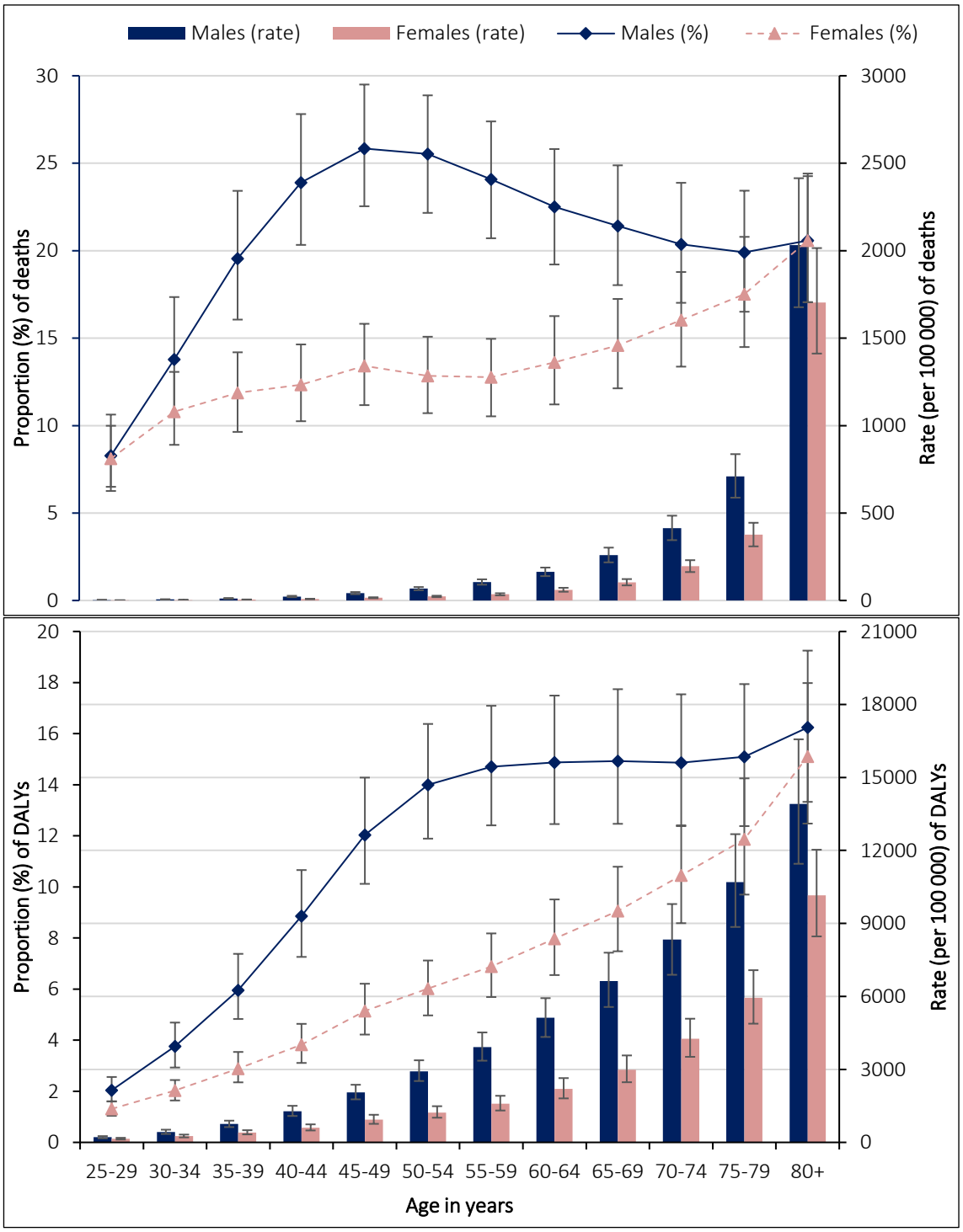

Figure 4.2 Burden of disease (death and disability-adjusted life years (DALYs)) related to dietary risks and proportion of contribution to the burden of non – communicable disease by age and sex in Australia in 2015
[Proportions were calculated out of all NCD-related deaths/DALYs.]

The leading dietary risk factors for mortality from NCDs in Australia in 2015 were diets low in FV, nuts and seeds and whole grains, and high in sodium (Table 4.2). An estimated number of 6185 (4.2%) and 6247 (4.2%) NCD deaths were attributable to diets low in FV, respectively. NCD deaths attributable to diets low in nuts and seeds (3.9%) and high in sodium (3.2%) were also major contributors. We found a relatively low burden of NCD deaths (0.1%) attributable to a diet high in SSBs. The burden of disease attributable to specific dietary risks was generally higher in males than females (Supplementary Figure 4.1).

Table 4.2 Burden of non-communicable diseases (NCDs) associated with specific dietary risk factors (deaths and disability-adjusted life years) in Australia, 2015

	Deaths (95% UI)			DALYs (95% UI)		
Dietary risks	**Number**	**Crude rate per 100,000**	**Crude proportion (%)**	**Number**	**Crude rate per 100,000**	**Crude proportion (%)**
Diet low in vegetables	6247 (2959-9997)	26 (12-41)	4.2 (2.0-6.7)	84,173 (41,272-132,633)	346 (170-545)	1.8 (0.8-2.9)
Diet low in fruits	6185 (3647-9204)	25 (15-38)	4.2 (2.5-6.2)	103,554 (62,802-150,775)	426 (258-620)	2.2 (1.3-3.3)
Diet low in nuts and seeds	5836 (3503-8592)	24 (14-35)	3.9 (2.4-5.8)	84,720 (53,657-121,269)	348 (221-499)	1.8 (1.1-2.7)
Diet high in sodium	4746 (1319-10789)	20 (5-44)	3.2 (0.9-7.2)	66,686 (20,060-143,025)	274 (82-588)	1.4 (0.4-3.1)
Diet low in whole grains	4341 (2448-6672)	18 (10-27)	2.9 (1.6-4.5)	77,875 (45,758-115,333)	320 (188-474)	1.7 (1.0-2.5)
Diet low in seafood omega-3 fatty acids	3342 (1325-5728)	14 (5-24)	2.2 (0.9-3.8)	43,144 (17,083-73,549)	177 (70-302)	0.9 (0.4-1.6)
Diet low in fibre	2346 (1220-3815)	10 (5-16)	1.6 (0.8-2.6)	32,543 (16,924-52,916)	134 (70-218)	0.7 (0.4-1.2)
Diet high in processed meat	1889 (592-3146)	8 (2-13)	1.3 (0.4-2.1)	38,633 (19,035-58,628)	159 (78-241)	0.8 (0.4-1.3)
Diet high in *trans* fatty acids	1194 (379-2416)	5 (2-10)	0.8 (0.3-1.6)	18,622 (6294-35,900)	77 (26-148)	0.4 (0.1-0.8)
Diet suboptimal in calcium	952 (509-1472)	4 (2-6)	0.6 (0.3-1.0)	16,356 (8642-25,832)	67 (36-106)	0.4 (0.2-0.6)
Diet low in polyunsaturated fatty acids	908 (349-1526)	4 (1-6)	0.6 (0.2-1.0)	6935 (2689-11,813)	29 (11-49)	0.2 (0.1-0.3)
Diet low in milk	742 (247-1305)	3 (1-5)	0.5 (0.2-0.9)	13,317 (4306-23,389)	55 (18-96)	0.3 (0.1-0.5)
Diet high in red meat	606 (256-975)	2 (1-4)	0.4 (0.2-0.7)	18,985 (8417-30,338)	78 (35-125)	0.4 (0.2-0.6)
Diet high in sugar-sweetened beverages	165 (109-240)	1 (0-1)	0.1 (0.1-0.2)	5978 (3942-8768)	25 (16-36)	0.1 (0.1-0.2)

DALYs – disability-adjusted life years; UI – uncertainty interval; The sum of percentages in rows exceeds the total for all dietary risk factors combined because of overlap between various risk factors. Proportions were calculated out of all NCD-related deaths/DALYs.

In 2015, 42.3% (35.3-49.1) of all CVD deaths in Australia were related to dietary risks. Of all NCD deaths attributable to dietary risks, 80.5% were caused by CVD. The relative contribution of dietary risks to CVD deaths was higher among people aged 25-49 (61.7%; 55.7-67.3) and 50-69 (55.4%; 47.3-63.2) years than those aged 70 years and over (40.0%; 33.2-46.9). On the other hand, 8.7% of all cancer deaths and 14.2% of deaths related to diabetes, urogenital, blood and endocrine were attributable to dietary risk factors (Supplementary Table 4.4).

Trend of diet-related NCD burden between 1990 and 2015 in Australia

The period 1990-2015 was characterized by a major downward shift in the diet-related burden of disease in Australia. Age-standardized rates of mortality and DALYs attributed to dietary risks decreased by half during this period (165 to 78). The age-standardized attributable fraction of NCD deaths was 27.0% (22.9-31.1) and 19.4% (16.4-22.4) in 1990 and 2015, respectively (Table 4.3**)**, representing a decrease of 28.2% ([19.4-27.0]/27.0 x 100). However, the rate of decrease appears to have slowed down in recent years, particularly since 2000. For instance, the decrease in the fraction of diet-related deaths between 2005 (21.0%; 17.7-24.2) and 2015 (19.4%; 16.4-22.4) was 7.4%, which was much lower compared to the 15.1% decrease recorded between 1990 (27.0%; 22.9-31.1) and 2000 (23.0%; 19.4-26.4) (Supplementary Table 4.5 and Supplementary Figure 4.2).

Between 1990 and 2015, the proportion of deaths attributable to dietary risks decreased for diets low in fruits (5.5% vs. 4.3%), vegetables (6.4% vs. 4.1%), and nuts and seeds (5.8% vs. 3.9%). The relative fraction of NCD deaths attributable to diets high in sodium and low in whole grains decreased from 4.6% to 3.2% and 4.3% to 2.9%, respectively, in the period (Supplementary Figure 4.3).

Over the same period, the estimated number of diet-related CVD deaths decreased from

25,660 to 23,665, reflecting a 56.9% decrease in the age-standardized rate of diet-related CVD deaths during this period. In contrast, diet-related cancer deaths increased from 2897 in 1990 to 4121 in 2015. However, despite the modest increase in absolute numbers, the age-standardized proportion of cancer deaths related to dietary risk factors decreased by 13.5% **(**Supplementary Table 4.5**)**.

Comparison with OECD countries

Table 4.3 and Supplementary Table 4.5 compare age-standardized fraction, rank and percentage change of diet-related NCD burden between 1990 and 2015 for 35 countries and the mean of global, high-income, OECD and European countries. For both sexes combined, Australia had one of the more favourable dietary profiles in 2015 ranked behind only 11 and three other countries in terms of deaths and DALYs, respectively. Compared to the global average and averages of high-income, OECD and Europe countries, the estimated attributable deaths and DALYs for Australia in 2015 were lower. When stratified by sex, Australia ranked ninth for male and 15th for female deaths attributable to dietary risks. The rank in terms of death in 2015 represents an improvement over the results in 1990 for males; however, these results remained nearly the same for females. Australia ranked second (behind Switzerland) in terms of diet-related NCD DALYs for males in 2015. Australia ranked 11th in males and 14th in females for diet-related NCD deaths in 1990. In 2015, the rank for males jumped two levels to ninth; the rank for females moved down marginally to 15th.

In seven out of 35 countries (including Australia), a diet low in fruits was the leading dietary risk. While a diet high in sodium is the fourth most important dietary factor in Australia, it was the leading dietary risk factor at a global level and in 12 OECD countries. A diet low in fruits was the leading dietary factor for NCD DALYs in ten countries,

including Australia **(**Supplementary Figure 4.4**)**.

The absolute number of deaths and DALYs in 1990 and 2015 in all countries is provided in Supplementary Table 4.6. We also present age-specific burden of NCDs and age-standardized specific causes of death attributable to dietary risks for all countries in Supplementary Figure 4.5 and Supplementary Figure 4.6.

Table 4.3 Age-standardized burden of non-communicable diseases (expressed as percentage of deaths and disability-adjusted life years) associated with dietary risks, related rank and percentage change of the burden for OECD countries between 1990 and 2015

Country	Death (95% UI)					DALYs (95% UI)				
	1990		2015			1990		2015		
	Proportion (%)	Rank	Proportion (%)	Rank	Change (%)	Proportion (%)	Rank	Proportion (%)	Rank	Change (%)
Netherlands	23.7 (20.0-27.4)	4 (4-4)	16.1 (13.4-19.0)*	1 (1-1)	-32.1 (-35.3 to -29.3)	14.1 (11.8-16.6)	5 (5-5)	8.4 (6.9-10.0)*	3 (3-4)	-40.4 (-43.4 to -37.6)
France	20.7 (17.6-24.1)	2 (2-2)	17.0 (14.4-19.7)	2 (2-2)	-17.9 (-20.6 to -15)	11.2 (9.3-13.3)	1 (1-1)	8.2 (6.7-9.8)	2 (2-2)	-26.7 (-29.2 to -24.1)
Israel	27.1 (22.5-31.8)	14 (11-14)	17.4 (14.4-20.8)*	3 (3-4)	-35.8 (-38.8 to -33)	15.7 (13.0-18.7)	15 (13-15)	8.7 (7.2-10.5)*	6 (5-6)	-44.5 (-47.5 to -41.2)
Spain	23.1 (19.5-27.0)	3 (3-3)	17.6 (14.8-20.7)	4 (3-4)	-23.8 (-26.5 to -21.2)	13.5 (11.3-16.0)	4 (4-4)	9.0 (7.5-10.7)*	7 (7-7)	-33.4 (-35.9 to -30.7)
Denmark	28.6 (24.6-32.4)	21 (17-22)	18.4 (15.8-21.1)*	5 (5-5)	-35.7 (-38.4 to -33.1)	16.5 (13.9-19.1)	20 (20-21)	9.2 (7.7-11.0)*	10 (9-10)	-43.9 (-46.5 to -41.1)
Switzerland	24.1 (20.4-27.8)	5 (5-5)	18.5 (15.7-21.6)	6 (6-6)	-23.2 (-26.1 to -20.1)	12.4 (10.3-14.7)	3 (2-3)	7.7 (6.4-9.3)*	1 (1-1)	-37.4 (-40.2 to -34.8)
Mexico	19.2 (16.3-22.4)	1 (1-1)	18.8 (15.9-22.0)	7 (7-10)	-1.8 (-3.9 to 0.4)	12.3 (10.4-14.4)	2 (2-3)	11.9 (10.0-14.0)	26 (26-26)	-3.3 (-5.5 to -1.1)
Norway	29.1 (24.9-33.2)	23 (24-24)	18.8 (16.0-21.7)*	8 (7-8)	-35.3 (-37.6 to -32.9)	16.2 (13.6-18.9)	18 (17-18)	8.7 (7.2-10.2)*	5 (5-6)	-46.5 (-48.8 to -44.0)
Belgium	25.0 (21.5-28.5)	6 (6-7)	18.8 (16.1-21.7)	9 (7-9)	-24.8 (-27.2 to -22.4)	14.7 (12.4-17.1)	8 (7-9)	9.6 (8.0-11.3)*	12 (12-14)	-34.6 (-37.2 to -32.0)
United Kingdom	29.3 (25.4-33.1)	24 (25-23)	19.0 (16.3-21.6)*	10 (7-10)	-35.4 (-37.3 to -33.5)	17.8 (15.1-20.4)	26 (26-26)	9.6 (8.1-11.3)*	13 (12-13)	-45.9 (-47.7 to -43.9)
Canada	26.6 (22.8-30.3)	11 (9-12)	19.4 (16.6-22.3)*	11 (11-11)	-27.1 (-29.5 to -24.8)	15.1 (12.8-17.5)	11 (9-12)	9.6 (8.1-11.3)*	14 (13-14)	-36.2 (-38.4 to -33.8)
Australia	27.0 (22.9-31.1)	13 (13-14)	19.4 (16.4-22.4)*	12 (11-12)	-28.2 (-30.6 to -25.7)	14.3 (11.9-16.8)	6 (6-6)	8.4 (7.0-9.9)*	4 (3-4)	-41 (-43.5 to -38.5)
Chile	26.4 (22.5-30.7)	10 (10-12)	19.4 (16.3-23.3)	13 (11-15)	-26.2 (-29.5 to -23.1)	15.5 (13.1-18.2)	13 (13-14)	10.8 (9.0-13.0)*	21 (21-21)	-30.3 (-33.4 to -27.1)
New Zealand	26.1 (22.1-30.1)	9 (7-9)	19.7 (16.7-22.9)	14 (14-14)	-24.8 (-26.9 to -22.6)	15.1 (12.6-17.6)	10 (10-10)	9.3 (7.7-11.0)*	11 (11-11)	-38.3 (-41.0 to -35.6)
Luxembourg	26.7 (22.9-30.6)	12 (11-13)	19.7 (16.9-22.8)*	15 (13-15)	-26.1 (-28.6 to -23.6)	15.7 (13.2-18.4)	14 (14-16)	9.1 (7.6-10.8)*	8 (8-9)	-41.7 (-44.0 to -39.4)
Portugal	27.9 (23.3-32.9)	16 (16-21)	20.7 (17.4-24.4)	16 (16-17)	-25.7 (-28.3 to -22.8)	16.6 (13.9-19.9)	23 (20-24)	10.5 (8.7-12.6)*	19 (19-20)	-37.1 (-39.8 to -34.4)
United States	28.0 (24.1-31.8)	17 (15-19)	21.0 (18.0-24.0)*	17 (16-17)	-25.1 (-26.9 to -23.3)	16.3 (14.0-18.8)	19 (16-23)	11.9 (10.2-13.7)*	25 (24-27)	-27 (-29.2 to -24.8)
Germany	28.6 (24.3-32.8)	20 (20-20)	21.3 (18.0-25.0)	18 (18-19)	-25.5 (-28.0 to -23.1)	16.5 (13.9-19.5)	21 (19-21)	10.2 (8.4-12.2)*	16 (15-17)	-38.7 (-40.9 to -36.5)
Italy	25.9 (21.9-30.2)	8 (8-8)	21.4 (18.2-25.3)	19 (19-20)	-17.2 (-20.1 to -14.5)	14.6 (12.3-17.3)	7 (8-8)	10.1 (8.4-12.0)*	15 (15-16)	-31.0 (-33.3 to -28.5)
Iceland	28.8 (24.5-33.0)	22 (21-22)	21.5 (18.3-24.7)	20 (18-20)	-25.4 (-27.7 to -23.1)	15.3 (12.8-18.0)	12 (11-12)	9.2 (7.6-11.0)*	9 (8-10)	-39.9 (-42.3 to -37.5)
Ireland	30.1 (26.0-34.0)	26 (25-26)	22.2 (19.1-25.3)*	21 (21-21)	-26.3 (-28.6 to -23.8)	17.2 (14.5-19.9)	24 (23-24)	10.2 (8.5-12.1)*	17 (16-17)	-40.5 (-43.4 to -37.8)
Japan	28.1 (23.6-32.8)	18 (17-19)	22.8 (19.2-26.4)	22 (22-22)	-19.2 (-21.5 to -16.8)	15.8 (13.2-18.9)	16 (15-18)	11.5 (9.6-13.7)	24 (24-25)	-27.1 (-29.3 to -24.9)
Slovenia	27.3 (23.0-31.9)	15 (15-16)	23.0 (19.3-27.2)	23 (23-27)	-15.7 (-19.1 to -11.7)	17.2 (14.5-20.3)	25 (25-25)	11.5 (9.5-13.7)*	23 (23-23)	-33.6 (-37.0 to -30.2)
Austria	28.2 (24.0-32.6)	19 (18-18)	23.1 (19.4-26.8)	24 (23-24)	-18.3 (-20.9 to -15.3)	16.2 (13.5-19.1)	17 (17-19)	10.4 (8.6-12.4)*	18 (18-18)	-35.8 (-38.1 to -33.6)
South Korea	33.6 (28.5-39.0)	28 (28-30)	23.2 (19.5-27.1)*	25 (25-25)	-31.1 (-34.2 to -28.0)	23.2 (19.8-27.0)	30 (30-30)	12.6 (10.6-15.0)*	28 (28-28)	-45.4 (-48.7 to -42.3)
Sweden	31.1 (26.6-35.5)	27 (27-27)	23.3 (19.8-26.9)	26 (24-26)	-25.2 (-27.4 to -22.8)	16.6 (13.9-19.5)	22 (21-22)	10.6 (8.8-12.5)*	20 (19-20)	-36.4 (-38.7 to -34.1)
Greece	25.4 (20.9-30.3)	7 (6-10)	23.3 (19.4-27.7)	27 (26-28)	-8.0 (-10.8 to -4.6)	14.7 (12.1-17.8)	9 (7-11)	12.0 (9.9-14.5)	27 (25-27)	-18.3 (-21.5 to -14.9)
Finland	33.7 (28.9-38.2)	29 (28-29)	23.5 (19.9-27.1)*	28 (26-28)	-30.4 (-32.7 to -27.9)	20.4 (17.2-23.6)	28 (28-28)	11.2 (9.3-13.1)*	22 (22-22)	-45.2 (-47.4 to -42.7)
Turkey	29.5 (24.9-34.1)	25 (23-26)	24.2 (20.3-28.4)	29 (29-29)	-17.9 (-22.9 to -13.1)	19.4 (16.4-22.5)	27 (27-27)	13.4 (11.2-15.9)*	29 (29-29)	-30.7 (-36.4 to -25.1)
Singapore	34.2 (29.9-38.5)	30 (29-30)	28.2 (24.3-32.4)	30 (30-30)	-17.3 (-20.2 to -14.4)	22.7 (19.6-26.0)	29 (29-29)	14.4 (12.0-17.2)*	30 (30-30)	-36.6 (-39.5 to -33.5)
Poland	39.6 (34.7-44.3)	32 (32-32)	31.2 (27.1-35.2)	31 (31-31)	-21.2 (-23.1 to -19.3)	25.9 (22.5-29.4)	32 (32-32)	17.4 (14.9- 20.0)*	31 (31-32)	-32.9 (-35.1 to -30.7)
Hungary	36.8 (32.4-41.0)	31 (31-31)	32.8 (28.7-36.9)	32 (32-32)	-10.7 (-13.1 to -8.5)	25.0 (21.9-28.2)	31 (31-31)	18.9 (16.4-21.6)*	34 (34-34)	-24.4 (-27.4 to -21.6)
Czech Republic	40.6 (36.0-45.2)	33 (33-33)	34.1 (29.9-38.0)	33 (33-33)	-16.1 (-18.0 to -14.1)	26.8 (23.4-30.2)	33 (33-33)	17.8 (15.2-20.6)*	33 (33-32)	-33.5 (-35.9 to -31.1)
Estonia	44.9 (39.4-50.1)	35 (35-35)	34.8 (29.4-40.9)	34 (34-35)	-22.4 (-27 to -16.2)	28.1 (24.3-32.0)	35 (35-35)	17.5 (14.7-20.9)*	32 (31-33)	-37.9 (-41.6 to -33.0)
Slovakia	42.7 (37.8-47.5)	34 (34-34)	36.2 (31.7-40.6)	35 (34-35)	-15.3 (-17.9 to -11.6)	27.8 (24.0-31.3)	34 (34-34)	19.4 (16.6-22.3)*	35 (35-35)	-30.3 (-33.4 to -26.8)
OECD Countries	28.2 (24.2-32.2)		21.4 (18.4-24.7)		-23.9 (-25.3 to -22.4)	16.6 (14.2-19.3)		11.3 (9.6-13.3)*		-31.8 (-33.5 to -30.0)
High-income	27.4 (23.5-31.4)		20.8 (17.8-24.1)		-24.0 (-25.6 to -22.5)	16.0 (13.6-18.6)		10.8 (9.1-12.7)*		-32.2 (-33.9 to -30.5)

Country	Death (95% UI)					DALYs (95% UI)				
	1990		2015			1990		2015		
	Proportion (%)	Rank	Proportion (%)	Rank	Change (%)	Proportion (%)	Rank	Proportion (%)	Rank	Change (%)
Europe	33.3 (28.9-37.6)		29.3 (25.6-33.2)		-11.9 (-13 to -10.6)	20.5 (17.7-23.6)		16.4 (14.0-19.0)		-20.2 (-22.0 to -18.3)
Global	30.6 (26.8-34.5)		30.3 (26.6-34.0)		-1.0 (-2.2 to 0.3)	19.8 (17.3-22.7)		18.5 (16.1-21.2)		-6.9 (-9.0 to -4.6)

*- Changes that are statistically significant (i.e., the changes were outside the 95% UI range). DALYs – disability-adjusted life years; OECD – Organization for Economic Cooperation and Development; UI – uncertainty interval; Ranking was based on the age-standardized relative contribution (population attributable fraction) to deaths and DALYs. Proportions were calculated out of all non-communicable disease (NCD)-related deaths/DALYs.

Discussion

Compared to other OECD nations, Australia was one of the countries with a relatively low burden of NCDs attributable to dietary risks. Over the past 25 years, the burden of diet-related NCDs in Australia has declined. However, despite improvements in Australia's global standing and a decline in diet-related NCD burden over the past 25 years, the relative contribution of dietary risk factors to NCD burden is still high in Australia. In 2015, nearly one-fifth (19.7%) of NCD deaths were attributable to dietary risk factors. Young (25-49 years) and middle-age (50-69 years) male adults had a higher PAF of diet-related NCD deaths and DALYs than their female counterparts. Overall, more than three-quarters (80.5%) of diet-related NCD deaths were caused by CVD and 42.3% of all CVD deaths were attributable to dietary risks. Diets low in FV, nuts and seeds, and whole grains, and high in sodium were the major contributors to both NCD deaths and DALYs.

Dietary risks were the most important behavioural risk factors for deaths and DALYs in Australia in all age groups and both sexes [297, 316]. In people aged 25-49 and 50-69 years, the risk factors were the second (behind alcohol and drug use, and tobacco use, respectively) most important behavioural risks of mortality while being the highest ranked risk factor among those aged 70 years and over [316]. These findings highlight the potential to reduce the burden of NCDs and improve population health through the implementation of effective community-based strategies that target improving dietary behaviours. Because metabolic factors mediate dietary risk factors [317] and dietary factors are the most common modifiable risks in Australia, interventions prioritizing better dietary behaviours can produce greater impact. Studies in other developed countries have also shown that such interventions can be effective [318, 319]. The interventions

first and foremost can assist in preventing and optimizing metabolic risk factors. Most importantly, with such interventions, we can reduce the cost related to diet-related disease, which is the most costly compared to the other behavioural and metabolic risk factors [320].

Our study showed a higher proportion of diet-related NCD burden among males at a younger age when compared to their female counterparts in Australia. The sex difference in the burden of diet-related NCDs in Australia was also shown in the GBD 2013 and 2015 risk factor studies at the global level [24, 297], which could be linked to more prevalent consumption of unhealthy diets among young people and males [50, 321] than their female counterparts. For instance, sodium consumption in Australia was higher in males (3.59 g/day) than females (3.26 g/day) [311, 322]. Meat consumption by Australian males was also remarkably higher than females [323]. These two dietary risks are closely linked with CVD [324], diabetes mellitus [325] and cancer [326]. Recently, the WHO reported that increased consumption of red and processed meat increases the risk of cancer [326]. A systematic review also reported an increased risk of cancer of as much as 18% for a 50 g increase of consumption of processed meat per day [309]. Processed foods are also known to have high salt content [258], which further increase the risk of NCD. These findings suggest that preventive interventions to reduce exposure to dietary risks should be a priority for younger males to reduce the risk of NCDs.

In the current study, a low consumption of FV was the leading dietary risk, which is consistent with findings obtained from a recent Australian report [307]. High levels of co-morbidity and premature mortality from NCDs are attributable to the low consumption of FV [303, 327]. The Australian dietary guidelines recommend consuming two servings of fruits and five servings of vegetables per day [328]. However, despite this and other

recommendations from relevant international organizations (i.e., WHO and FAO) [329] and thus intervention efforts [321, 330, 331], the 2011/12 Australian Health Survey indicated that only 5.5% of Australian adults had an adequate daily intake of FV [332]. *Taylor* and *colleagues* [330] also reported that the proportion of adults consuming the recommended level of vegetables and/or fruits in an Australian state (South Australia) has not changed between 2004 and 2013. Consistent with this finding, the attributed burden of disease in Australia also remained the same between 2005 and 2015. Similarly, the finding on gender differences in the burden of NCD due to a low consumption of FV is consistent with sex differentials in FV consumption patterns in Australia [332] and elsewhere [333]. Further intervention options, particularly community-based programmes, to increase the consumption of FV in the country should be reconsidered, as alternative strategies may provide different levels of effectiveness [334-336].

The relatively low proportion of NCD burden attributable to SSBs observed in this study is consistent with other findings in Australia (0.3% of the total DALYs) [307] and the UK [337]. In 2011/12, 32% of adults (i.e., aged 19 years and above) were reported to have consumed SSBs [338], and the proportion of people and the amount of SSB consumption tended to decline with age among South Australian adults [247]. Despite the robust methods in the GBD and a demonstrated prospective association between SSB consumption and the risk of NCDs [339], the relatively low attributable NCD burden in Australia could be due to a number of factors. First, the reported level of SSB consumption could be underestimated due to social desirability bias in the original studies used in this study, which eventually leads to an underestimated attributable burden of diseases. Second, given that the consumption of SSBs is associated with a high consumption of other components of poor quality (processed) diet [340, 341], such as high sodium intakes [342], the independent effect of SSBs on NCD risks may have been

masked by these associations. However, these limitations might also apply to the other dietary risks included in this study. Third, it is also possible that the estimates used in the study may have been affected by the indirect approach used to estimate the burden attributable to SSBs [297, 310]. In this approach, NCD risk was estimated using BMI although this may not be the only causal mechanism. For instance, SSBs could affect health through change in blood glucose level [343].

A recent study in Mexico asserted that interventions, such as taxing SSBs would reduce consumption [344]. In addition, a modelling study on the effect of taxing SSBs on health and associated expenses showed gains in health-adjusted life years and a reduction of health care costs in Australia [345]. However, another study suggested that dietary behaviours may not be dependent only on pricing in the country [335]. Studies also found a minimal impact of soft drink taxes in reducing weight at the population level [346]. Therefore, it is important to consider available policy options that target dietary behaviours comprehensively for their impact at the population level, specifically in adults. Interventions targeted at increasing the consumption of diets rich in FV, nuts and seeds and whole grains, and decreasing intakes of sodium may have a notable additional contribution to reducing NCD burden [303, 327, 347]. Combined interventions, such as appropriate food labelling, tax legislation (e.g., minimizing taxes for vegetables, fruit and nuts and increasing taxes for sugary and salted food items), and increasing community awareness and knowledge of diets and their effects on health are likely to be more effective than individual interventions in improving dietary behaviours and reducing NCD burden [336, 344, 348-352]. In addition, the experience of a successful anti-smoking intervention in Australia [353] could be replicated to improve dietary behaviours of the population and promote healthy foods.

In Australia, the burden of diet-related NCDs has declined between 1990 and 2015 and its rank among OECD countries has improved over this time period. In addition to the potential impact of the modest reduction in consumption of unhealthy foods among the Australian population [50], the factors that drove the decline could be multifaceted, including decreases in age-standardized death (611 to 404 per 100,000) and DALY (20 453 to 16,045 per 100,000) rates of NCDs [312], and increases in the relative contribution of other risk factors (for instance, alcohol and drug use) between 1990 and 2015 [297]. However, further study is warranted to clearly identify and quantify the drivers.

As detailed and discussed in the GBD 2015 risk factors study, this study has important limitations [24, 297, 308]. Some of the most important limitations specific to this study are discussed below. For some of the dietary components, such as a diet low in whole grains, the data representativeness index was low, but it was high for overall dietary risks. However, 95% UIs of the estimates can provide the extent of available information for the overall and each of the dietary components. The absence of intervention studies on some of the dietary components, such as a diet high in SSBs, could produce residual confounding. Although exposure and effect size data were adjusted for study- and country-level relevant covariates and potential mediators, adjustments were not undertaken to account for interactions between dietary components and residual confounding could exist. Furthermore, the burden of sodium and SSBs was assessed using a different approach compared to other dietary risk factors and this may affect the comparability of disease burden estimates across the dietary components. The use of a universal effect size (relative risks) across countries for a given age-sex group could be another shortfall of this study because dietary risks could have a different effect on disease outcomes across different population subgroups. Relative risks were also not corrected for publication bias [24, 297].

In conclusion, notwithstanding these limitations, and the progress in reducing the diet-related burden of NCDs in Australia, almost one-fifth of NCD mortalities and 42.3% of CVD deaths are still attributed to dietary risk factors. Although commendable gains have been made within the past 25 years, the continuing effect of dietary behaviours and the discrepancy between sexes will require strong national and local commitments. Except for sodium, the majority of NCD burden was attributable to a low intake of healthy diets than the high intake of unhealthy ones. There is a need to give priority to dietary behaviours with tailored approaches focusing on specific components of dietary risks—diets low in FV, nuts and seeds and whole grains and high in sodium—and specific population subgroups (e.g., young males). Current and intended policy options to improve dietary behaviours in adults also need a careful consideration if they are meant to bring substantial impact. Multisectoral collaboration is also a key to improving dietary quality and eating behaviours. Considering the expansion and use of appropriate technology to improve dietary behaviours could be helpful in achieving the intended outcomes [354, 355].

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Conflict of interest

All authors declare they have no competing interests. The authors are solely responsible for the views expressed in this article, and they do not necessarily represent the views, decisions, or policies of their institutions.

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Informed consent

Not applicable because the manuscript does not include details, images, or videos relating to individual participants.

Ethics and consent

Not applicable.

CHAPTER 5 DIETARY PATTERNS AND BONE MINERAL DENSITY

5.1 Publication

Melaku YA, Gill TK, Adams R, Shi Z: Association between dietary patterns and low bone mineral density among adults aged 50 years and above: findings from the North West Adelaide Health Study (NWAHS). Br J Nutr 2016; DOI:10.1017/S0007114516003366.

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Overall percentage (%)	50%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	23/07/2018

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Association between dietary patterns and low bone mineral density among adults aged 50 years and above: findings from the North West Adelaide Health Study (NWAHS)

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Abstract

Studies on the association between dietary patterns and bone mineral density (BMD) have reported inconsistent findings. Data from the North West Adelaide Health Study, a population-based cohort study undertaken in Australia, were used to assess this association among adults aged 50 years and above. In this specific study, 1182 adults (545 males, 45.9%) had dietary data collected using a food frequency questionnaire and also had BMD measurements taken using Dual-energy X-ray absorptiometry. Factor analysis with PCA method was applied to ascertain dietary patterns. Two distinct dietary patterns were identified. Pattern 1 ('prudent' pattern) was characterised by high intake of fruit, vegetables, sugar, nut-based milk, fish, legumes and high-fibre bread. In contrast, pattern 2 ('Western' pattern) was characterised by high levels of processed and red meat, snacks, takeaway foods, jam, beer, soft drinks, white bread, poultry, potato with fat, high-fat dairy products and eggs. Compared with the study participants in the first tertile (T1, lowest consumption) of the 'prudent' pattern, participants in the third tertile (T3) had a lower prevalence of low BMD (prevalence ratio (PR) = 0.52; 95% confidence interval (CI): 0.33, 0.83) after adjusting for sociodemographic, lifestyle and behavioural characteristics, chronic conditions and energy intake. Participants in T3 of the 'Western' pattern had a higher prevalence of low BMD (PR = 1.68; 95% CI: 1.02, 2.77) compared with those in T1. In contrast to the 'Western' diet, a dietary pattern characterised by high intake of FV and dairy products is positively associated with BMD.

Keywords: Dietary patterns, bone mineral density, adults, Australia

Bone is a dynamic tissue comprised of cellular, organic and inorganic components with a complex internal structure. Disruption of the balance between bone formation and resorption due to excessive production of osteoclasts or inadequate presence of osteoblasts leads to bone loss, and hence osteoporosis [12]. The level of osteoporosis is increasing worldwide, with more than 200 million people living with osteoporosis in 2010 [14]. Despite underestimations in reports of osteoporosis prevalence [78], available epidemiological evidence has shown that the magnitude has increased in Australia. In 2012, 3.3% (5.3% men and 1.2% women) of the general Australian population self-reported that they had osteoporosis, which was double the estimate of 1.6% from the year 2000. This figure was higher among those aged 50 years and above (15 and 3% in women and men, respectively) [71].

Determinants of osteoporosis are multifaceted and interlinked. Genetic, lifestyle, nutritional, medical disorders, medication use and metabolic (biological) risks are identified as major contributors for osteoporosis [97]. Evidence has demonstrated the importance of specific food items, nutrients and non-nutritive substances in maintaining BMD and preventing osteoporosis and osteoporotic fractures [143]. For instance, high consumption of soya [217] and dairy products [25] has been found to be important in the prevention of osteoporosis. Nutrients and non-nutritive substances, such as calcium [203], PUFA [165] and isoflavones [214], were also found to have an important role in the prevention of osteoporosis.

Recent epidemiological studies have focused on the effect of the overall nature of food consumption habits on disease outcomes, instead of specific foods or nutrients [51]. This is because an outcome (disease) usually occurs as a result of natural interactions or patterns of nutrients and other components of diets rather than intake of single foods or

nutrients. In line with this, new dietary analysis methods have been introduced. These methods are either *a posteriori* analyses (data-driven techniques), such as factor, PCA and cluster analysis, or *a priori* analyses, which include dietary indices or dietary scores. Most recently, RRR, which combines the above two, has also been used [356].

Studies have reported different patterns of diet that are associated with BMD [271, 357]. However, findings are inconsistent. For example, a study in South Korea among postmenopausal women showed a direct association between dairy-rich dietary patterns and BMD [271]. However, another study found no such association among Canadian women [357]. The effect of dietary patterns on BMD can also vary by communities as the food that is available in one location may not be found in others. Hence, tailored dietary patterns that are useful for optimal bone mass should be developed for specific groups/populations.

In Australia, a few studies have explored the association between dietary patterns and BMD, and the available studies are generally conducted among children and young adults [157, 358]. The present study, therefore, aims to assess the association between dietary patterns and low BMD among adults aged 50 years and above in Australia.

Methods

Study design and population

The NWAHS data were used for this analysis. The NWAHS recruited participants from the northern and 'Western' suburbs of Adelaide, South Australia. The region represents a third of the South Australian population and half of the metropolitan area of the city of Adelaide, and was established with the purpose of providing valid and reliable data on chronic diseases and their risk factors. It is a community-based cohort study that

incorporates clinical, public health, social and biochemical data. Three stages of data collection have been conducted: 1999–2003, 2004–2006 and 2008–2010. Data were collected using a self-completed questionnaire, computer-assisted telephone interview and clinical assessments (CATI) [73].

Details on the objectives and methods of the NWAHS are published elsewhere [73]; however, in brief, the study participants were adults aged 18 years and above when first recruited. Random sampling was initially undertaken at the household level. All households that were not connected to a landline telephone were excluded from the sampling frame (using Electronic White Pages). At the time of recruitment (1999), 97.9% of households in South Australia were connected with a landline telephone [359]. Randomly selected households were screened for individuals aged 18 years and above. All these individuals were then invited to participate in the study. Those who could not communicate in English were excluded. At the initial stage, 4056 males and females participated. This study used BMD data collected from those aged 50 years and over as part of Stage 2 (2004–2006, n = 1588), and dietary data was collected as part of Stage 3 (2008–2010, n = 2500). In total, 1182 adults (545 males, 45.9%) aged 50 years and above provided data related to BMD and nutrition.

Dietary assessment and food groups

Dietary intake was assessed using validated DQES-V3.1. The DQES-V3.1 was self-completed and designed to assess intake over the preceding 12 months. Portion size was assessed using four questions and by calculating a single portion size factor, which helps in estimating a median-sized serving of food an individual eats [360]. The completed forms were sent to Cancer Council Victoria for analyses of total daily intakes of food items and nutrients using the Australian NUTTAB95 (Australian Government Publishing

Service, Canberra) food composition database. The amount of food items consumed per day was calculated in grams for each study participant. Food items were categorised into thirty-nine food groups [295]. Data on vitamin D and calcium supplementation were also collected.

Assessment of other covariates

Stage 2 covariates

Sex, age and family history of osteoporosis were determined. Annual household income was categorised as follows: up to $20,000, $20,001–$40,000, $40,001–$60,000 and more than $60,000. Marital status was determined and categorised into married or living together with partner (in union), separated/divorced, widowed and never married. Alcohol intake risk was assessed using the frequency and number of standard drinks [361]. Smoking status was classified into non-smokers, ex-smokers and current smokers. Height and weight of the study participants were obtained to calculate the BMI. BMI was further classified on the basis of the WHO standard [362]. Identification of participants with diabetes was by either doctor-diagnosed self-report of diabetes or laboratory diagnosis using blood samples collected during the clinic visit, with diabetes defined as fasting plasma glucose ≥7.0 mmol/L.

Assessment of leisure-time physical activity levels (PAL) was performed using the Australian NHS questions [363]. This was assessed considering the number of times a person exercised in the last 2 weeks and the total amount of time spent walking for exercise and performing moderate and vigorous exercise. Job-related PAL was also assessed from data related to occupation, which were obtained in Stage 1, by two occupational physicians based on the type of professions the study participants had. Both PAL were classified as sedentary or low and medium or high. In this particular analysis,

home duties were considered as sedentary or low PAL. Detailed methods of both PAL are published elsewhere [364]. Total number of medications prescribed over the past 6 months (including for hypertension, high cholesterol, mental health problems, osteoporosis and asthma), menopausal status and sunlight exposure were also assessed at this stage. Data on medication use were obtained from pharmaceutical benefits scheme. Sunlight exposure was assessed using questions including average duration of direct sunlight exposure during winter and summer and timing (week day and weekend).

Stage 3 covariates

Health literacy was assessed using the Newest Vital Sign test tool [365]. For thirty-one cases with missing values, we used data collected with the short Test of Functional Health Literacy in Adults tool (sTOFHLA) [366]. Health literacy was classified as limited or adequate.

Assessment of bone mineral density

BMD of the whole body was measured using Prodigy and DPX+ DXA (GE Lunar) as part of the clinic visit at Stage 2. DXA was calibrated, and measurements were verified to check correct operation at the beginning of each scan day. Details of the DXA measurement procedures can be found elsewhere [367]. Participants were categorised into two groups using T–scores of BMD. Those who had T-scores of less than −1 were considered as osteopenic (between −1 and −2.5) or osteoporotic (less than or equal to –2.5) [58] and were classified as having low BMD.

Dietary and statistical analysis

To evaluate dietary misreporting, the Goldberg method was used. In this method, the ratio of actual energy intake (EI):basal metabolic rate (BMR) and PAL were considered [368].

To take account of variations in methods, the 95% CI of PAL was calculated. Both leisure-time and job-related PAL were considered in the calculation. Next, the ratio of EI:BMR was compared against the 95% CI of PAL. On the basis of the recommendation by Black et al., the following values for PAL were determined: sedentary = 1.4, light = 1.6, medium = 1.8 and strenuous = 2. Individuals were classified as plausible if the ratio was in the CI range. However, if the ratio was below or above the 95% CI, it was classified as under-reported or over-reported, respectively [369].

To represent population-level dietary patterns, factor scores and dietary patterns were calculated and constructed among 2453 (forty-seven cases with considerable (>30) missing values were excluded) study participants who provided dietary information. Data reduction technique using factor analysis with PCA was used to identify dietary patterns out of the 39 food groups; two dietary patterns were determined on the basis of the scree plot, an eigenvalue (>1) and interpretability. To attain optimal structure and increase the interpretability of factors, varimax rotation was applied. Factor scores for each of the participants and factors were calculated as the sum of the products of factor loading coefficients, which was standardised by daily intake of each food item. Tertiles were constructed for each factor. Factor loadings are the correlation coefficients between factors (identified dietary patterns) and food groups. Factor loadings of each food group on each factor (dietary pattern) were graphically presented. Sample adequacy was checked using the Kaiser–Mayer–Olkin (KMO) test.

Descriptive analysis of sociodemographic and lifestyle characteristics and chronic conditions was performed across the tertiles of the factors. Mean values and standard deviations (continuous and normally distributed variables), medians and interquartile ranges (continuous and non-normally distributed variables) and proportions were

calculated (categorical variables). Chi-square, Kruskal–Wallis tests and ANOVA were used to identify significant differences across different levels of dietary pattern scores.

To assess the association between intake of different levels of dietary patterns and low BMD, Poisson regression models were used [370]. For dietary patterns, we developed four regression models in addition to the unadjusted model. The first model was adjusted for sex and age. Model two was additionally adjusted for socio-economic and lifestyle factors (smoking status, alcohol intake, marital status, income, health literacy and job-related PAL). In addition to the variables in the second model, chronic conditions (diabetes mellitus, family history of osteoporosis and BMI) were adjusted in the third model. To assess whether the association between dietary patterns and outcomes was confounded by total EI, we additionally adjusted for EI in the fourth model.

Subgroup analyses were performed to assess the association of dietary patterns with low BMD in various subgroups of the study participants. In the final models, multiplicative terms for each dietary pattern and each of the variables were used to assess the interaction in predicting low BMD. Missing data were identified across all variables. Except for leisure-time PAL, which had the highest number of missing values, others were imputed using data from the other stage of the study or were otherwise reported as ‘missing’. We did not impute leisure-time PAL in the analysis because the approaches used to assess the PAL at different stages were not the same, and it had a high number of missing values (n = 128). A sensitivity analysis was undertaken by including and excluding the missing values and variables, including season of birth and DXA measurement, leisure-time PAL, vitamin D and calcium supplementation, menopausal status, medication use and sunlight exposure, in the final models. All analyses were conducted using STATA/SE version 14.1 (Stata, StataCorp LP).

Results

A total of 1182 (45.9%, males) study participants provided dietary and BMD data and were included in the analysis. However, the total number of study participants in the multivariable analysis was 1066. Therefore, 116 (9.8%) cases had at least one missing value among the other covariates. Variables such as leisure time PAL (128, 10.8%) and health literacy (34, 2.9%) had the highest proportion of missing values (Table 5.1). Missing values of variables including smoking status (five cases), alcohol intake risk (39 cases), diabetes (five cases), family history of osteoporosis (four cases) and marital status (four cases) were identified and imputed using data from the third stage.

Table 5.1 Participants' characteristics across tertiles of dietary patterns in adults 50 years and above, South Australia

Characteristics	Over all	'Prudent' pattern			*P* value	'Western' pattern			*P* value
		T1	T2	T3		T1	T2	T3	
N	1182	395	396	391		395	396	391	
Sex[†]					<0.001				<0.001
Male	543 (45.9)	232 (58.7)	156 (39.4)	155 (39.6)		116 (29.4)	174 (43.9)	253 (64.7)	
Age in years, median (IQR)[¥]	62.0 (56.0, 69.0)	62.0 (56.0, 70.0)	62.0 (55.5, 68.5)	61.0 (56.0, 67.0)	0.150	62.0 (56.0, 70.0)	62.0 (56.0, 68.5)	61.0 (56.0, 68.0)	0.710
Income[†]					0.066				0.480
Up to $20,000	363 (30.7)	137 (34.7)	114 (28.8)	112 (28.6)		134 (33.9)	123 (31.1)	106 (27.1)	
$20,001-$40,000	382 (32.3)	136 (34.4)	128 (32.3)	118 (30.2)		116 (29.4)	131 (33.1)	135 (34.5)	
$40,001-$60,000	206 (17.4)	62 (15.7)	74 (18.7)	70 (17.9)		65 (16.5)	67 (16.9)	74 (18.9)	
More than $60,000	215 (18.2)	56 (14.2)	73 (18.4)	86 (22.0)		70 (17.7)	72 (18.2)	73 (18.7)	
Missing	16 (1.4)	4 (1.0)	7 (1.8)	5 (1.3)		10 (2.5)	3 (0.8)	3 (0.8)	
Marital status[†]					0.062				0.041
In union	783 (66.2)	246 (62.3)	274 (69.2)	263 (67.3)		240 (60.8)	275 (69.4)	268 (68.5)	
Separated/divorced/widowed	350 (29.6)	126 (31.9)	106 (26.8)	118 (30.2)		140 (35.4)	105 (26.5)	105 (26.9)	
Never married	45 (3.8)	22 (5.6)	14 (3.5)	9 (2.3)		14 (3.5)	14 (3.5)	17 (4.3)	
Missing	4 (0.3)	1 (0.3)	2 (0.5)	1 (0.3)		1 (0.3)	2 (0.5)	1 (0.3)	
Had family history of osteoporosis[†]	228 (19.3)	54 (13.7)	79 (19.9)	95 (24.3)	0.001	79 (20.0)	80 (20.2)	69 (17.6)	0.600
Smoking[†]					<0.001				<0.001
Non-smoker	583 (49.3)	172 (43.5)	207 (52.3)	204 (52.2)		213 (53.9)	196 (49.5)	174 (44.5)	
Ex-smoker	476 (40.3)	165 (41.8)	148 (37.4)	163 (41.7)		159 (40.3)	158 (39.9)	159 (40.7)	
Smoker	123 (10.4)	58 (14.7)	41 (10.4)	24 (6.1)		23 (5.8)	42 (10.6)	58 (14.8)	
Alcohol risk[†]					0.006				<0.001
Non-drinkers (no risk)	628 (53.1)	231 (58.5)	191 (48.2)	206 (52.7)		186 (47.1)	207 (52.3)	235 (60.1)	
Low risk	493 (41.7)	138 (34.9)	183 (46.2)	172 (44.0)		192 (48.6)	175 (44.2)	126 (32.2)	
Intermediate to high risk	60 (5.1)	25 (6.3)	22 (5.6)	13 (3.3)		16 (4.1)	14 (3.5)	30 (7.7)	
Missing	1 (0.1)	1 (0.3)	0 (0.0)	0 (0.0)		1 (0.3)	0 (0.0)	0 (0.0)	
BMI (Kg/m^2), mean (SD)[£]	28.2 (4.7)	28.4 (4.6)	28.3 (4.6)	27.9 (5.0)	0.330	28.2 (4.9)	28.1 (4.8)	28.3 (4.5)	0.930
Had diabetes mellitus[†]	139 (11.8)	44 (11.1)	39 (9.8)	56 (14.3)	0.134	39 (9.9)	49 (12.4)	51 (13.0)	0.350
					0.028				0.651
Leisure time physical activity[†]									

Characteristics	Over all	'Prudent' pattern			*P* value	'Western' pattern			*P* value
		T1	T2	T3		T1	T2	T3	
N	**1182**	**395**	**396**	**391**		**395**	**396**	**391**	
Sedentary to Low	667 (56.4)	238 (60.3)	229 (57.8)	200 (51.2)		225 (57.0)	224 (56.6)	218 (55.8)	
Moderate to high	387 (32.7)	110 (27.9)	126 (31.8)	151 (38.6)		128 (32.4)	123 (31.1)	136 (34.8)	
Missing	128 (10.8)	47 (11.9)	41 (10.4)	40 (10.2)		42 (10.6)	49 (12.4)	37 (9.5)	
Job related physical activity level[†]					0.001				0.043
Sedentary to low	689 (58.3)	201 (50.9)	241 (60.9)	247 (63.2)		247 (62.5)	223 (56.3)	219 (56.0)	
Moderate to high	472 (39.9)	189 (47.8)	147 (37.1)	136 (34.8)		136 (34.4)	168 (42.4)	168 (43.0)	
Missing	21 (1.8)	5 (1.3)	8 (2.0)	8 (2.0)		12 (3.0)	5 (1.3)	4 (1.0)	
Health literacy [†]					<0.001				0.300
Limited	405 (34.3)	173 (43.8)	120 (30.3)	112 (28.6)		142 (35.9)	124 (31.3)	139 (35.5)	
Adequate	743 (62.9)	211 (53.4)	263 (66.4)	269 (68.8)		242 (61.3)	261 (65.9)	240 (61.4)	
Missing	34 (2.9)	11 (2.8)	13 (3.3)	10 (2.6)		11 (2.8)	11 (2.8)	12 (3.1)	
Total energy (KJ/day), mean (SD) [£]	8665.4 (2611.3)	7509.5 (2184.1)	8405.9 (2193.1)	10082.3 (2747.2)	<0.001	6818.7 (1814.1)	8435.1 (1834.0)	10640.2 (2534.4)	<0.001
Protein (gram/day), mean (SD) [£]	94.5 (33.0)	78.7 (24.1)	92.5 (26.4)	112.3 (40.5)	<0.001	74.8 (22.3)	92.4 (21.8)	115.1 (40.7)	<0.001
Carbohydrate (gram/day), mean (SD) [£]	210.1 (93.1)	173.9 (69.0)	204.1 (90.4)	251.3 (99.9)	<0.001	163.6 (66.3)	207.9 (94.4)	256.4 (88.9)	<0.001
Fat (gram/day), mean (SD) [£]	88.5 (30.3)	81.2 (27.6)	85.4 (26.2)	99.0 (33.7)	<0.001	70.0 (23.7)	85.2 (21.4)	109.4 (30.6)	<0.001
Vegetable (gram/day), mean (SD) [£]	211.0 (122.7)	105.6 (53.5)	199.1 (71.5)	329.5 (109.7)	<0.001	209.7 (122.9)	207.0 (122.3)	216.3 (123.0)	0.5474
Fruit (gram/day), mean (SD) [£]	328.1 (230.6)	216.3 (141.1)	307.1 (190.4)	462.3 (270.2)	<0.001	291.8 (186.9)	320.2 (210.4)	372.9 (278.3)	<0.001
Total BMD (gm/cm^2), mean (SD)[£]	1.20 (0.12)	1.20 (0.12)	1.19 (0.12)	1.19 (0.12)	0.170	1.18 (0.12)	1.19 (0.11)	1.22 (0.12)	<0.001
T-score, mean (SD)[£]	0.34 (1.32)	0.30 (1.30)	0.34 (1.35)	0.39 (1.31)	0.608	0.32 (1.37)	0.29 (1.28)	0.42 (1.31)	0.360
Low BMD[†]	188 (15.9)	73 (18.5)	65 (16.4)	50 (12.8)	0.087	69 (17.5)	62 (15.7)	57 (14.6)	0.530
Osteoporosis (T-score ≤ -2.5) [†]	23 (2.0)	8 (2.0)	9 (2.3)	6 (1.5)	0.748	8 (2.0)	7 (1.8)	8 (2.1)	0.951

[†] – Chi-square test; [¥] – Kruskal-Wallis; [£] – ANOVA – IQR-interquartile range; BMD – bone mineral density; BMI – body mass index; SD – standard deviation; T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence); All values are displayed as frequency (percent) or n (%) unless specified.

Sociodemographic characteristics

The median age of the participants at the second stage of assessment was 62 years (interquartile range 56.0, 69.0). Almost half (47.7%) of the study participants reported a household income between $20,001 and $60,000. More than two-thirds (779, 65.9%) of the study participants were married or living with a partner (Table 5.1).

Dietary patterns and characteristics of study participants

Assessment of dietary misreporting showed that only 7 (0.6%) participants had under-reporting (2) or over-reporting (5) of EI. We identified two dietary patterns. These patterns explained a total of 17.0% variance in total food intake (10.3% in the first and 6.7% in the second patterns).

Figure 5.1 shows the factor loadings for each pattern. Pattern 1 (‘prudent’ pattern) was characterised by high intake of FV, sugar, nut-based milk, fish, legumes and high-fibre bread. In contrast, pattern 2 (‘Western’ pattern) was high in processed and red meat, snacks, takeaway foods, jam, vegemite (a brewers’ yeast extract commonly used as a spread in Australia), beer, soft drinks, white bread, poultry, potato with fat, high-fat dairy and eggs. Cross-loading (factor loading >0.30 in each pattern) was found for sugar, tea and water. Food groups with their constituents are provided in the Supplementary Table 5.1.

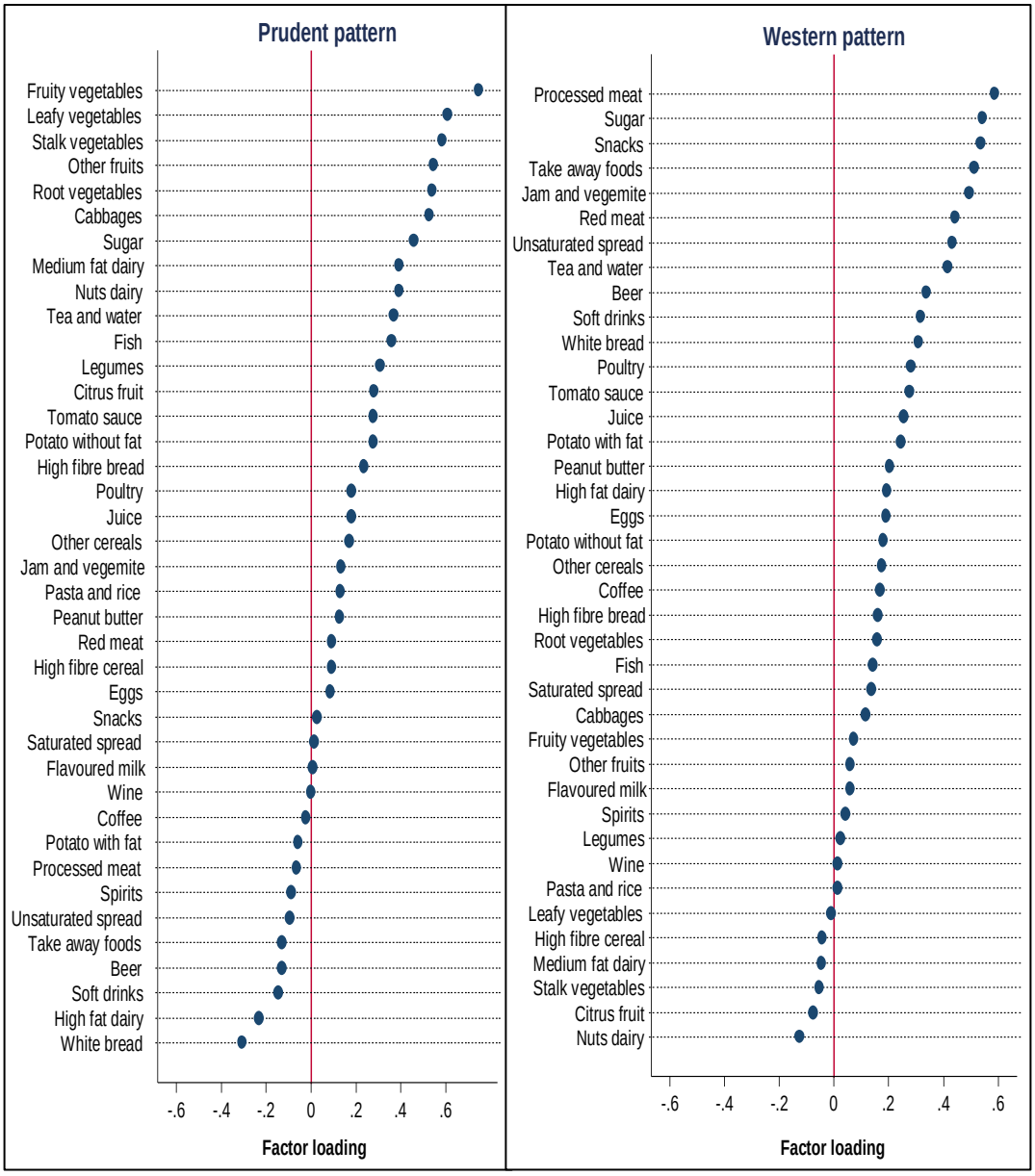

Figure 5.1 Factor loadings for two food patterns among adults aged 50 years and above, South Australia (n = 2453)

Sociodemographic characteristics, chronic conditions, EI and BMD across intake levels of the two dietary patterns are shown in Table 5.1. The overall prevalence of low BMD and osteoporosis was 15.9 (12.7% in men and 18.6% in women) and 2.0%, respectively. More than half (53.1%) of the study participants had no risk of harm from alcohol. The mean BMI was 28.2 (SD = 4.7) kg/m^2. The prevalence of diabetes mellitus was 11.8%. The mean whole-body BMD was 1.20 (SD = 0.12) g/cm^2. Family history of osteoporosis

was reported in 19.3% of the participants, with almost a quarter (24.0%) of study participants in the third tertile (T3) of the 'prudent' pattern having a family history of osteoporosis compared with 13.7% in the first tertile (T1). More than two-thirds (68.8%) of participants in T3 of the 'prudent' pattern had adequate health literacy.

There were significant differences in dietary pattern intake by sex, smoking status, alcohol intake risk and job-related PAL. A significant difference in energy, protein, fat, carbohydrate and fruit intakes was found across the tertiles of both dietary patterns. Vegetable intake was significantly different across tertiles of the 'prudent' pattern but not the 'Western' pattern. In addition, family history of osteoporosis ($P < 0.001$) and health literacy ($P < 0.001$) had crude, significant, positive associations with different levels of the 'prudent' dietary intake. Total BMD ($P < 0.001$) had crude, significant, positive associations with tertiles of the 'Western' dietary pattern.

Dietary patterns and bone mineral density

The prevalence of low BMD was 18.5%, 16.4% and 12.8% across tertiles of the 'prudent' dietary pattern and 17.5%, 15.7% and 14.6% across the tertiles of the 'Western' pattern. In the univariate regression analysis, those in T3 of the 'prudent' pattern had a low prevalence ratio (PR) of low BMD (PR = 0.69; 95% confidence interval (CI): 0.48, 0.99) compared with those in T1. There was no crude significant association between 'Western' pattern and low BMD (Table 5.2).

Significant inverse associations between 'prudent' pattern and low BMD were observed in multivariable regression models (Table 5.2). After adjustment for sociodemographic and lifestyle factors, chronic conditions and EI, participants in T3 had a significantly lower prevalence of low BMD (PR = 0.52; 95% CI: 0.33, 0.83) compared with those in T1. No significant association between 'Western' pattern and low BMD was observed

after adjusting for sociodemographic, lifestyle and chronic condition covariates. However, after adjustment for EI, the study participants in T3 were 68% more likely to have low BMD (PR = 1.68; 95% CI: 1.02, 2.77) compared with those in T1.

Table 5.2 Prevalence ratio [95% confidence interval (CI)] for the association between tertiles of food patterns and low bone mineral density among adults 50 years and above, South Australia (n = 1066)

	'Prudent' pattern				'Western' pattern			
	T_1	T_2	T_3	*P*-trend	T_1	T_2	T_3	*P*-trend
Crude	1.00	0.89(0.64, 1.24)	0.69(0.48, 0.99)*	0.046	1.00	0.90(0.64, 1.26)	0.84(0.59, 1.19)	0.310
Model 1	1.00	0.85(0.61, 1.19)	0.69(0.48, 0.99)*	0.046	1.00	0.99(0.70, 1.40)	1.00(0.69, 1.43)	0.974
Model 2	1.00	0.86(0.60, 1.24)	0.66(0.45, 0.98)*	0.038	1.00	1.05(0.73, 1.51)	1.01(0.69, 1.48)	0.952
Model 3	1.00	0.82(0.57, 1.17)	0.53(0.36, 0.79)**	0.002	1.00	0.99(0.69, 1.43)	1.01(0.68, 1.48)	0.975
Model 4	1.00	0.79(0.54, 1.17)	0.52(0.33, 0.83)**	0.006	1.00	1.26(0.84, 1.89)	1.68(1.02, 2.77)*	0.044

*$P < 0.05$;**$P < 0.01$; T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence)

Model 1: adjusted for sex and age

Model 2: additionally adjusted for socio-economic and life style factors (smoking, alcohol intake (no risk, low risk, medium/very high risk), marital status, income, health literacy, leisure time and job related physical activity levels)

Model 3: additionally adjusted for chronic conditions (diabetes mellitus, family history of osteoporosis and body mass index (continuous))

Model 4: additionally adjusted for energy intake (continuous)

P-trend was calculated by including the tertiles of the patterns as continuous variables in the models.

We further conducted two sensitivity analyses: (1) by adjusting for season of birth, DXA measurement, vitamin D and Ca supplementation, total number of medications prescribed, sunlight exposure, menopausal status and leisure-time PAL in the final models; and (2) by excluding the missing values of covariates. The association between dietary patterns and low BMD remained in both sensitivity analyses (data not shown).

Interaction was examined between dietary patterns and sociodemographic and lifestyle factors. No interactions were found and these are shown in Figure 5.2.

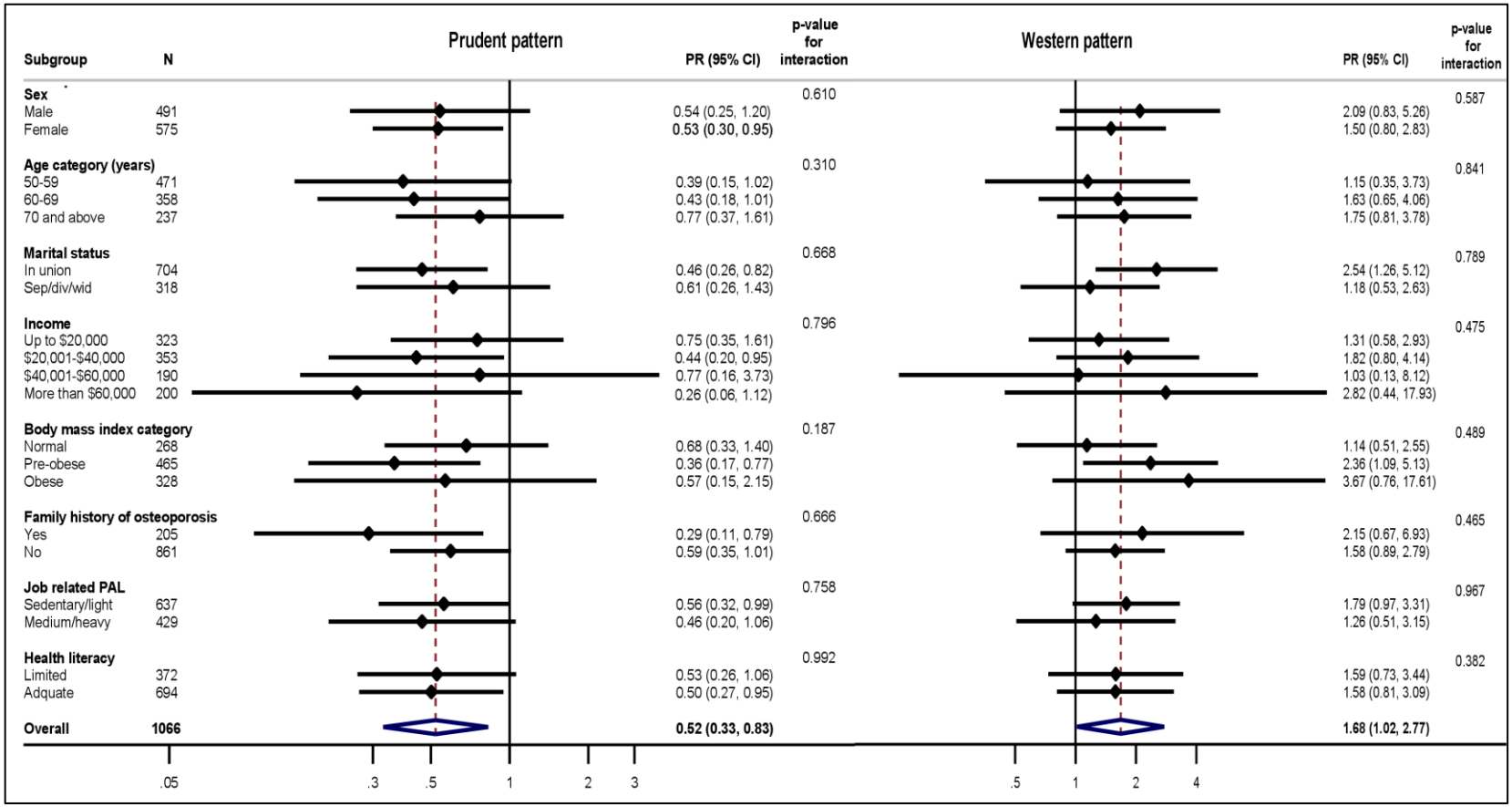

Figure 5.2 Subgroup analysis of the association of third tertiles (highest intake) of 'prudent' (left) and 'Western' (right) dietary patterns with low BMD among adults 50 years and above, South Australia.

[PAL – physical activity level; PR – prevalence ratio (adjusted); Sep/div/wid – separated or divorced or widowed. The first tertiles of pattern scores (lowest intake of 'prudent' and 'Western' dietary patterns) were the references. Poisson regression was used to compute PR.]

Discussion

In this study, we identified dietary patterns and the association with low BMD among adults aged 50 years and over. We identified two major dietary patterns: a 'prudent' (healthy) pattern characterised by a high intake of FV, fish, medium-fat dairy products, nut-based milk, high-fibre bread and legumes and a 'Western' pattern characterised by a high consumption of processed and red meat, fast foods (snacks and takeaway foods), soft drinks, white bread and high-fat dairy products. A significant inverse association between 'prudent' pattern and low BMD was observed. In contrast, a positive association between 'Western' pattern and low BMD was found.

The finding that the 'prudent' pattern was inversely associated with low BMD is consistent with previous studies [275, 286]. The Rotterdam Study in the Netherlands reported that a diet with a high intake of FV, fish, wholegrains, legumes/beans and dairy products was positively associated with BMD [275]. Among Korean adults, a positive association between a food pattern characterised by high dairy products, fruits and wholegrains and BMD was found [286]. It may be that the 'prudent' pattern prevents low BMD because of a large number of food groups within this pattern having high nutrient constituents, such as dairy products [213] and fish [227], and low energy [157], which play an important role in bone mass.

The 'prudent' pattern was also characterised by a high intake of dairy products. A study among postmenopausal women found that a high intake of milk and dairy products reduced the risk of osteoporosis [288]. Dairy products contain good sources of protein and calcium. Furthermore, the nutrient density of protein, calcium, magnesium, potassium, zinc and phosphorous is higher than any other food. Vitamins, calcium and polysaccharides are also constituents of nut-based, particularly soyabean milk [213]. In

addition, flavonoids in soyabeans, particularly isoflavones, mimic oestrogenic activity and are believed to have an effect in maintaining bone health and in preventing osteoporosis in elderly women [214].

A high consumption of FV was also the characteristic of the 'prudent' pattern. FV are comprised of nutrients and non-nutritive substances, such as vitamin potassium, magnesium, polyphenols and phyto-oestrogens, which are important for bone metabolism [260]. Moreover, FV have an alkaline effect due to magnesium and potassium, which buffers the acidic condition that causes bone resorption [269]. However, it has been proposed that the effect of FV on bone mass is not due to its buffering nature but rather because of the nutrients (e.g. calcium and vitamin C) they contain [263]. Current evidence regarding the role of FV in bone health is inconsistent [35, 143]. The extent of the association between 'prudent' pattern and BMD, due to high intake of FV, requires further investigation and so does the mechanism of action. Nonetheless, public health efforts should target increasing the consumption of FV. In South Australia, the proportion of the population consuming the recommended level of FV (consuming ≥5 vegetable servings and/or ≥2 fruit servings/d) has been consistently approximately 50% over the past 10 years, among middle-age and ageing people [330].

Although there were no significant interactions between the 'prudent' pattern and the sociodemographic and lifestyle factors in our subgroup analysis, the associations were stronger in certain groups. For instance, in the subgroup of participants who had a family history of osteoporosis, those in T3 of the 'prudent' pattern were found to have significantly lower PR (71% reduction in PR) of low BMD compared with those in T1. The direction of the association in those who had no family history was also similar, although the magnitude was smaller (41% reduction in PR) and not statistically

significant. We also found that the proportion of study participants who had a family history of osteoporosis and adequate health literacy significantly increased across the tertiles of the 'prudent' pattern. Thus, the PR difference between those who had and did not have a family history could be explained by the fact that those who had a family history were aware of their susceptibility to low BMD and reduced the risk by following healthy dietary patterns.

In this study, our analysis showed a significant positive association between 'Western' pattern and low BMD. This was observed after adjustment for all the covariates and EI, showing that the association was independent of EI, which could have arisen from differences in body size, physical activity and metabolic efficiency [40]. The association in different subgroups was also consistent with low BMD. Consistent positive associations between similar dietary patterns and low BMD have been reported in previous studies [157, 254]. Food items (such as soft drinks) in the 'Western' pattern are characterised by low content of important nutrients such as calcium and high levels of energy content and phosphorus, resulting in low serum calcium, which causes bone resorption [239]. In addition, evidence shows that high EI is also an important factor in the homoeostasis of nutrients (particularly macrominerals), resulting in reduced BMD [248].

It is important to recognise some of the important limitations of this study: one of these is the time lapse between collection of dietary and DXA information. Although dietary data were collected between 2008 and 2010, BMD using DXA was determined between 2004 and 2006 with a 4.3-year median difference (minimum = 2.8 and maximum = 6.1 years). Between these years, eating behaviours of the study participants could have changed. Although habits of elderly people in relation to the choice of food groups have

been found to be stable over years [371], individuals diagnosed with chronic diseases may change their diet towards a healthy one, and this may result in an underestimation of association estimates. In addition, although studies on the effect of retirement on food habits are limited [372], the available evidence shows that more healthy food habits are likely to be developed among women while it remains similar for men [373]. In our study, a total of 175 (14.8%; 44.9% men and 55.1% women) participants retired between the two stages of assessment, which could potentially cause an underestimation of the inverse association between 'prudent' dietary pattern and low BMD.

Although FFQ have limitations in providing valid dietary information, they are widely used to measure the usual dietary exposures and behaviours [374]. To evaluate the robustness of the dietary data, analysis of dietary misreporting was also conducted to identify misreporting. Furthermore, the dietary analysis we conducted was for a large population group, which can represent the consumption behaviour of the community over time [375]. Another potential limitation of this study is the number of cases with missing values of covariates and exclusion of leisure-time PAL from the analysis. However, sensitivity analyses with imputed and excluded covariates suggested that the findings remained similar.

In conclusion, to the best of our knowledge, this is the first study that assessed the association between dietary patterns and BMD among Australians aged 50 years and above. In this community-based study, we found that a dietary pattern characterised by high intakes of FV, medium-fat dairy products and fish was associated with higher BMD. A dietary pattern characterised by high intakes of processed and red meat, fast foods (snacks and takeaway foods), soft drinks, white bread and high-fat dairy products was inversely associated with BMD. Further longitudinal research among ageing populations

is warranted.

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Conflict of interest

The authors have no financial or personal conflicts of interest to declare.

Authors' contribution

All authors conceived the study. YAM conducted all analyses and wrote all drafts of the paper. ZS assisted with analysis and reviewed and provided comment on all drafts. TKG and RJA reviewed and commented on all drafts. All authors read and approved the final manuscript.

CHAPTER 6 NUTRIENT PATTERNS AND BONE MINERAL DENSITY

6.1 Publication

Melaku YA, Gill TK, Taylor AW, Adams R, Shi Z: Association between nutrient patterns and bone mineral density among aging adults. Clin Nutr ESPEN (2017), doi: 10.1016/ j.clnesp.2017.08.001.

Statement of Authorship

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Name of Principal Author (Candidate)	Yohannes Adama Melaku		
Contribution to the Paper	Conception and design, statistical analysis, interpretation of data, manuscript preparation, contribution to the materials/analysis tools and critical revision and editing of the manuscript		
Overall percentage (%)	50%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	23/07/2018

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Signature		Date	20/07/2018

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Contribution to the Paper	Supervised the development of the work. Conception and design, statistical assistance and contribution to the materials/analysis tools, interpretation of results and critical revision of the manuscript		
Signature		Date	20/07/2018

Association between nutrient patterns and bone mineral density among aging adults

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Summary

Background and aim

There is limited evidence on the link between the overall nutrients intake from diet and bone mineral density (BMD). We assessed the association between nutrient patterns and BMD among an ageing Australian population.

Methods

Participants (n = 1135; males, 45.8%; median age, 62.0 years) with dietary and BMD data in the North West Adelaide Health Study were included. Dietary intake was assessed using a food frequency questionnaire. BMD was measured using Dual-energy X-ray absorptiometry. Nutrient patterns were identified by factor analysis. Linear regression analyses were conducted to assess the association between nutrient patterns and BMD (mg/cm^2). Multiple imputation and sensitivity analyses were conducted to investigate the effect of missing data on the estimates.

Results

Three nutrient patterns (mixed-source [potassium, calcium, fibre, retinol and Vitamin B_{12}], animal-sourced [cholesterol, protein, Vitamin B_{12} and fat] and plant-sourced [fibre, carotene, vitamin C and Lutein]) were identified. After adjusting for sociodemographic, lifestyle and behavioural characteristics, chronic conditions and energy intake, animal ($\beta = -4.07$; 95% confidence interval (CI): −11.89, 3.76) and plant-sourced ($\beta = -0.99$; 95% CI: −7.43, 5.45) patterns were not associated with BMD. However, we found that the mixed-source pattern was positively associated with BMD ($\beta = 10.86$; 95% CI: 1.91, 19.80). We did not find interactions between the pattern, other covariates and BMD. The multiple imputation and sensitivity analyses including missing data identified similar

patterns of association between nutrient patterns and BMD.

Conclusions

Whereas animal- and plant-sourced nutrient patterns are not associated with BMD, mixed-source pattern may have benefit in prevention of reduced BMD.

1. Introduction

Studies have focused on individual food items and nutrients to investigate their impact on bone mass and fracture risks [202, 248, 376, 377]. However, in recent years, interest has grown to determine the combined effect of the whole diet and nutrients that are consumed on bone mass [205, 378] and risk of fractures [204]. In this regard, evidence suggests that particular dietary patterns have effect on bone mass [209, 288] and fracture risks [204]. For instance, there is a growing evidence that shows a dietary pattern characterized by a high intake of FV, whole grains and dairy products benefits the maintenance of bone mass in adults [209, 281, 378]. Identifying dietary patterns that consider the overall eating habits, rather than focussing on individual foods, better reflects the complexity of dietary intakes and helps to understand the combined effect of diet components.

Previous studies have also focused on assessing the impact of individual nutrients on bone mass [379, 380] and fracture risks [381, 382]. The Framingham Study demonstrated the importance and role of PUFA in maintaining bone mass [161]. Other studies have also demonstrated the association between particular nutrients, such as protein [380], phosphorous [191], magnesium [383] and potassium [384], and bone mass and fracture risks. These studies however assessed the link between a single nutrient or few nutrients and bone mass/fracture risks without considering other nutrients that could have had a potential role.

People do not consume individual nutrients, rather a mixture of multiple nutrients. In addition, investigating a single nutrient does not consider the antagonist, additive and synergistic effects of nutrients. Therefore, assessing the combined effect of nutrients, taking into account the whole intake pattern, is important in order to address these effects. Some previous studies have determined the combined impact of nutrients (nutrient

patterns) on chronic inflammation [385], cancer [386, 387] and obesity [388]. These studies demonstrated the importance of identifying nutrient patterns and their associations with disease outcomes.

Assessment of associations between nutrient patterns and bone mass, in particular, is important because bone metabolism and structure depends on a diverse range of nutrients. Furthermore, identifying nutrient patterns that are associated with bone mass will allow mapping of particular nutrient combinations that could have a substantial influence. Previous studies have assessed the association of nutrient patterns with bone mass in post-menopausal women [205] and self-reported fracture risk [94], but the limitations of these studies do not allow for firm conclusions. Therefore, this study aimed to identify nutrient patterns and investigate their associations with BMD in an ageing population.

2. Methods

2.1. Study design and population

We used data from the NWAHS, which is a community-based follow-up investigation with the purpose of providing social, behavioural, clinical and biomedical data. Details of the study are published elsewhere [378, 389]. In brief, three stages of data collections were undertaken—each occurred approximately five years apart (1999–2003, 2004–2006 and 2008–2010). Initially, households from the northern and 'Western' part of Adelaide city (South Australia) which were connected to a landline telephone were randomly selected using Electronic White Pages. Individuals residing in the selected household and aged 18 years were candidates for study participation. With the exception of health literacy and nutrient data (assessed at Stage 3), all other measurements used in this study were collected at Stage 2. At this stage, all study participants aged 50 years and above

were invited to undergo an assessment of BMD by DXA; 1588 undertook the measurement. At Stage 3, 2500 study participants had dietary assessment, of which 2364 had complete nutrient data. Both dietary and BMD data were available for 1135 study participants aged 50 years and over (Figure 6.1). Ethics approval was provided by Ethics of Human Research Committee of The Queen Elizabeth Hospital, Adelaide, South Australia. Participants provided a written informed consent.

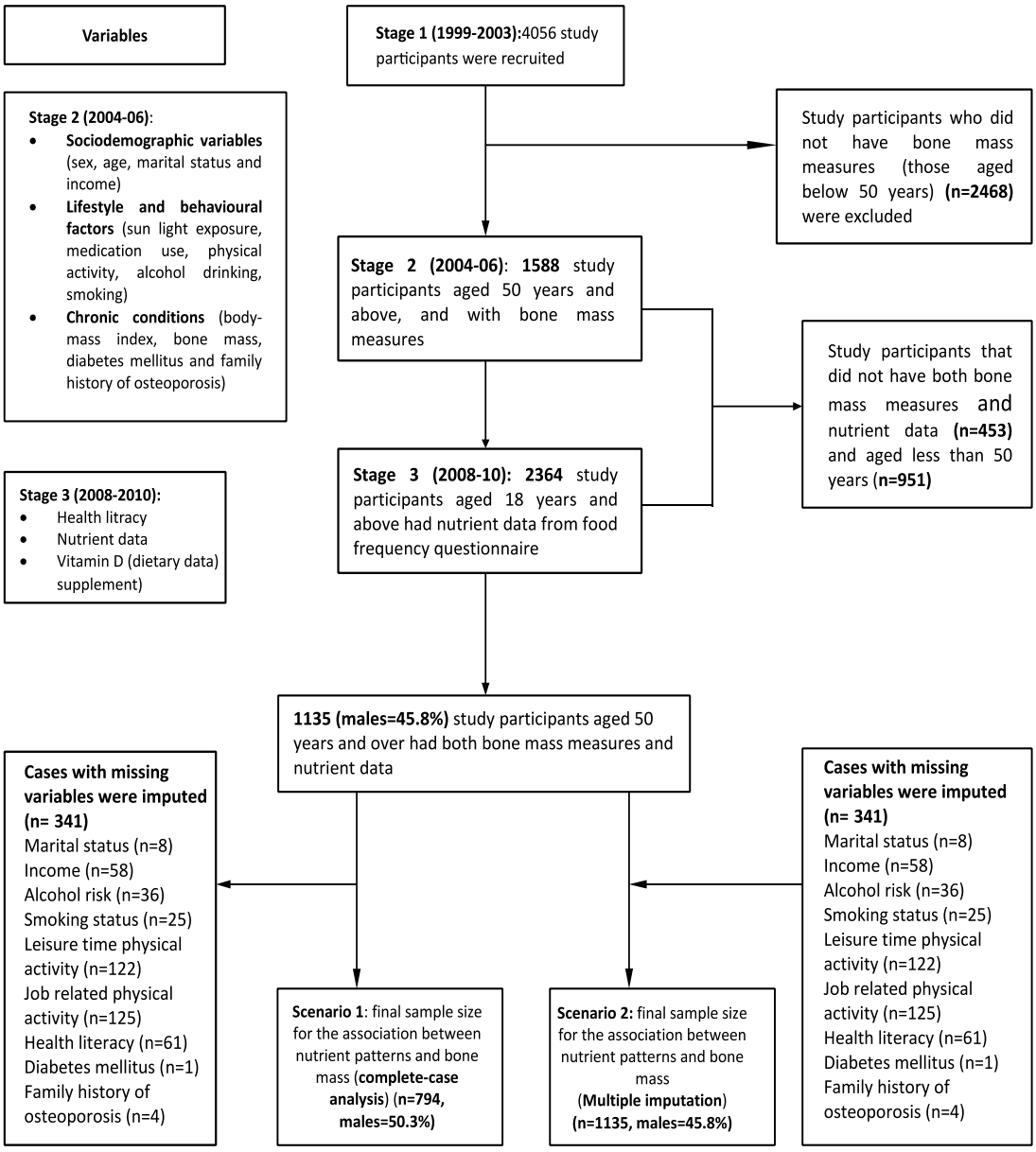

Figure 6.1 Sample description

2.2. Dietary and nutrient intake assessments

At Stage 3, dietary intake was assessed using a paper-based validated DQES-V3.1 [390]. The questionnaire assesses intake of 167 foods and beverages with 10 frequency categories over the previous 12 months. Portion sizes were illustrated using photographs of six foods. Nutrient intakes were calculated from the dietary data using NUTTAB95 database (Food Standards Australia New Zealand, Canberra, 1995). Intake of nutrients

from supplements (vitamin D) was not considered as part of the factor analysis because limited information was collected (i.e. only categorical response (yes/no) without dose).

2.3. Other measurements

Details of social, behavioural, clinical and biochemical assessment methods are described elsewhere [367, 378, 389]. In summary, a self-report questionnaire, clinic visits, as well as a CATI were used to collect the data. At Stage 2, participants' sociodemographic (sex, age, income, and marital status) and behavioural characteristics PAL, alcohol risk, smoking and sun light exposure), biomedical (family history of osteoporosis, diabetes, weight, height and BMD) data were collected. Income was categorized as $20,000, $20,001–$40,000, $40,001–$60,000 and more than $60,000. Marital status was classified as married/living with partner and single/separated/widowed/divorced. Leisure PAL was determined using Australian NHS questions [71]. Detailed methods of PAL are published elsewhere [364]. Job-related PAL was determined and coded based on the type of occupation of participants by two occupational physicians. Both PALs were categorized sedentary/low and moderate/high for each study participant. Diabetes cases were either doctor-diagnosed self-reported or diagnosed during the clinic visit (fasting plasma glucose ≥7.0 mmol/L). The total number of medications prescribed in the past 6 months was obtained from the pharmaceutical benefits scheme. Menopausal status was defined as not having menstruation for 12 months or more preceding the data collection.

BMD was assessed using Prodigy and DPX+ DXA (GE Lunar) as part of the clinic visit at Stage 2. BMD was measured in g/cm^2, however, we converted to mg/cm^2 (i.e. 1 g/cm^2 = 1000 mg/cm^2) in the current analysis. Osteopenia and osteoporosis were based on T-scores; ≤ -1 and > -2.5 and ≤ -2.5, respectively [58].

Data on dietary supplementation (vitamin D) and health literacy were collected at Stage

3. Data on health literacy were collected using Newest Vital Sign test tool [365] and categorized into limited and adequate.

2.4. Statistical analyses

2.4.1. Identification of nutrient patterns

Factor analysis was used to identify nutrient patterns using 33 nutrients that were collated from all measured nutrients. The analysis was performed for 2364 study participants to reflect the nutrient patterns of the whole study population at large. Orthogonal (varimax) rotation was used to reduce the correlation between the factors, attain optimal structure and increase interpretability. An eigenvalue >1, scree plot and interpretability were used to determine the number of factors. Factor loadings of the nutrients in each factors were calculated. For each participant and factor, we computed factor scores by summing the products of factor loading coefficients and standardizing it by the daily intake of each nutrient. Tertiles of each dietary pattern were constructed based on the factor scores of study participants. Names were given to each of the nutrient patterns based on the highest nutrient groups loading.

2.4.2. Data analyses

Data were summarized using means and standard deviations (for continuous normally distributed variables), medians and interquartile ranges (for continuous non-normally distributed variables) and proportions (for categorical variables). The chi-square test and ANOVA were used to compare differences between groups for categorical and continuous variables, respectively. The Kruskal–Wallis test was used for variables which were continuous but not normally distributed.

Linear regression analyses were used to assess the association between nutrient pattern

scores (continuous variable) and BMD. In addition to the crude model, four additional multivariable models were developed. Model 1 was adjusted for age and sex; model 2 was additionally adjusted for other socio-economic behavioural factors (marital status, income, job related and leisure time PAL levels, smoking, alcohol intake and health literacy); model 3 was additionally adjusted for chronic conditions (diabetes mellitus, family history of osteoporosis, and body-mass index). The final model (model 4) was additionally adjusted for total energy intake.

Subgroup analyses were conducted to investigate the association between nutrient patterns and BMD in different subgroups. To assess interactions between nutrient patterns, BMD and other sociodemographic, behavioural and chronic conditions, the multiplicative terms of the factor scores (continuous variable) for the patterns and the covariates were used. We conducted four sensitivity analyses to assess the robustness of the results in model 4: 1) by labelling missing values of covariates as "missing" and including in the model; 2) by including and excluding some of the covariates that can potentially affect the outcome variables (medication use, dietary supplementation (vitamin D), sunlight exposure and menopausal status); 3) since there was time gap between DXA measure and dietary assessment, we dichotomized the study participants below and above the median time between assessments (those with early assessment, that is the 50% of the participants who had dietary information prior to and including the median time] and those with late assessment [the remaining 50% of the participants]). We then undertook a linear regression model for both groups separately to investigate this effect of the time difference on the association; 4) by performing multiple imputation on the covariates with missing values using the Markov chain Monte Carlo (MCMC) method. All the analyses were conducted using STATA 14.1 (Stata Corporation, College Station, TX, USA).

3. Results

Of the 1135 study participants, 341 (30.0%) had at least one missing value of the covariates. Variables such as job related PAL (125, 11.0%), leisure time PAL (122, 10.7%), health literacy (61, 5.4%), income (58, 5.1%) and alcohol risk (36, 3.2%) had higher proportion of missing values. Missing values for marital status (8) and family history of osteoporosis (4) were also identified (Table 6.1). We conducted multivariable analysis for the 794 participants that had complete values for all variables. We then used multiple imputation to assign values for all missing values of the covariates (n = 341).

Table 6.1 presents the characteristics of study participants by sex. The median age of the participants was 62.0 years (interquartile range = 56.0, 69.0). More than half (615, 54.2%) of the participants were females and 56.7% of the participants had low leisure time PAL. Almost one-fifth (18.9%) of the participants had a family history of osteoporosis. The prevalence of osteopenia and osteoporosis was 14.3% and 1.9%, respectively. The mean (SD) BMD was 1196 (119) mg/cm^2.

Table 6.1 Sociodemographic, lifestyle, behavioural and chronic diseases related characteristics of study participants aged 50 years and over, the North West Adelaide Health Study (n = 1135)

Characteristics	Total	Male	Female	*P* value
	1135	520 (45.8%)	615 (54.2%)	
Age in years, median (IQR)*	62.0 (56.0, 69.0)	62.0 (56.0, 69.0)	61.0 (55.0, 68.0)	0.049
Marital status[¥]				
Married/partnered	746 (65.7%)	363 (69.8%)	383 (62.3%)	0.007
Single/separated/widowed/divorced	381 (33.6%)	153 (29.4%)	228 (37.1%)	
Missing	8 (0.7%)	4 (0.8%)	4 (0.7%)	
Annual household gross income[¥]				
Up to $20,000	335 (29.5%)	122 (23.5%)	213 (34.6%)	<0.001
$20,001-$40,000	348 (30.7%)	168 (32.3%)	180 (29.3%)	
$40,001-$60,000	195 (17.2%)	104 (20.0%)	91 (14.8%)	
More than $60,000	199 (17.5%)	104 (20.0%)	95 (15.4%)	
Missing	58 (5.1%)	22 (4.2%)	36 (5.9%)	
Job related physical activity level [¥]				
Low	558 (49.2%)	226 (43.5%)	332 (54.0%)	<0.001
Moderate to high	452 (39.8%)	285 (54.8%)	167 (27.2%)	
Missing	125 (11.0%)	9 (1.7%)	116 (18.9%)	
Leisure time physical activity level [¥]				
Low	643 (56.7%)	268 (51.5%)	375 (61.0%)	0.010
Moderate to high	370 (32.6%)	185 (35.6%)	185 (30.1%)	
Missing	122 (10.7%)	67 (12.9%)	55 (8.9%)	
Health literacy[¥] (Stage 3)				
Limited	384 (33.8%)	187 (36.0%)	197 (32.0%)	0.140
Adequate	690 (60.8%)	304 (58.5%)	386 (62.8%)	
Missing	61 (5.4%)	29 (5.6%)	32 (5.2%)	
Alcohol risk[¥]				
Non-drinker/low	1039 (91.5%)	470 (90.4%)	569 (92.5%)	0.006
Moderate to high	60 (5.3%)	38 (7.3%)	22 (3.6%)	
Missing	36 (3.2%)	12 (2.3%)	24 (3.9%)	
Smoking[¥]				
Non-smoker	566 (49.9%)	205 (39.4%)	361 (58.7%)	<0.001
Ex-smoker/current smoker	564 (49.7%)	312 (60.0%)	252 (41.0%)	
Missing	5 (0.4%)	3 (0.6%)	2 (0.3%)	
Sunlight exposure (hours/week), median (IQR)*	2.50 (2.00, 3.50)	3 (2.00, 4.00)	2.5 (1.75, 3.00)	<0.001
Menopause (women, n = 615)				
Yes		N/A	555 (90.2%)	N/A
No			48 (7.8%)	
Missing			12 (2.0%)	
Family history of osteoporosis[¥]				
Yes	215 (18.9%)	61 (11.7%)	154 (25.0%)	<0.001
No	916 (80.7%)	457 (87.9%)	459 (74.6%)	
Missing	4 (0.4%)	2 (0.4%)	2 (0.3%)	
Had diabetes[¥]				
Yes	68 (6.0%)	45 (8.7%)	23 (3.7%)	<0.001
No	1066 (93.9%)	475 (91.3%)	591 (96.1%)	
Missing	1 (0.1%)	0 (0.0%)	1 (0.2%)	
Body mass index (kg/m^2), mean (SD) [#]	28.2 (4.8)	28.1 (3.9)	28.2 (5.4)	0.720
Took vitamin D supplement[¥] (Stage 3)				
Yes	87 (7.7%)	21 (4.0%)	66 (10.7%)	<0.001
No	1048 (92.3%)	499 (96.0%)	549 (89.3%)	
Osteopenia[¥]				
Yes	162 (14.3%)	58 (11.2%)	104 (16.9%)	0.006

Characteristics	Total	Male	Female	*P* value
	1135	520 (45.8%)	615 (54.2%)	
No	972 (85.6%)	462 (88.8%)	510 (82.9%)	
Missing	1 (0.1%)	0 (0.0%)	1 (0.2%)	
Osteoporosis[¥]				
Yes	22 (1.9%)	11 (2.1%)	11 (1.8%)	0.690
No	1112 (98.0%)	509 (97.9%)	603 (98.0%)	
Missing	1 (0.1%)	0 (0.0%)	1 (0.2%)	
BMD (mg/cm2), mean (SD) (n = 1135) [#]	1196 (119)	1255 (103)	1146 (109)	<0.001
T-score, mean (SD) (n = 1135)[#]	0.35 (1.33)	0.44 (1.28)	0.27 (1.35)	0.035

* – Wilcoxon rank-sum test; [¥] – chi-square test; [#] – Two sample t test; BMD – bone mineral density; N/A – not applicable. Except for those indicated, the other variables were collected at Stage 2.

3.1. Nutrient patterns

We identified three nutrient patterns–mixed-source, animal- and plant-sourced. Overall, these patterns explained 62.7% of the variance in the total nutrient intake (26.0%, 23.5% and 13.2%, respectively). Figure 6.2 shows the factor loadings for each pattern. The plant sourced pattern was characterized by high intakes of potassium, fibre, carotene, lutein and zeaxanthin and vitamin C. The animal-sourced pattern was characterized by high levels of palmitoleic acid, cholesterol, PUFA, protein, vitamin B_{12}, saturated and monounsaturated fats, zinc and retinol. The mixed-source pattern was characterized by a high intake of both animal- and plant-sourced nutrients, including phosphorous, potassium, calcium, niacin, starch and dextrins, vitamin B_1, B_2, B_3, B_7 and B_{12}, fibre, protein and retinol.

3.2. Participants' characteristics and nutrient and food intake across tertiles of nutrient patterns

The proportion of study participants who had moderate to high leisure time PAL increased across the tertiles of the mixed-source pattern ($P = 0.034$). Across the plant-sourced pattern, there was a significant decrease in median age ($P = 0.005$) and the proportion of participants who had moderate or high job related PAL and limited health literacy decreased across tertiles of this pattern ($P < 0.001$) (Supplementary Table 6.1). Nutrient and food intake across tertiles of each nutrient pattern are presented in Table 6.2 and Supplementary Table 6.2. The mean (SD) energy intake was 8671 kJ (2615.8) overall, and varied significantly across the tertiles of the nutrient patterns (Supplementary Table 6.3). More specifically, the overall average protein intake was 94.5 g/d and there was a significant increase across tertiles of the mixed-source nutrient pattern. There was also a significant increase in the intake of omega-6 ($P < 0.018$), vitamin D, calcium,

magnesium, phosphorous, vitamins C, B7 and B12 and fibre across tertiles of the mixed-pattern ($P < 0.001$). Intake levels of dairy, fruits, high fibre bread, fruity and root vegetables ($P < 0.001$) and legumes ($P < 0.004$) also significantly increased across the tertiles of the mixed-source pattern.

	Mixed-source	Animal-sourced	Plant-sourced
Nutrients		**Factor loadings**	
Phosphorous	0.78	0.44	0.26
Potassium	0.77	0.21	0.48
Niacin (vitamin B_3)	0.76	0.40	0.24
Starch & dextrins	0.76	0.09	0.16
Riboflavin (vitamin B_2)	0.73	0.31	0.09
Magnesium	0.72	0.19	0.33
Calcium	0.72	0.29	0.05
Folate	0.71	0.12	0.24
Fibre	0.67	0.08	0.62
Iron	0.67	0.40	0.41
Sugar	0.64	0.27	0.22
Iodine	0.63	0.41	-0.17
Biotin (vitamin B_7)	0.62	0.26	0.34
Thiamine (vitamin B_1)	0.55	0.17	0.12
Palmitoleic acid	0.23	0.88	0.18
Cholesterol	0.21	0.86	0.07
Omega-6	0.07	0.84	0.14
Protein	0.48	0.78	0.26
Cobalamin (vitamin B_{12})	0.27	0.77	-0.07
Saturated fat	0.45	0.70	-0.04
Monounsaturated fat	0.30	0.70	0.21
Zinc	0.47	0.70	0.23
Vitamin D	0.25	0.63	-0.04
Sodium	0.57	0.61	0.18
Retinol	0.47	0.56	-0.20
Omega-3	-0.02	0.54	0.32
Vitamin E	0.28	0.53	0.44
Beta-carotene	0.20	0.06	0.86
Lutein and zeaxanthin	0.05	0.07	0.71
Vitamin C	0.23	0.08	0.71
Alpha-carotene	0.14	-0.06	0.68
Lycopene	0.22	0.25	0.39
Pyridoxine	0.14	0.19	0.24

Figure 6.2 Nutrient patterns and factor loadings (correlations) of nutrients among adults aged 50 years and above (n = 2364), the North West Adelaide Health Study

[The colour gradation reflects how large and in which direction the correlation was between the nutrients and the nutrient patterns. Deep green colour refers relatively a higher correlation (a higher intake) of the nutrients with the corresponding pattern. Deep red refers to relatively a lower correlation (a lower intake) of the nutrients with the corresponding nutrient pattern.]

Table 6.2 Mean (SD) of selected food and nutrient intake across tertiles of nutrient pattern scores among adults aged 50 years and over, the North West Adelaide Health Study (n = 1135)

		Mixed-source				Animal-sourced			
	Total	**T1**	**T2**	**T3**	***P* value**	**T1**	**T2**	**T3**	***P* value**
N	**1135**	**379**	**378**	**378**		**379**	**378**	**378**	
					Mean (SD)				
Nutrients									
Protein (g/d)	94.5 (34.0)	78.5 (30.9)	92.2 (31.2)	112.8 (30.8)	<0.001	74.1 (23.0)	90.3 (18.0)	119.0 (39.8)	<0.001
Vitamin D (mcg/d)	3.49 (2.02)								
		2.96 (1.83)	3.40 (1.95)	4.11 (2.10)	<0.001	2.21 (1.10)	3.30 (1.38)	4.97 (2.29)	<0.001
Calcium (mg/d)	879 (329)	607 (202)	878 (240)	1151 (281)	<0.001	793 (336)	864 (296)	980 (327)	<0.001
Magnesium (mg/d)	450 (161)	339 (108)	442 (120)	570 (159)	<0.001	431 (178)	436 (142)	483 (157)	<0.001
Phosphorous (mg/d)	1607 (578)	1212 (385)	1550 (390)	2061 (581)	<0.001	1406 (651)	1538 (403)	1878 (547)	<0.001
Potassium (mg/d)	3919 (1452)	2981 (912)	3768 (961)	5011 (1576)	<0.001	3772 (1791)	3738 (1118)	4248 (1309)	<0.001
Omega-3	579 (487)	589 (519)	567 (514)	581 (421)	0.810	352 (240)	545 (302)	841 (665)	<0.001
Omega-6	246 (144)	243 (142)	233 (149)	263 (141)	0.018	157 (63)	231 (63)	351 (188)	<0.001
Beta-carotene (mcg/d)	3428 (1910)	3038 (1829)	3377 (1815)	3870 (1992)	<0.001	3463 (2244)	3323 (1621)	3498 (1809)	0.420
Alpha-carotene (mcg/d)	792 (623)	712 (647)	770 (633)	894 (575)	<0.001	853 (707)	757 (541)	767 (607)	0.064
Biotin (vitamin B_7) (mcg/d)	34.1 (16.8)	26.0 (10.7)	31.5 (12.2)	44.8 (19.8)	<0.001	30.6 (18.0)	31.3 (12.2)	40.5 (17.6)	<0.001
Vitamin C (mg/d)	135.5 (75.6)	112.9 (59.9)	137.1 (79.0)	156.5 (80.1)	<0.001	137.1 (84.2)	131.1 (67.7)	138.3 (74.0)	0.370
Cobalamin (vitamin B_{12}) (mcg/d)	3.40 (1.86)	2.84 (1.52)	3.23 (1.79)	4.12 (2.02)	<0.001	2.14 (1.06)	3.28 (1.19)	4.77 (2.10)	<0.001
Saturated fat (g/d)	28.5 (12.0)	23.1 (9.1)	27.4 (9.2)	35.2 (13.9)	<0.001	20.4 (6.5)	27.2 (7.0)	38.0 (13.6)	<0.001
Cholesterol (mg/d)	278 (118)	253 (115)	266 (109)	314 (122)	<0.001	192 (60)	265 (62)	376 (133)	<0.001
Fibre (g/d)	28.3 (11.2)	21.9 (7.8)	27.5 (8.1)	35.6 (12.4)	<0.001	28.4 (13.4)	27.0 (9.3)	29.6 (10.3)	0.007
Energy (kj/d)	8664 (2611)	6973 (2052)	8367 (1920)	10656 (2377)	<0.001	7358 (2445)	8277 (1785)	10360 (2563)	<0.001
Food groups									
Take away foods (g/d)	33.6 (31.3)	28.9 (25.7)	31.5 (32.5)	40.5 (33.9)	<0.001	23.0 (19.7)	32.5 (24.2)	45.4 (41.4)	<0.001
Red meat (g/d)	78.7 (71.7)	79.5 (65.7)	73.9 (74.8)	82.7 (74.3)	0.230	43.8 (32.6)	71.6 (36.6)	120.8 (100.1)	<0.001
Processed meat (g/d)	24.3 (22.8)	20.7 (22.7)	24.3 (22.4)	28.0 (22.7)	<0.001	15.1 (15.8)	22.2 (17.6)	35.7 (27.9)	<0.001
Soft drinks (g/d)	183 (309)	168 (264)	176 (298)	204 (358)	0.250	168 (313)	174 (302)	206 (313)	0.180
High fat dairy (g/d)	90.1 (174.6)	63.1 (121.0)	85.0 (164.3)	122.3 (219.5)	<0.001	39.5 (100.2)	79.2 (154.6)	151.7 (226.3)	<0.001
Fish (g/d)	27.2 (31.3)	27.9 (32.8)	27.4 (33.3)	26.2 (27.3)	0.750	16.2 (17.2)	25.3 (21.6)	40.1 (43.4)	<0.001
Medium fat dairy (g/d)	262 (232)	144 (137)	275 (219)	369 (263)	<0.001	269 (227)	273 (227)	245 (240)	0.180

	Mixed-source					Animal-sourced			
	Total	**T1**	**T2**	**T3**	***P* value**	**T1**	**T2**	**T3**	***P* value**
N	**1135**	**379**	**378**	**378**		**379**	**378**	**378**	
					Mean (SD)				
Leafy vegetables (g/d)	26.3 (26.1)	24.3 (25.8)	26.4 (26.9)	28.1 (25.6)	0.140	25.2 (26.7)	26.3 (25.8)	27.3 (25.9)	0.550
Other fruits (g/d)	222 (159)	187 (131)	224 (137)	255 (193)	<0.001	234 (191)	214 (136)	218 (143)	0.160
High fibre cereal (g/d)	2.14 (7.49)	1.35 (5.92)	2.83 (8.56)	2.24 (7.71)	0.023	2.47 (7.50)	2.14 (8.01)	1.81 (6.92)	0.480
High fibre bread (g/d)	56.6 (44.3)	39.3 (33.2)	55.4 (39.6)	75.2 (50.7)	<0.001	52.6 (42.4)	55.7 (42.1)	61.6 (47.7)	0.017
Fruity vegetables (g/d)	115 (71)	100 (62)	115 (71)	129 (76)	<0.001	113 (73)	111 (62)	119 (77)	0.260
Citrus fruit (g/d)	20.5 (29.3)	17.2 (28.3)	21.9 (30.5)	22.4 (28.8)	0.027	22.8 (33.5)	19.8 (29.6)	18.9 (23.9)	0.150
Legumes (g/d)	38.6 (73.0)	33.6 (55.8)	33.3 (51.6)	48.9 (100.5)	0.004	38.1 (63.5)	31.3 (45.3)	46.4 (99.1)	0.017
Root vegetables (g/d)	15.3 (13.2)	13.7 (13.5)	14.8 (13.4)	17.4 (12.4)	<0.001	16.6 (14.7)	14.6 (11.4)	14.9 (13.2)	0.078
Stalk vegetables (g/d)	10.9 (9.9)	10.0 (10.3)	11.5 (9.6)	11.2 (9.7)	0.098	9.5 (8.7)	11.6 (10.3)	11.5 (10.5)	0.004
Cabbages (g/d)	34.6 (30.7)	31.9 (31.2)	32.8 (30.1)	39.1 (30.4)	0.002	36.4 (33.1)	34.1 (28.6)	33.3 (30.2)	0.350
				Plant-sourced					
Nutrients		**379**	**378**	**378**					
Protein (g/d)		83.8 (25.6)	92.8 (29.1)	106.8 (41.2)	<0.001				
Vitamin D (mcg/d)		3.69 (2.15)	3.17 (1.71)	3.61 (2.13)	<0.001				
Calcium (mg/d)		845 (323)	852 (319)	939 (337)	<0.001				
Magnesium (mg/d)		387 (133)	443 (151)	520 (169)	<0.001				
Phosphorous (mg/d)		1420 (436)	1583 (555)	1819 (652)	<0.001				
Potassium (mg/d)		3142 (951)	3838 (1304)	4780 (1542)	<0.001				
Omega-3		428 (277)	541 (360)	768 (668)	<0.001				
Omega-6		220 (106)	244 (118)	275 (189)	<0.001				
Beta carotene (mcg/d)		1872 (761)	3143 (986)	5273 (1868)	<0.001				
Alpha-carotene (mcg/d)		395 (268)	691 (368)	1292 (737)	<0.001				
Biotin (vitamin B_7) (mcg/d)		28.3 (13.7)	32.5 (14.8)	41.5 (18.6)	<0.001				
Vitamin C (mg/d)		81.1 (39.5)	130.4 (52.5)	195.1 (79.5)	<0.001				
Cobalamin (vitamin B_{12}) (mcg/d)		3.53 (1.78)	3.30 (1.68)	3.37 (2.11)	0.220				
Saturated fat (g/d)		28.9 (13.6)	28.1 (11.1)	28.7 (11.3)	0.660				
Cholesterol (mg/d)		266 (101)	273 (114)	293 (136)	0.004				
Fibre (g/d)		20.9 (7.1)	27.9 (8.8)	36.4 (11.3)	<0.001				
Energy (kj/d)		7850 (2213)	8555 (2443)	9589 (2844)	<0.001				
Food groups									
Take away foods (g/d)		34.4 (28.0)	33.8 (34.8)	32.8 (30.7)	0.780				
Red meat (g/d)		67.1 (52.2)	80.1 (61.9)	88.8 (93.1)	<0.001				

		Mixed-source				Animal-sourced			
	Total	**T1**	**T2**	**T3**	***P* value**	**T1**	**T2**	**T3**	***P* value**
N	**1135**	**379**	**378**	**378**		**379**	**378**	**378**	
				Mean (SD)					
Processed meat (g/d)		25.1 (22.5)	23.6 (21.2)	24.2 (24.5)	0.660				
Soft drinks (g/d)		216 (351)	168 (286)	163 (284)	0.033				
High fat dairy (g/d)		154.6 (220.1)	66.3 (147.2)	49.2 (122.3)	<0.001				
Fish (g/d)		18.2 (18.5)	24.2 (23.3)	39.2 (42.6)	<0.001				
Medium fat dairy (g/d)		248 (257)	269 (222)	270 (214)	0.340				
Leafy vegetables (g/d)		12.0 (12.0)	23.7 (18.5)	43.1 (32.8)	<0.001				
Other fruits (g/d)		151 (97)	221 (127)	294 (200)	<0.001				
High fibre cereal (g/d)		1.29 (5.43)	2.10 (7.03)	3.03 (9.40)	0.006				
High fibre bread (g/d)		52.7 (46.9)	56.0 (41.7)	61.2 (43.8)	0.029				
Fruity vegetables (g/d)		59 (36)	112 (50)	172 (71)	<0.001				
Citrus fruit (g/d)		13.9 (25.5)	20.4 (27.1)	27.2 (33.2)	<0.001				
Legumes (g/d)		22.1 (35.6)	33.4 (45.5)	60.3 (109.2)	<0.001				
Root vegetables (g/d)		7.5 (5.9)	13.2 (8.1)	25.4 (16.0)	<0.001				
Stalk vegetables (g/d)		5.8 (5.5)	11.0 (8.5)	15.9 (11.8)	<0.001				
Cabbages (g/d)		17.9 (15.0)	31.3 (22.8)	54.6 (37.3)	<0.001				

ANOVA was used to test the difference across tertiles. T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence)

Intake levels of protein, PUFA, saturated fat and cholesterol increased across the tertiles of the animal-sourced pattern ($P < 0.001$) as did take-away foods, meats, fish and high fat dairy consumption ($P < 0.001$). Across the tertiles of the plant-sourced pattern, a significant reduction in vitamin D and retinol, and increase in intakes of omega-3 and -6, beta- and alpha-carotene, vitamin C and fibre ($P < 0.001$) were found. Although there is an increase in cholesterol and saturated fat across tertiles of the pattern ($P < 0.001$), the amount was lower compared to the animal-sourced pattern. Consumption of FV, cereal, high fibre bread and legumes increased across the tertiles of the plant-sourced nutrient pattern ($P < 0.001$) (Table 6.2).

3.3. Nutrient patterns and bone mineral density

Regression coefficients for the association between each nutrient pattern z score and BMD (mg/cm^2) are presented in Table 6.3. After adjusting for sociodemographic, behavioural, and chronic conditions, a unit increase in z score of mixed-source nutrient pattern was associated with a 9.5 mg/cm^2 (9.53; 95% CI: 3.09, 5.97) ($P < 0.01$) increase in BMD. After adjustment for energy, a unit increase of the z score was associated with a 10.9 mg/cm^2 ($\beta = 10.86$; 95% CI: 1.91, 19.80) increase in BMD ($P < 0.05$). Although z scores of the animal- ($\beta = -4.07$; 95% CI: −11.89, 3.76) and plant-sourced ($\beta = -0.99$; 95% CI: −7.43, 5.45) patterns were inversely associated with BMD, the associations were not statistically significant.

Among those who had early dietary assessment after DXA measure (n = 398), the association between mixed–source nutrient pattern and BMD was found to be stronger ($\beta = 19.42$; 95% CI; 6.36, 32.48; $P < 0.01$) compared to the whole samples and those with late dietary assessment (n = 396; $\beta = 0.23$; 95% CI: −12.18, 12.63) (Supplementary Table 6.3).

Table 6.3 Regression coefficients (β) [95% confidence interval (CI)] for the association between z scores of nutrient patterns and bone mineral density among adults aged 50 years and over, the North West Adelaide Health Study

Nutrient patterns	β (95%CI)				
	Complete-case analysis				
	Crude model (n = 1135)	Model 1 (n = 1135)	Model 2 (n = 794)	Model 3 (n = 794)	Model 4 (n = 794)
Mixed-source	6.74 (-0.47, 13.9)	4.04 (-2.01, 10.10)	6.97 (-0.25, 14.19)	9.53 (3.09, 15.97)**	10.86 (1.91, 19.80)*
Animal-sourced	10.8 (4.0, 17.6)**	0.90 (-4.91, 6.72)	1.98 (-5.66, 9.62)	-0.02 (-6.76, 6.72)	-4.07 (-11.89, 3.76)
Plant-sourced	-0.06 (-07.0, 06.20)	0.47 (-5.27, 6.22)	-1.17 (-8.18, 5.84)	0.61 (-5.58, 6.79)	-0.99 (-7.43, 5.45)
	Multiple imputation (n = 1135)				
	Crude model	Model 1	Model 2	Model 3	Model 4
Mixed-source	6.74 (-0.47, 13.94)	4.15 (-1.91, 10.22)	3.80 (-2.28, 9.87)	6.76 (1.33, 12.19)*	7.75 (0.49, 15.02)*
Animal-sourced	10.8 (3.96, 17.58)**	0.08(-5.76, 5.91)	0.80 (-5.08, 6.68)	-0.13 (-5.36, 5.10)	-3.16 (-9.53, 3.21)
Plant-sourced	-0.60 (-7.39, 6.20)	0.58 (-5.18, 6.34)	0.05 (-5.78, 5.88)	1.40 (-3.79, 6.59)	0.32 (-5.16, 5.80)

* $P < 0.05$; ** $P < 0.01$; T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence)

Model 1: adjusted for sex and age

Model 2: additionally adjusted for socio-economic and life style factors [smoking, alcohol intake (no/low risk, medium/very high risk), marital status, income, health literacy (limited, adequate), leisure time and job related physical activity levels (low, moderate/high)]

Model 3: additionally adjusted for chronic conditions [diabetes mellitus, family history of osteoporosis and body mass index (continuous)]

Model 4: additionally adjusted for energy intake (continuous)

Using multiple imputation, similar association patterns were detected with the mixed-source (β = 7.75; 95% CI: 0.49, 15.02) and the animal-sourced (β = −3.16; 95% CI: −9.53, 3.21) patterns, and a slight difference was found for the plant-sourced pattern (β = 0.32; 95% CI: −5.16, 5.80) compared to the analysis without multiple imputation (n = 341) (Table 6.3), but remained non-significant.

Subgroup analyses adjusting for all potential cofounders found that the positive association between the mixed-sourced nutrient pattern and BMD was stronger for certain subgroups. Among those with low work related PAL, there was a 15.0 mg/cm^2 (β = 14.96; 95% CI: 2.87, 27.04) increase in BMD, although the interaction was not statistically significant (P = 0.6613) Among those without family history of osteoporosis, a unit increase in the z score of mixed-source pattern was associated with a 14.2 mg/cm^2 (β = 14.19; 95% CI: 3.95, 24.42) increase in BMD, with a non-significant interaction term (P = 0.3443) (Supplementary Figure 6.1).

Sensitivity analyses (by labelling missing values as "missing" and by including and excluding medication use, dietary supplementation (vitamin D), sunlight exposure and menopausal status) provided similar patterns of associations for all nutrient patterns compared to the initial analysis (data not shown).

4. Discussion

In this study, we identified three nutrient patterns: plant-sourced (characterized by high intake of potassium, fibre, carotene, lutein and zeaxanthin, and vitamin C), animal-sourced (which includes high intake of palmitoleic acid, cholesterol, PUFA, protein, vitamin B_{12}, saturated and monounsaturated fats, zinc and retinol) and mixed-source (characterized by high intake of both plant-sourced and animal-sourced nutrients,

including phosphorous, potassium, calcium, niacin, starch and dextrins, vitamin B_1, B_2, B_3, B_7 and B_{12}, fibre, protein and retinol). We found that the mixed-source nutrient pattern was positively associated with BMD. No independent and statistically significant associations between animal- and plant-sourced nutrient patterns and BMD were found.

4.1. Nutrient patterns

Multivariable data reduction methods in nutritional epidemiology allow summarizing the complexity, relationships and patterns of diet and nutrients and comparing across population groups [45, 51]. Particularly, application of these methods to identify nutrient patterns captures a better explanation of the variation (the proportion of variability in each nutrient pattern that can be explained by the included nutrients) [391] compared to using the methods in identifying dietary patterns [378, 392], which is also reflected in the current study (62.7%). The other characteristic of nutrient patterns derived by these methods is the similarity across the population groups that is evident in the current and other studies [205, 393]. This implies the consistent nature of nutrient patterns across populations, which leads to a premise that generalizability of findings on the association between nutrient patterns and disease outcomes across populations could be possible.

4.2. Association between mixed-source nutrient pattern and BMD

We found that the mixed-source pattern was associated with increased BMD. The finding is consistent with a study conducted among Iranian postmenopausal women that found a positive association between a nutrient pattern characterized by high intake of fibre, folate vitamins A, K, B_2, B_6 and B_{12}, magnesium and potassium and lumbar spine BMD [205]. A French prospective investigation among those aged 65 years and over (The Three-City Study) reported that a similar nutrient pattern was associated with a 13% reduction in

fracture risk [94].

The mixed-source pattern identified by this study was characterized by a high intake of nutrients that are important to bone metabolism [143]. In the pattern, minerals, including phosphorus, potassium, magnesium and calcium, were the major components. Phosphorus is known to have a primary role in building and maintaining bone mass [394] through hydroxyapatite formation [395]. Potassium and magnesium are also the important minerals for bone mass [396], by reducing calcium excretion [397] and hydroxyapatite crystal formation [398]. Furthermore, although evidence is not conclusive, metabolic alkalosis [152] created by potassium and magnesium [399] could be another explanation. It is important to note that dietary sources of these nutrients (such as dairy products, nuts, and seeds) are common and nutritional recommendations can be easily made to protect bone loss in ageing populations. Most of these nutrients can also be found by consuming Mediterranean diet which have shown a positive correlation with bone health [400].

Other nutrients that were highly loaded to the mixed-source pattern were B vitamins (B_1, B_2, B_3, B_7 and B_{12}), protein, saturated fat, fibre and retinol. In the Framingham Osteoporosis Study, a lower plasma vitamin B_{12} concentration was associated with a lower BMD [401]. A review by Fratoni and Brandi also showed a strong positive association between low levels of vitamin B_{12} serum concentration and fracture risks [402]. In previous studies, nutrient patterns that were high in fibre and vitamin A were also positively associated with BMD [205, 403]. In addition, the antioxidant characteristics of the nutrients in the mixed-source pattern (with high load of vitamins A, C and E, beta-carotene and lycopene) can play an important role in maintaining bone mass [174, 176]. Furthermore, dietary protein is an important factor in increasing

intracellular and extracellular bone proteins. It also raises the level of insulin-like growth factor-I (IGF-I) which promotes production of 1, 25 dihydroxyvitamin D (1,25D) and reabsorption of inorganic phosphate by the kidney [154]. The importance of protein in bone formation is supported by epidemiological studies [154, 380] although the overall evidence is limited [19].

Another characteristic of the mixed-source pattern in this study was low loadings of PUFA (particularly omega-3). Although studies support the importance of PUFA in maintaining bone mass and minimizing fracture risks, evidence of the association between PUFA and bone health is inconclusive [33, 143, 161, 404].

Taken together, nutrients that were highly loaded in the mixed-source pattern not only benefit bone health but also are important for overall health. Given the diverse dietary source of these nutrients, nutrition messages targeting ageing people should encourage the intake of both animal and plant source foods.

4.3. Association between plant-/animal-sourced nutrient patterns and BMD

We did not find any significant associations between plant- and animal-sourced patterns and BMD. In Iranian postmenopausal women, similar nutrient patterns were also not associated with BMD [205]. The animal-sourced pattern in our study was not highly loaded with important nutrients such as potassium, magnesium, fibre and anti-oxidants. In addition, this nutrient pattern was characterized by a high intake of take-away food, red meat, soft drinks and high fat dairy that our previous study found to be positively associated with low BMD [378]. Although FV intake increased across tertiles of the plant-sourced pattern, the low intake of diets that are main sources of nutrients for bone health

was the main characteristic of the pattern.

The limitations of this study should be considered while interpreting the findings. First, the time of dietary assessment was after the DXA measurement (median = 4.3 years, minimum = 2.8 and maximum = 6.1 years). However, to investigate the effect of this time gap, we conducted a sensitivity analysis by segregating the study participants into two categories, those with early dietary assessment and those with late assessment (above and below 50%). The analysis suggested that the time gap could actually underestimate the association between mixed-source nutrient pattern and BMD. In our study, 162 (14.3%) of the study participants retired within this time frame. It has been previously shown that women are more likely to change their eating habit towards a healthy one while it remains stable for men after retirement [373]. Further adjustment for retirement did not change the estimates of the associations between nutrient patterns and BMD. A study has also found a stable dietary habit existed over a period of five years among men and women aged 64–85 years [371], indicating that it is unlikely that people do change eating habits when they age. However, it must be acknowledged that, in the time gap, change in dietary behaviour, and hence nutrient intake, as a result of multiple factors, including change in socio-economic status and physiological changes, could exist. In addition, study participants who had a new diagnosis of a disease that could be impacted by a dietary change and those who were told the result of DXA measurements could change their eating habit and other lifestyle behaviours. Particularly, those participants who knew that they were osteopenic or osteoporotic may have been more likely to take supplements (such as, vitamin D) at Stage 2 for which we did not have the data.

Secondly, the number of cases with missing values was a limitation. However, to investigate the influence of the missing values on the estimates, we conducted sensitivity

analyses (including multiple imputation) which suggested a similar pattern of association to that which we reported. Thirdly, although FFQ is widely used and it captures the usual intake of food and the relative consumption pattern at the population level [40], the inherent limitations of recall bias in accurately measuring the amount of food and nutrients should be noted. Fourthly, measurement errors associated with dietary assessment could be introduced because of potentially diminished cognitive function of the study participants (e.g. those aged 70 years and over) despite the majority (80.3%) of our study participants were aged 50–69 years and the acceptable validity of FFQ use among older people reported in previous studies [374, 405]. Formal cognitive testing was not undertaken in this study and thus we are not able to determine the impact of this on results. However, we assume that mental health conditions may impact on cognitive status and we identified those with a possible mental health condition through use of relevant medication. When adjusting for the medication use in the analysis, there was no impact on the estimates. However, we acknowledge that this is not a replacement for formal cognitive testing and the impact that this may have on dietary assessment. Fifthly, because of the cross-sectional analysis of the study, cause-effect relationships cannot be declared.

In summary, we found that the mixed-source nutrient pattern was positively associated with BMD but both plant- and animal-sourced patterns were not significantly associated. This study shows the potential benefit of nutrients from both animal and plant source foods in maintaining bone mass and hence the prevention of bone fragility and reducing fracture risk. This highlights that a balanced diet (from both plant and animal sources) is important in maintaining bone mass in the aging population. To prevent the development of osteoporosis/osteopenia, dietary approaches should be part of the targeted strategies for both clinical and public health interventions. Further longitudinal studies are warranted to support these findings.

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Conflict of interest

The authors have no financial or personal conflicts of interest to declare.

Authors' contribution

YAM, TKG, RA and ZS conceived the study. YAM conducted all analyses and wrote all drafts of the paper. ZS assisted with analysis and reviewed and provided comment on all drafts. TKG, AWT and RJA reviewed and commented on all drafts. All authors read and approved the final manuscript.

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CHAPTER 7 DIETARY AND NUTRIENT PATTERNS AND FRACTURE

7.1 Publication

Melaku YA, Gill TK, Appleton SL, Taylor AW, Adams R, Shi Z: Prospective Associations of Dietary and Nutrient Patterns with Fracture Risk: A 20-Year Follow-Up Study. Nutrients 2017, 9(11).

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Name of Principal Author (Candidate)	Yohannes Adama Melaku		
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Overall percentage (%)	50%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	23/07/2018

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Signature		Date	20/07/2017

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Signature		Date	20/07/2017

Prospective Associations of Dietary and Nutrient Patterns with Fracture Risk: A 20-Year Follow-Up Study

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Abstract: Studies on long-term exposure to foods/nutrients and its associations with fracture risk are scarce. Using data from the China Health and Nutrition Survey (CHNS), we determined the prospective association of dietary and nutrient patterns with fractures. Data from 15,572 adults aged ≥18 years were analysed. Fracture occurrence was self-reported and dietary intake data were collected using a 24-hour (24-h) recall method for three consecutive days, for each individual across nine waves (1989–2011). We used cumulative and overall mean, recent and baseline dietary and nutrient exposures. Hazard ratios (HR) were used to determine the associations. Two dietary (traditional and modern) and two nutrient (plant- and animal-sourced) patterns were identified. After adjusting for potential confounders, study participants in the third tertiles (highest intake) of the modern dietary and animal-sourced nutrient patterns' cumulative scores had a 34% (HR = 1.34; 95% confidence interval (CI): 1.06–1.71) and 37% (HR = 1.37; 95% CI: 1.08–1.72) increase in fracture risks compared to those in the first tertiles, respectively. While the overall mean factor scores of dietary and nutrient patterns had a similar (or stronger) pattern of association as the cumulative scores, no association between recent and baseline scores and fracture was found. Greater adherence to a modern dietary and/or an animal-sourced nutrient pattern is associated with a higher risk of total fractures. This suggests that a modern animal based diet is related to bone fragility. A repeated three-day 24-h recall dietary assessment provides a stronger association with fracture compared to a recent or baseline exposure.

Keywords: dietary pattern, nutrient pattern, fracture, China Health and Nutrition Survey

1. Introduction

Lifestyle and behavioural factors are associated with fracture risk [406, 407]. Of the lifestyle and behavioural factors, diet is of a particular significance [204, 408, 409]. Previous studies have generally focused on the associations between individual diets or nutrients with fractures [28, 32, 190, 410, 411]. This approach does not consider other food items or nutrients that could have a potential influence on fracture risk; and the interactions of food items or nutrients are ignored resulting in a biased (confounded) association with fracture risk. Realistically, people do not consume individual foods or nutrients but rather a mixture of foods with multiple nutrients. Furthermore, bone physiology is not dependent on individual nutrients, thus these combinations provide a further challenge for clinical and public health recommendations to improve bone strength.

Studies have shown inconsistent findings on the association between dietary patterns and fracture risks [204, 280, 281, 412]. In terms of nutrient patterns, to the best of our knowledge, with the exception of one study [94], no other studies have investigated the association with fracture risks. A thorough investigation of an association between patterns of nutrient and food intakes over the long term, and fractures, is essential as bone is a complex structure composed of multiple nutrients. In addition, diet and/or nutrients that are associated with muscle mass or strength could also determine fracture risks [413]. Focusing on the overall dietary and nutrient patterns assists dietary counselling and recommendations for individuals and population groups and this approach can also detect a potential positive impact of minimal changes across foods or nutrients, rather than a major change in a few food or nutrient groups on health outcomes, which might result in a better compliance of dietary recommendations [414]. In this study, we aimed to assess

prospective associations between long term dietary and nutrient patterns and fracture risk among adults (18 years and above) using the CHNS.

2. Materials and methods

2.1. Study design and population

We used longitudinal data from the CHNS, which is an open prospective cohort study and represents nine provinces of China [415]. There were nine waves (two to three years apart) of data collection between 1989 and 2011. A multistage random-cluster sampling technique was used to select households in the study. All members of the selected households were eligible to be included in the study. Between 1989 and 2011, 35,703 study participants were involved in at least one study wave. After excluding those who were not eligible, the analysis sample was 15,572 in this specific study (Figure 7.1). The response rate based on those who participated in previous waves staying in the subsequent survey was around 88%. However, the response rate out of the participants included at baseline (1989) and remained in 2006 was more than 60% [298]. The CHNS was approved by the institutional review committees of the University of North Carolina (Chapel Hill, NC, USA) and the National Institute of Nutrition and Food Safety (Beijing, China). Prior to the survey, informed consent was obtained from all participants.

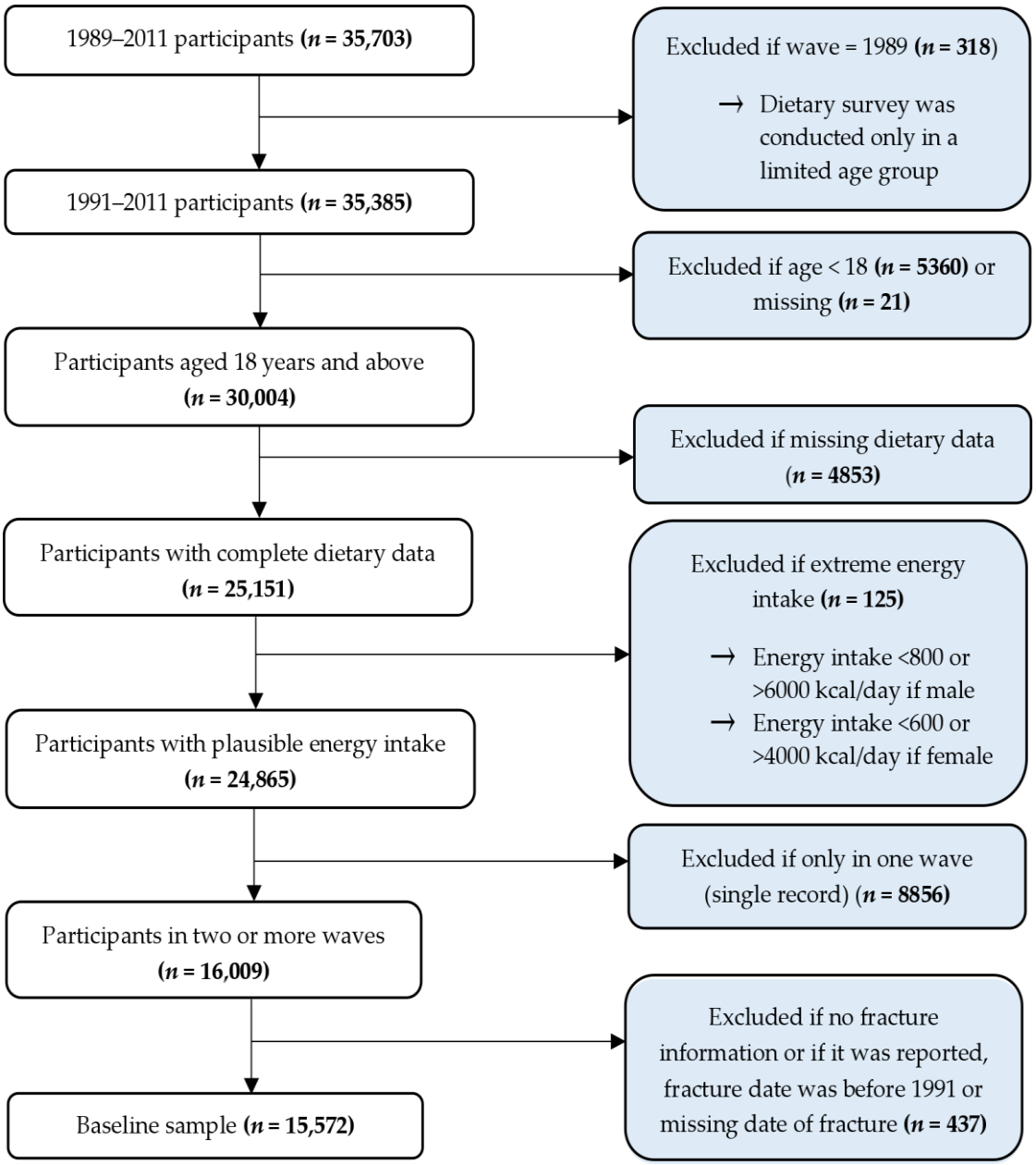

Figure 7.1 Sampling description

2.2. Outcome variable

Fracture was self-reported in each wave by the study participants for a question "Have you ever had fracture?" along with age when the first fracture occurred. To determine the calendar year of fracture, first we calculated the difference between the current age (at the interview) and age at first fracture. Then, we subtracted the age differences (in years) from the respective calendar years or waves (when the interview was conducted). This

provided us the calendar year of the first facture. We assumed that the date of fracture was on 1 July of each year. In a previous large cohort study, a self-reported assessment of lifetime fractures, along with age at fractures, was found to be a feasible method to establish incident cases [416]. We excluded those participants who had the first fractures before the first interview date for each wave (when dietary data were collected) and those with less than 0.5 years of follow-up after the interviews.

2.3. Assessment of dietary and nutrient intakes

Detailed descriptions of dietary measurements are provided elsewhere [417]. In short, dietary intake data were collected using a 24-h dietary recall method for three consecutive days at each wave for each individual. At the beginning and end of the three days, interviewers weighed/recorded all available and wasted foods at home. These data were linked and harmonized with the dietary recall data to determine individuals' dietary intake levels. The Chinese Food Composition Table was used to analyse the food consumption data (g/day) and to determine the intake levels of nutrients. Foods and nutrients were categorized into 34 and 21 groups for further analysis, respectively.

2.4. Covariates

At each wave, data on sociodemographic, lifestyle, physical measurements and chronic conditions were collected. Individual level income was classified into tertiles (low, middle and high) at each wave. The highest level of education achieved was categorized into low (illiterate or primary school), medium (junior middle school) and high (high middle school or higher). Residency was classified into two categories (urban and rural) based on an urbanization index which is a composite of 12 components that included population and other socioeconomic characteristics [417]. Lifestyle factors included smoking, alcohol consumption and PAL. We categorized smoking status as non-smokers

and current smokers/ex-smokers. Frequency of alcohol consumption was categorized as "none", "<1/week", "1–2/week", "3–4/week" and "daily". PAL, in terms of metabolic equivalent of task (MET-hours per week), was determined based on self-reported job and leisure time activities, intensity and duration of the activities.

Height and weight were measured based on a protocol recommended by WHO. BMI was calculated as weight (kg) divided by the square of height (m). Hypertension was determined based on systolic (above 140 mmHg) and/or diastolic (above 90 mmHg) blood pressure measures, or having doctor diagnosed hypertension.

2.5. Statistical analysis

Dietary and nutrient patterns were identified across the seven waves (1991–2009) by factor analysis using the PCA method. An eigenvalue (>1.5), scree plot, and interpretability of the factors were used to determine the number of dietary and nutrient patterns. Factor loadings (the correlation between each pattern and the food and nutrient groups) were calculated. Percentages of variances (the variations that were explained by the identified dietary and nutrient patterns) were also computed. For each dietary and nutrient pattern, factor scores were assigned across all study participants. Factor scores show the relative position of the study participants in each of the identified patterns reflecting adherence to the patterns. Pattern-specific factor scores are calculated as the sum of the products of the factor loading coefficients and standardized daily consumption of food and nutrient groups related with the pattern. The factor scores were orthogonally (varimax) rotated to create less correlation among the patterns and to facilitate their interpretability.

Based on the factor scores for the dietary and nutrient patterns, four approaches were used to determine the exposure levels (measured in scores) of dietary and nutrient patterns and

assess the association between the patterns and fracture risk. The first approach was to calculate the cumulative exposure level. To represent the usual relative position (factor scores or adherence to the patterns) of the study participants in the factors [418], we calculated cumulative mean factor scores. The cumulative scores were calculated by summing factor scores and dividing by the number of waves contributing to the scores for each study participant. For example, for the second wave (1993), factor scores of the first wave (1991) were used; for the third wave (1997), an average of scores of waves one (1991) and two (1993) was used; and, for the fourth wave (2000), an average of factors of waves one, two and three (1997) was used. Correlations between cumulative scores of dietary and nutrient patterns were investigated with Spearman rank correlations.

The second approach was using the overall mean of the dietary and nutrient pattern scores. The overall mean was calculated by summing factor scores until the wave just prior to the fracture or censoring occurred and dividing by the number of waves contributing to the scores for each study participant. The third and fourth approaches used the recent and baseline factor scores. The participants were then allocated into tertiles (first (lowest intake); second; and third (highest intake) tertiles) based on the factor scores.

Chi-square (categorical variables), analysis of variance (ANOVA) (normally distributed continuous variables) and Kruskal–Wallis (continuous but not normally distributed) tests were used where appropriate to compare the differences in proportions, means and medians of the groups at baseline. Time to the incident event was determined as the time from enrolment to the first occurrence of incident fracture. Follow-up was censored at the date of the outcome event, end of follow-up, date of outmigration, or date of death whichever came first.

We calculated the incidence rate (per 1000 person-years) of fractures by tertiles of dietary

and nutrient patterns and the log-rank test was used to investigate the differences. Nelson–Aalen cumulative hazard estimates were calculated by tertiles of the patterns across the follow-up time. To assess the associations of dietary and nutrient patterns with incident fractures, hazard ratios (HRs) for fractures and tertiles of the cumulative and overall mean, recent, and baseline factor scores were determined using Cox proportional hazard regression models. The first tertile was used as reference category. Three models were used to determine HRs: Model 1 adjusted for age, sex and daily energy intake; Model 2 additionally adjusted for education status, income, alcohol intake, residency and PAL; and Model 3 was further adjusted for BMI and hypertension. Using Model 3, we also conducted stratified analyses using age group (age < 50 and ≥ 50) and sex to explore and compare the associations in the respective groups. We tested interactions between dietary and nutrient patterns, other covariates and fracture risks using multiplicative terms in the last model (Model 3). The assumption of proportionality was tested by including time-dependant covariates in the final models and was valid for all analyses. To assess the quality of models (Model 3), we determined Akaike's information criterion (AIC). We estimated the absolute risk differences for fractures between the third and first tertiles and the number of individuals needed to get one fracture case as a consequence of being in the third tertiles of dietary and nutrient patterns. Participants were also jointly classified across tertiles of dietary and nutrient patterns and used in the Cox regression (Model 3). Statistical analyses were performed using Stata version 14 (Stata Corporation, College Station, TX, USA). All *P* values are two-sided.

3. Results

3.1. Baseline characteristics

Baseline characteristics of the study participants are shown in Table 7.1. The study

participants were followed for 20.2 years (median follow-up time = 8.9 years), which equates to a total of 162,416.3 person-years.

Table 7.1 Baseline sociodemographic characteristics across tertiles of dietary and nutrient patterns among adults 18 years and above, the China Health and Nutrition Survey

Characteristics	Overall		T1	T2	T3	*P* value	T1	T2	T3	*P* value
	Category	Value	Traditional dietary pattern				Modern dietary pattern			
N		15,572	5476	5164	4932		6019	4796	4757	
Sex [#]	Male	7627 (49.0%)	2613 (47.7%)	2192 (42.4%)	2822 (57.2%)	<0.001	3000 (49.8%)	2213 (46.1%)	2414 (50.7%)	<0.001
Age in years, median (IQR) [$]		37.6 (27.5, 51.1)	37.9 (27.5, 51.7)	38.6 (27.9, 53.3)	36.3 (26.7, 47.9)	<0.001	36.5 (26.8, 48.4)	37.7 (27.2, 51.5)	39.2 (28.6, 53.5)	<0.001
Income [#]	Low	4537 (29.1%)	2010 (36.7%)	1335 (25.9%)	1192 (24.2%)	<0.001	2409 (40.0%)	1481 (30.9%)	647 (13.6%)	<0.001
	Medium	5083 (32.6%)	1739 (31.8%)	1728 (33.5%)	1616 (32.8%)		2066 (34.3%)	1651 (34.4%)	1366 (28.7%)	
	High	5842 (37.5%)	1674 (30.6%)	2065 (40.0%)	2103 (42.6%)		1522 (25.3%)	1624 (33.9%)	2696 (56.7%)	
	Missing	110 (0.7%)	53 (1.0%)	36 (0.7%)	21 (0.4%)		22 (0.4%)	40 (0.8%)	48 (1.0%)	
Residency [#]	Urban	5578 (35.8%)	1610 (29.4%)	2150 (41.6%)	1818 (36.9%)	<0.001	999 (16.6%)	1839 (38.3%)	2740 (57.6%)	<0.001
Education [#]	Low	6496 (41.7%)	2514 (45.9%)	2042 (39.5%)	1940 (39.3%)	<0.001	3311 (55.0%)	2036 (42.5%)	1149 (24.2%)	<0.001
	Medium	4601 (29.5%)	1630 (29.8%)	1470 (28.5%)	1501 (30.4%)		1751 (29.1%)	1458 (30.4%)	1392 (29.3%)	
	High	3086 (19.8%)	847 (15.5%)	1099 (21.3%)	1140 (23.1%)		603 (10.0%)	846 (17.6%)	1637 (34.4%)	
	Missing	1389 (8.9%)	485 (8.9%)	553 (10.7%)	351 (7.1%)		354 (5.9%)	456 (9.5%)	579 (12.2%)	
Physical activity (MET-hours/week), mean (SD) (*n* = 14,930) [@]		201.1 (174.1)	212.4 (185.2)	192.3 (169.5)	197.9 (165.4)	<0.001	236.8 (183.0)	202.4 (173.9)	153.7 (149.6)	<0.001
Alcohol consumption [#]	None	9327 (59.9%)	3247 (59.3%)	3311 (64.1%)	2769 (56.1%)	<0.001	3663 (60.9%)	3002 (62.6%)	2662 (56.0%)	<0.001
	<1/week	1826 (11.7%)	653 (11.9%)	534 (10.3%)	639 (13.0%)		740 (12.3%)	515 (10.7%)	571 (12.0%)	
	1–2/week	1256 (8.1%)	390 (7.1%)	401 (7.8%)	465 (9.4%)		449 (7.5%)	334 (7.0%)	473 (9.9%)	
	3–4/week	705 (4.5%)	220 (4.0%)	216 (4.2%)	269 (5.5%)		264 (4.4%)	178 (3.7%)	263 (5.5%)	
	Daily	1299 (8.3%)	412 (7.5%)	400 (7.7%)	487 (9.9%)		424 (7.0%)	369 (7.7%)	506 (10.6%)	
	Missing	1159 (7.4%)	554 (10.1%)	302 (5.8%)	303 (6.1%)		479 (8.0%)	398 (8.3%)	282 (5.9%)	
Smoking [#]	Current/ex-smoker	4759 (30.6%)	1606 (29.3%)	1411 (27.3%)	1742 (35.3%)	<0.001	1916 (31.8%)	1379 (28.8%)	1464 (30.8%)	0.002
	Missing	957 (6.1%)	463 (8.5%)	252 (4.9%)	242 (4.9%)		415 (6.9%)	329 (6.9%)	213 (4.5%)	
Body-mass index (kg/m^2), mean (SD) (*n* = 14,045) [@]		22.1 (3.1)	22.6 (3.1)	22.0 (3.2)	21.7 (2.9)	<0.001	21.4 (2.7)	22.2 (3.1)	23.0 (3.3)	<0.001
Hypertension [#]	Yes	1725 (11.1%)	634 (11.6%)	611 (11.8%)	480 (9.7%)	<0.001	466 (7.7%)	529 (11.0%)	730 (15.3%)	<0.001
	Missing	1401 (9.0%)	623 (11.4%)	406 (7.9%)	372 (7.5%)		555 (9.2%)	481 (10.0%)	365 (7.7%)	
Energy (kcal), mean (SD) [@]		2448.2 (708.4)	2452.8 (750.7)	2212.2 (595.9)	2690.2 (685.5)	<0.001	2597.3 (692.4)	2356.5 (714.5)	2351.9 (689.7)	<0.001
			Plant-sourced nutrient pattern				Animal-sourced nutrient pattern			
N		15,571	5661	4210	5700		6026	4170	5375	
Sex [#]	Men		2146 (37.9%)	2200 (52.3%)	3280 (57.5%)	<0.001	2435 (40.4%)	1973 (47.3%)	3218 (59.9%)	<0.001
Age in years, median (IQR) [$]			39.4 (28.2, 55.5)	36.9 (26.8, 49.4)	36.7 (27.1, 47.9)	<0.001	38.6 (27.9, 53.5)	37.3 (27.3, 51.2)	36.7 (26.9, 48.4)	<0.001
Income [#]	Low		1377 (24.3%)	1147 (27.2%)	2013 (35.3%)	<0.001	2121 (35.2%)	1169 (28.0%)	1247 (23.2%)	<0.001
	Medium		1814 (32.0%)	1414 (33.6%)	1854 (32.5%)		2017 (33.5%)	1381 (33.1%)	1684 (31.3%)	
	High		2415 (42.7%)	1625 (38.6%)	1802 (31.6%)		1852 (30.7%)	1588 (38.1%)	2402 (44.7%)	
	Missing		55 (1.0%)	24 (0.6%)	31 (0.5%)		36 (0.6%)	32 (0.8%)	42 (0.8%)	
Residency [#]	Urban		2721 (48.1%)	1491 (35.4%)	1365 (23.9%)	<0.001	1708 (28.3%)	1599 (38.3%)	2270 (42.2%)	<0.001
Education [#]	Low		2014 (35.6%)	1671 (39.7%)	2811 (49.3%)	<0.001	3008 (49.9%)	1684 (40.4%)	1804 (33.6%)	<0.001
	Medium		1592 (28.1%)	1285 (30.5%)	1724 (30.2%)		1673 (27.8%)	1249 (30.0%)	1679 (31.2%)	
	High		1414 (25.0%)	820 (19.5%)	851 (14.9%)		853 (14.2%)	851 (20.4%)	1381 (25.7%)	
	Missing		641 (11.3%)	434 (10.3%)	314 (5.5%)		492 (8.2%)	386 (9.3%)	511 (9.5%)	

Characteristics	Overall		T1	T2	T3	*P* value	T1	T2	T3	*P* value
	Category	Value	Traditional dietary pattern				Modern dietary pattern			
Physical activity (MET-hours), mean (SD) (*n* = 14,930) [@]			165.9 (162.8)	199.1 (167.0)	236.5 (182.5)	<0.001	214.2 (180.6)	197.8 (172.8)	189.2 (166.6)	<0.001
Alcohol consumption [#]	None		3845 (67.9%)	2422 (57.5%)	3060 (53.7%)	<0.001	3952 (65.6%)	2559 (61.4%)	2816 (52.4%)	<0.001
	<1/week		517 (9.1%)	503 (11.9%)	806 (14.1%)		599 (9.9%)	486 (11.7%)	741 (13.8%)	
	1–2/week		354 (6.3%)	393 (9.3%)	508 (8.9%)		383 (6.4%)	324 (7.8%)	548 (10.2%)	
	3–4/week		206 (3.6%)	197 (4.7%)	302 (5.3%)		222 (3.7%)	188 (4.5%)	295 (5.5%)	
	Daily		419 (7.4%)	376 (8.9%)	504 (8.8%)		398 (6.6%)	312 (7.5%)	589 (11.0%)	
	Missing		320 (5.7%)	319 (7.6%)	520 (9.1%)		472 (7.8%)	301 (7.2%)	386 (7.2%)	
Smoking [#]	Current/ex-smoke		1344 (23.7%)	1345 (31.9%)	2069 (36.3%)	<0.001	1599 (26.5%)	1199 (28.8%)	1960 (36.5%)	<0.001
	Missing		259 (4.6%)	265 (6.3%)	433 (7.6%)		402 (6.7%)	244 (5.9%)	311 (5.8%)	
Body-mass index (kg/m^2), mean (SD) (*n* = 14,045) [@]			22.3 (3.3)	22.3 (3.1)	21.9 (2.9)	<0.001	21.8 (3.0)	22.2 (3.2)	22.4 (3.1)	<0.001
Hypertension [#]	Yes		781 (13.8%)	449 (10.7%)	495 (8.7%)	<0.001	698 (11.6%)	454 (10.9%)	573 (10.7%)	0.190
	Missing		499 (8.8%)	378 (9.0%)	524 (9.2%)		566 (9.4%)	387 (9.3%)	448 (8.3%)	
Energy (kcal), mean (SD) [@]			1943.5 (492.3)	2491.4 (491.0)	2917.9 (690.5)	<0.001	2136.7 (624.0)	2385.8 (557.8)	2846.1 (710.9)	<0.001

[#] – Pearson's chi-square test; [$] – Kruskal – Wallis test; [@] – analysis of variance (ANOVA); IQR – interquartile range; MET – metabolic equivalent task; SD – standard deviation; T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence)

3.2. Dietary and nutrient patterns

Figure 7.2 depicts the identified dietary and nutrient patterns and factor loadings of food groups and nutrients. Two dietary patterns were identified. Whereas the first pattern (traditional) was characterized by a high intake of rice, pork, fish, poultry, dry tofu, beef, fresh vegetables and offal, the second pattern (modern) was characterized by a high intake of fruits, milk, cake, fast foods, eggs, soy milk and deep fried products. The two patterns explained 11.9% of variance. Two nutrient patterns (plant- and animal-sourced) were determined. The two nutrient patterns explained 59.1% of nutrient intake variance. The correlations between the traditional dietary pattern and the plant- and animal-sourced nutrient pattern cumulative scores were −0.051 and 0.127, respectively; and between the modern dietary pattern and plant- and animal-sourced nutrient patterns were −0.306 and 0.462, respectively ($p \leq 0.0001$) (Supplementary Table 7.1).

Consumption patterns of selected food and nutrient groups across the tertiles of dietary and nutrient patterns are also shown in Table 7.2. Overall, the consumption of milk was very low (5.8 millilitre/day). There was a significant reduction of calcium, fiber and vitamin C intake across the tertiles of animal-sourced nutrient pattern ($P < 0.001$).

3.3. Dietary and nutrient patterns and fracture rate

During the follow-up, there were 649 incident cases of fractures (males = 311 and females = 338). The rate of fracture was 4.0 (95% CI: 3.7–4.3) per 1000 person-years (Table 7.3). While males (3.8 per 1000 person-years) below 50 years of age had a higher fracture rate compared to their female (2.9 per 1000 person-years) counterparts, the reverse (2.8 (males) vs. 6.4 (females) per 1000 person-years) was found for those 50 years and over (Supplementary Table 7.2). Nelson–Aalen cumulative hazard estimates by tertiles of dietary and nutrient patterns are depicted in Supplementary Figure 7.1 and Supplementary

Figure 7.2.

Food groups	Dietary patterns and factor loadings		Nutrients	Nutrient patterns and factor loadings	
	Traditional	Modern		Plant-sourced	Animal-sourced
Rice	0.71	−0.40	Potassium	0.93	−0.08
Pork	0.48	0.21	Phosphorus	0.93	0.26
Fish	0.41	0.19	Magnesium	0.93	0.08
Poultry	0.29	0.21	Zinc	0.87	0.32
Dry tofu	0.29	0.03	Calcium	0.87	−0.17
Beef	0.24	0.16	Iron	0.86	0.19
Fresh vegetable	0.24	−0.20	Copper	0.82	0.25
Offal	0.24	0.03	Fiber	0.79	0.08
Mushroom	0.16	0.29	Manganese	0.78	0.11
Spirit	0.12	0.10	Vitamin C	0.78	−0.26
Shrimp	0.11	0.22	Carbohydrate	0.73	0.17
Nuts	0.09	0.23	Niacin (vitamin B_3)	0.72	0.39
Beer	0.09	0.23	Thiamine (vitamin B_1)	0.70	0.37
Fruit	0.08	0.44	Sodium	0.25	0.11
Salted vegetable	0.07	−0.21	Riboflavin (vitamin B_2)	0.22	0.79
Milk	0.05	0.40	Protein	0.61	0.70
Beverage	0.04	0.12	Fat	0.08	0.66
Yoghurt	0.03	0.16	Selenium	0.30	0.52
Sugar	0.03	0.11	Vitamin E	0.34	0.51
Wine	0.02	0.03	Vitamin A	−0.07	0.47
Milk powder	0.02	0.06	Folate	−0.04	0.11
Lamb	0.01	0.18			
Fresh bean	0.00	0.03			
Cake	−0.02	0.31			
Legume	−0.02	−0.11			
Fast food	−0.03	0.40			
Eggs	−0.03	0.44			
Tofu	−0.05	0.05			
Soy milk	−0.07	0.42			
Bean thread noodle	−0.09	0.07			
Tubers	−0.19	−0.13			
Deep fried products	−0.20	0.41			
Whole grain	−0.47	−0.04			
Wheat	−0.73	0.07			

Figure 7.2 Factor loadings of food groups and nutrients to patterns

[The colour gradation reflects how big and in which direction was the correlation between the food groups and nutrients, and the patterns. Deep green colour refers to a relatively higher correlation (higher intake) of the food groups and nutrients with the dietary and nutrient patterns, respectively. Deep red colour refers to a relatively lower correlation (a lower intake) of the food groups and nutrients with the patterns.]

Table 7.2 Selected baseline (1991) food and nutrient intake across tertiles of dietary and nutrient pattern scores among adults 18 years and above, the China Health and Nutrition Survey

		T1	T2	T3	*P* value	T1	T2	T3	*P* value
		Traditional dietary pattern				Modern dietary pattern			
N	**15,572**	**5476**	**5164**	**4932**		**6019**	**4796**	**4757**	
Food Groups, Mean (SD)									
Rice (g/day)	286.9 (211.4)	100.6 (119.7)	324.1 (137.9)	454.9 (192.5)	<0.001	422.5 (212.2)	212.2 (171.7)	190.7 (146.4)	<0.001
Fish (g/day)	24.1 (47.2)	6.4 (21.0)	20.0 (36.4)	47.9 (65.1)	<0.001	13.8 (33.3)	22.5 (42.4)	38.8 (61.1)	<0.001
Tofu (g/day)	22.7 (42.4)	25.1 (46.0)	24.3 (42.4)	18.4 (37.6)	<0.001	21.4 (45.1)	22.3 (40.3)	24.8 (40.9)	<0.001
Dry tofu (g/day)	10.0 (26.3)	3.1 (15.2)	8.4 (20.9)	19.3 (36.4)	<0.001	10.1 (26.3)	8.7 (24.9)	11.2 (27.5)	<0.001
Fresh vegetable (g/day)	279.1 (179.0)	238.2 (168.0)	256.7 (151.7)	347.8 (196.6)	<0.001	338.4 (204.8)	239.7 (145.7)	243.7 (152.3)	<0.001
Salted vegetable (g/day)	15.7 (46.7)	13.1 (53.7)	13.3 (34.5)	21.1 (48.9)	<0.001	29.6 (68.1)	7.5 (21.6)	6.4 (20.2)	<0.001
Fruit (g/day)	19.4 (72.2)	12.5 (48.0)	20.1 (62.3)	26.3 (98.6)	<0.001	2.2 (15.6)	7.3 (29.5)	53.2 (119.1)	<0.001
Soy milk (mL/day)	5.6 (29.2)	7.5 (36.8)	6.0 (28.0)	2.9 (18.9)	<0.001	0.4 (6.0)	1.3 (9.8)	16.4 (49.8)	<0.001
Milk (mL/day)	5.8 (35.3)	3.5 (28.0)	7.1 (37.2)	6.9 (40.2)	<0.001	0.0 (0.3)	0.1 (2.5)	18.8 (62.0)	<0.001
Milk powder (g/day)	0.4 (5.5)	0.3 (4.2)	0.4 (4.6)	0.4 (7.4)	0.360	0.0 (1.4)	0.1 (2.1)	1.0 (9.6)	<0.001
Whole grain (g/day)	26.7 (82.4)	70.0 (126.2)	5.0 (20.3)	1.5 (11.6)	<0.001	29.8 (101.8)	33.3 (78.4)	16.2 (52.6)	<0.001
Nutrients									
Calcium (mg/day)	639.2 (780.3)	608.2 (838.3)	564.1 (641.9)	752.3 (831.3)	<0.001	774.6 (952.5)	543.2 (653.2)	564.7 (614.2)	<0.001
Magnesium (mg/day)	381.8 (239.9)	451.8 (277.9)	318.9 (186.7)	370.1 (222.9)	<0.001	421.4 (283.6)	367.3 (213.3)	346.4 (193.0)	<0.001
Phosphorus (mg/day)	1266.8 (595.0)	1335.5 (669.4)	1083.6 (471.3)	1382.2 (578.1)	<0.001	1378.1 (668.9)	1204.3 (551.0)	1188.8 (511.1)	<0.001
Potassium (mg/day)	2419.5 (2032.4)	2479.1 (2231.7)	2104.9 (1655.9)	2682.8 (2113.4)	<0.001	2858.1 (2464.2)	2127.5 (1693.5)	2159.0 (1597.4)	<0.001
Fiber (g/day)	15.4 (11.4)	18.9 (12.9)	12.6 (9.2)	14.3 (10.7)	<0.001	17.7 (13.2)	14.4 (10.1)	13.4 (9.4)	<0.001
Vitamin A (mg/day)	200.6 (738.4)	106.5 (225.3)	162.1 (353.4)	345.3 (1225.6)	<0.001	106.3 (605.1)	174.5 (504.8)	346.2 (1015.7)	<0.001
Vitamin C (mg/day)	142.1 (178.0)	129.6 (185.8)	129.7 (155.7)	169.1 (187.9)	<0.001	187.5 (214.2)	114.4 (143.0)	112.7 (144.5)	<0.001
Protein (g/day)	73.4 (26.0)	74.9 (28.6)	63.2 (20.9)	82.2 (24.0)	<0.001	71.0 (25.0)	71.3 (25.6)	78.4 (26.8)	<0.001
Fat (g/day)	33.6 (25.0)	26.7 (19.2)	30.2 (22.6)	44.7 (29.1)	<0.001	25.1 (22.2)	30.8 (21.4)	47.1 (26.2)	<0.001
Carbohydrate(g/day)	394.1 (160.9)	437.2 (180.9)	346.7 (127.6)	395.9 (154.8)	<0.001	453.0 (166.6)	383.5 (156.5)	330.2 (127.9)	<0.001
		Plant-sourced nutrient pattern				Animal-sourced nutrient pattern			
N	**15,571**	**5661**	**4210**	**5700**		**6026**	**4170**	**5375**	
Food Groups									
Rice (g/day)		242.3 (145.8)	309.8 (202.2)	314.4 (260.1)	<0.001	308.8 (200.3)	278.0 (207.8)	269.4 (223.7)	<0.001
Fish (g/day)		25.3 (43.2)	26.7 (48.6)	20.9 (49.8)	<0.001	16.4 (36.2)	23.4 (44.1)	33.2 (57.8)	<0.001
Tofu (g/day)		18.5 (33.4)	24.1 (42.7)	25.9 (49.3)	<0.001	18.0 (37.8)	23.8 (41.8)	27.1 (47.0)	<0.001
Dry tofu (g/day)		7.0 (18.7)	11.9 (28.7)	11.6 (30.3)	<0.001	6.1 (18.7)	8.7 (22.4)	15.5 (34.2)	<0.001
Fresh vegetable (g/day)		224.0 (130.9)	294.2 (178.9)	322.6 (204.6)	<0.001	278.6 (176.1)	274.4 (181.3)	283.2 (180.4)	0.057
Salted vegetable (g/day)		8.8 (24.7)	12.8 (36.4)	24.8 (65.1)	<0.001	15.7 (42.6)	15.3 (46.7)	16.0 (50.9)	0.740

	T1	T2	T3	*P* value	T1	T2	T3	*P* value
Fruit (g/day)	21.4 (62.6)	22.5 (74.9)	15.0 (78.5)	<0.001	11.0 (46.8)	17.9 (79.0)	29.9 (87.2)	<0.001
Soy milk (g/day)	7.1 (31.2)	6.1 (29.1)	3.6 (27.0)	<0.001	2.7 (17.9)	4.7 (24.2)	9.4 (40.5)	<0.001
Milk (g/day)	8.0 (40.5)	6.8 (39.4)	2.7 (25.0)	<0.001	1.4 (15.2)	4.4 (28.3)	11.7 (51.8)	<0.001
Milk powder (g/day)	0.4 (4.1)	0.3 (4.5)	0.4 (7.1)	0.930	0.1 (2.2)	0.2 (2.9)	0.7 (8.7)	<0.001
Whole grain (g/day),	8.8 (30.6)	18.9 (54.5)	50.3 (120.5)	<0.001	21.3 (68.3)	32.1 (90.4)	28.7 (89.8)	<0.001
Nutrients								
Calcium (mg/day)	280.1 (128.1)	401.9 (182.0)	1171.1 (1081.7)	<0.001	873.1 (1116.6)	454.5 (415.5)	520.2 (360.7)	<0.001
Magnesium (mg/day)	218.9 (64.5)	319.3 (83.4)	589.9 (274.5)	<0.001	394.1 (314.7)	337.5 (165.3)	402.6 (179.9)	<0.001
Phosphorus (mg/day)	816.9 (192.0)	1135.5 (188.3)	1810.5 (628.4)	<0.001	1234.5 (773.8)	1132.4 (385.7)	1407.1 (451.7)	<0.001
Potassium (mg/day)	1271.3 (331.5)	1809.8 (383.1)	4010.3 (2636.8)	<0.001	2900.2 (2912.9)	1920.6 (1116.3)	2267.8 (1006.6)	<0.001
Fiber (g/day)	7.9 (3.0)	12.3 (4.6)	25.1 (13.1)	<0.001	16.2 (13.4)	13.4 (8.4)	16.0 (10.7)	<0.001
Vitamin A (mg/day)	281.7 (1068.4)	186.0 (407.9)	130.8 (470.7)	<0.001	66.8 (131.3)	137.7 (228.3)	399.4 (1207.2)	<0.001
Vitamin C (mg/day)	63.9 (37.6)	94.1 (56.6)	255.3 (249.5)	<0.001	207.8 (249.0)	104.3 (101.5)	97.9 (80.0)	<0.001
Protein (g/day)	55.6 (15.6)	72.9 (17.8)	91.3 (27.0)	<0.001	58.3 (20.6)	69.1 (14.6)	93.5 (25.2)	<0.001
Fat (g/day)	31.6 (21.1)	34.6 (27.1)	34.8 (26.8)	<0.001	19.4 (14.3)	30.4 (15.8)	51.9 (28.7)	<0.001
Carbohydrate (g/day)	271.9 (75.5)	377.8 (85.3)	527.5 (163.9)	<0.001	375.9 (163.0)	378.5 (132.3)	426.6 (173.3)	<0.001

P values were calculated using analysis of variance (ANOVA). SD – standard deviation; T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence)

Table 7.3 Median follow-up time and crude incidence of fractures by tertiles of dietary and nutrient patterns among adults 18 years and above, the China Health and Nutrition Survey (1991–2011)

		T1	T2	T3	Log-rank test	T1	T2	T3	Log-rank test
	Total	**Traditional dietary pattern**				**Modern dietary pattern**			
N	**15,572**	**5476**	**5164**	**4932**	***P* value**	**6019**	**4796**	**4757**	***P* value**
Median follow-up time (years)	8.9	8.8	8.9	9.0		8.9	9.0	7.0	
Number of fractures	649	220	214	215	0.8441	227	216	206	0.0230
Person-years at risk	162,416.3	54,925.4	52,208.0	55,282.9		63,297.3	54,385.8	44,733.2	
Rate of fracture per 1000 person-years (95% CI)	4.0 (3.7, 4.3)	4.0 (3.5, 4.6)	4.0 (3.6, 4.7)	3.9 (3.4, 4.5)		3.6 (3.2, 4.1)	4.0 (3.5, 4.5)	4.6 (4.0, 5.3)	
		Plant-sourced nutrient pattern				**Animal-sourced nutrient patterns**			
N	**15,571**	**5661**	**4210**	**5700**		**6026**	**4170**	**5375**	
Median follow-up time (years)	8.9	7.0	9.0	8.9		7.1	9.0	7.1	
Number of fractures	649	198	189	262	0.2531	221	214	214	0.4048
Person-years at risk	162,416.3	46,670.8	51,462.5	64,281.0		59,501.7	51,064.5	51,848.1	
Rate of fracture per 1000 person-years (95% CI)	4.0 (3.7, 4.3)	4.2 (3.7, 4.9)	3.7 (3.2, 4.2)	4.1 (3.6, 4.6)		3.7 (3.3, 4.2)	4.2 (3.7, 4.8)	4.1 (3.6, 4.7)	

CI – confidence interval; T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence)

After adjusting for potential confounders (sociodemographic, lifestyle and chronic conditions), participants in the third tertile of modern dietary pattern scores (cumulative mean) had a 34% increased fracture risk (HR = 1.34; 95% CI: 1.06–1.71) compared to those in the first tertile (Table 7.4). The absolute risk increase was 0.30% (95% CI: 0.06–0.54) and a number needed to have one fracture case was 339 (95% CI: 188–1785). Participants in the second (HR = 1.29; 95% CI: 1.04–1.60) and third tertiles (HR = 1.37; 95% CI: 1.08–1.72) of animal-sourced nutrient pattern cumulative scores had a higher risk of fracture compared to those in the first tertile with an absolute risk increase of 0.31% (95% CI: 0.08–0.55) and a number needed to have one case of fracture of 321 (95% CI: 184–1285).

In joint classification of study participants according to adherence to different dietary and nutrient patterns, the risk of fracture was a higher with higher adherence to the modern pattern in each stratum of traditional dietary and animal-sourced nutrient patterns. We found a 32% (95% CI: 52–1%) reduction of fracture rate for those who had simultaneous category of lowest adherence to plant- and animal-sourced nutrient patterns (Supplementary Figure 7.3**,** Supplementary Figure 7.4 and Supplementary Figure 7.5).

The estimates of association between tertiles of overall mean factor scores and fracture provided a similar pattern to the cumulative factor scores of dietary and nutrient patterns. However, there was no association between the recent and baseline factor scores of dietary and nutrient patterns and fracture (Table 7.4). There were no interactions between the dietary/nutrient patterns, other covariates and fracture risk (data not shown). Stratified analyses by age and sex are provided in Supplementary Table 7.3.

Table 7.4 Hazard ratios (HRs) [95% confidence interval (CI)] for tertiles of dietary and nutrient pattern scores and fracture among adults 18 years and above, the China Health and Nutrition Survey (1991–2011)

		HR 95% CI			*P*-trend	AIC	HR 95% CI		*P*-trend	AIC
		T1	T2	T3			T2	T3		
Models	**Person-years; number of study participants (number of cases)**	**Cumulative mean scores**					**Overall mean scores**			
					Traditional Dietary Pattern					
Model 1	162,416.3; 15,572 (649)	1.00	1.00 (0.82–1.20)	1.01 (0.84–1.23)	0.887		0.97 (0.80–1.17)	1.10 (0.91–1.33)	0.361	
Model 2	136,542.0; 14,506 (559)	1.00	1.00 (0.82–1.23)	0.99 (0.80–1.22)	0.927		0.98 (0.80–1.21)	1.08 (0.88–1.33)	0.470	
Model 3	130,075.1; 14,193 (540)	1.00	1.05 (0.85–1.30)	1.03 (0.83–1.28)	0.757	9565	1.00 (0.81–1.24)	1.12 (0.90–1.39)	0.313	9564
					Modern dietary pattern					
Model 1	162,414.3; 15,571 (649)	1.00	1.08 (0.90–1.30)	1.26 (1.04–1.52) *	0.020		1.25 (1.03–1.52) *	1.48 (1.22–1.80) **	<0.0001	
Model 2	136,542.0; 14,506 (559)	1.00	1.05 (0.85–1.29)	1.31 (1.04–1.65) *	0.029		1.25 (1.01–1.55) *	1.59 (1.26–2.01) **	<0.0001	
Model 3	130,075.1; 14,193 (540)	1.00	1.06 (0.85–1.31)	1.34 (1.06–1.71) *	0.019	9559	1.29 (1.04–1.61) *	1.63 (1.28–2.07) **	<0.0001	9550
					Plant-sourced nutrient pattern					
Model 1	162,414.3; 15,571 (649)	1.00	0.91 (0.74–1.12)	1.06 (0.86–1.30)	0.487		1.08 (0.89–1.31)	0.95 (0.77–1.17)	0.618	
Model 2	136,540.0; 14,505 (559)	1.00	0.94 (0.75–1.18)	1.08 (0.86–1.36)	0.427		1.11 (0.90–1.37)	0.96 (0.76–1.21)	0.687	
Model 3	130,073.1; 14,192 (540)	1.00	0.94 (0.75–1.19)	1.08 (0.86–1.37)	0.438	9564	1.09 (0.88–1.35)	0.93 (0.74–1.19)	0.551	9563
					Animal-sourced nutrient pattern					
Model 1	162,414.3; 15,571 (649)	1.00	1.18 (0.98–1.43)	1.25 (1.02–1.54) *	0.026		1.15 (0.94–1.40)	1.49 (1.22–1.83) **	<0.0001	
Model 2	136,540.0; 14,505 (559)	1.00	1.27 (1.03–1.56) *	1.32 (1.05–1.66) *	0.016		1.18 (0.95–1.47)	1.54 (1.22–1.94) **	<0.0001	
Model 3	130,073.1; 14,192 (540)	1.00	1.29 (1.04–1.60) *	1.37 (1.08–1.72) *	0.008	9557	1.22 (0.98–1.52)	1.61 (1.27–2.04) **	<0.0001	9549
		Recent scores					**Baseline Scores**			
					Traditional dietary pattern					
Model 1		1.00	0.98 (0.81–1.19)	1.05 (0.87–1.28)	0.600		1.09 (0.90–1.31)	1.06 (0.87–1.28)	0.566	
Model 2		1.00	1.00 (0.81–1.23)	1.04 (0.85–1.29)	0.691		1.07 (0.87–1.31)	1.07 (0.87–1.31)	0.546	
Model 3		1.00	1.02 (0.83–1.27)	1.08 (0.87–1.34)	0.498	9565	1.11 (0.90–1.38)	1.11 (0.90–1.38)	0.337	9564
					Modern dietary pattern					
Model 1		1.00	1.04 (0.86–1.25)	1.19 (0.98–1.44)	0.083		1.15 (0.95–1.40)	1.20 (0.98–1.45)	0.072	
Model 2		1.00	1.05 (0.85–1.29)	1.18 (0.94–1.48)	0.172		1.19 (0.97–1.46)	1.22 (0.97–1.53)	0.086	
Model 3		1.00	1.02 (0.83–1.26)	1.15 (0.91–1.46)	0.252	9564	1.18 (0.95–1.45)	1.23 (0.97–1.55)	0.084	9562
					Plant-sourced nutrient pattern					
Model 1		1.00	1.08 (0.88–1.33)	1.06 (0.83–1.36)	0.664		1.00 (0.82–1.22)	1.22 (1.00–1.49) *	0.037	
Model 2		1.00	1.16 (0.92–1.46)	1.13 (0.86–1.49)	0.411		1.03 (0.82–1.28)	1.27 (1.02–1.58) *	0.027	
Model 3		1.00	1.15 (0.91–1.46)	1.12 (0.85–1.48)	0.455	9564	1.02 (0.81–1.27)	1.24 (0.99–1.54)	0.051	9561

	HR 95% CI			*P*-trend	AIC	HR 95% CI		*P*-trend	AIC
	T1	T2	T3			T2	T3		
					Animal-sourced nutrient pattern				
Model 1	1.00	1.01 (0.83–1.22)	1.04 (0.83–1.29)	0.747		1.04 (0.86–1.26)	1.09 (0.90–1.32)	0.373	
Model 2	1.00	0.97 (0.79–1.19)	0.99 (0.77–1.26)	0.901		1.10 (0.90–1.35)	1.14 (0.93–1.41)	0.209	
Model 3	1.00	0.95 (0.77–1.18)	0.99 (0.77–1.27)	0.909	9565	1.10 (0.89–1.35)	1.18 (0.95–1.47)	0.126	9563

* $P < 0.05$; ** $P < 0.001$. AIC – Akaike's information criterion; T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence); Model 1: adjusted for sex, age (continuous) and energy intake (continuous). Model 2: additionally adjusted for educational status (low, medium and high), income (low, medium and high), alcohol consumption (none, <1, 1–2, 3–4 per week and daily), smoking (non-smoker and current/ex-smoker), residency (rural and urban) and physical activity level (metabolic equivalent task-hours/week, continuous). Model 3: additionally adjusted for body-mass index (continuous) and high blood pressure (yes/no). *P* for trend was obtained by adjusting the tertiles of the pattern scores as continuous variables.

4. Discussion

Two dietary (traditional and modern) and two nutrient (plant- and animal-sourced) patterns were identified using the CHNS data. In this analysis, with up to 20 years of follow-up, we found that a greater adherence to a modern dietary (characterized by a high intake of fruits, milk, cake, fast foods, eggs, soy milk and deep fried products) and/or animal-sourced nutrient patterns (a high intake of protein, fat, vitamins A, B_2 and E, and low intake of potassium, calcium, magnesium and vitamin C) was prospectively associated with an increased risk of fractures among adults. In this study, we demonstrated that, compared to a single three-day 24-h dietary assessment method (at baseline or recent), a repeated three-day 24-h dietary assessment provided a stronger estimate of the association with fracture risk as it reflected a usual food intake more closely. This highlights the problem of using a baseline or a recent dietary exposure to estimate the association between diet and fracture in cohort studies which could provide a biased estimate leading to a wrong conclusion.

4.1. Comparison with other studies

Studies among men and women in the US and Sweden found a lower risk of hip fractures among those who had a higher adherence to a Mediterranean diet [31, 204]. Studies have also shown the benefit of vegetables, legumes and whole grains as part of a healthy dietary pattern in maintaining bone mass and preventing osteoporotic fractures [204, 281, 412]. Thus, a low intake of vegetables, legumes and whole grains could explain the positive association between the modern pattern and fracture in our study. In studies among Chinese populations, it has also been found that favourable dietary patterns (a high intake of FV, nuts, soy and seafood) were inversely associated with hip fractures [408, 409]. It is of note however that the intake of milk in our study was highly correlated with the

modern dietary pattern, although milk is largely considered to be an essential part of a favourable dietary pattern for bone health in many studies [287, 288]. However, the overall milk consumption among the study participants in the current study was very low (5.8 millilitre/day) which may contribute to the findings.

4.2. Potential mechanisms

The increased risk of fracture associated with a higher adherence to the modern dietary pattern could be explained by the direct effect of food groups on bone mass and/or indirect influence on skeletal muscle. Previous studies have shown inverse association between modern and processed dietary patterns with bone mass [26, 378], which consequently lead to a higher risk of osteoporotic fractures. These dietary patterns are mainly loaded with a high intake of suboptimal diets, such as energy-dense or nutrient-poor foods [157, 248], which have been associated with reduced bone mass. On the other hand, risk factors for fractures are multifaceted and might not necessarily be associated with a lower bone mass [419].

Because of the fact that fractures could be related with falls as a result of a lower muscle mass/strength [413], diets could have also indirect effect on fracture risk through their impact on muscle. For instance, a 'Western' type of dietary pattern (characterized by high intake of red meats, potato, gravy and butter) was negatively associated with muscle strength [420]. Similarly, a higher risk of fall-related fractures was reported among elderly Japanese who had a higher adherence to a "meat" based dietary pattern [421]. On the other hand, a higher adherence to Mediterranean diet was associated with a lower risk of frailty [422].

The effect of dietary patterns on body acid-base balance [267] and inflammation [36] could be another possible indirect pathway through which dietary patterns affect bone

mass, and eventually fracture risk. In people with a low intake of calcium, a higher dietary acid load was associated with a lower BMD [423]. A higher net endogenous acid production would result in decreased extracellular pH, creating an acidic environment. This phenomenon could facilitate the release of calcium from bone matrix in order to buffer the higher acid levels. In addition, it might also increase osteoclast and decrease osteoblast activities (i.e., facilitated bone resorption), eventually resulting in increased calcium excretion [424] and reduced bone mass [425]. However, the epidemiological evidence remains inconclusive, pending further investigation [426]. In recent studies, pro-inflammatory diets were associated with a lower BMD [427] and an increased risk of hip fractures in women [36]. In addition to non-nutritive substances in dietary patterns, the combination of nutrients may take a major role on fracture risks directly through affecting bone mass or indirectly through increasing body acid and/or inflammation.

In the current study, we found that a higher adherence to an animal-sourced nutrient pattern was associated with a higher risk of fractures. The factor scores of this nutrient pattern were also positively and moderately correlated with the scores of the modern dietary pattern. A nutrient pattern characterized by a high intake of calcium, phosphorous, vitamin B_{12}, proteins and saturated fats was related with a lower risk of wrist and hip fracture among French older people (aged 65 and over) [94]. The difference in calcium, phosphorous, protein and fat content of nutrient patterns associated with the fracture risk in this and our current studies could be explained by the general difference in population groups, such as age, eating habit and race. Protein (93.5 g/day) and fat (51.9 g/day) intake was found to be higher among study participants in the third tertile of the animal-sourced nutrient pattern compared to those in the first tertile in the current study. Although the evidence on the effect of high protein intake on bone mass is inconsistent [151, 428, 429], it is believed that higher protein intake can lead to calciuria [152], causing bone

resorption. In addition, a low-fat diet was associated with reduced risk of multiple falls among postmenopausal women [412].

Inflammation of the body can also increase bone resorption and decrease bone formation through various pathways [430] making the bone more susceptible to a low-trauma fracture. A study among Australian men found that animal-sourced nutrient pattern was associated with enhanced inflammatory markers [385]. In another prospective cohort study in the US, increased inflammatory markers were positively associated with incident fracture risks among older men and women [431], further supporting the fact that the pro-inflammatory effect of the animal-sourced nutrient pattern in the current study may explain the positive association with fracture risks. In line with our study, a higher adherence to an inflammatory diet (mainly containing high animal-sourced nutrients) was associated with an increased risk of hip fracture in younger women (less than 63 years) [36]. This suggests that clinical and public health interventions and strategies should consider dietary approaches in prevention of fractures among high risk adults.

Interactions between dietary and nutrient patterns and other covariates in predicting fracture risk were not found. Stratified analyses by sex and age, however, gave a slightly different result. Modern dietary and animal-sourced patterns were significantly associated with fracture risks in males, but not in females (although the association remained in the same direction). In females, a higher adherence to a plant-sourced nutrient pattern was significantly associated with an increased risk of fractures. Although the direction of association remained the same in those aged less than 50 years, the association between the modern dietary pattern and fracture risk was significant only in those aged 50 years or over. The difference in the associations may be attributable to differences in body physiology (including bone physiology), hormonal changes, change in dietary habit

and/or a low number of fracture cases in the stratified analyses. In addition, causes (low-energy vs. high-energy injury) of fractures might be different in different age categories and sexes. In this regard, our study showed that the risk of fracture was higher in males than females at a younger age while the vice versa was found for the older age bracket. This may indicate that most of the fractures in young males could be due to high-energy traumas. Further research is warranted in this regard. An animal-sourced nutrient pattern remained significantly and positively associated with fracture risks in both age brackets (<50 and ≥50 years and over).

4.3. Dietary exposure measurement

Our study also demonstrates that the identification of dietary risks of a disease outcome (in this case fracture) using a repeated 24-h dietary recall method is likely to provide a stronger estimate of an association compared to a baseline or recent dietary exposure. Dietary data collected using a repeated three-day 24-h recall method give a better picture of the usual food intake compared to a baseline or a recent dietary exposure using a single three-day 24-h dietary assessment method, which eventually provides a stronger association estimate for a disease outcome [40]. In our study, use of recent or baseline dietary that rely on a static eating behaviours (exposure) underestimated the associations. This is supported by a previous study which used multiple dietary measurements during a follow-up period to assess the effect of dietary fat on coronary heart disease. It was found that this approach provided a better estimate compared to a baseline or recent dietary exposure [418].

It is important to note the following limitations of this study when interpreting the findings. First, data on fractures were self-reported. The dates of the fractures were determined based on participants' recall of ages at which the fractures occurred, which

may be impacted by a recall bias. In addition, the dates of fractures might not be accurate. However, this approach has previously been found to be a feasible alternative to hospital and X-ray records in determining a relative fracture incidence across population subgroups, particularly for recent fractures, in a large cohort study [416]. Secondly, since fractures were not segregated into low- and high-trauma injuries, it was not possible to determine the specific low-trauma trauma fracture cases potentially due to a reduced bone mass. However, a study reported that most fracture cases (58%) in China (2014) were caused by low-trauma injuries (slip, trip, or fall) [88]. Body sites of fractures were also not reported in the survey—fractures of toe, finger, sternum, and clavicle are less likely to be linked with osteoporosis [432, 433]. However, this method of fracture reporting has been used in a previous study [36] and in China the highest incidence rates of fracture occurred on tibia and fibula (0.76 fractures per 1000 people) and radius and ulna (0.63 per 1000 people) [88]. Thirdly, although we adjusted for potential confounders, residual confounding and other confounding from unmeasured lifestyle variables (such as from duration of sleep [44, 88]) are still possible. In addition, not being able to adjust for medication (such as psychoactive medications) and supplement (hormonal and dietary) use could potentially overestimate the associations. However, in China, the proportion of women using, for example, hormonal replacement therapy has previously been reported as being 2.1% [434]. Thus, the effect of this confounder may be small.

5. Conclusions

In summary, modern dietary and animal-sourced nutrient patterns are prospectively associated with an increased risk of fractures. This study highlights the important role of diet and nutrients in fracture risk among adults. Clinical and public health interventions that target increasing or maintaining bone mass and lowering fracture risks should take

into account dietary approaches as important strategies at individual and population levels. Repeated measures of dietary exposure provide a stronger estimate in determining an association with a disease outcome. On the contrary, using a baseline or a recent exposure of dietary score to estimate the association between diet and a disease outcome in prospective studies could provide a biased estimate.

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Author contributions

Y.A.M., T.K.G., R.A. and Z.S. conceived the study. Y.A.M. and Z.S. conducted the analyses. Y.A.M. wrote all drafts of the paper. T.K.G., A.W.T., S.L.A., R.A. and Z.S. critically reviewed and commented on all drafts. All authors read and approved the final manuscript.

Conflicts of interest

The authors declare no conflict of interest.

CHAPTER 8 DIETARY PATTERN ANALYSIS METHODS

8.1 Publication

Melaku YA, Gill TK, Taylor AW, Adams R, Shi Z: A comparison of principal component analysis, partial least-squares and reduced-rank regressions in the identification of dietary patterns associated with bone mass in aging Australians. Eur J Nutr 2017; DOI: 10.1007/s00394-017-1478-z.

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Contribution to the Paper	Conception and design, statistical analysis, interpretation of data, manuscript preparation, contribution to the materials/analysis tools and critical revision and editing of the manuscript		
Overall percentage (%)	50%		
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.		
Signature		Date	23/07/2018

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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A comparison of principal component analysis, partial least-squares and reduced-rank regressions in the identification of dietary patterns associated with bone mass in ageing Australians

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Abstract

Purpose

The relative advantages of dietary analysis methods, particularly in identifying dietary patterns associated with bone mass, have not been investigated. We evaluated principal component analysis (PCA), partial least-squares (PLS) and reduced-rank regressions (RRR) in determining dietary patterns associated with bone mass.

Methods

Data from 1182 study participants (45.9% males; aged 50 years and above) from the North West Adelaide Health Study were used. Dietary data were collected using a food frequency questionnaire. Dietary patterns were constructed using PCA, PLS and RRR and compared based on the performance to identify plausible patterns associated with bone mineral density (BMD) and content (BMC).

Results

PCA, PLS and RRR identified two, four and four dietary patterns, respectively. All methods identified similar patterns for the first two factors (factor 1, 'prudent' and factor 2, 'Western' patterns). Three, one and none of the patterns derived by RRR, PLS and PCA were significantly associated with bone mass, respectively. The 'prudent' and dairy (factor 3) patterns determined by RRR were positively and significantly associated with BMD and BMC. Vegetables and fruit pattern (factor 4) of PLS and RRR was negatively and significantly associated with BMD and BMC, respectively.

Conclusions

RRR was found to be more appropriate in identifying more (plausible) dietary patterns that are associated with bone mass than PCA and PLS. Nevertheless, the advantage of RRR over the other two methods (PCA and PLS) should be confirmed in future studies.

Keywords

Dietary analysis methods, principal component analysis, partial least-squares regression, reduced-rank regression, bone mass, ageing population

Introduction

Assessment of food habits and nutrients and their associations with a specific disease outcome can be determined based on pre-existing evidence, that is, *a priori* methods. This is usually done by constructing scores and indices based on food guidelines and nutritional recommendations [435]. This method is useful to evaluate adherence and the magnitude of the effect of dietary recommendations on disease outcomes [436]. However, because it is only based on a prior selection of foods and nutrients, it does not consider and describe the overall dietary patterns of the population group under the study [259, 436]. Therefore, methods to explore the association between overall diet intake and disease outcomes through a systematic consideration of the correlations between components are increasingly used [51]. Such methods are referred to as *a posteriori*—a method based on collected data (data-driven) in a specific group of population.

There are two main approaches to *a posterior*i methods [51]. In the first approach, the dietary variables are combined into fewer variables (or factors) based on their correlation, and the latent variables are virtually constructed to represent the original dietary variables [294]. PCA and explanatory factor analysis (EFA) are examples of these approaches [51]. The second approach is cluster analysis, where unlike PCA and EFA approaches, non-overlapping clusters of individuals are constructed [437].

Another approach in dietary data analysis is a hybrid method of the *a priori* and *a posteriori* methods. In this approach, response variables that mediate dietary risks and outcomes are determined based on a "priori" knowledge. These variables can be biomarkers, nutrient intakes or an overall dietary quality that are known to have association with the outcome of interest [259]. These methods mathematically work by creating a linear combination of the predictors (food groups) and response variables [259,

438]. The two most common examples of these methods are PLS and RRR. The two methods are considered as alternatives for PCA [259].

Studies have reported different recommendations in terms of the utility of the methods [53, 259]. When investigating the association between dietary patterns and bone mass, most studies have used *a posteriori* methods, although hybrid methods are being increasingly used in recent years [275, 358]. However, the relative advantages and a thorough evaluation of the methods used to identify dietary patterns associated with bone mass have not been investigated. Thus, for the first time, we evaluated the three dietary analysis methods (PCA, PLS and RRR), in this study, to determine dietary patterns associated with bone mass among ageing Australian population.

Methods

Detailed methods are presented previously [378]; however, some of the important issues in this specific study are highlighted below.

Study design and population

The study population was selected from participants of the NWAHS, which is a community-based cohort study. Three major stages of data collection have been conducted between 1999 and 2003, 2004 and 2006 and 2008 and 2010. In the cohort, data were collected using self-complete questionnaire, CATI and clinical assessments. Adults (both sexes and aged 18 years and above; n = 4056) from randomly selected households were recruited at the inception of the study [73]. The focus of this specific study is the BMD and BMC collected at Stage 2 from those aged 50 years and over (2004–2006, n = 1,588). Data related to both BMD/BMC and diet were provided in a total of 1182 adults (545 males, 45.9%) aged 50 years and above. Dietary data were collected at Stage

3 (2008–2010, *n* = 2500) (Figure 8.1).

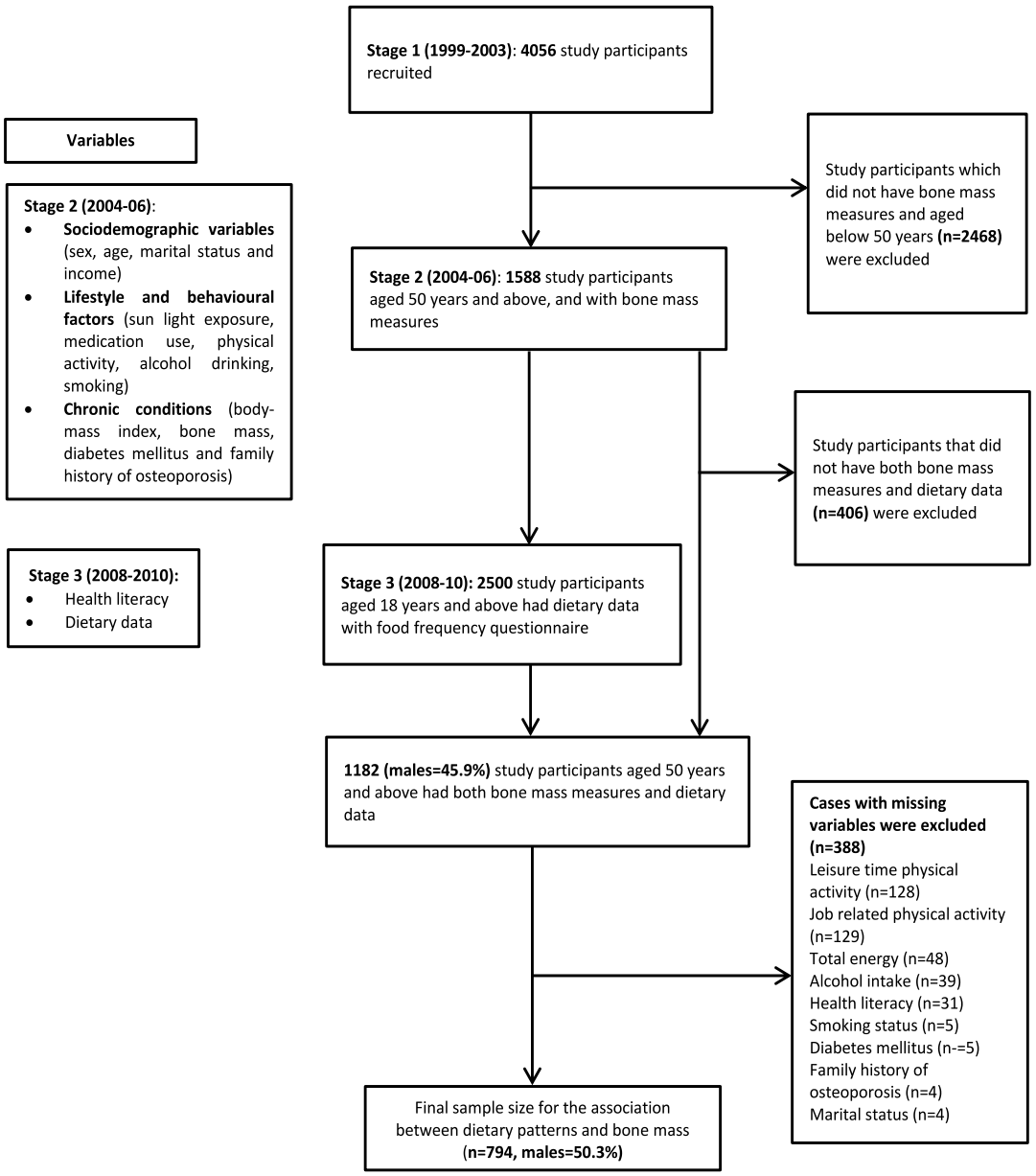

Figure 8.1 Sampling description of study participants with dietary intake and bone mass records, the North West Adelaide Health Study, South Australia

Diet and other covariates assessment

Dietary intake was assessed using the DQES-V3.1 from Cancer Council of Victoria [390]. The questionnaire assesses intake of foods and beverages over the previous 12 months. Analyses of total daily intake of food items and nutrients were performed using the

Australian NUTTAB 95 (Food Standards Australia New Zealand, Canberra, 1995) food composition database. For each study participant, the amount of food items consumed per day was calculated in grams and aggregated into 39 food groups [295].

At Stage 2 of the NWAHS, sex, age and family history of osteoporosis were assessed. Annual household income was determined and categorized as up to $20,000, $20,001–$40,000, $40,001–$60,000, and more than $60,000. Marital status was classified as married or living together with partner (in union), separated/divorced, widowed or never married. Alcohol risk was assessed using frequency and number of standard drinks [361]. Smoking was defined as non-smokers, ex-smokers and current smokers. Height and weight of the study participants were measured during the clinic assessment. BMI was calculated and classified based on the WHO standard [362]. Participants with diabetes were identified by either self-report or laboratory diagnosis using blood samples collected at the clinic visit.

Assessment of leisure time PAL was undertaken using the Australian NHS questions [363], considering the number of times a person exercised in the last two weeks and the total amount of time spent walking or doing moderate or vigorous exercise at Stage 2. Job-related PAL was also assessed based on the type of profession. Detailed methods of both forms of PAL are published elsewhere [364]. Medication use (for hypertension, high cholesterol, mental health problems and asthma) and sun light exposure were also assessed at this stage.

At Stage 3, health literacy was assessed using the Newest Vital Sign test tool [365]. For 31 cases with missing values, we used data collected from the sTOFHLA tool [366], which was also collected at this stage. Health literacy was classified as limited or adequate.

The number of missing values for each variable includes smoking status (n = 5 cases), alcohol risk (n = 39), diabetes (n = 5), family history of osteoporosis (n = 4), marital status (4), leisure time PAL (n = 128), job-related PAL (n = 129), total energy (n = 48) and health literacy (n = 31). We excluded all cases which had at least one missing value of these variables from the analysis (n = 388, 32.8%).

Prodigy and DPX + DXA (GE Lunar, Madison, WI) was used to assess whole body BMD/BMC as part of the clinic visit at Stage 2. Details of the DXA measurement procedures can be found elsewhere [367]. BMD and BMC were reported as grams/cm^2 and grams, respectively. T-scores for BMD were also reported for each study participant. Study participants who were osteopenic or osteoporotic (T-scores of less than -1) [58] were classified as having low BMD.

Response variables for PLS and RRR analyses

To identify potential response variables, we reviewed previously published studies and chose the dietary intake of four nutrients (protein, calcium, potassium and vitamin D). These nutrients have been strongly linked with bone mass [43, 153, 439-441]. Diet was also found to be a considerable source of vitamin D in the study population [mean intake = 3.5 mcg/day (140 international unit/day)]. We calculated the percentage of energy from total protein intake, and calcium, potassium and vitamin D densities and used these values as response variables. The percentage of energy from total protein intake was calculated as follows: total energy intake from protein (kJ) divided by total energy intake, multiplied by 100. Calcium, potassium and vitamin D densities were expressed as absolute intakes of calcium (mg/day), potassium (mg/day) and vitamin D (ng/day), respectively, divided by total daily energy intake (kJ/d) [358].

Statistical analysis

Dietary analysis

To reflect the larger population dietary intake, factor scores and dietary patterns were calculated and constructed for 2453 study participants after excluding 47 participants who had a significant amount of missing dietary data. Data reduction techniques using PCA, PLS and RRR were used to identify dietary patterns out of 39 food groups. Using PCA, a similar number of factors (39 factors) to food groups were produced; however, we retained four factors, of which the first two were chosen based on scree plot, an eigenvalue (>1) and interpretability. These two factors were used to investigate the association between dietary patterns and bone mass as only these gave meaningful interpretations of the dietary groups [378]. Varimax rotation was applied, and sample adequacy was checked using the KMO test. Linear regression analysis of the factor scores and response variables described above (percentage of energy from total protein intake, calcium, potassium and vitamin D densities) was used to obtain the variance of the response variables explained by the two factors of PCA. An explained variance measures the proportion of variation of a dietary pattern that can be attributable to the food groups or response variables (in this case, nutrients).

The *PROC PLS* statement in SAS (SAS Institute Inc., Cary, NC, USA) was used to conduct both PLS and RRR analysis, defining each in turn in the "method=" [259]. In the analysis, we used a dietary data file containing the 39 food groups coded as *fg1, fg2…fg39* and the four response variables. Four factors were specified and retained in each method.

Different algorisms are applied to construct the scores in each of the three methods. For each method, we calculated the continuous factor scores [the linear functions of food groups (predictors)] and response scores were used in the subsequent statistical analyses

and interpretations.

In PCA, the factors explain as much variation as possible of the food groups [438]. Unlike PCA, RRR uses a covariance matrix of responses and predictors (food groups) in calculating the scores. PLS combines the two methods and produces scores considering both the predictor (food group) and response matrixes simultaneously [259]. In this case, the explained variance of both the response variables and food groups is expected to be between the other two methods. Tertiles [T1 (lowest intake), T2 and T3 (highest intake)] of each of the factor scores were constructed. Factor loadings of each food group on the factors were also calculated. Factor loadings are the correlation between the factors and food groups. The proportion of factor-specific and all factor variances across all three methods that explain the response variables and food groups was also determined. Correlations (response scores) between the factors of each method and the response variables were computed. Pearson correlation coefficients for the response variables were also calculated.

Descriptive analysis and modelling

Mean and standard deviation (for continuous normally distributed variables), median and interquartile ranges (for continuous non-normally distributed variables) and proportions (for categorical variables) were calculated. The tertiles of factor scores produced by PCA, PLS, and RRR analyses were used to assess the association of dietary patterns with bone mass. We applied linear regression models to evaluate the associations between tertiles of each factor scores, and BMD and BMC. The initial models (model 1) were adjusted for sex and age. Model 2 was additionally adjusted for socio-economic and lifestyle factors (income, marital status, smoking, alcohol intake, health literacy, leisure time and job-related PAL), chronic conditions (diabetes mellitus, family history of osteoporosis

and BMI) and height (BMC). The last model (model 3) was additionally adjusted for total energy intake to assess the potential confounding effect of energy intake in the associations. To compare the relative quality of the models, AIC was determined for each model.

Trend of associations across tertiles of each factor was assessed by entering the tertiles of factor scores as continuous variables in the models. Additional adjustments for medications, season of DXA measurement, sunlight exposure and dietary supplements did not materially affect estimates and were not retained in the final models. PLS and RRR analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, North Carolina). All other statistical analyses were conducted with Stata/SE version 14.1 (StataCorp, College Station, TX, USA).

Comparison of methods

Previous studies have used different approaches to evaluate and compare dietary assessment methods [53, 259]. In this study, we compared PCA, PLS and RRR methods mainly based on the relative loading of food groups within each dietary pattern and its association with bone mass [442]. We additionally evaluated the methods based on the magnitude of variances of each method that explained the response variables and food groups.

Ethical considerations

Ethics approval for the NWAHS was provided by The Queen Elizabeth Hospital, Ethics of Human Research Committee. Participants provided written informed consent.

Results

A total of 1182 (45.9%, males) study participants provided dietary and BMD data. In the multivariable analysis, we excluded those who had missing data from covariates, leaving a total of 794 (67.2%) of participants. The median age of the participants was 62 years (interquartile range = 56.0, 69.0). One-fifth (19.2%) of the participants reported a family history of osteoporosis (Table 8.1).

Dietary patterns

Food groups are provided in the Supplementary Table 5.1 and Supplementary Table 8.1. Factor loadings (standardized correlations of the food groups with the dietary patterns) derived by PCA, PLS and RRR methods are shown in Figure 8.2. The first factor (dairy, vegetables and fruit pattern—'prudent' pattern) was similar across the three methods and was characterized primarily by a high intake of medium fat dairy, vegetables and fish and, a low intake of soft drinks, processed meat and take away foods. Factor 2 of each of the three methods was also similar in terms of the constituents of the food groups. Factor 2 ('Western' pattern) of the PCA method was characterized by a high intake of processed meat, take away foods, white bread, red meat and soft drinks and a low intake of dairy products and nuts. Factor 2 ('Western' pattern) of the other two methods was characterized by a high consumption of animal foods (poultry, eggs, red and processed meat, fish and high fat dairy) and a low intake of medium fat dairy, fruit and nuts.

Table 8.1 Participants' characteristics of adults 50 years and above, South Australia (n = 1182)

Characteristics	Level	Value
N		1182
sex	Male	543 (45.9%)
Age category (years)	50-59 years	513 (43.4%)
	60-69 years	400 (33.8%)
	70 and above	269 (22.8%)
Age in years, median (IQR)		62.0 (56.0, 69.0)
Monthly income category	Up to $20,000	352 (29.8%)
	$20,001-$40,000	361 (30.5%)
	$40,001-$60,000	203 (17.2%)
	More than $60,000	206 (17.4%)
	Missing	60 (5.1%)
Marital status	Married or living with a partner	779 (65.9%)
	Separated / Divorced	196 (16.6%)
	Widowed	154 (13.0%)
	Never married	45 (3.8%)
	Missing	8 (0.7%)
Smoking status	Non smoker	581 (49.2%)
	Ex-smoker	476 (40.3%)
	Current smoker	120 (10.2%)
	Missing	5 (0.4%)
Alcohol risk level	Non-drinkers, no risk	609 (51.5%)
	Low risk	474 (40.1%)
	Intermediate to very high risk	60 (5.1%)
	Missing	39 (3.3%)
Leisure time PAL	Sedentary/low	667 (56.4%)
	Moderate/high	387 (32.7%)
	Missing	128 (10.8%)
Work related PAL	Sedentary/light	581 (49.2%)
	Medium/heavy	472 (39.9%)
	Missing	129 (10.9%)
Health literacy	Limited	402 (34.0%)
	Adequate	715 (60.5%)
	Missing	65 (5.5%)
Diabetes mellitus	no	1040 (88.0%)
	yes	137 (11.6%)
	Missing	5 (0.4%)
Family history of osteoporosis	Yes	227 (19.2%)
	No	951 (80.5%)
	Missing	4 (0.3%)
Bone mineral category	Normal	299 (25.3%)
	Pre-obese	524 (44.3%)
	Obese	359 (30.4%)
Body mass index, mean (SD) (kg/m^2)		28.2 (4.7)
Total energy, mean (SD), (kJ/day)		8665.4 (2611.3)
Percent of energy from protein, mean (SD)		18.6 (3.3)
Protein (g/d), mean (SD)		94.5 (34.0)
Calcium density, mean (SD), (mg/kJ/day)		0.4 (0.1)
Calcium (mg/d), mean (SD)		878.6 (329.1)
Potassium density, mean (SD), (mg/kJ/day)		1.9 (0.4)
Potassium (mg/d), mean (SD)		3919.9 (1452.4)
Vitamin D density, mean (SD), (ng/kJ/day)		1.7 (0.9)
Vitamin D (mcg/d), mean (SD)		3.5 (2.0)
Bone mineral density, mean (SD) (mg/cm^2)		1195.6 (118.4)
DXA T-score, mean (SD)		0.34 (1.32)
Bone mineral content, mean (SD) (g)		2755.4 (550.8)
Low bone mineral density		188 (15.9%)
Height, mean (SD) (cm)		166.7 (9.5)

DXA – Dual-energy X-ray absorptiometry; IQR – interquartile range; PAL – physical activity level; SD-standard deviation

Food groups	Principal component analysis		Partial least-squares				Reduced-rank regression			
	'Prudent' pattern	'Western' pattern	'Prudent' pattern	'Western' pattern	Dairy pattern	Vegetables and fruit pattern	'Prudent' pattern	'Western' pattern	Dairy pattern	Vegetables and fruit
Medium fat dairy	0.39	-0.05	0.33	-0.19	0.35	0.03	0.57	-0.39	0.04	-0.3
Fruity vegetables	0.75	0.07	0.33	0.01	-0.31	0.21	0.18	-0.16	-0.09	0.35
Stalk vegetables	0.58	-0.05	0.28	0.07	-0.27	0.11	0.14	-0.07	-0.06	0.23
Leafy vegetables	0.61	-0.01	0.27	0.10	-0.26	0.14	0.17	-0.07	-0.08	0.28
Cabbages	0.53	0.12	0.27	0.04	-0.22	0.10	0.20	-0.09	-0.08	0.28
Root vegetables	0.54	0.16	0.26	-0.06	-0.25	0.12	0.13	-0.14	-0.05	0.26
Other fruits	0.55	0.06	0.23	-0.15	-0.27	0.08	0.05	-0.15	0.05	0.29
Potato without fat	0.28	0.18	0.15	-0.07	-0.13	0.03	0.08	-0.08	-0.01	0.15
Tea and water	0.37	0.42	0.13	-0.10	-0.14	0.05	0.12	-0.11	0.09	0.16
Citrus fruit	0.28	-0.08	0.13	-0.09	-0.15	0.03	0.05	-0.08	0.02	0.15
Nuts dairy	0.39	-0.13	0.12	-0.16	-0.15	0.14	-0.05	-0.14	0.03	0.06
Fish	0.36	0.14	0.12	0.34	-0.18	0.03	0.18	0.39	-0.17	0.15
Legumes	0.31	0.02	0.10	-0.01	-0.14	0.09	0.05	-0.05	-0.03	0.13
High fibre cereal	0.09	-0.04	0.08	0.03	0.02	-0.02	0.08	-0.03	0.00	0.03
Sugar	0.46	0.54	0.07	-0.33	-0.17	0.12	-0.01	-0.17	0.27	0.01
Tomato sauce	0.28	0.28	0.07	0.09	-0.17	0.17	0.04	-0.01	-0.08	0.15
High fibre bread	0.24	0.16	0.06	-0.16	-0.15	0.04	-0.08	-0.02	0.10	-0.06
Other cereal	0.17	0.18	0.06	-0.14	-0.06	-0.01	0.00	-0.06	0.07	-0.03
Coffee	-0.02	0.17	0.05	0.08	0.01	-0.11	0.18	-0.02	0.01	0.25
Poultry	0.18	0.28	0.04	0.37	0.10	0.33	0.11	0.1	-0.48	-0.10
Wine	0.00	0.01	0.01	0.11	-0.04	0.14	-0.03	0	-0.10	0.06
Juice	0.18	0.25	0.00	-0.11	-0.12	0.11	-0.05	-0.06	0.00	0.11
Eggs	0.08	0.19	-0.02	0.14	-0.13	0.02	-0.01	0.16	-0.05	0.00
Flavoured milk	0.01	0.06	-0.03	-0.15	0.15	-0.06	0.07	-0.1	0.15	-0.24
Saturated spread	0.01	0.14	-0.04	-0.12	-0.08	0.06	-0.12	-0.06	0.06	-0.05
Jam and vegemite	0.13	0.49	-0.04	-0.18	-0.18	0.18	-0.13	-0.04	0.02	0.05
Potato with fat	-0.06	0.24	-0.04	-0.07	-0.05	0.05	-0.07	-0.03	0.02	0.04
Red meat	0.09	0.44	-0.04	0.38	0.04	0.39	0.02	0.17	-0.57	-0.11
Pasta and rice	0.13	0.01	-0.04	-0.04	-0.10	0.18	-0.16	-0.02	-0.04	-0.06
peanut butter	0.13	0.20	-0.05	-0.15	-0.10	0.18	-0.15	-0.04	-0.01	-0.06
Spirits	-0.09	0.04	-0.07	0.07	0.04	-0.02	0.00	0.07	-0.02	-0.04
Snacks	0.02	0.54	-0.13	-0.28	-0.05	0.28	-0.29	-0.11	0.08	-0.17
Beer	-0.13	0.34	-0.16	0.07	-0.06	0.07	-0.15	0.1	-0.02	-0.04
Unsaturated spread	-0.09	0.43	-0.16	-0.10	-0.12	0.05	-0.20	0.13	0.11	-0.09
Soft drinks	-0.15	0.32	-0.17	-0.13	0.03	0.11	-0.21	-0.01	0.02	-0.14
Processed meat	-0.06	0.59	-0.18	0.14	-0.01	0.31	-0.14	0.15	-0.22	-0.14
Take away foods	-0.13	0.51	-0.22	-0.04	-0.03	0.23	-0.22	0.08	-0.08	-0.14
High fat dairy	-0.23	0.19	-0.22	0.19	-0.29	-0.40	-0.01	0.6	0.40	0.05
White bread	-0.31	0.31	-0.25	-0.04	-0.05	0.05	-0.27	0.11	0.05	-0.12

Figure 8.2 Factor loadings of food groups in dietary patterns identified using principal component analysis, partial least-squares and reduced-rank regressions, the North West Adelaide Health Study, South Australia (*n* = 2453)

[The colour gradation denotes the strength and direction of the correlation between the food groups and the dietary patterns. Deep green colour represents a relatively higher correlation (a higher intake) of the food groups with the corresponding dietary patterns. Deep red represents relatively a lower correlation (a lower intake) of the food groups with the corresponding patterns.]

Factor 3 (dairy pattern) was generally characterised by a high intake of dairy products; however, a slight difference in food groups was identified using PLS and RRR. Factor 4

(vegetables and fruit pattern) was primarily characterized by a low intake of dairy products and a high consumption of vegetables (Figure 8.2). The intake of major foods and nutrients across tertiles of dietary patterns is provided in the Supplementary Table 8.1, Supplementary Table 8.2 and Supplementary Table 8.3.

Explained variations in response variables and food groups

The two factors of PCA explained 37.1% of the response variable variation (proportion of energy from protein, calcium, potassium and vitamin D densities). Both PLS (75.5%) and RRR (70.6%) explained a larger amount of variation in the response variables. In PLS and RRR, the largest explained variations of responses were observed in vitamin D (65.2%) and calcium (80.0%) densities, respectively. Potassium density was the most explained response in the other two methods (22.7% in PCA and 43.4% in PLS) in the 'prudent' pattern; however, calcium density was the most explained (56.5%) response in RRR (Table 8.2).

Using PLS, 21.1% of variation in predictors (food groups) was found, compared to 16.7% of PCA and 14.0% of RRR. Whereas factor 1 explained 10.3% of variation of predictors in PCA, only 3.4 and 7.3% variations were explained by this factor for RRR and PLS, respectively **(**Table 8.2**)**.

The correlation (response scores) between factors and response variables estimated using PCA, PLS and RRR methods are depicted Figure 8.3. Factor 1 of the PCA was positively correlated with protein energy, calcium and potassium densities. Using PLS, the proportion of energy from protein was positively correlated with all factors. RRR analysis estimated a positive correlation between calcium density and factors 1 and 3. We also found positive and moderate correlations among proportion of energy from protein, calcium and potassium densities (Supplementary Table 8.4).

Table 8.2 Explained variation in responses and food groups in dietary patterns identified using principal component analysis, partial least-squares regression and reduced-rank regression in aging people, South Australia

Dietary pattern	Explained variation in responses															Explained variation in food groups		
	Principal component analysis					Partial least-squares					Reduced-rank regression							
	Energy from protein (%/day)	Calcium density	Potassium density	Vitamin D density	Total	Energy from protein (%/day)	Calcium density	Potassium density	Vitamin D density	Total	Energy from protein (%/day)	Calcium density	Potassium density	Vitamin D density	Total	Partial least-squares	Reduced-rank regression	Principal component analysis
'Prudent'	2.1%	3.8%	22.7%	3.3%	24.9%	7.0%	18.6%	43.4%	6.0%	18.8%	26.2%	56.5%	29.0%	1.4%	28.3%	7.3%	3.4%	10.3%
'Western'	0.0%	7.8%	7.2%	0.4%	12.2%	41.6%	1.0%	0.6%	21.9%	16.3%	5.5%	1.4%	5.6%	65.5%	19.5%	3.9%	3.4%	6.7%
Dairy pattern (Factor 3[a])	(3.8%)[a]	(2.2%)[a]	(0.0%)[a]	(0.0%)[a]	(8.1%)[a]	9.5%	16.1%	0.3%	12.6%	9.6%	36.2%	13.8%	0.0%	5.3%	13.8%	5.4%	3.3%	(5.0%)[a]
Vegetables and fruit pattern (Factor 4[a])	(8.6%)[a]	(2.6%)[a]	(0.0%)[a]	(3.1%)[a]	(17.2%)[a]	3.1%	21.1%	2.8%	24.6%	12.9%	1.5%	8.4%	24.1%	1.9%	9.0%	4.5%	4.0%	(4.4%)[a]
Total	**2.1% (14.5%)[a]**	**11.6% (16.4%)[a]**	**29.9% (29.9%)[a]**	**3.7% (6.8%)[a]**	**37.1% (62.4%)[a]**	**61.1%**	**56.8%**	**47.1%**	**65.2%**	**57.5%**	**69.5%**	**80.0%**	**58.6%**	**74.1%**	**70.6%**	**21.1%**	**14%**	**16.7% (26.3%)[a]**

[a]These are results from factors 3 and 4 of principal component analysis. Factors 3 and 4 of Principal component analysis were neither interpretable nor considered in the analysis that assesses the association between dietary patterns and bone mass. We present the explained variations due to these factors for comparison purpose in brackets.

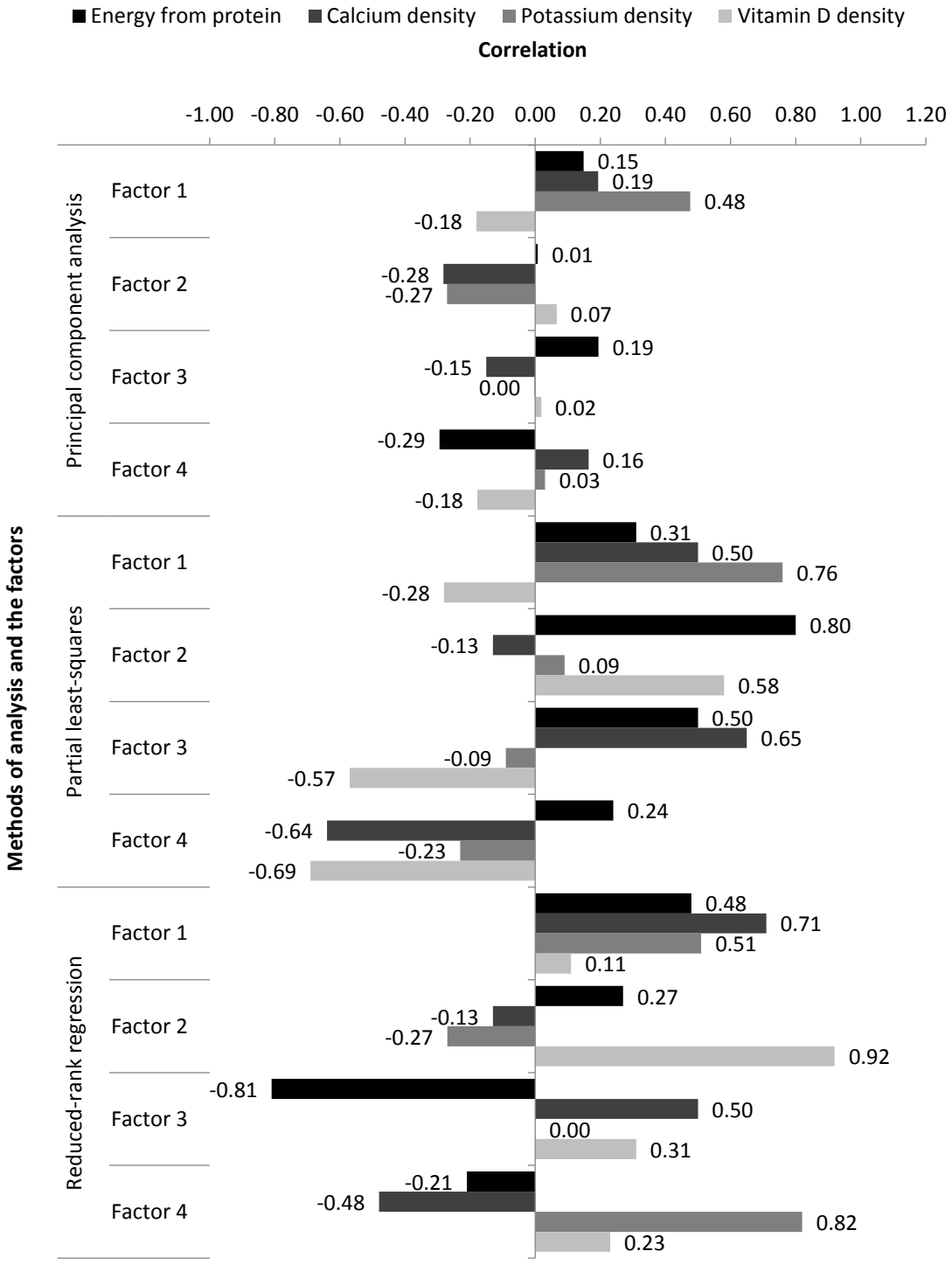

Figure 8.3 Correlation (response scores) between factors and response variables obtained from principal component analysis, partial least-squares and reduced-rank regressions, the North West Adelaide Health Study, South Australia

Dietary patterns and bone mass

Table 8.3 provides the different associations of factors identified by PCA, PLS and RRR with BMD and BMC. In the most adjusted models, none of the factors of PCA was significantly associated with bone mass; and more dietary factors determined by RRR compared to PLS were found to be associated with BMD and BMC. However, in all methods, the coefficients increased across tertiles of the 'prudent' and dairy patterns, and decreased across the tertiles of vegetables and fruit patterns. Participants in T3 of vegetables and fruit pattern determined by PLS had a 17.3 mg/cm^2 (β = −17.29; 95% CI: −34.0, −0.58) decrease in BMD compared to those in T1 (model 3). No significant association of this dietary pattern determined by PLS with BMC was observed.

Table 8.3 Coefficients (β) [95% confidence interval (CI)] for BMD and BMC and tertiles of factors derived using principal component analysis, partial least-squares and reduced-rank regressions (n = 794)

	BMD, mg/cm^2					BMC$^{\#}$, g			
	T_1	T_2	T_3	*P-trend*	AIC	T_2	T_3	*P-trend*	AIC
Principal component analysis									
Model 1									
'Prudent' pattern	Ref.	3.94 (-13.73, 21.60)	9.68 (-7.78, 27.15)	0.276	9601	43.80 (-25.94, 113.55)	44.20 (-24.76, 113.16)	0.210	11782
'Western' pattern	Ref.	-18.14 (-35.90, -0.39)*	0.19 (-18.10, 18.48)	0.962	9597	-71.00 (-140.98, -1.03)*	33.34 (-38.75, 105.43)	0.349	11775
Model 2									
'Prudent' pattern	Ref.	-0.74 (-16.87, 15.39)	8.65 (-7.64, 24.94)	0.293	9438	-9.48 (-62.42, 43.46)	1.23 (-52.28, 54.73)	0.959	11324
'Western' pattern	Ref.	-10.80 (-26.90, 5.30)	2.04 (-14.57, 18.66)	0.794	9437	-25.88 (-78.65, 26.89)	12.91 (-41.62, 67.44)	0.635	11322
Model 3									
'Prudent' pattern	Ref.	-2.50 (-18.91, 13.92)	4.25 (-13.74, 22.24)	0.649	9439	-12.48 (-66.38, 41.41)	-6.30 (-65.40, 52.81)	0.831	11326
'Western' pattern	Ref.	-15.33 (-32.35, 1.68)	-8.45 (-29.46, 12.56)	0.403	9436	-28.41 (-84.28, 27.46)	7.04 (-62.01, 76.10)	0.878	11324
Partial least-square									
Model 1									
'Prudent' pattern	Ref.	-0.32 (-17.75, 17.10)	15.76 (-2.11, 33.63)	0.087	9598	7.62 (-61.15, 76.39)	78.85 (8.33, 149.38)*	0.030	11778
'Western' pattern	Ref.	-9.37 (-26.81, 8.06)	3.70 (-13.69, 21.10)	0.678	9600	-19.18 (-88.14, 49.77)	-5.59 (-74.41, 63.23)	0.873	11784
Dairy pattern	Ref.	9.16 (-8.37, 26.69)	12.09 (-5.34, 29.53)	0.175	9600	17.37 (-51.92, 86.66)	41.49 (-27.42, 110.40)	0.237	11782
Vegetables and fruit pattern	Ref.	8.40 (-9.03, 25.83)	-3.01 (-20.48, 14.47)	0.741	9600	22.17 (-46.68, 91.01)	-30.77 (-99.79, 38.24)	0.385	11782
Model 2									
'Prudent' pattern	Ref.	-6.02 (-21.95, 9.91)	14.87 (-1.69, 31.42)	0.081	9433	-3.73 (-56.08, 48.61)	30.22 (-24.30, 84.74)	0.281	11323
'Western' pattern	Ref.	-13.22 (-28.85, 2.41)	-2.96 (-18.75, 12.82)	0.699	9436	-8.17 (-59.49, 43.15)	11.80 (-40.05, 63.64)	0.660	11324
Dairy pattern	Ref.	-0.19 (-16.08, 15.70)	4.28 (-11.58, 20.15)	0.592	9439	-18.52 (-70.51, 33.48)	16.75 (-35.16, 68.67)	0.515	11323
Vegetables and fruit pattern	Ref.	-1.19 (-17.00, 14.62)	-12.25 (-28.31, 3.81)	0.135	9437	17.62 (-34.12, 69.36)	-41.84 (-94.37, 10.70)	0.119	11319
Model 3									
'Prudent' pattern	Ref.	-6.02 (-21.94, 9.91)	13.71 (-2.95, 30.37)	0.113	9433	-3.73 (-56.11, 48.65)	28.95 (-25.96, 83.85)	0.308	11324
'Western' pattern	Ref.	-11.07 (-27.05, 4.91)	-0.72 (-16.88, 15.44)	0.948	9437	-4.74 (-57.22, 47.74)	15.38 (-37.71, 68.48)	0.564	11325
Dairy pattern	Ref.	4.77 (-12.04, 21.59)	9.47 (-7.40, 26.33)	0.269	9438	-12.65 (-67.78, 42.48)	22.88 (-32.44, 78.20)	0.369	11324
Vegetables and fruit pattern	Ref.	-2.47 (-18.30, 13.36)	-17.29 (-34.00, -0.58)*	0.045	9434	15.12 (-36.76, 67.00)	-51.53 (-106.33, 3.27)	0.073	11319
Reduced-rank regression									
Model 1									
'Prudent' pattern	Ref.	28.02 (10.84, 45.19)**	30.58 (13.07, 48.08)**	0.001	9587	88.92 (20.99, 156.84)*	122.00 (52.78, 191.22)**	0.001	11771
'Western' pattern	Ref.	-12.37 (-29.59, 4.85)	-10.97 (-28.62, 6.67)	0.217	9600	-25.91 (-94.02, 42.20)	-16.01 (-85.80, 53.78)	0.645	11783
Dairy pattern	Ref.	2.66 (-14.95, 20.26)	12.71 (-5.02, 30.45)	0.155	9600	29.12 (-40.38-98.63)	61.13 (-8.89, 131.16)	0.086	11781

	BMD, mg/cm^2					BMC$^{\#}$, g			
	T_1	**T_2**	**T_3**	***P-trend***	**AIC**	**T_2**	**T_3**	***P-trend***	**AIC**
Vegetables and fruit pattern	Ref.	-15.14 (-32.42, 2.13)	-16.36 (-34.11, 1.39)	0.070	9598	-85.92 (-154.08, -17.75)*	-47.21 (-117.25, 22.83)	0.186	11778
Model 2									
'Prudent' pattern	Ref.	20.26 (4.64, 35.88)*	26.84 (10.77, 42.91)**	0.001	9427	45.66 (-5.70, 97.02)	69.40 (16.44, 122.35)*	0.010	11317
'Western' pattern	Ref.	-9.50 (-25.08-6.09)	-8.96 (-24.98, 7.07)	0.268	9438	8.79 (-42.37, 59.95)	14.95 (-37.63, 67.54)	0.576	11324
Dairy pattern	Ref.	6.67 (-9.13, 22.47)	25.46 (9.39, 41.54)**	0.002	9429	14.88 (-37.11, 66.87)	56.34 (3.35, 109.33)*	0.035	11320
Vegetables and fruit pattern	Ref.	-9.00 (-24.61, 6.61)	-10.14 (-26.27, 5.98)	0.218	9438	-53.71 (-104.79, -2.62)*	-27.89 (-80.65, 24.86)	0.302	11320
Model 3									
'Prudent' pattern	Ref.	21.36 (5.70, 37.02)**	26.99 (10.94, 43.04)**	0.001	9427	47.14 (-4.42, 98.70)	69.65 (16.67, 122.63)*	0.009	11319
'Western' pattern	Ref.	-7.55 (-23.39, 8.29)	-8.26 (-24.31, 7.78)	0.312	9438	11.82 (-40.21, 63.86)	16.03 (-36.68, 68.74)	0.550	11326
Dairy pattern	Ref.	6.76 (-9.04, 22.56)	24.58 (8.44, 40.72)**	0.003	9429	14.97 (-37.05, 66.99)	55.49 (2.26, 108.73)*	0.040	11321
Vegetables and fruit pattern	Ref.	-7.96 (-23.62, 7.71)	-10.19 (-26.31, 5.92)	0.215	9437	-52.79 (-104.10, -1.47)*	-27.95 (-80.73, 24.84)	0.301	11322

* $P < 0.05$;** $P < 0.01$; AIC – Akaike's information criterion; BMC - bone mineral content; BMD – bone mineral density; Ref. – reference

Model 1: adjusted for sex and age

Model 2: additionally adjusted for socio-economic and lifestyle factors (smoking, alcohol risk, marital status, income, health literacy, leisure time and job related physical activity levels), chronic conditions (diabetes mellitus, family history of osteoporosis and body mass index)

Model 3: additionally adjusted for total energy intake

$^{\#}$Models 2 and 3 of bone mineral content were additionally adjusted for height (cm).

P for trend was calculated by including the tertiles of the patterns as continuous variables in the models.

In model 3, the ‘prudent’ and dairy patterns of RRR were significantly and positively associated with BMD and BMC. Participants in T2 and T3 of ‘prudent’ pattern had a 21.4 mg/cm^2 (β = 21.36; 95% CI: 5.70, 37.02) and 27.0 mg/cm^2 (β = 26.99; 95% CI: 10.94, 43.04) increased BMD than those in T1, respectively. Those in T3 of dairy pattern had a 24.6 mg/cm^2 (β = 24.58; 95% CI: 8.44, 40.72) higher BMD than those in T1. Compared to those in T1 of ‘prudent’ and dairy patterns, a 69.7 g (β = 69.65; 95% CI: 16.67, 122.63) and a 55.5 g (β = 55.49; 95% CI: 2.26, 108.73) increase in BMC was found among participants in T3, respectively. Vegetables and fruit pattern was negatively and significantly associated with BMC. Participants in T2 of vegetables and fruit pattern had a 52.8 g (β = −52.79; 95% CI: −104.10, −1.47) decrease in BMC compared to those in T1. The AIC was comparable across the corresponding dietary patterns of each of the dietary analysis methods (Table 8.3).

Discussion

We identified and compared dietary patterns (PCA = 2; PLS = 4; RRR = 4 patterns) using three analysis methods. The first pattern (‘prudent’ pattern) of all methods was characterized by a high intake of dairy products, FV. The second pattern (‘Western’ pattern) was characterized by a high intake of fish, poultry, high fat dairy, processed and red meat and a low intake of medium fat dairy and FV. In assessing the association between factors and bone mass, RRR identified more (plausible) factors which were significantly associated with bone mass than the other two methods.

Whereas the ‘prudent’ pattern of RRR was significantly and positively associated with bone mass, the one computed by PCA and PLS was not. This dietary pattern was characterized by a high intake of FV and dairy products. In numerous studies, an intake of these food groups has been linked with a decreased risk of reduced bone mass [43, 288,

392, 443]. However, despite the similarity in contents of the food groups, only the 'prudent' pattern determined by RRR was significantly and positively associated with bone mass. In line with this finding, an absence of association between Mediterranean dietary pattern derived by PCA and indices of bone mass was reported [284]. Furthermore, in the RRR analysis, the correlation of factor scores of 'prudent' pattern with calcium density—which has an indispensable role as a component of bone mass—was the highest (0.71) compared to the other two methods (PCA = 0.19 and PLS = 0.50). As there was a low correlation between the 'prudent' pattern with protein in the PCA and PLS, this may also be an explanation for the absence of a significant positive association, as evidence suggests that the role of calcium on bone mass is enhanced when there is an adequate intake of protein and vice versa [147]. In addition, RRR extracts dietary patterns that combine eating behaviours and the pathway to the outcome (through the response variables) taking into account the physiological importance.

Our findings show that the dairy pattern of RRR was positively associated with bone mass. However, there was a non-significant positive association across the tertiles of the dairy pattern and bone mass with PLS. This could be due to the following reasons. First, a careful observation of the factor loadings of FV showed that the intake of FV in the RRR analysis was not as low as those in PLS. Second, we also found an inverse correlation between potassium and vitamin D densities, and the dairy pattern of PLS. With regard to this, evidence has shown a significant positive role of FV [288] as well as potassium [384] and vitamin D on bone mass. Third, despite these two methods use existing knowledge of the association between nutrients and diseases, the fact that RRR mainly focuses on explaining variation in the responses (nutrients) [259] rather than the food groups can partly explain why the dairy pattern of RRR analysis is significantly associated with bone mass.

Dairy products are the most important food groups which assist in the prevention of osteoporosis [443]. In line with this, our finding also supports the importance of dairy products in building bone mass. The vegetables and fruit pattern of RRR, which is characterized by low consumption of dairy products and high consumption of FV, was negatively and significantly associated with bone mass, highlighting the imperative role of dairy on bone mass. In our previous study, we have also highlighted the importance of dairy products as part of 'prudent' dietary pattern [378].

Information obtained by PCA can give clearer understanding of dietary patterns within a specific population which helps in the formulation of tailored nutrition interventions [444, 445]. However, PCA does not necessarily explain the variation and amount of nutrient intake in the identified patterns, rather it explains the cultural and behavioural aspects of food [40]. The effects of diet could be also mediated through specific nutrients which cannot be captured by this method [442] and could create difficulty in providing a plausible interpretation of findings. In line with this, our results showed that although PCA explains the highest variation in food groups (considering all four factors), no factor was significantly associated with bone mass in the most adjusted models. This supports the view that PCA is unlikely to identify dietary patterns associated with bone mass. The selection of the dietary patterns in PCA is subjective, although aided by methods such as eigenvalues and scree plots. However, these subjective decisions could introduce a bias in identifying the optimal number of dietary patterns. Without due consideration of selecting the optimal number of factors, investigators could also miss disease-related dietary patterns. Thus, it is important to note that critical evaluation is required when selecting the number of patterns using this method.

PLS, a method mathematically thought to be between PCA and RRR, is an alternative

method for deriving dietary patterns. In this method, the covariance matrixes of both response (nutrients) and predictors (food groups) are explained in the latent variables [259]. In the current study, none of the factors identified by PLS was significantly associated with BMD and BMC. Although no study has evaluated dietary analysis methods in association with bone mass, some studies have used these types of analyses for different outcomes. For instance, DiBello et al. claimed that PCA and PLS were found to be more appropriate in identifying dietary patterns associated with CVD [53]. However, it may be that the differences in the findings of our study and this study could be impacted by the disease outcome used and the types of response variables.

In the current study, we found more dietary patterns associated with bone mass using RRR which are plausible in the context of existing evidence. In line with our findings, a study by Hoffmann et al. compared PCA, PLS and RRR in identifying dietary patterns associated with diabetes and concluded that RRR is the most appropriate method in extracting more dietary patterns that are significantly associated with diabetes [259]. RRR is also the most commonly used hybrid method in nutritional epidemiology [275, 358]. The method is better to explain the dietary patterns in the responses [53] and dietary patterns can be evaluated based on the response variables for their plausibility in their association with disease outcomes. Although most of the previous studies used *a posteriori* methods [254, 446], in recent years, RRR is being increasingly used in identifying plausible dietary patterns associated with bone mass [26, 43, 275, 358].

Some limitations should be acknowledged when interpreting the findings. First, dietary information was collected between 2008 and 2010 while bone mass was determined between 2004 and 2006 with a 4.3-year median difference (minimum = 2.8 and maximum = 6.1 years). Although habits of elderly people in relation to the choice of the

food groups have been found to be stable over years [371], eating behaviours of the study participants, particularly change of behaviours towards a healthy pattern among participants diagnosed with chronic diseases, could exist. In addition, since study participants were told the result of DXA measurements, those who knew they had low BMD could also change their behaviour towards a favourable diet. Thus, the association between a dietary pattern and bone mass in our study may be underestimated. To investigate the effect, we did a sensitivity analysis by dividing study participants into two groups based on the median gap of time (i.e. early and late measures of dietary data after bone mass measurement). The estimates of associations for the early measures were either consistent or stronger compared with the whole sample. On the other hand, estimates of participants with late measures were attenuated, further highlighting the underestimated associations between the dietary patterns and bone mass.

Although FFQs have limitations in providing valid dietary information, they are commonly used to measure the usual dietary habits [374]. In this regard, measurement error for every diet component will tend to underestimate the effects in the statistical analysis [292]. However, in the presence of correlation between dietary variables, the direction of bias associated with measurement error is unknown [447, 448]. Furthermore, in ranking intake levels of dietary components, FFQ is relatively robust [40]. Recall bias is also another potential limitation associated with FFQ.

In conclusion, although PCA, PLS and RRR are similar in terms of their mathematical foundations (use of covariance matrix to reduce dimensionality) and extraction of factors that are not correlated, studies have reported different recommendations regarding their utility. In this particular study, RRR was found to be more appropriate in identifying dietary patterns that are associated with bone mass than the other two methods.

Nevertheless, the advantage of RRR over the other two methods (PCA and PLS) should be confirmed in future studies in different settings, population groups, response variables and disease outcomes.

Notes

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Authors' contribution

YAM, TKG, RA and ZS conceived the study. YAM conducted all analyses and wrote all drafts of the paper. ZS assisted with analysis and reviewed and provided comment on all drafts. TKG, AWT and RA reviewed and commented on all drafts. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest

The authors have no financial or personal conflicts of interest to declare.

CHAPTER 9 DISCUSSION, FUTURE DIRECTIONS AND CONCLUSION

9.1 Summary of findings

The findings in this thesis can be summarized in three major parts: 1) the impact of suboptimal diet on the current burden of NCDs; 2) associations of dietary/nutrient patterns with BMD/BMC and fracture risk; 3) evaluation of dietary pattern analysis methods (PCA, PLS and RRR). The results reveal that a fifth of NCD and 42.3% of CVD deaths, and one-tenth of NCD DALYs were attributable to dietary risk factors in Australia. Diet-related burden of diseases is higher in male adults compared to their female counterparts. Diets low in FV, nuts and seeds and whole grains and high sodium were the most common contributors. A low intake of healthy dietary components contributes to the majority of the NCD burden.

The main findings of the association between dietary/nutrient patterns with musculoskeletal outcomes are summarized in Figure 9.1. The findings show that a 'prudent' dietary pattern characterized by a high intake of FV, medium fat diary is beneficial in preventing low BMD. On the other hand, a 'Western' dietary pattern, characterized by a high intake of processed, takeaway foods and soft drinks is associated with low BMD. In general, milk and FV are indispensable components of a dietary pattern that benefits bone mass in aging adults.

A modern dietary pattern (characterized by a high intake of fast food, eggs, deep fried foods, milk and fruit, and a low intake of vegetable and rice) was positively associated with bone fracture in the Chinese population. Although this pattern was positively correlated with milk intake, in general, milk consumption was minimal in the study population. In addition, this pattern was positively correlated with animal-sourced nutrient pattern (a high intake of protein, total fat and riboflavin (B_2); and a low intake of potassium, calcium and vitamin C and fibre) (Figure 9.1).

Figure 9.1 Relative factor loading of dietary and nutrient components of dietary and nutrient patterns and associations with musculoskeletal outcomes

[The colour gradation reflects how big and in which direction was the correlation of the food groups and nutrients with the patterns. A deep green colour refers to a relatively higher correlation or factor loading (higher intake) of the food groups and nutrients within the dietary and nutrient patterns, respectively. A deep red colour refers to a relatively lower correlation or factor loading (a lower intake) of the food groups and nutrients with the patterns. "+" indicates a positive association. "-" indicates a negative association. "Nu" indicates no statistically significant association. BMC – bone mineral content; BMD – bone mineral density; CHNS – Chana Health and Nutrition Survey; NWAHS – North West Adelaide Health Study; PCA – principal component analysis; PLS – partial least-squares; RRR – reduced-rank regression]

It is also important to note some inconsistent findings of the associations between dietary patterns and BMD/BMC when different dietary analysis methods are used. As such, RRR was found to be more appropriate than PCA and PLS in identifying plausible dietary patterns associated with BMD and BMC. Plausible dietary patterns are characterized by a high intake of food items that contain nutrients and non-nutritive substances which are biologically known to have a positive contribution to bone mass.

In addition to dietary patterns that mirror overall sociodemographic, lifestyle and health-related behaviours, exploring the association between nutrient patterns with bone fragility, advances the understanding how diet is related with disease outcomes and helps to mechanistically understand the pathophysiological basis. In this thesis, a mixed-source nutrient pattern (characterized by a high intake of potassium, calcium, retinol and vitamin B_{12}) was shown to be positively associated with BMD. Conversely, an animal-sourced nutrient pattern was positively associated with a greater risk of bone fracture.

Components of dietary and nutrient patterns are also important to further interpret findings and to identify foods and nutrients that are more important in association with bone fragility. Figure 9.1 summarizes the relative contribution of foods and nutrients to dietary and nutrient patterns in studies CHAPTER 5, CHAPTER 6, CHAPTER 7 and CHAPTER 8. In general, while a high intake of dairy, FV, fish and legumes is pivotal for bone health, a high intake of poultry, red and processed meat, snacks, beer, soft drinks, spreads, takeaways foods and white bread are detrimental foods. Any dietary pattern without fruit or/and dairy products is harmful, or not beneficial, to bone health. Food patterns characterised by these food items are nutrient dense. In this thesis, a high intake of phosphorous, potassium, niacin, riboflavin, magnesium, fibre and calcium was positively associated with bone health. The importance of complementing dietary patterns

with nutrient patterns and investigating their associations with bone fragility is also highlighted in further exploring potential mechanism between diet and bone health.

Further, a range of factors, including sociodemographic, lifestyle and chronic conditions, were considered in assessing the association between diet and bone fragility. Figure 9.2 shows the association of diet with BMD, BMC and bone fracture, and clustering with other sociodemographic, lifestyle and chronic conditions. There are also correlations between dietary and nutrient patterns. For instance, there is a positive correlation between 'prudent' dietary and mixed-source nutrient patterns both of which are positively associated with bone mass.

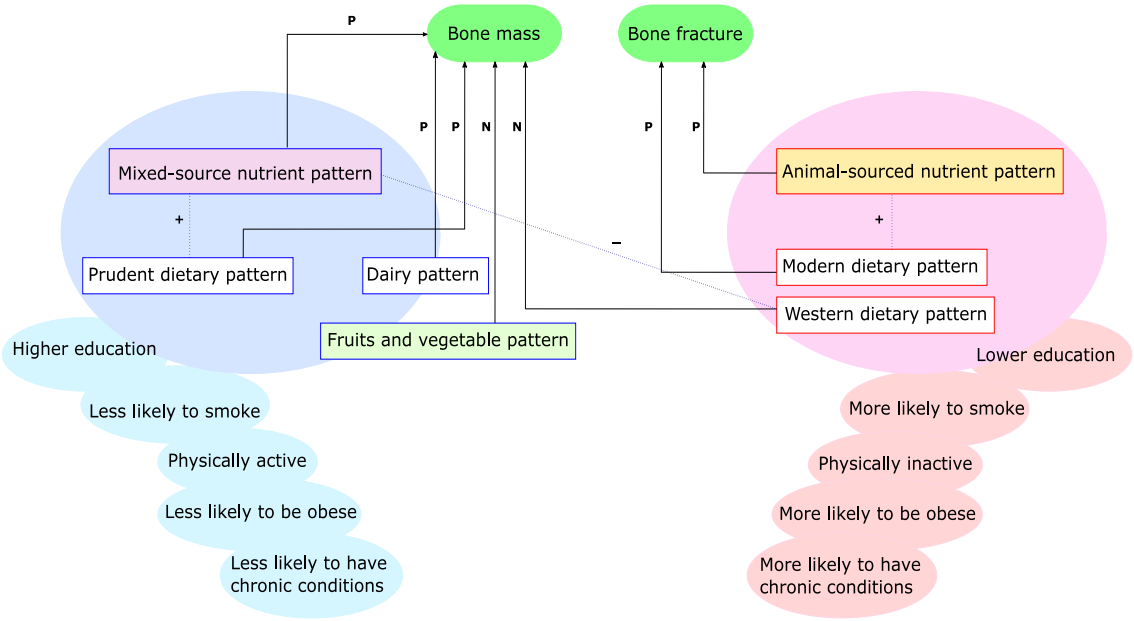

Figure 9.2 Associations of dietary/nutrient patterns with bone mass and bone fracture risk and clustering of sociodemographic and lifestyle factors
["P" indicates a positive association. "N" indicates a negative association. "+" indicates a positive correlation. "-" indicates a negative correlation.]

9.2 Impact of diet on the burden of disease

The study in CHAPTER 4 extends the understanding of the effects of diet on the current burden of disease at community level in terms of disabilities and deaths. There have been a range of population-based interventions to improve dietary habits [336, 344]. However, despite these interventions, this study reveals the high burden of NCDs due to dietary factors. Considering the burden of disease attributable to specific dietary components, designing tailored and comprehensive interventions is needed. These interventions may further create synergy with other interventions, such as measures to reduce metabolic risks of NCDs, because these factors are the ones through which diet can have an association with disease outcomes. Extension and implementation of dietary interventions and strategies, and evaluating the measures used to reduce diet-attributable diseases and economic burden should be the focus areas. Further, I suggest that diet (nutrition) should be considered as a core training program in clinical training and practice for three reasons: 1) diet is a modifiable risk factor; 2) there are effective interventions to improve dietary behaviours at community and individual levels; and 3) dietary risk factors are the main contributors (both at individual and community levels) for the current NCD burden.

9.3 Potential mechanisms for the link between diet and bone fragility

There are two potential mechanisms how diet affects bone fragility: 1) direct effect of foods and nutrients on the bone and/or; 2) indirectly through, a) inflammation, b) endogenous acid load, c) its effect on skeletal muscle mass and strength, d) the link with chronic conditions. Figure 9.3 summarizes these mechanisms.

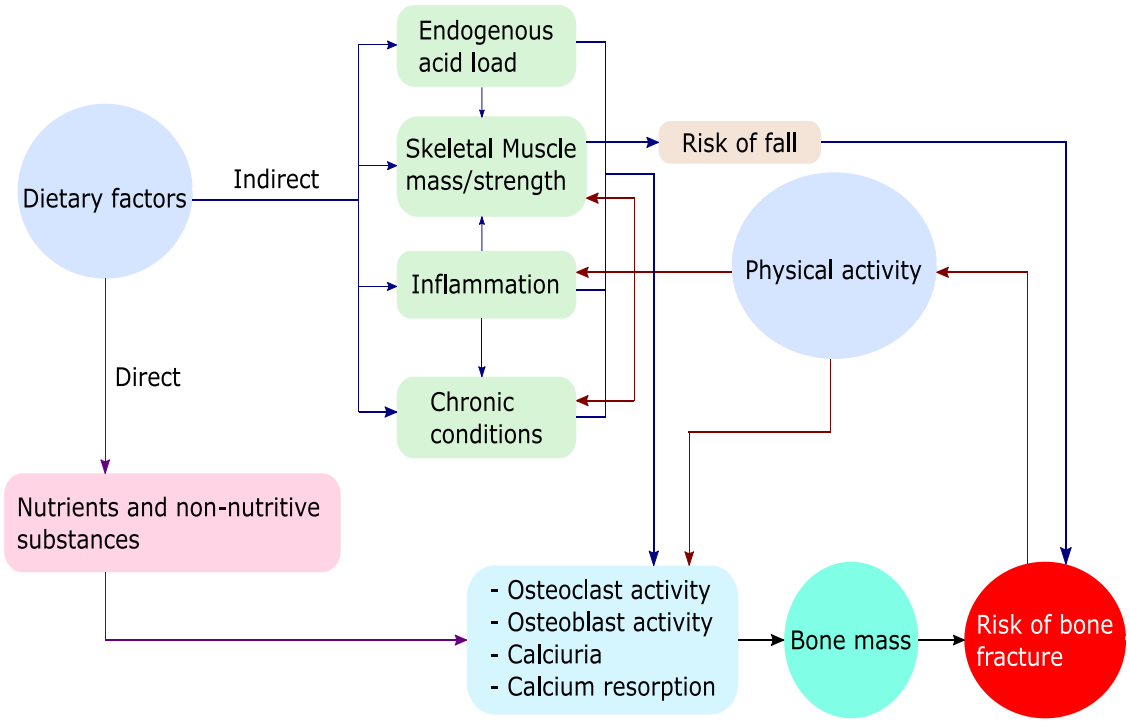

Figure 9.3 Potential mechanisms which diet is associated with bone fragility

9.3.1 Direct effect of diet on bone fragility

Diet plays a direct role in determining bone fragility through nutritive and non-nutritive substances. FV and dairy contain most important nutrients that are indispensable and main constitutes of the bone matrix, such as calcium, vitamin D, potassium, magnesium and phosphorus [182]. These dietary components and nutrients are the core constituents of dietary and nutrient patterns that are positively associated with an increased bone mass in the studies included in this thesis. In addition to these, non-nutritive substances, such as dietary phytoestrogens [214], may contribute to this mechanism. Like any other tissues, bone cells are responsible for building or deposition of bone tissue and these functions are mainly dependent on nutrients and non-nutritive substances. For instance, the production of bone matrix require nutrients, such as protein, vitamin C, D and K. In addition, calcium, magnesium phosphorous and potassium are used in bone matrix development and mineral deposition.

Intake of diets that constitute nutrients and non-nutritive substances and are important for bone health is low. For instance, FV consumption is low worldwide [50] and in Australia [330]. In addition, diet has been more frequently linked with metabolic diseases and less commonly associated with bone fragility in literature and policies [20, 414]. However, this phenomena should be changed so that dietary components are considered as major risk factors for bone fragility in addition to calcium and vitamin D. Interventions should target aging adults to encourage consumption of recommended levels of FV, dairy products and other healthy foods to prevent bone fragility. Achieving optimal bone mass (both amount and quality) at an early age by consuming the important dietary components should also be one of the strategies to decrease the burden of bone fragility in later life [19].

9.3.2 Indirect effect of diet on bone fragility

It is also equally important to consider the indirect pathophysiological pathways and impact of diet on bone health. Pro-/anti-inflammatory properties of diet and nutrients may have indirect effects [36] through stimulating or suppressing osteoclast activity. The activities of osteoclasts are affected by a systematic inflammation as a result of C-reactive protein and E-selectin [430]. In this thesis, dietary patterns that are characterized by a high intake of takeaway foods, snacks, soft drinks, and red meat ('Western' pattern) are positively associated with low BMD. A mixed-source nutrient pattern that is characterized by a high intake of calcium, vitamin D, potassium, magnesium and phosphorus is also positively associated with BMD. On the other hand, an animal-sourced nutrient pattern was positively associated with bone fracture. A previous study that included approximately half of the participants of NWAHS indicated that an animal-sourced nutrient pattern was found to be pro-inflammatory [385]. In this thesis, the animal-sourced nutrient pattern was negatively associated with an increased risk of

fractures (CHAPTER 7) and a mixed-source nutrient pattern was positively associated with bone mass (CHAPTER 6). These show that a diet that balances nutrient intake from both animal- and plant-sources is optimal for bone health. Future studies that assess the associations of diet and bone health should consider the inflammatory properties of food and nutrient constituents in addition to their direct role.

On the other hand, diet could affect endogenous acid load which in turn affects bone mass and fracture risk [423, 449]. Although dietary acid load was not assessed in the studies of this thesis, modern and 'Western' dietary and animal-sourced nutrient patterns, which are characterized by a high intake of food items (such as red meat) and nutrients (such as protein) that increase endogenous acid load [429], were positively associated with bone fragility. Balancing those food items and nutrients with alkaline producing diets may buffer the endogenous acid production and offset the effect on bone fragility [424], which is in line with the study in CHAPTER 6, where the mixed-source nutrient pattern is positively associated with bone mass.

Muscle mass/strength could be another pathway through which diet is associated with bone health. Diet is associated with muscle mass and this, in turn, could be associated with risks of fall and fracture [413, 420]. In this thesis, the 'Western' dietary pattern was characterized by a high intake of calorie and a low consumption of nutrient-dense food items. In a previous study, this dietary pattern was positively associated with low muscle strength [420]. Low muscle mass/strength that leads to an increased risk of fractures that could also have an association with NCDs (e.g. CVDs and neoplasms) through limiting physical activity [6]. This may lead to functionality loss and dependency ultimately resulting in multimorbidity and mortality due to NCD [6-9]. However, further evidence that leads to a better understanding should be generated. Figure 9.3 summarizes the

potential mechanisms through which diet could have an indirect effect on bone fragility.

9.4 Implications

The implications of the studies in this thesis are in two parts: implications of the findings for nutrition-related interventions in public health and clinical settings and methodological implications in nutritional epidemiology.

9.4.1 Public health and clinical significance

This thesis addresses one of the most important factors of NCDs with a special focus on bone fragility. In general, dietary habits are the most important modifiable behaviour for which there are effective interventions. However, tailored utilization of these interventions to reduce associated burden of diseases should be expanded and additional strategies from other successful risk factor intervention packages, such an anti-smoking measure in Australia, could be adopted. In addition to the current focus on reducing unhealthy diet consumption, equal or greater attention is required to increase the intake of a healthy diet. Clinicians also should consider providing dietary advice in their routine practice.

Comprehensive public health and clinical interventions may lead to a successful reduction of diet-related NCD burden and associated costs. The findings in this thesis provide unequivocal evidence for the necessity of these interventions and potential areas (in terms of identifying the leading dietary risk factors that have a large contribution in the current burden of NCDs) of interventions through which diet-related diseases could be effectively addressed.

To prevent NCDs burden in adults and bone fragility in ageing population, diet should be a priority area of intervention. There are effective interventions that could have a potential

impact to improve consumption of healthy diet and reduce intake of unhealthy ones [336, 344, 348-352]. This thesis highlights the need to implement these interventions and novel strategies. Increasing awareness on diet and its health impact should be a main focus and utilization of multiple channels of communication, including the application of new technologies, is important.

9.4.2 Methodological significance in nutritional epidemiology

The thesis also assesses some of the methodological issues, particularly dietary data collection and analysis methods. Using baseline and recent dietary data in longitudinal studies may lead to a biased association with a disease outcome as they do not reflect a habitual intake. On the other hand, future studies that investigate the association of dietary and nutrient patterns and disease outcomes should select/compare appropriate statistical methods to conduct a dietary pattern analysis. Utilization of these methods in different disease outcomes should be evaluated because the findings on a diet-disease association may vary due to the application of different dietary analysis methods.

Interpretation of dietary patterns and their associations with disease outcomes should be seen broadly and should not be limited to the patterns only. Thus, it is crucial to cautiously evaluate the following six aspects of dietary patterns when investigating their associations with disease outcomes. These are: 1) the whole characteristics of dietary patterns and appropriate labelling; 2) the relative contribution of each food item within dietary patterns; 3) the absolute intake of each food item in a study population and comparison with recommended food intakes; 4) complementing a dietary pattern analysis with nutrient patterns and investigating the relation between the two and with disease outcomes; 5) the food landscape of the community in which the study was conducted; and 6) dynamism of food patterns and associated drivers (such as agricultural production)

over time and its potential impact on health outcomes.

Dietary patterns provide comparative contributions of food items within an umbrella of general food habits. However, considering the absolute intake of each food item is also crucial. For instance, in this thesis, a modern dietary pattern (characterized by a high intake of fast food, eggs, deep-fried foods, milk and fruit, and a low intake of vegetable and rice) was positively associated with bone fracture in the Chinese population. This means that the intake of milk was higher in those study participants who had a high adherence of this pattern. However, the average consumption of milk was very low (5.8 mL/day) in the study population. This information provides a further understanding of the dietary pattern and its association with bone fracture.

In addition, the utilization of a complex system model [450] in dietary pattern analyses could be a potential approach to include some of the aforementioned aspects of dietary patterns. In this case, the drivers of dietary patterns and their multiple interactions (such as food policy, economic intervention and agricultural production), the dynamism of dietary patterns across lifetime and their consequences can be considered. However, features of dietary patterns should not be limited to these aspects only.

9.5 Limitations

Although the limitations of each study are detailed in the respective chapters, I mention some of the major ones below. Inability to account for correlations among dietary components and not be able to allow for time lag in determining diet-related burden of NCDs were the major limitations in the first study (CHAPTER 4). In addition, the interaction of dietary components and nutrients was not considered in this study. Therefore, future studies on diet-disease relationship should consider the

comprehensiveness of food and nutrient intakes. This also enables us to consider recipes of mixed dishes.

Cross-sectional analysis of NWAHS data does not enable us to claim causality. However, the associations we found in these studies will help future causal investigations between diet and bone fragility and contribute to the design of intervention studies. Although FFQ is the most common dietary data collection method, it has limitations in measuring usual intakes of food and nutrients. However, unlike a single dietary component or nutrient, dietary and nutrient patterns reflect relative consumption of foods and nutrients, which makes this concern less worrisome. In all studies that assess the association between diet and bone fragility in this study, mediation analysis was not conducted. However, we interpreted and explained the results considering these factors. Determining the number of dietary factors and labelling the components in the dietary data analysis are subjective. However, we used the recommended approaches (scree plot, an eigenvalue and interpretability) to minimize subjectivity.

9.6 Future directions

Future studies should consider incorporating dietary and nutrient patterns simultaneously to determine their associations with a disease outcome. Combining these methods will provide additional insights on the disease mechanism of diet as only using dietary patterns to identify disease aetiology could compromise the understanding of the mechanisms. Subjectivity in determining the number of factors to be included in the subsequent diet-disease association analyses and labelling of the identified factors is another challenge. Future studies should focus on addressing these factors by enriching existing methods and developing new techniques. Dietary pattern analysis should also consider contextual attributes of diet, such the food chain system, cooking methods, food contamination and

other lifestyle factors [451].

There is no common understanding and conceptual framework for dietary/nutrient patterns to determine the translation of findings into policy, guidelines and interventions. Development of the framework will help to shape and standardize dietary analysis methods and consequent translation of findings into interventions. Further, diet is multidimensional and dynamic. Therefore, the analysis methods should be able to capture these characteristics. Dynamicity (meal timing and frequency), in addition to its dimensionality (amount and type), should be considered in investigating the association between diet and bone fragility [451]. In this regard, evidence shows the former has a major role in diet-disease associations [452].

Data on the impact of sleep parameters (sleep duration, sleep quality and circadian rhythm) on disease outcomes have grown in recent years. Evidence suggests that circadian disruption and sleep deprivation cause changes in metabolome and increased risk of metabolic syndrome [453]. In addition, the interaction of chorotype (diurnal inclination for activities in the morning or evening) and diet has an effect on health outcomes, such as cancer risk [454]. Evidence on the association between sleep parameters and bone health is scarce. A recent study reported that a short sleep duration was positively associated with bone fracture in the Chinese population [88]. However, further investigation is required in this matter. In addition, evidence on the interaction effect of diet (type and amount of food and timing of meal) and sleep parameters on bone health is limited, warranting further studies.

Tools should be developed and improved to capture the changes of the diet over time and other closely related behaviours, including timing of eating and sleep patterns. The collaboration among nutritionists, statisticians, epidemiologists and computer experts to

create the innovative approaches in dietary data collection and analysis is essential. Application of machine-learning in nutritional epidemiology should be considered in solving challenges related to dietary analysis methods and interpretation of findings. In this regard, utilization of machine-learning has been used in identifying dietary patterns associated with cardiometabolic risks [455] and this should be applied in musculoskeletal health outcomes as well. Extensive evaluation of statistical methods that are applied to identify dietary patterns is also warranted.

Long-term prospective studies with a repeated dietary assessment approach are required to extensively evaluate the causal associations between diet and bone fragility, particularly BMD and BMC. Associated with this, time-varying models of dietary patterns that can account for short- and long-term dynamicity of dietary intake should be developed. Further studies on intergenerational and early-life effects of diet on bone fragility are needed.

9.7 Conclusion

This thesis supports the fact that diet is a major contributor for the current burden of NCDs in Australia, particularly in middle-aged males. A low intake of healthy diet is the most important contributor which implies that dietary interventions could be benefited if the targets are males and healthy dietary components, like FV, whole grains and nuts in addition to measures that reduce the consumption of unhealthy diets.

There is inconsistent evidence on the association between diet and bone fragility. The sources of this inconstancy are partially clarified in this thesis. Different factors may attribute for this varying evidence, including study design, study population and dietary analysis methods. In this thesis, whereas a ‘prudent’ dietary pattern (predominantly FV

and dairy) and a mixed-source nutrient pattern (potassium, calcium, potassium, fibre and protein) are beneficial for bone health, 'Western' and modern dietary patterns and an animal-sourced nutrient pattern are detrimental factors. These dietary and nutrient patterns could have direct and/or indirect effects on the bone. Clustering and correlation of other lifestyle factors may also contribute for this associations. Future studies should focus on analysing mediators of these associations. Clinical and public health interventions to bone health (particularly to prevent bone fragility in population groups that are at risk) should consider the importance of diet.

Dietary data collection and analysis methods are growing areas of nutritional epidemiology. Long-term assessment of diet and determining its association with a disease outcome may provide unbiased estimates. In evaluating three dietary pattern analysis methods (PCA, PLS and RRR), RRR is more appropriate in constructing plausible dietary patterns that are associated with bone mass. Despite their wide use in the literature, there is a lack of evidence that explicitly assesses the relative advantages and disadvantages of using these methods, warranting further methodological evaluation of the approaches in future studies.

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APPENDIXES

Appendix I – Supplementary Tables

Supplementary Table 3.1 Theoretical minimum risk exposure levels (TMREL) used in GBD risk factors study 2015

Risk factors	Definition	Theoretical minimum risk exposure level	Data representative index
Overall dietary risks			**92.9%**
Diet low in fruits	Average daily consumption of fruits (fresh, frozen, cooked, canned, or dried, excluding fruit juices and salted or pickled fruits)	Consumption of fruit between 200 g and 300 g per day	88.9%
Diet low in vegetables	Average daily consumption of vegetables (fresh, frozen, cooked, canned, or dried vegetables, including legumes but excluding salted or pickled vegetables, juices, nuts and seeds, and starchy vegetables such as potatoes or corn)	Consumption of vegetables between 340 g and 500 g per day	88.9%
Diet low in whole grains	Average daily consumption of whole grains (bran, germ, and endosperm in their natural proportion) from breakfast cereals, bread, rice, pasta, biscuits, muffins, tortillas, pancakes, and other sources	Consumption of whole grains between 100 g and 150 g per day	16.2%
Diet low in nuts and seeds	Average daily consumption of nut and seed foods	Consumption of nuts and seeds between 16 g and 25 g per day	88.9%
Diet low in milk	Average daily consumption of milk, including non-fat, low fat, and full-fat milk, excluding soy milk and other plant Derivatives	Consumption of milk between 350 g and 520 g per day	88.9%
Diet high in red meat	Average daily consumption of red meat (beef, pork, lamb, and, goat but excluding poultry, fish, eggs, and all processed meats)	Consumption of red meat between 18 g and 27 g per day	88.9%
Diet high in processed meat	Average daily consumption of meat preserved by smoking, curing, salting, or addition of chemical preservatives	Consumption of processed meat between 0 g and 4 g per day	27.3%
Diet high in sugar sweetened beverages	Average daily consumption of beverages with ≥50 kcal per 226.8 g serving, including carbonated beverages, sodas, energy drinks, and fruit drinks, but excluding 100% fruit and vegetable juices	Consumption of sugar-sweetened beverages between 0 g and 5 g per day	26.8%

Diet low in fibre	Average daily intake of fibre from all sources including fruits, vegetables, grains, legumes, and pulses	Consumption of fibre between 19 g and 28 g per day	88.9%
Diet suboptimal in calcium	Average daily intake of calcium from all sources, including milk, yogurt, and cheese	Consumption of calcium between 1.0 g and 1.50 g per day	88.9%
Diet low in seafood omega-3 fatty acids	Average daily intake of eicosapentaenoic acid and docosahexaenoic acid	Consumption of seafood omega-3 fatty acids between 200 mg and 300 mg per day	88.9%
Diet low in polyunsaturated fatty acids	Average daily intake of omega-6 fatty acids from all sources, mainly liquid vegetable oils, including soybean oil, corn oil, and safflower oil	Consumption of polyunsaturated fatty acids between 9% and 13% of total daily energy	88.9%
Diet high in *trans* fatty acids	Average daily intake of *trans* fat from all sources, mainly partially hydrogenated vegetable oils and ruminant products	Consumption of *trans* fatty acids between 0% and 1% of total daily energy	39.9%
Diet high in sodium	24 h urinary sodium measured in mg per day	Consumption of sodium between 1 g and 5 g per day	32.3%

Source: GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016; 388:1659–1724. GBD-Global Burden of Disease

Supplementary Table 4.1 Epidemiological evidence supporting causality between dietary risk-outcome pairs included in the Global Burden of Disease 2015 study

Risk	Outcome	Citation
Diet low in fruits	Lip and oral cavity cancer, Nasopharynx cancer, Other pharynx cancer, and Larynx cancer	Key TJ. Fruit and vegetables and cancer risk. British Journal of Cancer 2011; 104: 6–11.
Diet low in fruits	Oesophageal cancer	Liu J, Wang J, Leng Y, Lv C. Intake of fruit and vegetables and risk of esophageal squamous cell carcinoma: a meta-analysis of observational studies. Int J Cancer 2013; 133: 473–85.
Diet low in fruits	Tracheal, bronchus and lung cancer	Vieira AR, Abar L, Vingeliene S, et al. Fruits, vegetables and lung cancer risk: a systematic review and metaanalysis.Ann Oncol 2016; 27: 81–96.
Diet low in fruits	Ischaemic heart disease	Wang X, Ouyang Y, Liu J, et al. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies. BMJ 2014; 349: g4490.
Diet low in fruits	Ischaemic stroke	Hu D, Huang J, Wang Y, Zhang D, Qu Y. Fruits and vegetables consumption and risk of stroke: a metaanalysis of prospective cohort studies. Stroke 2014; 45: 1613–9.
Diet low in fruits	Hemorrhagic stroke	Hu D, Huang J, Wang Y, Zhang D, Qu Y. Fruits and vegetables consumption and risk of stroke: a metaanalysis of prospective cohort studies. Stroke 2014; 45: 1613–9.
Diet low in fruits	Diabetes	Li M, Fan Y, Zhang X, Hou W, Tang Z. Fruit and vegetable intake and risk of type 2 diabetes mellitus: metaanalysis of prospective cohort studies. BMJ open 2014; 4(11): e005497.
Diet low in vegetables	Oesophageal cancer	Liu J, Wang J, Leng Y, Lv C. Intake of fruit and vegetables and risk of esophageal squamous cell carcinoma: a meta-analysis of observational studies. Int J Cancer 2013; 133: 473–85.
Diet low in vegetables	Ischaemic heart disease	Wang X, Ouyang Y, Liu J, et al. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies. BMJ 2014; 349: g4490.
Diet low in vegetables	Ischaemic stroke, Hemorrhagic stroke	Hu D, Huang J, Wang Y, Zhang D, Qu Y. Fruits and vegetables consumption and risk of stroke: a metaanalysis of prospective cohort studies. Stroke 2014; 45: 1613–9.
Diet low in whole grains	Diabetes	Aune D, Norat T, Romundstad P, Vatten LJ. Whole grain and refined grain consumption and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. Eur J Epidemiol 2013; 28: 845–58.
Diet low in whole grains	Ischaemic heart disease	Aune D, Keum N, Giovannucci E, et al. Whole grain consumption and risk of cardiovascular disease, cancer, and all cause and cause specific mortality: systematic review and dose-response meta-analysis of prospective studies. BMJ 2016; 353: i2716.

Risk	Outcome	Citation
Diet low in whole grains	Ischaemic heart disease, Diabetes	Afshin A, Micha R, Khatibzadeh S, Mozaffarian D. Consumption of nuts and legumes and risk of incident ischemic heart disease, stroke, and diabetes: a systematic review and meta-analysis. Am J Clin Nutr 2014; 100: 278–88.
Diet low in milk	Colon and rectum cancer	World Cancer Research Fund, American Institute for Cancer Research, Imperial College London. WCRF/AICR Systematic Literature Review Continuous Update Project Report: The Associations between Food, Nutrition and Physical Activity and the Risk of Colorectal Cancer. Oct 2010.
Diet high in red meat	Colon and rectum cancer	World Cancer Research Fund, American Institute for Cancer Research, Imperial College London. WCRF/AICR Systematic Literature Review Continuous Update Project Report: The Associations between Food, Nutrition and Physical Activity and the Risk of Colorectal Cancer. Oct 2010.
Diet high in red meat	Diabetes	Pan A, Sun Q, Bernstein AM, et al. Red meat consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. Am J Clin Nutr 2011; 94: 1088–96.
Diet high in processed meat	Colon and rectum cancer	World Cancer Research Fund, American Institute for Cancer Research, Imperial College London. WCRF/AICR Systematic Literature Review Continuous Update Project Report: The Associations between Food, Nutrition and Physical Activity and the Risk of Colorectal Cancer. Oct 2010.
Diet high in processed meat	Ischaemic heart disease	Micha R, Wallace SK, Mozaffarian D. Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes mellitus: a systematic review and meta-analysis. Circulation 2010; 121: 2271–83.
Diet high in processed meat	Diabetes	Pan A, Sun Q, Bernstein AM, et al. Red meat consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. Am J Clin Nutr 2011; 94: 1088–96.
Diet high in sugar-sweetened beverages and high body-mass index	Not applicable	Malik VS, Pan A, Willett WC, Hu FB. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. Am J Clin Nutr 2013; 98: 1084–102.
Diet low fibre	Colon and rectum cancer	World Cancer Research Fund, American Institute for Cancer Research, Imperial College London. WCRF/AICR Systematic Literature Review Continuous Update Project Report: The Associations between Food, Nutrition and Physical Activity and the Risk of Colorectal Cancer. Oct 2010.
Diet low in fibre	Ischaemic heart disease	Threapleton DE, Greenwood DC, Evans CE, et al. Dietary fibre intake and risk of cardiovascular disease: systematic review and meta-analysis. BMJ (Clinical research ed) 2013; 347: f6879.
Diet low in calcium	Colon and rectum cancer	World Cancer Research Fund, American Institute for Cancer Research, Imperial College London. WCRF/AICR Systematic Literature Review Continuous Update Project Report: The Associations between Food, Nutrition and Physical Activity and the Risk of Colorectal Cancer. Oct 2010.
Diet low in seafood omega-3 fats	Ischaemic heart disease	Chowdhury R, Stevens S, Gorman D, et al. Association between fish consumption, long chain omega 3 fatty acids, and risk of cerebrovascular disease: systematic review and meta-analysis. BMJ (Clinical research ed) 2012; 345: e6698.

Risk	Outcome	Citation
Diet low in polyunsaturated fats	Ischaemic heart disease	Farvid MS, Ding M, Pan A, et al. Dietary linoleic acid and risk of coronary heart disease: a systematic review and meta-analysis of prospective cohort studies. Circulation 2014; 130: 1568–78.
Diet low in polyunsaturated fats	Ischaemic heart disease	Mozaffarian D, Micha R, Wallace S. Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials. PLoS Med 2010; 7: e1000252.
Diet high in *trans* fats	Ischaemic heart disease	Mozaffarian D, Clarke R. Quantitative effects on cardiovascular risk factors and coronary heart disease risk of replacing partially hydrogenated vegetable oils with other fats and oils. Eur J Clin Nutr. 2009; 63(Suppl 2): S22-33.
Diet high in sodium and high systolic blood pressure	Not applicable	Aburto NJ, Ziolkovska A, Hooper L, Elliott P, Cappuccio FP, Meerpohl JJ. Effect of lower sodium intake on health: systematic review and meta-analyses. BMJ 2013; 346: f1326.
Diet high in sodium	Stomach cancer	World Cancer Research Fund, American Institute for Cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington DC: AICR, 2007.

Source: GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016; 388:1659–172.

Supplementary Table 4.2 List of data sources for exposure levels used in Global Burden of Disease 2015 study for Australia

N	Sources
1	Australia National Nutrition Survey 1995-1996 as it appears in Global Dietary Database Consortium, Nutrition and Chronic Disease Expert Group (NutriCoDE). Global Dietary Database 1980-2011. [Unpublished]
2	Beard TC, Eickhoff R, Mejglo ZA, Jones M, Bennett SA, Dwyer T. Population-based survey of human sodium and potassium excretion. Clin Exp Pharmacol Physiol. 1992; 19(5): 327-30 as it appears in Global Dietary Database Consortium, Nutrition and Chronic Disease Expert Group (NutriCoDE). Global Dietary Database 1980-2011. [Unpublished]
3	Beard TC, Woodward DR, Ball PJ, Hornsby H, von Witt RJ, Dwyer T. The Hobart Salt Study 1995: few meet national sodium intake target. Med J Aust. 1997; 166(8): 404-7 as it appears in Global Dietary Database Consortium, Nutrition and Chronic Disease Expert Group (NutriCoDE). Global Dietary Database 1980-2011. [Unpublished]
4	Charlton K, Yeatman H, Houweling F, Guenon S. Urinary sodium excretion, dietary sources of sodium intake and knowledge and practices around salt use in a group of healthy Australian women. Aust N Z J Public Health. 2010; 34(4): 356Â–63 as it appears in Global Dietary Database Consortium, Nutrition and Chronic Disease Expert Group (NutriCoDE). Global Dietary Database 1980-2011. [Unpublished]
5	Euromonitor International. Partially Hydrogenated Vegetable Oil Sales Database
6	Food and Agriculture Organization of the United Nations (FAO). FAOSTAT Food Balance Sheets, May 2013. Rome, Italy: Food and Agriculture Organization of the United Nations (FAO)
7	Margerison C, Nowson C. Dietary intake and 24-hour excretion of sodium and potassium. Asia Pac J Clin Nutr. 2006; 15(Suppl 3): S37 as it appears in Global Dietary Database Consortium, Nutrition and Chronic Disease Expert Group (NutriCoDE). Global Dietary Database 1980-2011. [Unpublished]
8	Notowidjojo L, Truswell A. Urinary sodium and potassium in a sample of healthy adults in Sydney, Australia. Asia Pac J Clin Nutr. 1993; 2(1): 25-33 as it appears in Global Dietary Database Consortium, Nutrition and Chronic Disease Expert Group (NutriCoDE). Global Dietary Database 1980-2011. [Unpublished]
9	Salt Intake in New South Wales, Australia - Results of a 24-Hour Urinary Sodium Excretion Study in a Representative Adult Population Sample as it appears in Global Dietary Database Consortium, Nutrition and Chronic Disease Expert Group (NutriCoDE). Global Dietary Database 1980-2011. [Unpublished]

Source: http://ghdx.healthdata.org/

Supplementary Table 4.3 Covariates and mediators used in Global Burden of Disease 2015 dietary risk factors study

Dietary risk	Covariates used in the modelling							Metabolic mediators used			
	sex	Suboptimal metric	Nationally Representativeness	Data from FFQ	Data from HBS	Data from FAO	Country level covariate	Body Mass Index	Total Serum Cholesterol	Fasting Plasma Glucose	Systolic Blood Pressure
Diet low in fruits	√	√	√	√	√	√		√	√	√	√
Diet low in vegetables	√	√	√	√	√	√		√	√	√	√
Diet low in whole grains	√	√	√	√	√	x		√	√	√	x
Diet low in nuts and seeds	√	√	√	√	√	√		√	√	√	√
Diet low in milk	√	√	√	√	√	√		x	x	x	x
Diet high in red meat	√	√	√	√	√	√		√	x	√	x
Diet high in processed meat	√	√	√	√	√	x	National availability of red meat (grams/person/day) National availability of pig meat (% of energy/person/day)	√	x	√	√
Diet high in sugar-sweetened beverages	√	√	√	√	√	x	National availability of sugar (Kcal/person/day)	x	x	x	x
Diet low in fiber	√	√	√	√	√	√		x	√	x	x
Diet suboptimal in calcium	√	√	√	√	√	√		x	x	x	x
Diet low in seafood omega-3 fatty acids	√	√	√	√	√	√	Landlocked nation (Yes,/No)	√	x	x	√
Diet low in polyunsaturated fatty acids	√	√	√	√	√	√		x	√	√	x

Diet high in *trans* fatty acids	√	√	√	√	√	x	National availability of hydrogenated oil (% of energy/person/day)	√	√	x	x
Diet high in sodium	√	x	√	x	x	x		x	x	x	x

Source: GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016; 388:1659–1724. FAO – Food and Agriculture Organization; FFQ – food frequency questionnaire; HBS – household budget survey; √ – used ; x – not used

Supplementary Table 4.4 Diet-related deaths from specific causes (diseases) in Australia by age in 1990 and 2015

Age category	Metric	1990 (95% UI)			2015 (95% UI)			Percent of change (95% UI)		
		Diabetes, urogenital, blood, and endocrine diseases	Cardiovasular disease	Cancer	Diabetes, urogenital, blood, and endocrine diseases	Cardiovasular disease	Cancer	Diabetes, urogenital, blood, and endocrine diseases	Cardiovasular disease	Cancer
25-49 years	Number	53 (42 - 64)	1065 (958 - 1165)	168 (127 - 210)	70 (55 - 85)	754 (664 - 851)	164 (122 - 204)	32.3 (30.1 to 33.8)	-29.2 (-30.6 to -27)	-2.7 (-4.4 to -2.9)
	Rate (per 100,000)	1 (0 - 1)	12 (11 - 13)	2 (1 - 2)	1 (0 - 1)	6 (5 - 7)	1 (1 - 2)	0 (-2.2 to 0)	-46.6 (-47.7 to -44.9)	-27 (-27.9 to -26.5)
50-69 years	Number	280 (212 - 348)	6794 (5777 - 7704)	1214 (894 - 1560)	363 (274 - 451)	3602 (3051 - 4106)	1308 (952 - 1672)	29.8 (29.6 to 29.6)	-47 (-47.2 to -46.7)	7.7 (6.5 to 7.2)
	Proportion (%)	23.9 (18.3 - 29.4)	58.9 (50.2 - 66.7)	10.3 (7.6 - 13.3)	22.9 (17.5 - 28.4)	55.4 (47.3 - 63.2)	8.7 (6.4 - 11.2)	-3.9 (-4.5 to -3.4)	-6 (-5.8 to -5.3)	-15.4 (-16.3 to -15.8)
	Rate (per 100,000)	9 (7 - 12)	230 (196 - 261)	41 (30 - 53)	7 (5 - 8)	65 (55 - 74)	24 (17 - 30)	-31 (-31.2 to -31.2)	-71.8 (-71.9 to -71.7)	-42.8 (-43.4 to -43)
70+ years	Number	542 (382 - 724)	17802 (14718 - 20936)	1515 (1110 - 1942)	1195 (821 - 1614)	19309 (15892 - 22694)	2649 (1959 - 3383)	120.4 (114.9 to 122.9)	8.5 (8 to 8.4)	74.9 (76.5 to 74.2)
	Proportion (%)	14.6 (10.3 - 19.5)	44.4 (36.9 - 51.6)	10.1 (7.5 - 12.9)	12.6 (8.7 - 17.2)	40 (33.2 - 46.9)	8.9 (6.5 - 11.2)	-13.6 (-16 to -11.7)	-9.9 (-10.1 to -9)	-12.7 (-12.6 to -13.1)
	Rate (per 100,000)	44 (31 - 59)	1446 (1196 - 1701)	123 (90 - 158)	52 (35 - 70)	833 (686 - 979)	114 (85 - 146)	17.1 (14.1 to 18.4)	-42.4 (-42.6 to -42.4)	-7.1 (-6.2 to -7.5)
All Ages	Number	874 (647 - 1127)	25660 (21472 - 29680)	2897 (2167 - 3666)	1627 (1162 - 2133)	23665 (19622 - 27590)	4121 (3044 - 5165)	86.1 (79.6 to 89.3)	-7.8 (-8.6 to -7)	42.2 (40.5 to 40.9)
	Proportion (%)	16.8 (12.5 - 21.7)	48.1 (40.4 - 55.3)	9.9 (7.4 - 12.4)	14.2 (10.2 - 18.8)	42.3 (35.3 - 49.1)	8.7 (6.4 - 10.9)	-15.6 (-18.5 to -13.3)	-12.2 (-12.6 to -11.2)	-12.2 (-12.7 to -12.1)
	Rate (per 100,000)	5 (4 - 7)	151 (126 - 174)	17 (13 - 22)	7 (5 - 9)	97 (81 - 113)	17 (13 - 21)	30.2 (25.8 to 32.5)	-35.4 (-36 to -34.9)	-0.5 (-1.6 to -1.3)
Age-standardized	Proportion (%)	16.6 (12.3 - 21.4)	47.9 (40.3 - 55.1)	9.9 (7.4 - 12.4)	14.8 (10.8 - 19.4)	43.1 (36.1 - 49.9)	8.6 (6.3 - 10.8)	-10.6 (-12.2 to -9.4)	-10.1 (-10.4 to -9.3)	-13.5 (-14.2 to -13.3)
	Rate (per 100,000)	5 (4 - 6)	144 (121 - 167)	16 (12 - 20)	5 (3 - 6)	62 (52 - 72)	12 (9 - 15)	-7.2 (-8.9 to -7)	-56.9 (-57.1 to -56.8)	-27.1 (-28.1 to -27.5)

UI – uncertainty interval

Supplementary Table 4.5 Age-standardized burden of non-communicable diseases (expressed as percentage of deaths and disability-adjusted life years) associated with dietary risks by sex, and rank and burden percentage change of OECD countries between 1990 and 2015

Country	Sex	Death (95% UI)					DALYs (95% UI)				
		1990		2015			1990		2015		
		Proportion (%)	Rank	Proportion (%)	Rank	Change (%)	Proportion (%)	Rank	Proportion (%)	Rank	Change (%)
Netherlands	Males	25.9 (21.9 - 29.9)	4 (4 - 4)	18.2 (15.1 - 21.2)	1 (1 - 1)	-29.8 (-33.4 to -26.8)	18.2 (15.3 - 21.2)	9 (8 - 8)	11.0 (9.1 – 13.0)	4 (4 - 4)	-39.5 (-42.6 to -36.5)
	Females	20.5 (17.3 – 24.0)	3 (3 - 3)	13.5 (11.2 - 16.1)	1 (1 - 1)	-33.9 (-38.1 to -30.0)	9.5 (7.9 - 11.4)	3 (3 - 3)	5.7 (4.7 - 6.9)	4 (4 - 4)	-39.6 (-43.5 to -35.5)
	Both	23.7 (20.0 - 27.4)	4 (4 - 4)	16.1 (13.4 – 19.0)	1 (1 - 1)	-32.1 (-35.3 to -29.3)	14.1 (11.8 - 16.6)	5 (5 - 5)	8.4 (6.9 – 10.0)	3 (3 - 4)	-40.4 (-43.4 to -37.6)
France	Males	21.8 (18.6 - 25.3)	2 (2 - 2)	18.4 (15.7 - 21.2)	2 (1 - 2)	-15.7 (-19.1 to -12.3)	14.4 (12.1 - 16.8)	2 (2 - 2)	10.9 (9 - 12.8)	3 (3 - 3)	-24.3 (-27.3 to -21.1)
	Females	19.0 (16.0 - 22.5)	1 (2 - 2)	15.0 (12.7 - 17.8)	2 (2 - 3)	-20.8 (-24.4 to -16.9)	7.6 (6.2 - 9.2)	1 (1 - 1)	5.3 (4.3 - 6.4)	2 (3 - 3)	-29.8 (-33 to -26.6)
	Both	20.7 (17.6 - 24.1)	2 (2 - 2)	17.0 (14.4 - 19.7)	2 (2 - 2)	-17.9 (-20.6 to -15.0)	11.2 (9.3 - 13.3)	1 (1 - 1)	8.2 (6.7 - 9.8)	2 (2 - 2)	-26.7 (-29.2 to -24.1)
Israel	Males	29.3 (24.6 - 34.1)	17 (15 - 17)	19.4 (16.2 - 22.9)	4 (4 - 5)	-33.6 (-36.6 to -30.4)	19.2 (16.1 - 22.7)	14 (12 - 15)	11.4 (9.5 - 13.6)	6 (6 - 6)	-40.7 (-43.8 to -37.3)
	Females	24.7 (20.3 - 29.3)	13 (10 - 19)	15.2 (12.5 - 18.5)	3 (2 - 4)	-38.6 (-42.2 to -35.2)	12.2 (10.0 - 14.9)	20 (18 - 21)	6.1 (4.9 - 7.5)	8 (5 - 8)	-50.2 (-53.6 to -46.5)
	Both	27.1 (22.5 - 31.8)	14 (11 - 14)	17.4 (14.4 - 20.8)	3 (3 - 4)	-35.8 (-38.8 to -33.0)	15.7 (13.0 - 18.7)	15 (13 - 15)	8.7 (7.2 - 10.5)	6 (5 - 6)	-44.5 (-47.5 to -41.2)
Spain	Males	24.1 (20.4 – 28.0)	3 (3 - 3)	18.9 (16.0 – 22.0)	3 (3 - 3)	-21.6 (-24.9 to -18.4)	16.7 (14.0 - 19.4)	4 (4 - 4)	11.7 (9.8 - 13.8)	7 (7 - 8)	-29.8 (-32.9 to -26.7)
	Females	21.6 (18.0 - 25.8)	5 (5 - 5)	15.8 (13.0 – 19.0)	5 (4 - 7)	-27.0 (-30.3 to -23.2)	9.9 (8.1 - 12.1)	4 (4 - 4)	6.0 (4.9 - 7.4)	6 (5 - 7)	-38.8 (-41.5 to -36.1)
	Both	23.1 (19.5 – 27.0)	3 (3 - 3)	17.6 (14.8 - 20.7)	4 (3 - 4)	-23.8 (-26.5 to -21.2)	13.5 (11.3 – 16.0)	4 (4 - 4)	9.0 (7.5 - 10.7)	7 (7 - 7)	-33.4 (-35.9 to -30.7)
Denmark	Males	31.5 (27.0 - 35.7)	22 (22 - 22)	20.4 (17.4 - 23.4)	6 (6 - 7)	-35.1 (-38.2 to -31.8)	20.9 (17.8 – 24.0)	21 (21 - 21)	11.8 (9.9 - 13.9)	9 (9 - 9)	-43.5 (-46.1 to -40.4)
	Females	25.1 (21.4 - 28.7)	16 (12 - 17)	16.1 (13.7 - 18.6)	7 (5 - 7)	-35.9 (-39.2 to -32.5)	11.7 (9.8 - 13.8)	16 (15 - 16)	6.6 (5.4 - 7.8)	12 (11 - 12)	-43.8 (-47.1 to -40.5)
	Both	28.6 (24.6 - 32.4)	21 (17 - 22)	18.4 (15.8 - 21.1)	5 (5 - 5)	-35.7 (-38.4 to -33.1)	16.5 (13.9 - 19.1)	20 (20 - 21)	9.2 (7.7 – 11.0)	10 (9 - 10)	-43.9 (-46.5 to -41.1)
Switzerland	Males	26.3 (22.4 - 30.4)	5 (5 - 6)	20.8 (17.6 - 24.1)	10 (10 - 10)	-21.1 (-24.3 to -17.6)	16.3 (13.7 - 19.2)	3 (3 - 3)	10.5 (8.7 - 12.6)	1 (1 - 2)	-35.6 (-38.8 to -32.6)
	Females	21.2 (17.9 - 24.7)	4 (4 - 4)	15.9 (13.3 - 18.9)	6 (5 - 6)	-25.0 (-28.8 to -20.7)	8.2 (6.7 - 9.9)	2 (2 - 2)	5.0 (4.1 - 6.1)	1 (1 - 1)	-39.1 (-42.6 to -35.5)
	Both	24.1 (20.4 - 27.8)	5 (5 - 5)	18.5 (15.7 - 21.6)	6 (6 - 6)	-23.2 (-26.1 to -20.1)	12.4 (10.3 - 14.7)	3 (2 - 3)	7.7 (6.4 - 9.3)	1 (1 - 1)	-37.4 (-40.2 to -34.8)
Mexico	Males	19.3 (16.5 - 22.3)	1 (1 - 1)	19.5 (16.5 - 22.6)	5 (4 - 5)	0.9 (-1.6 to 3.3)	13.6 (11.6 - 15.7)	1 (1 - 1)	13.6 (11.6 - 15.8)	21 (19 - 21)	0.5 (-2.3 to 3.0)
	Females	19.0 (16.0 - 22.3)	1 (1 - 1)	18.0 (15.1 - 21.3)	16 (16 - 16)	-5.1 (-7.6 to -2.3)	11.1 (9.2 - 13.1)	13 (12 - 13)	10.1 (8.3 - 12.1)	28 (28 - 29)	-8.4 (-10.8 to -5.6)
	Both	19.2 (16.3 - 22.4)	1 (1 - 1)	18.8 (15.9 – 22.0)	7 (7 - 10)	-1.8 (-3.9 to 0.4)	12.3 (10.4 - 14.4)	2 (2 - 3)	11.9 (10.0 – 14.0)	26 (26 - 26)	-3.3 (-5.5 to -1.1)
Norway	Males	31.9 (27.4 - 36.3)	23 (23 - 24)	20.6 (17.6 - 23.6)	7 (8 - 9)	-35.7 (-38.3 to -32.9)	21.1 (17.9 - 24.3)	23 (23 - 23)	11.2 (9.4 - 13.1)	5 (5 - 5)	-47 (-49.4 to -44.5)
	Females	25.0 (21.2 - 28.9)	15 (13 - 15)	16.7 (14.2 - 19.4)	9 (9 - 10)	-33.3 (-36.3 to -29.9)	10.6 (8.7 - 12.6)	7 (7 - 8)	6.0 (4.9 - 7.2)	5 (5 - 7)	-43.2 (-46.4 to -39.8)
	Both	29.1 (24.9 - 33.2)	23 (24 - 24)	18.8 (16.0 - 21.7)	7 (7 - 8)	-35.3 (-37.6 to -32.9)	16.2 (13.6 - 18.9)	18 (17 - 18)	8.7 (7.2 - 10.2)	5 (5 - 6)	-46.5 (-48.8 to -44.0)
Belgium	Males	26.3 (22.6 – 30.0)	6 (5 - 6)	20.6 (17.7 - 23.5)	8 (7 - 11)	-21.7 (-24.9 to -18.9)	18.1 (15.4 - 20.9)	7 (6 - 9)	12.3 (10.4 - 14.3)	11 (11 - 11)	-32 (-35.0 to -29.1)
	Females	23.1 (19.7 - 26.7)	7 (6 - 8)	16.5 (14.0 - 19.4)	8 (8 - 9)	-28.4 (-31.8 to -25.4)	10.9 (9.1 - 12.9)	11 (10 - 12)	6.7 (5.5 – 8.0)	13 (13 - 13)	-38.2 (-41.2 to -35.2)
	Both	25.0 (21.5 - 28.5)	6 (6 - 7)	18.8 (16.1 - 21.7)	9 (7 - 9)	-24.8 (-27.2 to -22.4)	14.7 (12.4 - 17.1)	8 (7 - 9)	9.6 (8 - 11.3)	12 (12 - 14)	-34.6 (-37.2 to -32.0)
United Kingdom	Males	32.3 (28.1 - 36.3)	24 (23 - 25)	21.9 (18.9 - 24.8)	15 (14 - 16)	-32.3 (-34.3 to -30.0)	22.6 (19.5 - 25.7)	26 (26 - 26)	12.6 (10.7 - 14.6)	13 (13 - 13)	-44.2 (-46.3 to -41.7)
	Females	25.4 (21.9 – 29.0)	18 (16 - 21)	15.7 (13.4 - 18.2)	4 (3 - 6)	-38.1 (-40.4 to -35.9)	12.5 (10.4 - 14.6)	22 (20 - 22)	6.6 (5.4 - 7.8)	11 (11 - 12)	-47.3 (-49.3 to -45.2)
	Both	29.3 (25.4 - 33.1)	24 (25 - 23)	19.0 (16.3 - 21.6)	10 (7 - 10)	-35.4 (-37.3 to -33.5)	17.8 (15.1 - 20.4)	26 (26 - 26)	9.6 (8.1 - 11.3)	13 (12 - 13)	-45.9 (-47.7 to -43.9)
Canada	Males	28.8 (24.8 - 32.5)	15 (12 - 17)	21.5 (18.5 - 24.5)	12 (11 - 14)	-25.3 (-27.9 to -22.6)	19.2 (16.5 – 22.0)	13 (11 - 14)	12.4 (10.5 - 14.4)	12 (12 - 12)	-35.2 (-37.8 to -32.4)
	Females	23.5 (19.9 - 27.2)	9 (8 - 9)	16.8 (14.2 - 19.6)	11 (10 - 11)	-28.5 (-31.8 to -25.4)	10.6 (8.9 - 12.6)	8 (7 - 11)	6.8 (5.7 - 8.1)	15 (14 - 15)	-36.3 (-39.2 to -33.3)
	Both	26.6 (22.8 - 30.3)	11 (9 - 12)	19.4 (16.6 - 22.3)	11 (11 - 11)	-27.1 (-29.5 to -24.8)	15.1 (12.8 - 17.5)	11 (9 - 12)	9.6 (8.1 - 11.3)	14 (13 - 14)	-36.2 (-38.4 to -33.8)
Australia	Males	28.4 (24.1 - 32.6)	11 (11 - 13)	20.7 (17.5 - 23.8)	9 (8 - 9)	-27.2 (-29.8 to -24.5)	17.8 (15.0 - 20.7)	5 (5 - 5)	10.7 (9.0 - 12.5)	2 (1 - 2)	-39.8 (-42.6 to -37.2)
	Females	24.9 (21.0 - 28.9)	14 (14 - 14)	17.7 (15.0 - 20.6)	15 (13 - 15)	-28.8 (-31.9 to -25.4)	10.4 (8.6 - 12.4)	6 (6 - 6)	6.1 (5.0 - 7.3)	7 (6 - 8)	-41.4 (-44.6 to -38.1)
	Both	27.0 (22.9 - 31.1)	13 (13 - 14)	19.4 (16.4 - 22.4)	12 (11 - 12)	-28.2 (-30.6 to -25.7)	14.3 (11.9 - 16.8)	6 (6 - 6)	8.4 (7.0 - 9.9)	4 (3 - 4)	-41.0 (-43.5 to -38.5)
Chile	Males	27.4 (23.2 - 32.2)	9 (9 - 9)	21.0 (17.4 - 25.2)	11 (6 - 15)	-23.5 (-27.5 to -19.6)	18.1 (15.3 - 21.3)	6 (7 - 9)	13.4 (11.1 – 16.0)	20 (17 - 21)	-26.1 (-29.9 to -22.3)
	Females	25.1 (21.5 – 29.0)	17 (17 - 18)	17.6 (14.9 – 21.0)	14 (15 - 13)	-29.8 (-33.6 to -26.0)	12.9 (10.9 - 15.2)	24 (23 - 25)	8.3 (7.0 – 10.0)	24 (23 - 25)	-35.7 (-39.2 to -32.0)
	Both	26.4 (22.5 - 30.7)	10 (10 - 12)	19.4 (16.3 - 23.3)	13 (11 - 15)	-26.2 (-29.5 to -23.1)	15.5 (13.1 - 18.2)	13 (13 - 14)	10.8 (9.0 – 13.0)	21 (21 - 21)	-30.3 (-33.4 to -27.1)
New Zealand	Males	28.4 (24.1 - 32.4)	10 (11 - 12)	21.5 (18.4 - 24.8)	13 (12 - 13)	-24.1 (-26.8 to -21.4)	19.1 (16.1 - 22.1)	12 (13 - 13)	11.9 (10.0 – 14.0)	10 (10 - 10)	-37.6 (-40.4 to -34.5)
	Females	22.9 (19.2 – 27.0)	6 (7 - 7)	17.4 (14.6 - 20.6)	12 (12 - 12)	-23.8 (-26.9 to -20.9)	10.7 (8.8 - 12.8)	9 (9 - 9)	6.7 (5.5 - 8.1)	14 (15 - 14)	-36.8 (-40.4 to -33.1)

Country	Sex	Death (95% UI)					DALYs (95% UI)				
		1990		2015			1990		2015		
		Proportion (%)	Rank	Proportion (%)	Rank	Change (%)	Proportion (%)	Rank	Proportion (%)	Rank	Change (%)
	Both	26.1 (22.1 - 30.1)	9 (7 - 9)	19.7 (16.7 - 22.9)	14 (14 - 14)	-24.8 (-26.9 to -22.6)	15.1 (12.6 - 17.6)	10 (10 - 10)	9.3 (7.7 – 11.0)	11 (11 - 11)	-38.3 (-41 to -35.6)
Luxembourg	Males	28.5 (24.5 - 32.3)	12 (10 - 14)	21.5 (18.5 - 24.7)	13 (12 - 15)	-24.3 (-27.4 to -21.5)	19.4 (16.6 - 22.4)	15 (14 - 15)	11.7 (9.8 - 13.6)	7 (7 - 7)	-39.8 (-42.7 to -37)
	Females	24.5 (20.9 - 28.6)	12 (11 - 13)	17.6 (14.9 - 20.7)	13 (14 - 14)	-28.2 (-31.5 to -24.5)	11.6 (9.6 - 13.9)	15 (15 - 16)	6.5 (5.3 - 7.8)	10 (9 - 10)	-44 (-47 to -41.0)
	Both	26.7 (22.9 - 30.6)	12 (11 - 13)	19.7 (16.9 - 22.8)	15 (13 - 14)	-26.1 (-28.6 to -23.6)	15.7 (13.2 - 18.4)	14 (14 - 16)	9.1 (7.6 - 10.8)	8 (8 - 9)	-41.7 (-44 to -39.4)
Portugal	Males	29.2 (24.7 - 34.2)	16 (16 - 19)	22.0 (18.5 - 25.6)	16 (13 - 16)	-24.8 (-27.8 to -21.7)	20.1 (16.9 - 23.7)	17 (17 - 18)	13.4 (11.1 - 15.9)	19 (19 - 20)	-33.5 (-36.7 to -30.2)
	Females	26.3 (21.7 - 31.4)	23 (19 - 24)	19.1 (15.8 - 23.1)	20 (17 - 20)	-27.4 (-30.6 to -23.9)	13.0 (10.7 - 15.9)	25 (24 - 25)	7.4 (6.1 - 9.2)	19 (19 - 19)	-43.0 (-45.6 to -40.3)
	Both	27.9 (23.3 - 32.9)	16 (16 - 21)	20.7 (17.4 - 24.4)	16 (16 - 17)	-25.7 (-28.3 to -22.8)	16.6 (13.9 - 19.9)	23 (20 - 24)	10.5 (8.7 - 12.6)	19 (19 - 20)	-37.1 (-39.8 to -34.4)
United States	Males	30.0 (25.9 - 33.9)	19 (16 - 19)	22.9 (19.9 – 26.0)	18 (17 - 20)	-23.4 (-25.5 to -21.6)	20.2 (17.5 - 23.1)	18 (16 - 20)	14.8 (12.8 - 16.9)	26 (24 - 26)	-27.0 (-29.3 to -24.6)
	Females	25.5 (21.7 - 29.2)	19 (20 - 18)	18.7 (16.0 - 21.7)	17 (17 - 19)	-26.5 (-28.6 to -24.6)	12.2 (10.3 - 14.3)	19 (17 - 21)	9.0 (7.6 - 10.5)	26 (26 - 26)	-26.5 (-29.3 to -23.9)
	Both	28.0 (24.1 - 31.8)	17 (15 - 19)	21.0 (18.0 – 24.0)	17 (16 - 17)	-25.1 (-26.9 to -23.3)	16.3 (14.0 - 18.8)	19 (16 - 23)	11.9 (10.2 - 13.7)	25 (24 - 27)	-27.0 (-29.2 to -24.8)
Germany	Males	30.9 (26.4 - 35.4)	20 (20 - 21)	23.2 (19.8 - 26.9)	20 (19 - 20)	-24.9 (-27.4 to -22.3)	21.0 (17.8 - 24.3)	22 (22 - 22)	13.2 (11 - 15.5)	17 (16 - 17)	-37.3 (-39.9 to -34.9)
	Females	26.1 (22.0 - 30.3)	21 (21 - 22)	19.1 (15.9 - 22.6)	19 (18 - 19)	-26.9 (-30.1 to -23.5)	12.0 (9.9 - 14.4)	17 (17 - 19)	7.0 (5.7 - 8.5)	16 (16 - 16)	-42.1 (-44.6 to -39.6)
	Both	28.6 (24.3 - 32.8)	20 (20 - 20)	21.3 (18.0 – 25.0)	18 (18 - 19)	-25.5 (-28.0 to -23.1)	16.5 (13.9 - 19.5)	21 (19 - 21)	10.2 (8.4 - 12.2)	16 (15 - 17)	-38.7 (-40.9 to -36.5)
Italy	Males	27.0 (23.0 - 31.2)	7 (7 - 8)	22.8 (19.5 - 26.4)	17 (17 - 18)	-15.7 (-18.8 to -12.4)	18.2 (15.5 - 21.1)	8 (7 - 10)	13.1 (11.1 - 15.4)	16 (16 - 18)	-27.8 (-30.6 to -24.7)
	Females	24.3 (20.3 - 28.9)	11 (10 - 14)	19.7 (16.4 - 23.9)	21 (21 - 21)	-19.2 (-22.8 to -15.3)	10.8 (8.8 – 13.0)	10 (10 - 11)	7.1 (5.8 - 8.6)	17 (17 - 17)	-34.5 (-37.1 to -31.7)
	Both	25.9 (21.9 - 30.2)	8 (8 - 8)	21.4 (18.2 - 25.3)	19 (19 - 20)	-17.2 (-20.1 to -14.5)	14.6 (12.3 - 17.3)	7 (8 - 8)	10.1 (8.4 – 12.0)	15 (15 - 16)	-31.0 (-33.3 to -28.5)
Iceland	Males	32.5 (27.8 – 37.0)	25 (24 - 25)	25.0 (21.2 - 28.6)	26 (25 - 25)	-23.3 (-25.7 to -20.9)	20.3 (17.0 - 23.7)	19 (18 - 19)	13.0 (10.8 - 15.3)	14 (14 - 14)	-35.9 (-38.7 to -33.4)
	Females	24.2 (20.4 – 28.0)	10 (9 - 12)	16.8 (14.0 - 19.8)	10 (8 - 11)	-30.7 (-34.1 to -27.1)	10.1 (8.3 - 12.1)	5 (5 - 5)	5.3 (4.3 - 6.4)	2 (2 - 2)	-47.7 (-51 to -44.0)
	Both	28.8 (24.5 – 33.0)	22 (21 - 22)	21.5 (18.3 - 24.7)	20 (18 - 20)	-25.4 (-27.7 to -23.1)	15.3 (12.8 – 18.0)	12 (11 - 12)	9.2 (7.6 – 11.0)	9 (8 - 10)	-39.9 (-42.3 to -37.5)
Ireland	Males	33.0 (28.8 - 37.1)	26 (26 - 27)	24.6 (21.3 – 28.0)	24 (23 - 26)	-25.5 (-28.2 to -22.9)	21.9 (18.6 - 25.2)	25 (25 - 25)	13.7 (11.6 - 16.1)	22 (22 - 22)	-37.2 (-40.4 to -33.9)
	Females	26.2 (22.5 - 30.1)	22 (25 - 20)	18.8 (16.1 - 21.7)	18 (18 - 20)	-28.4 (-31.5 to -25.2)	12.1 (10.1 - 14.4)	18 (18 - 19)	6.4 (5.3 - 7.8)	9 (9 - 10)	-46.9 (-51.4 to -42.5)
	Both	30.1 (26.0 – 34.0)	26 (25 - 26)	22.2 (19.1 - 25.3)	21 (21 - 21)	-26.3 (-28.6 to -23.8)	17.2 (14.5 - 19.9)	24 (23 - 24)	10.2 (8.5 - 12.1)	17 (16 - 17)	-40.5 (-43.4 to -37.8)
Japan	Males	28.5 (24.0 - 33.2)	13 (10 - 15)	23.8 (20.1 - 27.5)	21 (21 - 21)	-16.6 (-18.9 to -14.2)	18.7 (15.8 – 22.0)	11 (11 - 12)	14.6 (12.3 - 17.3)	24 (24 - 26)	-21.9 (-24.3 to -19.3)
	Females	27.5 (23.0 - 32.3)	27 (26 - 27)	20.9 (17.6 - 24.7)	24 (24 - 25)	-23.8 (-26.3 to -21.2)	12.6 (10.4 - 15.3)	23 (22 - 24)	7.9 (6.5 - 9.7)	22 (22 - 23)	-37.1 (-39.1 to -35.0)
	Both	28.1 (23.6 - 32.8)	18 (17 - 19)	22.8 (19.2 - 26.4)	22 (22 - 22)	-19.2 (-21.5 to -16.8)	15.8 (13.2 - 18.9)	16 (15 - 18)	11.5 (9.6 - 13.7)	24 (24 - 25)	-27.1 (-29.3 to -24.9)
Slovenia	Males	28.6 (24.3 - 33.2)	14 (13 - 14)	24.1 (20.3 - 28.1)	23 (22 - 24)	-16.0 (-20.3 to -11.3)	20.6 (17.4 - 23.9)	20 (19 - 20)	14.1 (11.7 - 16.7)	23 (23 - 23)	-31.5 (-35.8 to -27.5)
	Females	25.8 (21.2 - 30.6)	20 (16 - 22)	21.6 (17.9 - 25.8)	26 (25 - 26)	-16.3 (-20.2 to -11.6)	13.6 (11.3 - 16.4)	26 (26 - 26)	8.4 (6.9 - 10.2)	25 (24 - 25)	-38.2 (-41.0 to -35.0)
	Both	27.3 (23.0 - 31.9)	15 (15 - 16)	23.0 (19.3 - 27.2)	23 (23 - 27)	-15.7 (-19.1 to -11.7)	17.2 (14.5 - 20.3)	25 (25 - 25)	11.5 (9.5 - 13.7)	23 (23 - 23)	-33.6 (-37 to -30.2)
Austria	Males	29.7 (25.4 - 34.1)	18 (18 - 18)	23.9 (20.4 - 27.6)	22 (22 - 23)	-19.4 (-22.2 to -16.6)	20.0 (16.9 - 23.3)	16 (16 - 17)	13.0 (10.9 - 15.4)	15 (15 - 15)	-35.0 (-37.6 to -32.2)
	Females	26.5 (22.1 - 31.2)	24 (23 - 23)	22.0 (18.1 - 26.1)	27 (27 - 27)	-17.2 (-20.9 to -13.2)	12.3 (10.1 - 14.9)	21 (19 - 22)	7.6 (6.2 - 9.3)	20 (20 - 21)	-38.0 (-40.4 to -35.4)
	Both	28.2 (24.0 - 32.6)	19 (18 - 18)	23.1 (19.4 - 26.8)	24 (23 - 24)	-18.3 (-20.9 to -15.3)	16.2 (13.5 - 19.1)	17 (17 - 19)	10.4 (8.6 - 12.4)	18 (18 - 18)	-35.8 (-38.1 to -33.6)
South Korea	Males	33.3 (28.4 - 38.3)	27 (26 - 28)	23.2 (19.6 - 26.9)	19 (18 - 19)	-30.4 (-34.3 to -26.6)	25.5 (21.9 - 29.5)	28 (29 - 28)	15.3 (13.0 – 18.0)	27 (27 - 27)	-40.0 (-43.9 to -36.3)
	Females	33.8 (28.5 - 39.6)	30 (29 - 31)	22.8 (19.1 – 27.0)	29 (29 - 28)	-32.4 (-35.7 to -29.0)	20.4 (17.1 - 24.2)	32 (31 - 32)	9.5 (7.8 - 11.5)	27 (27 - 27)	-53.4 (-56.3 to -50.5)
	Both	33.6 (28.5 – 39.0)	28 (28 - 30)	23.2 (19.5 - 27.1)	25 (25 - 25)	-31.1 (-34.2 to -28.0)	23.2 (19.8 – 27.0)	30 (30 - 30)	12.6 (10.6 – 15.0)	28 (28 - 28)	-45.4 (-48.7 to -42.3)
Sweden	Males	34.2 (29.4 - 38.8)	29 (28 - 29)	25.4 (21.7 - 29.2)	28 (27 - 28)	-25.8 (-28.4 to -23.3)	21.3 (17.9 - 24.6)	24 (24 - 24)	13.3 (11.1 - 15.7)	18 (19 - 18)	-37.4 (-39.9 to -34.9)
	Females	27.2 (22.9 - 31.5)	25 (25 - 26)	20.8 (17.4 - 24.4)	23 (23 - 23)	-23.4 (-26.2 to -20.2)	11.5 (9.5 - 13.7)	14 (14 - 14)	7.7 (6.3 - 9.2)	21 (21 - 20)	-33.2 (-36.0 to -30.4)
	Both	31.1 (26.6 - 35.5)	27 (27 - 27)	23.3 (19.8 - 26.9)	26 (24 - 26)	-25.2 (-27.4 to -22.8)	16.6 (13.9 - 19.5)	22 (21 - 22)	10.6 (8.8 - 12.5)	20 (19 - 20)	-36.4 (-38.7 to -34.1)
Greece	Males	27.1 (22.6 - 31.9)	8 (7 - 8)	24.8 (20.8 - 29.1)	25 (24 - 26)	-8.3 (-11.3 to -5.1)	18.3 (15.2 - 21.6)	10 (6 - 10)	15.7 (13.0 - 18.5)	28 (28 - 28)	-14.5 (-17.9 to -11.1)
	Females	23.3 (18.8 - 28.5)	8 (6 - 10)	21.4 (17.6 - 25.9)	25 (24 - 26)	-8.1 (-12.0 to -3.2)	10.9 (8.6 - 13.5)	12 (7 - 13)	8.1 (6.5 - 10.1)	23 (24 - 22)	-25.4 (-29.1 to -21.4)
	Both	25.4 (20.9 - 30.3)	7 (6 - 10)	23.3 (19.4 - 27.7)	27 (26 - 28)	-8.0 (-10.8 to -4.6)	14.7 (12.1 - 17.8)	9 (7 - 11)	12.0 (9.9 - 14.5)	27 (25 - 27)	-18.3 (-21.5 to -14.9)
Finland	Males	36.8 (31.8 - 41.4)	30 (30 - 30)	26.0 (22.1 - 29.8)	29 (29 - 29)	-29.5 (-32.1 to -26.5)	26.1 (22.4 - 29.8)	30 (30 - 30)	14.7 (12.4 - 17.2)	25 (25 - 25)	-43.6 (-46.2 to -40.3)
	Females	29.8 (25.2 - 34.4)	28 (28 - 28)	20.4 (17.0 – 24.0)	22 (22 - 22)	-31.6 (-34.7 to -28.4)	14.0 (11.5 - 16.7)	27 (27 - 27)	7.3 (6.0 - 8.7)	18 (18 - 18)	-48.0 (-50.5 to -45.6)
	Both	33.7 (28.9 - 38.2)	29 (28 - 29)	23.5 (19.9 - 27.1)	28 (26 - 28)	-30.4 (-32.7 to -27.9)	20.4 (17.2 - 23.6)	28 (28 - 28)	11.2 (9.3 - 13.1)	22 (22 - 22)	-45.2 (-47.4 to -42.7)
Turkey	Males	31.0 (26.4 - 35.5)	21 (20 - 21)	25.3 (21.4 - 29.4)	27 (27 - 28)	-18.1 (-23.6 to -12.5)	23.1 (19.9 - 26.5)	27 (27 - 27)	16.5 (13.9 - 19.2)	29 (29 - 29)	-28.8 (-34.4 to -23.1)
	Females	27.3 (22.3 - 32.4)	26 (24 - 27)	22.6 (18.4 - 27.1)	28 (28 - 29)	-17.2 (-24.2 to -10.0)	14.9 (12.3 - 17.9)	28 (28 - 28)	10.2 (8.3 - 12.4)	29 (28 - 29)	-31.7 (-38.6 to -24.2)
	Both	29.5 (24.9 - 34.1)	25 (23 - 26)	24.2 (20.3 - 28.4)	29 (29 - 29)	-17.9 (-22.9 to -13.1)	19.4 (16.4 - 22.5)	27 (27 - 27)	13.4 (11.2 - 15.9)	29 (29 - 29)	-30.7 (-36.4 to -25.1)
Singapore	Males	34.1 (30.1 - 38.2)	28 (27 - 29)	30.1 (26.1 - 34.2)	30 (30 - 30)	-11.8 (-15.2 to -8.4)	25.6 (22.3 - 28.9)	29 (28 - 29)	18.0 (15.3 - 21.2)	30 (30 - 30)	-29.5 (-32.9 to -25.8)
	Females	33.6 (29.1 - 38.3)	29 (29 - 30)	25.8 (21.8 – 30.0)	30 (30 - 30)	-23.3 (-26.9 to -19.5)	19.1 (16.2 - 22.2)	29 (29 - 29)	10.5 (8.6 - 12.7)	30 (30 - 30)	-45.1 (-48.2 to -42.0)
	Both	34.2 (29.9 - 38.5)	30 (29 - 30)	28.2 (24.3 - 32.4)	30 (30 - 30)	-17.3 (-20.2 to -14.4)	22.7 (19.6 – 26.0)	29 (29 - 29)	14.4 (12.0 - 17.2)	30 (30 - 30)	-36.6 (-39.5 to -33.5)

Country	Sex	Death (95% UI)					DALYs (95% UI)				
		1990		2015			1990		2015		
		Proportion (%)	Rank	Proportion (%)	Rank	Change (%)	Proportion (%)	Rank	Proportion (%)	Rank	Change (%)
Poland	Males	41.8 (36.8 - 46.4)	32 (32 - 32)	33.1 (29.0 - 37.1)	31 (31 - 31)	-20.9 (-23.2 to -18.5)	30.7 (26.9 - 34.5)	32 (32 - 32)	21.6 (18.8 - 24.5)	33 (31 - 33)	-29.8 (-32.4 to -27.2)
	Females	36.9 (31.9 - 41.9)	32 (32 - 32)	28.7 (24.8 - 32.9)	31 (31 - 31)	-22.2 (-24.5 to -19.9)	19.9 (16.8 - 23.2)	30 (30 - 31)	12.4 (10.4 - 14.6)	31 (31 - 31)	-37.8 (-40.2 to -35.4)
	Both	39.6 (34.7 - 44.3)	32 (32 - 32)	31.2 (27.1 - 35.2)	31 (31 - 31)	-21.2 (-23.1 to -19.3)	25.9 (22.5 - 29.4)	32 (32 - 32)	17.4 (14.9 – 20.0)	31 (31 - 32)	-32.9 (-35.1 to -30.7)
Hungary	Males	38.8 (34.4 - 42.9)	31 (31 - 31)	34.4 (30.3 - 38.3)	32 (32 - 33)	-11.3 (-14.3 to -8.6)	29.2 (26.0 - 32.4)	31 (31 - 31)	22.8 (20.0 - 25.9)	34 (34 - 34)	-21.9 (-25.6 to -18.9)
	Females	34.4 (30.0 – 39.0)	31 (30 - 31)	31.1 (26.9 - 35.4)	32 (32 - 32)	-9.7 (-12.6 to -7.0)	20.0 (17.2 - 23.1)	31 (30 - 32)	14.7 (12.5 - 17.1)	34 (34 - 34)	-26.5 (-29.3 to -23.6)
	Both	36.8 (32.4 – 41.0)	31 (31 - 31)	32.8 (28.7 - 36.9)	32 (32 - 32)	-10.7 (-13.1 to -8.5)	25.0 (21.9 - 28.2)	31 (31 - 31)	18.9 (16.4 - 21.6)	34 (34 - 34)	-24.4 (-27.4 to -21.6)
Czech Republic	Males	42.4 (37.7 - 46.9)	33 (33 - 33)	35.6 (31.3 - 39.5)	34 (33 - 34)	-16.2 (-18.6 to -13.8)	31.4 (27.7 – 35.0)	33 (33 - 33)	21.5 (18.5 - 24.6)	32 (32 - 32)	-31.4 (-34.3 to -28.7)
	Females	38.3 (33.7 - 43.2)	33 (33 - 33)	32.1 (28.1 - 36.2)	33 (33 - 33)	-16.0 (-18.4 to -13.6)	21.4 (18.2 - 24.7)	33 (33 - 33)	13.6 (11.5 – 16.0)	32 (32 - 33)	-36.1 (-38.4 to -34.0)
	Both	40.6 (36.0 - 45.2)	33 (33 - 33)	34.1 (29.9 – 38.0)	33 (33 - 33)	-16.1 (-18.0 to -14.1)	26.8 (23.4 - 30.2)	33 (33 - 33)	17.8 (15.2 - 20.6)	33 (33 - 32)	-33.5 (-35.9 to -31.1)
Estonia	Males	45.7 (40.4 - 50.7)	35 (35 - 35)	35.1 (29.8 - 40.8)	33 (32 - 34)	-23.2 (-27.9 to -16.1)	33.0 (28.9 - 37.1)	35 (35 - 35)	21.1 (17.8 - 24.9)	31 (31 - 33)	-36.0 (-40.5 to -29.1)
	Females	43.9 (38.4 - 49.4)	35 (35 - 35)	34.5 (28.9 – 41.0)	34 (34 - 35)	-21.4 (-26.4 to -14.2)	23.0 (19.6 - 26.7)	35 (35 - 35)	14.0 (11.5 - 16.9)	33 (32 - 33)	-39.4 (-43.4 to -34.1)
	Both	44.9 (39.4 - 50.1)	35 (35 - 35)	34.8 (29.4 - 40.9)	34 (34 - 35)	-22.4 (-27.0 to -16.2)	28.1 (24.3 - 32)	35 (35 - 35)	17.5 (14.7 - 20.9)	32 (31 - 33)	-37.9 (-41.6 to -33)
Slovakia	Males	43.8 (38.9 - 48.5)	34 (34 - 34)	37.1 (32.5 - 41.4)	35 (35 - 35)	-15.2 (-18.5 to -11.6)	31.7 (27.8 - 35.6)	34 (34 - 34)	23.2 (20.1 - 26.4)	35 (35 - 35)	-26.9 (-30.5 to -23)
	Females	41.4 (36.3 - 46.6)	34 (34 - 34)	35.0 (30.5 - 39.6)	35 (34 - 35)	-15.4 (-18.2 to -11.2)	22.8 (19.4 - 26.4)	34 (34 - 34)	15.1 (12.7 - 17.6)	35 (35 - 35)	-34.0 (-36.8 to -30.4)
	Both	42.7 (37.8 - 47.5)	34 (34 - 34)	36.2 (31.7 - 40.6)	35 (34 - 35)	-15.3 (-17.9 to -11.6)	27.8 (24.0 - 31.3)	34 (34 - 34)	19.4 (16.6 - 22.3)	35 (35 - 35)	-30.3 (-33.4 to -26.8)
Europe	Males	34.1 (29.8 - 38.3)		30.2 (26.4 - 34.1)		-11.3 (-12.4 to -9.7)	24.2 (21.1 - 27.5)		19.8 (17.2 - 22.7)		-18.5 (-20.3 to -16.4)
	Females	32.0 (27.7 - 36.4)		27.9 (24.2 - 31.9)		-12.7 (-14.1 to -11.3)	16.3 (13.7 - 19.1)		12.5 (10.5 - 14.6)		-23.4 (-25.2 to -21.5)
	Both	33.3 (28.9 - 37.6)		29.3 (25.6 - 33.2)		-11.9 (-13 to -10.6)	20.5 (17.7 - 23.6)		16.4 (14 – 19.0)		-20.2 (-22.0 to -18.3)
Global	Males	31.5 (27.7 - 35.3)		31.7 (28.0 - 35.3)		0.6 (-1.0 to 2.2)	22.4 (19.7 - 25.4)		21.6 (19.0 - 24.4)		-3.7 (-6.1 to -1.4)
	Females	29.4 (25.5 - 33.4)		28.4 (24.7 - 32.2)		-3.4 (-5.0 to -1.6)	17.0 (14.6 - 19.6)		14.9 (12.7 - 17.3)		-12.6 (-15.3 to -9.6)
	Both	30.6 (26.8 - 34.5)		30.3 (26.6 – 34.0)		-1.0 (-2.2 to 0.3)	19.8 (17.3 - 22.7)		18.5 (16.1 - 21.2)		-6.9 (-9.0 to -4.6)
High-income	Males	29.0 (24.9 – 33.0)		22.5 (19.3 - 25.8)		-22.5 (-24.1 to -20.9)	19.7 (16.9 - 22.6)		13.7 (11.6 - 15.9)		-30.3 (-32.1 to -28.4)
	Females	25.3 (21.5 - 29.2)		18.7 (15.9 - 21.9)		-26.1 (-27.8 to -24.4)	11.9 (10.0 - 14.2)		7.8 (6.5 - 9.3)		-35.1 (-36.9 to -33.2)
	Both	27.4 (23.5 - 31.4)		20.8 (17.8 - 24.1)		-24.0 (-25.6 to -22.5)	16.0 (13.6 - 18.6)		10.8 (9.1 - 12.7)		-32.2 (-33.9 to -30.5)
OECD Countries	Males	29.7 (25.7 - 33.8)		23.0 (19.8 - 26.3)		-22.7 (-24.2 to -21.1)	20.4 (17.6 - 23.3)		14.2 (12.1 - 16.4)		-30.2 (-32.0 to -28.3)
	Females	26.1 (22.3 – 30.0)		19.4 (16.5 - 22.7)		-25.5 (-27.0 to -23.9)	12.5 (10.6 - 14.9)		8.3 (6.9 - 9.8)		-34.0 (-35.8 to -32.1)
	Both	28.2 (24.2 - 32.2)		21.4 (18.4 - 24.7)		-23.9 (-25.3 to -22.4)	16.6 (14.2 - 19.3)		11.3 (9.6 - 13.3)		-31.8 (-33.5 to -30.0)

Ranking was based on the age-standardized relative contribution (population attributable fraction) to deaths and DALYs. Lower rank shows lower burden and vice versa. DALY – disability-adjusted life years; OECD – Organization for Economic Cooperation and Development; UI – uncertainty interval

Supplementary Table 4.6 Number of deaths and disability-adjudged life years from non-communicable diseases associated with dietary risks by sex and age between 1990 and 2015 in Australia and across OECD countries

Country	Deaths (95% UI)		DALYs (95% UI)	
	1990	2015	1990	2015
Australia	29432 (33828 - 24933)	29414 (34058 - 24697)	523421 (593686 - 448831)	443385 (511388 - 377680)
Austria	21482 (25017 - 18157)	18484 (21609 - 15384)	345146 (396484 - 295933)	249205 (288547 - 210231)
Belgium	23470 (26889 - 20126)	18763 (21779 - 15920)	400885 (453067 - 347769)	287904 (332488 - 245885)
Canada	45110 (51319 - 38616)	48867 (56521 - 41844)	854788 (968675 - 744087)	820335 (941846 - 704716)
Chile	15834 (18326 - 13568)	20229 (24226 - 16909)	311565 (356435 - 271474)	368853 (436687 - 314739)
Czech Republic	46577 (51837 - 41243)	34675 (38814 - 30267)	853914 (945041 - 763155)	546292 (614560 - 480196)
Denmark	15342 (17473 - 13135)	8950 (10363 - 7615)	251147 (282266 - 217651)	143315 (164667 - 123128)
Estonia	7437 (8298 - 6537)	5256 (6216 - 4432)	134178 (148766 - 119287)	74968 (87742 - 63760)
Finland	14369 (16315 - 12360)	11802 (13614 - 9968)	262945 (296294 - 229552)	174636 (201278 - 149923)
France	89284 (104721 - 75765)	91674 (107430 - 77352)	1469873 (1696666 - 1257482)	1321093 (1534532 - 1120839)
Germany	242434 (279132 - 205186)	188447 (221382 - 158099)	3974235 (4538351 - 3410268)	2689041 (3118965 - 2281151)
Greece	21730 (26029 - 17893)	26507 (31817 - 21731)	372890 (440261 - 310994)	372774 (436935 - 310922)
Hungary	47763 (53287 - 42025)	38558 (43565 - 33484)	948832 (1047000 - 844281)	636369 (718886 - 560152)
Iceland	420 (482 - 357)	370 (428 - 309)	6964 (7897 - 6017)	5569 (6402 - 4763)
Ireland	6935 (7988 - 5932)	5617 (6467 - 4785)	127000 (144100 - 110646)	93152 (105663 - 80758)
Israel	6308 (7405 - 5236)	6840 (8180 - 5636)	115811 (135020 - 97231)	111408 (132465 - 92439)
Italy	130297 (152287 - 109914)	138163 (164100 - 115904)	2218729 (2556022 - 1905289)	1834218 (2142658 - 1566789)
Japan	194896 (227504 - 164067)	258690 (304044 - 216105)	3772149 (4361740 - 3221230)	3803621 (4441895 - 3217297)
Luxembourg	939 (1082 - 807)	671 (775 - 569)	16726 (19079 - 14535)	10951 (12660 - 9421)
Mexico	44947 (52141 - 38416)	101773 (118945 - 86149)	1187817 (1385442 - 763155)	2397321 (2822294 - 2028534)
Netherlands	27580 (31914 - 23237)	20959 (24725 - 17496)	503942 (574584 - 429460)	363364 (430270 - 305460)
New Zealand	6010 (6932 - 5069)	5814 (6785 - 4896)	113499 (129626 - 97527)	94481 (109929 - 81123)
Norway	11337 (12977 - 9672)	6962 (8061 - 5908)	185466 (210316 - 160024)	102916 (118329 - 88409)
Poland	136747 (152965 - 120008)	110725 (125159 - 96714)	2694422 (2998043 - 2387526)	1903649 (2143910 - 1668476)
Portugal	25125 (29683 - 20926)	19038 (22556 - 15883)	448695 (523227 - 380919)	302904 (356912 - 256231)
Singapore	3815 (4287 - 3340)	5011 (5795 - 4278)	88746 (98683 - 78980)	89718 (102528 - 77425)
Slovakia	20118 (22422 - 17803)	16339 (18382 - 14319)	384572 (426406 - 342595)	278879 (313643 - 244927)
Slovenia	4439 (5196 - 3737)	4062 (4778 - 3391)	85491 (98285 - 72864)	63492 (74676 - 52994)
South Korea	64202 (73991 - 55210)	61862 (72646 - 51999)	1574715 (1782369 - 1368878)	1218839 (1424169 - 1026955)
Spain	69596 (81577 - 58610)	66401 (78743 - 55522)	1226314 (1421834 - 1042330)	998825 (1169190 - 846922)
Sweden	26790 (30804 - 22810)	20085 (23431 - 16920)	402881 (459892 - 345271)	266616 (309861 - 225894)
Switzerland	13176 (15265 - 11122)	11261 (13249 - 9504)	206555 (237359 - 176738)	153575 (179147 - 130089)
Turkey	79274 (92597 - 65996)	70876 (83297 - 59102)	1907524 (2207122 - 1615627)	1716209 (2003778 - 1450618)

Country	Deaths (95% UI)		DALYs (95% UI)	
	1990	2015	1990	2015
United Kingdom	169077 (191222 - 146368)	101625 (116991 - 87221)	2925047 (3284132 - 2556333)	1568322 (1788351 - 1362644)
United States	521103 (592684 - 448242)	507755 (581533 - 434304)	9776120 (11020363 - 8511246)	9931490 (11431166 - 8608251)
Global	8220644 (9258165 - 7222868)	12058089 (13538388 - 10614994)	187258334 (209347869 - 166710512)	40197567 (45357115 - 35376425)
High-income	1865656 (2139046 - 1599286)	1776751 (2063023 - 1510466)	33891969 (38531314 - 29454213)	264411365 (294989032 - 236098327)
OECD Countries	2192608 (2505419 - 1884719)	2087552 (2418690 - 1780837)	40821481 (46221296 - 35616927)	29181343 (33630906 - 25105252)
Europe	2384519 (2696754 - 2073347)	2368072 (2697208 - 2053245)	44534503 (49827529 - 39168583)	35509668 (40948435 - 30582547)

DALY – disability-adjusted life years; OECD – Organization for Economic Cooperation and Development; UI – uncertainty interval;

Supplementary Table 5.1 Food groups used in the factor analysis and factor loadings for each of the identified dietary patterns among adults 50 years and above, South Australia

Food group	Foods items
Beer	Heavy beer, light beer, regular beer
Cabbages	Brussels, sprout, cauliflower, broccoli, coleslaw
Citrus fruit	oranges
Coffee	Coffee
Eggs	eggs
Fish	Steamed fish, tinned fish
Flavoured milk	Flavoured milk
Fruity vegetables	Avocado, fresh tomatoes, tomato products, cucumber, green beans, zucchini, squash, mushrooms, pumpkin, cantaloupe, capsicum, eggplant
High fat dairy	Full cream milk
High fibre bread	High fibre white bread, whole meal bread, multi-grain bread, rye bread, soy and linseed bread
High fibre cereals	Bran , sultana bran, other high fibre cereal
Jam and vegemite	Jam, vegemite
Juice	Orange juice, other fruit juice
Leafy vegetables	Iceberg lettuce, other lettuce, Asian greens, other cooked leafy vegetables
Legumes	Baked beans, dried beans, dried peas, chick dried beans, dried peas, chickpeas
Medium fat dairy	Reduced fat milk, soy milk, skim milk, other milk, yoghurt, ricotta, cottage all other cheeses, cream, sour cream
Nuts	Other nuts
Other cereals	Weet-bix, other weet-bix, regular cornflakes, Muesli, non-toasted commercial Muesli, non-toasted Homemade, muesli toasted, just right, sweet corn, other breakfast cereal
Other fruits	Tinned fruit salad, tinned peaches, apples, bananas, pineapple, strawberries, apricots, pears, peaches or nectarines, mango or pawpaw, berries, cherries, dried or tinned apricots, figs, grapes, other dried fruit plums, watermelon
Pasta and rice	Rice pasta, noodles, rice bubbles
Peanut butter	Peanuts, peanut butter
Potato with fat	Potato fat
Potato without fat	Potato no fat
Poultry	Chicken
Processed meat	Bacon, sausages, processed meat
Red meat	Beef or veal, pork lamb
Root vegetables	Beetroot, carrots
Saturated spread	Other margarine butter
Snacks	Cakes or sweet, pastries, chocolate, sweet biscuits, corn chips, etc ice cream, crackers not wholemeal, whole meal crackers, other confectionery
Soft drinks	Soft drink, spirits premix, sports plus, diet soft drink
Spirits	spirits
Stalk vegetables	Celery, onion or leeks, garlic, asparagus
Sugar	sugar
Take away foods	Pizza, fried fish, pastries with cheese, pastries with meat
Tea and water	Tea, water, herbal tea
Tomato sauce	Tomato sauce or ketchup, canned tomatoes
Unsaturated spread	Olive margarine, margarine on vegetables, mayonnaise, miracles spread, canola margarine, cholesterol lowering margarine, nut telex, poly margarine, soy margarine
White bread	White bread
Wine	White wine, red wine

Supplementary Table 6.1 Sociodemographic, lifestyle, behavioural and chronic diseases related characteristics of study participants aged 50 years and over across tertiles of the nutrient patterns, the North West Adelaide Health Study (n = 1135)

Factor		Mixed-source					Animal-sourced				Plant-sourced			
	Total	T1	T2	T3	*P* value	T1	T2	T3	*P* value	T1	T2	T3	*P* value
	1135	379	378	378		379	378	378		379	378	378	
Age in years, median (IQR)*	62.0 (56.0, 69.0)	62.0 (56.0, 68.0)	61.0 (55.0, 69.0)	62.0 (56.0, 69.0)	0.930	62.0 (56.0, 70.0)	62.0 (56.0, 69.0)	60.0 (56.0, 68.0)	0.160	63.0 (56.0, 71.0)	62.0 (56.0, 69.0)	60.5 (55.0, 67.0)	0.005
Marital status¥													
Married/partnered	746 (65.7%)	243 (64.1%)	243 (64.3%)	260 (68.8%)	0.380	238 (62.8%)	264 (69.8%)	244 (64.6%)	0.110	231 (60.9%)	257 (68.0%)	258 (68.3%)	0.046
Single/separated/widowed/divorced	381 (33.6%)	131 (34.6%)	133 (35.2%)	117 (31.0%)		139 (36.7%)	112 (29.6%)	130 (34.4%)		146 (38.5%)	119 (31.5%)	116 (30.7%)	
Missing	8 (0.7%)	5 (1.3%)	2 (0.5%)	1 (0.3%)		2 (0.5%)	2 (0.5%)	4 (1.1%)		2 (0.5%)	2 (0.5%)	4 (1.1%)	
Annual household gross income¥													
Up to $20,000	335 (29.5%)	127 (33.5%)	105 (27.8%)	103 (27.2%)	0.400	124 (32.7%)	112 (29.6%)	99 (26.2%)	0.320	120 (31.7%)	115 (30.4%)	100 (26.5%)	0.240
$20,001-$40,000	348 (30.7%)	109 (28.8%)	119 (31.5%)	120 (31.7%)		108 (28.5%)	115 (30.4%)	125 (33.1%)		123 (32.5%)	118 (31.2%)	107 (28.3%)	
$40,001-$60,000	195 (17.2%)	61 (16.1%)	63 (16.7%)	71 (18.8%)		69 (18.2%)	65 (17.2%)	61 (16.1%)		59 (15.6%)	61 (16.1%)	75 (19.8%)	
More than $60,000	199 (17.5%)	58 (15.3%)	72 (19.0%)	69 (18.3%)		56 (14.8%)	70 (18.5%)	73 (19.3%)		56 (14.8%)	69 (18.3%)	74 (19.6%)	
Missing	58 (5.1%)	24 (6.3%)	19 (5.0%)	15 (4.0%)		22 (5.8%)	16 (4.2%)	20 (5.3%)		21 (5.5%)	15 (4.0%)	22 (5.8%)	
Job related physical activity level ¥													
Low	558 (49.2%)	173 (45.6%)	191 (50.5%)	194 (51.3%)	0.190	180 (47.5%)	181 (47.9%)	197 (52.1%)	0.810	160 (42.2%)	198 (52.4%)	200 (52.9%)	<0.001
Moderate to high	452 (39.8%)	164 (43.3%)	138 (36.5%)	150 (39.7%)		148 (39.1%)	153 (40.5%)	151 (39.9%)		184 (48.5%)	133 (35.2%)	135 (35.7%)	
Missing	125 (11.0%)	42 (11.1%)	49 (13.0%)	34 (9.0%)		51 (13.5%)	44 (11.6%)	30 (7.9%)		35 (9.2%)	47 (12.4%)	43 (11.4%)	
Leisure time physical activity level ¥													
Low	643 (56.7%)	232 (61.2%)	211 (55.8%)	200 (52.9%)	0.034	207 (54.6%)	230 (60.8%)	206 (54.5%)	0.610	213 (56.2%)	230 (60.8%)	200 (52.9%)	0.050
Moderate to high	370 (32.6%)	105 (27.7%)	129 (34.1%)	136 (36.0%)		120 (31.7%)	122 (32.3%)	128 (33.9%)		121 (31.9%)	109 (28.8%)	140 (37.0%)	
Missing	122 (10.7%)	42 (11.1%)	38 (10.1%)	42 (11.1%)		52 (13.7%)	26 (6.9%)	44 (11.6%)		45 (11.9%)	39 (10.3%)	38 (10.1%)	
Health literacy¥													
Limited	384 (33.8%)	155 (40.9%)	118 (31.2%)	111 (29.4%)	0.002	134 (35.4%)	119 (31.5%)	131 (34.7%)	0.380	161 (42.5%)	111 (29.4%)	112 (29.6%)	<0.001
Adequate	690 (60.8%)	205 (54.1%)	245 (64.8%)	240 (63.5%)		222 (58.6%)	242 (64.0%)	226 (59.8%)		200 (52.8%)	245 (64.8%)	245 (64.8%)	
Missing	61 (5.4%)	19 (5.0%)	15 (4.0%)	27 (7.1%)		23 (6.1%)	17 (4.5%)	21 (5.6%)		18 (4.7%)	22 (5.8%)	21 (5.6%)	
Alcohol risk¥													
Non-drinker/low	1039 (91.5%)	340 (89.7%)	349 (92.3%)	350 (92.6%)	0.160	348 (91.8%)	349 (92.3%)	342 (90.5%)	0.150	352 (92.9%)	337 (89.2%)	350 (92.6%)	0.300
Moderate to high	60 (5.3%)	26 (6.9%)	14 (3.7%)	20 (5.3%)		16 (4.2%)	17 (4.5%)	27 (7.1%)		19 (5.0%)	25 (6.6%)	16 (4.2%)	
Missing	36 (3.2%)	13 (3.4%)	15 (4.0%)	8 (2.1%)		15 (4.0%)	12 (3.2%)	9 (2.4%)		8 (2.1%)	16 (4.2%)	12 (3.2%)	
Smoking¥													
Non-smoker	566 (49.9%)	176 (46.4%)	196 (51.9%)	194 (51.3%)	0.290	198 (52.2%)	179 (47.4%)	189 (50.0%)	0.410	175 (46.2%)	199 (52.6%)	192 (50.8%)	0.180
Ex-smoker/current smoker	564 (49.7%)	200 (52.8%)	180 (47.6%)	184 (48.7%)		181 (47.8%)	198 (52.4%)	185 (48.9%)		203 (53.6%)	178 (47.1%)	183 (48.4%)	
Missing	5 (0.4%)	3 (0.8%)	2 (0.5%)	0 (0.0%)		0 (0.0%)	1 (0.3%)	4 (1.1%)		1 (0.3%)	1 (0.3%)	3 (0.8%)	
Sunlight exposure (hours/week), median (IQR)*	2.50 (2.00, 3.50)	2.50 (2.00, 3.50)	2.50 (1.75, 3.50)	2.75 (2.00, 3.75)	0.130	2.50 (2.00, 3.50)	2.50 (1.75, 3.50)	2.75 (2.00, 3.75)	0.170	2.50 (2.00, 3.75)	2.50 (1.75, 3.50)	2.75 (2.00, 3.50)	0.260
Family history of osteoporosis¥													
Yes	916 (80.7%)	55 (14.5%)	83 (22.0%)	77 (20.4%)		68 (17.9%)	70 (18.5%)	77 (20.4%)		58 (15.3%)	80 (21.2%)	77 (20.4%)	0.076
No	215 (18.9%)	322 (85.0%)	293 (77.5%)	301 (79.6%)	0.023	311 (82.1%)	307 (81.2%)	298 (78.8%)	0.640	321 (84.7%)	297 (78.6%)	298 (78.8%)	
Missing	4 (0.4%)	2 (0.5%)	2 (0.5%)	0 (0.0%)		0 (0.0%)	1 (0.3%)	3 (0.8%)		0 (0.0%)	1 (0.3%)	3 (0.8%)	
Had diabetes¥													
Yes	68 (6.0%)	18 (4.7%)	22 (5.8%)	28 (7.4%)		23 (6.1%)	14 (3.7%)	31 (8.2%)		19 (5.0%)	21 (5.6%)	28 (7.4%)	0.350
No	1066 (93.9%)	361 (95.3%)	356 (94.2%)	349 (92.3%)	0.30	356 (93.9%)	364 (96.3%)	346 (91.5%)	0.033	360 (95.0%)	356 (94.2%)	350 (92.6%)	
Missing	1 (0.1%)	0 (0.0%)	0 (0.0%)	1 (0.3%)		0 (0.0%)	0 (0.0%)	1 (0.3%)		0 (0.0%)	1 (0.3%)	0 (0.0%)	
Body mass index (kg/m^2), mean (SD) #	28.2 (4.8)	28.6 (4.8)	28.2 (5.0)	27.7 (4.5)	0.039	28.0 (4.7)	28.4 (5.0)	28.1 (4.5)	0.500	28.3 (4.6)	28.1 (4.8)	28.1 (4.8)	0.860
Take vitamin D¥													

	Took	87 (7.7%)	28 (7.4%)	28 (7.4%)	31 (8.2%)		30 (7.9%)	33 (8.7%)	24 (6.3%)		29 (7.7%)	23 (6.1%)	35 (9.3%)	0.260
	Did not take	1048 (92.3%)	351 (92.6%)	350 (92.6%)	347 (91.8%)	0.890	349 (92.1%)	345 (91.3%)	354 (93.7%)	0.460	350 (92.3%)	355 (93.9%)	343 (90.7%)	
Osteopenia[¥]														
	Yes	162 (14.3%)	47 (12.4%)	59 (15.6%)	56 (14.8%)		55 (14.5%)	61 (16.1%)	46 (12.2%)		59 (15.6%)	54 (14.3%)	49 (13.0%)	0.580
	No	972 (85.6%)	332 (87.6%)	318 (84.1%)	322 (85.2%)	0.420	324 (85.5%)	316 (83.6%)	332 (87.8%)	0.290	319 (84.2%)	324 (85.7%)	329 (87.0%)	
	Missing	1 (0.1%)	0 (0.0%)	1 (0.3%)	0 (0.0%)		0 (0.0%)	1 (0.3%)	0 (0.0%)		1 (0.3%)	0 (0.0%)	0 (0.0%)	
Osteoporosis[¥]														
	Yes	22 (1.9%)	9 (2.4%)	5 (1.3%)	8 (2.1%)		7 (1.8%)	8 (2.1%)	7 (1.9%)		6 (1.6%)	6 (1.6%)	10 (2.6%)	0.480
	No	1112 (98.0%)	370 (97.6%)	372 (98.4%)	370 (97.9%)	0.550	372 (98.2%)	369 (97.6%)	371 (98.1%)	0.950	372 (98.2%)	372 (98.4%)	368 (97.4%)	
	Missing	1 (0.1%)	0 (0.0%)	1 (0.3%)	0 (0.0%)		0 (0.0%)	1 (0.3%)	0 (0.0%)		1 (0.3%)	0 (0.0%)	0 (0.0%)	
BMD (mg/cm2), mean (SD) (n = 1135) [#]		1196 (119)	1195.3 (116.9)	1187.2 (116.6)	1205.1 (122.8)	0.110	1184.4 (115.9)	1192.5 (122.1)	1210.7 (117.3)	0.007	1202.8 (123.1)	1189.0 (114.8)	1195.7 (118.5)	0.280
T-score, mean (SD) (n = 1135)[#]		0.35 (1.33)	0.35 (1.31)	0.31 (1.30)	0.39 (1.37)	0.680	0.30 (1.27)	0.33 (1.38)	0.40 (1.32)	0.580	0.33 (1.33)	0.35 (1.32)	0.35 (1.33)	0.970

* – Wilcoxon rank-sum test; [¥] – chi-square; [#] – ANOVA; BMD – bone mineral density; IQR – interquartile range; T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence)

Supplementary Table 6.2 Mean (SD) of selected nutrient intake across tertiles of nutrient patterns among adults 50 years and above, the North West Adelaide Health Study (n = 1135)

Factor	Mixed-source			*P* value	Animal-sourced			*P* value	Plant-sourced			*P* value
	T1	T2	T3		T1	T2	T3		T1	T2	T3	
N	379	378	378		379	378	378		379	378	378	
Nutrients	mean (SD)											
Monounsaturated fat (g/d)	37.5 (14.0)	34.0 (14.2)	36.1 (12.7)	42.4 (13.6)	<0.001	28.4 (9.3)	35.6 (8.7)	48.5 (14.7)	<0.001	34.0 (11.8)	37.2 (12.9)	41.3 (16.0)	<0.001
Starch & dextrins (g/d)	98.6 (46.6)	70.9 (23.5)	92.8 (26.1)	132.3 (58.0)	<0.001	95.7 (62.1)	93.6 (36.4)	106.7 (35.4)	<0.001	88.6 (34.9)	100.0 (49.5)	107.4 (51.9)	<0.001
Sugar (g/d)	102 (39)	74 (26)	101 (30)	130 (37)	<0.001	97 (42)	99 (34)	110 (39)	<0.001	91 (34)	99 (36)	115 (43)	<0.001
Riboflavin, B_2 (mg/d)	2.44 (1.18)	1.55 (0.57)	2.30 (0.75)	3.46 (1.22)	<0.001	2.13 (1.14)	2.34 (1.01)	2.84 (1.27)	<0.001	2.30 (1.08)	2.40 (1.18)	2.60 (1.27)	0.002
Pyridoxine, B_6 (mg/d)	1.33 (1.64)	1.20 (1.83)	1.21 (1.03)	1.57 (1.90)	0.002	1.06 (1.34)	1.35 (2.13)	1.58 (1.27)	<0.001	0.99 (0.81)	1.28 (1.79)	1.72 (1.99)	<0.001
Thiamin1	3.06 (2.12)	1.88 (0.97)	2.87 (1.40)	4.44 (2.70)	<0.001	2.83 (2.13)	2.87 (1.74)	3.49 (2.38)	<0.001	2.78 (1.89)	3.10 (2.16)	3.31 (2.26)	0.002
Vitamin E (mg/d)	11.5 (4.5)	10.5 (4.6)	11.0 (4.0)	13.0 (4.4)	<0.001	9.2 (3.5)	11.1 (3.3)	14.3 (5.0)	<0.001	9.4 (3.5)	11.3 (3.8)	13.9 (4.9)	<0.001
Zinc (mg/d)	10.5 (4.5)	8.5 (3.8)	10.1 (4.2)	13.0 (4.2)	<0.001	8.1 (3.2)	10.0 (2.8)	13.4 (5.3)	<0.001	9.1 (3.6)	10.5 (3.9)	12.0 (5.3)	<0.001
Iron (mg/d)	12.9 (4.8)	10.0 (3.6)	12.3 (3.6)	16.4 (4.6)	<0.001	11.5 (4.9)	12.3 (3.7)	14.9 (4.9)	<0.001	10.7 (3.8)	12.6 (4.1)	15.3 (5.1)	<0.001
Folate	537 (266)	366 (143)	501 (178)	744 (295)	<0.001	517 (280)	516 (236)	577 (276)	0.002	474 (231)	530 (264)	606 (285)	<0.001
Retinol (mcg/d)	333 (147)	254 (112)	325 (122)	421 (153)	<0.001	245 (102)	323 (118)	432 (153)	<0.001	369 (155)	322 (144)	308 (135)	<0.001
Niacin, B_3	83.5 (33.9)	62.2 (21.6)	78.7 (23.4)	109.7 (35.5)	<0.001	73.5 (36.1)	79.2 (24.4)	97.9 (34.9)	<0.001	73.8 (24.9)	82.9 (33.3)	93.8 (39.0)	<0.001
Sodium (mg/d)	2354 (905)	1854 (731)	2268 (722)	2943 (893)	<0.001	1896 (719)	2229 (632)	2939 (987)	<0.001	2160 (749)	2302 (842)	2602 (1043)	<0.001
Iodine (mcg/d)	121 (49)	86 (32)	118 (37)	158 (47)	<0.001	100 (41)	119 (43)	143 (53)	<0.001	129 (53)	116 (48)	117 (45)	<0.001
Lycopene(mcg/d)	8996 (10134)	7563 (8059)	8468 (9095)	10960 (12444)	<0.001	7568 (9016)	8130 (7528)	11292 (12753)	<0.001	5062 (4744)	8258 (6396)	13677 (14400)	<0.001
Palmitoleic acid (g/d)	1.31 (0.56)	1.18 (0.58)	1.28 (0.52)	1.46 (0.53)	<0.001	0.90 (0.28)	1.24 (0.25)	1.79 (0.62)	<0.001	1.19 (0.44)	1.29 (0.48)	1.45 (0.68)	<0.001
Lutein and zeaxanthin, (mcg/d)	1634 (1505)	1587 (1695)	1582 (1433)	1735 (1367)	0.28	1622 (1567)	1590 (1300)	1692 (1632)	0.630	722 (492)	1443 (801)	2741 (1957)	<0.001

ANOVA was used to test the mean difference across tertiles. T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence)

Supplementary Table 6.3 Regression coefficients (β) [95% confidence interval (CI)] for the association between z scores of nutrient patterns and bone mineral density by timing of dietary assessment after DXA measurement among study participants aged 50 years and over, the North West Adelaide Health Study (Early [before the median time of the gap] vs. late [after the median time of the gap] dietary assessment)

	Complete-case analysis (n = 794) β (95% CI)	
Nutrient pattern	**Early (n = 398)**	**Late (n = 396)**
Mixed-source	19.42 (6.36, 32.48)**	0.23 (-12.18, 12.63)
Animal-sourced	-10.87 (-22.97, 1.23)	3.15 (-7.33, 13.62)
Plant-sourced	-0.13(-9.91, 9.64)	-1.07 (-9.79, 7.64)

** $P < 0.01$

Results were adjusted for sex and age ,socio-economic and life style factors (smoking, alcohol intake (no/low risk, medium/very high risk), marital status, income, health literacy (limited, adequate), leisure time and job related physical activity levels (low, moderate/high), chronic conditions (diabetes mellitus, family history of osteoporosis and body mass index (continuous)), energy intake (continuous). DXA – dual-energy x-ray dual-energy x-ray absorptiometry

Supplementary Table 7.1 **Spearman rank correlation coefficients for cumulative factor score means of dietary and nutrient patterns among adults 18 years and above, the China Health and Nutrition Survey by age and sex (1991-2011)**

Dietary and nutrient patterns	Traditional dietary pattern Coefficients	*P* value	Modern dietary pattern Coefficients	*P* value	Plant-sourced nutrient pattern Coefficients	*P* value
Traditional dietary pattern						
Modern dietary pattern	-0.1389	<0.0001				
Plant-sourced nutrient pattern	-0.0513	<0.0001	-0.3060	<0.0001		
Animal-sourced nutrient pattern	0.1270	<0.0001	0.4617	<0.0001	0.0145	<0.001

Supplementary Table 7.2 Median follow-up time and crude incidence of fractures by age and sex categories among adults 18 years and above, the China Health and Nutrition Survey (1991-2011)*

	Males			Females		
	<50 years	**>50 years**	**Total**	**<50 years**	**>50 years**	**Total**
N	**5,656**	**3,371**	**7627**	**5,789**	**3371**	**7945**
Median follow-up time (years)	9.0	13.7	10.7	7.1	13.9	9.1
Number of fractures	204	107	311	144	194	338
Person-years at risk	53542.7	27534.0	81076.7	51008.7	30330.9	81339.6
Rate of fracture per 1000 person-years (95% CI)	3.8 (3.3, 4.4)	2.9 (3.2, 4.7)	3.8 (3.4, 4.3)	2.8 (2.4, 3.3)	6.4 (5.6, 7.4)	4.2 (3.7, 4.6)

*The analysis did not exclude those cases that had missing values of other covariates (sex, age, energy intake, educational status, income, alcohol consumption, smoking, residency and physical activity level, body-mass index and high blood pressure).

Supplementary Table 7.3 Hazard ratios (HRs) [95% confidence interval (CI)] for tertiles of dietary and nutrient patterns and fracture among adults 18 years and above, the China Health and Nutrition Survey by age and sex (1991-2011)[@]

	Person-years; number of study participants (number of cases)	HR (95% CI)			*P*-trend
		T1	T2	T3	
Traditional dietary pattern					
Sex					
Male	62475.2; 6893 (252)	1.00 [reference]	1.29(0.92-1.80)	1.19(0.87-1.63)	0.314
Female	67599.9; 7,300 (288)	1.00 [reference]	0.90(0.68-1.18)	0.91(0.67-1.24)	0.521
Age					
<50 years	83634.3; 10342 (293)	1.00 [reference]	1.14(0.85-1.54)	1.10(0.82-1.46)	0.556
≥50 years	46440.8; 6426 (247)	1.00 [reference]	0.96(0.71-1.30)	0.94(0.68-1.31)	0.717
Modern dietary pattern					
Sex					
Male	62475.2; 6893 (252)	1.00 [reference]	1.18(0.86-1.61)	1.63(1.16-2.30)**	0.006
Female	67599.9; 7,300 (288)	1.00 [reference]	0.96(0.72-1.29)	1.18(0.85-1.65)	0.361
Age					
<50 years	83634.3; 10342 (293)	1.00 [reference]	1.10(0.83-1.47)	1.28(0.93-1.77)	0.132
≥50 years	46440.8; 6426 (247)	1.00 [reference]	1.03(0.74-1.42)	1.45(1.01-2.09)*	0.049
Plant-sourced nutrient pattern					
Sex					
Male	62475.2; 6892 (252)	1.00 [reference]	0.77(0.54-1.10)	0.78(0.55-1.12)	0.269
Female	67599.9; 7300 (288)	1.00 [reference]	1.11(0.82-1.50)	1.41(1.03-1.92)*	0.030
Age					
<50 years	83634.3; 10341 (293)	1.00 [reference]	0.87(0.62-1.20)	1.02(0.74-1.42)	0.731
≥50 years	46440.8; 6425 (247)	1.00 [reference]	0.99(0.71-1.37)	1.09(0.78-1.53)	0.610
Animal-sourced nutrient pattern					
Sex					
Male	62475.2; 6892 (252)	1.00 [reference]	1.63(1.15-2.32)**	1.74(1.22-2.48)**	0.003
Female	67599.9; 7300 (288)	1.00 [reference]	1.13(0.85-1.49)	1.19(0.85-1.65)	0.280
Age					
<50 years	83634.3; 10341 (293)	1.00 [reference]	1.48(1.10-1.99)**	1.30(0.94-1.79)	0.113
≥50 years	46440.8; 6425 (247)	1.00 [reference]	1.12(0.81-1.53)	1.47(1.04-2.07)*	0.034

* $P < 0.05$; ** $P < 0.01$; T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence)

[@] The model was adjusted for sex, age (continuous), energy intake (continuous), educational status (low, medium and high), income (low, medium and high), alcohol consumption (none, <1, 1-2, 3-4 per week and daily), smoking (non-smoker and current/ex-smoker), residency (rural and urban) and physical activity level (metabolic equivalent task-hours/week, continuous), body-mass index (continuous) and high blood pressure (yes/no). *P* for trend was obtained by adjusting the tertiles of the pattern scores as a continuous variable. Exposure levels of dietary and nutrient patterns were determined based on cumulative mean.

Supplementary Table 8.1 Food and nutrient intake across tertiles of dietary patterns derived by principal component analysis

N		Principal component analysis							
		Factor 1				Factor 2			
	Overall (n = 1182)	T1	T2	T3	*P* value	T1	T2	T3	*P* value
Foods									
High fat dairy (g/d), mean (SD)	89.3 (174.5)	138.8 (207.6)	68.8 (148.7)	60.1 (149.8)	<0.001	51.8 (126.7)	77.2 (150.4)	139.5 (221.2)	<0.001
Medium fat dairy (g/d), mean (SD)	262.5 (232.2)	158.0 (184.7)	272.0 (227.4)	358.4 (236.7)	<0.001	264.2 (226.7)	279.2 (233.9)	243.8 (235.1)	0.10
Soft drinks (g/d), mean (SD)	183.0 (320.8)	242.4 (381.6)	159.1 (246.3)	147.2 (312.4)	<0.001	100.5 (179.0)	146.5 (190.6)	303.3 (468.8)	<0.001
Processed meat (g/d), mean (SD)	24.2 (22.5)	25.4 (22.5)	24.5 (21.3)	22.8 (23.7)	0.28	11.5 (11.2)	22.4 (16.0)	39.0 (27.6)	<0.001
High fibre cereal (g/d), mean (SD)	2.2 (7.7)	1.5 (6.2)	2.0 (6.8)	3.2 (9.7)	0.008	2.6 (8.3)	2.1 (7.7)	2.0 (7.2)	0.51
Take away foods (g/d), mean (SD)	33.8 (31.1)	37.7 (32.5)	33.9 (32.3)	29.9 (27.7)	0.002	19.5 (16.0)	30.1 (19.1)	52.1 (41.7)	<0.001
Citrus fruit (g/d), mean (SD)	20.6 (30.0)	11.0 (18.5)	20.7 (31.5)	30.2 (34.7)	<0.001	23.5 (35.1)	20.3 (27.8)	18.0 (26.2)	0.035
Fruity vegetables (g/d), mean (SD)	115.8 (71.6)	59.3 (34.4)	112.1 (52.2)	176.6 (68.0)	<0.001	113.7 (68.2)	115.4 (71.6)	118.3 (75.1)	0.66
Other fruits (g/d), mean (SD)	222.8 (161.2)	144.0 (94.4)	206.0 (118.1)	319.6 (199.1)	<0.001	217.8 (143.5)	217.4 (143.6)	233.4 (192.0)	0.29
Root vegetables (g/d), mean (SD)	15.5 (13.3)	8.1 (7.5)	14.2 (11.2)	24.2 (14.9)	<0.001	13.5 (11.6)	14.8 (12.8)	18.2 (15.0)	<0.001
Root vegetables (g/d), mean (SD)	15.5 (13.3)	8.1 (7.5)	14.2 (11.2)	24.2 (14.9)	<0.001	13.5 (11.6)	14.8 (12.8)	18.2 (15.0)	<0.001
Leafy vegetables (g/d), mean (SD)	26.5 (26.4)	11.9 (12.1)	23.0 (17.9)	44.7 (32.8)	<0.001	28.5 (27.8)	25.5 (26.6)	25.3 (24.5)	0.17
High fibre bread (g/d), mean (SD)	56.9 (44.5)	43.7 (44.2)	57.6 (41.0)	69.4 (44.6)	<0.001	47.1 (35.8)	58.2 (42.5)	65.3 (52.0)	<0.001
Cabbages (g/d), mean (SD)	34.7 (30.7)	18.0 (16.2)	32.8 (24.2)	53.6 (36.8)	<0.001	33.4 (30.4)	33.3 (27.7)	37.5 (33.7)	0.098
Legumes (g/d), mean (SD)	38.8 (72.3)	21.1 (27.9)	31.8 (44.9)	63.7 (109.6)	<0.001	40.1 (61.1)	34.5 (53.1)	41.8 (95.8)	0.34
Nutrients									
Protein (g/d), mean (SD)	94.5 (34.0)	78.7 (24.1)	92.5 (26.4)	112.3 (40.5)	<0.001	74.8 (22.3)	92.4 (21.8)	115.1 (40.7)	<0.001
Calcium (mg/d), mean (SD)	878.6 (329.1)	703.1 (266.5)	855.1 (298.9)	1077.3 (307.7)	<0.001	759.8 (312.4)	885.4 (314.0)	984.2 (322.7)	<0.001
Potassium (mg/d), mean (SD)	3919.9 (1452.4)	2928.9 (907.1)	3797.9 (1159.7)	5031.3 (1398.0)	<0.001	3311.0 (1114.4)	3867.6 (1455.5)	4547.6 (1477.5)	<0.001
Vitamin D (mcg/d), mean (SD)	3.5 (2.0)	3.4 (2.0)	3.3 (1.7)	3.8 (2.2)	<0.001	2.6 (1.4)	3.4 (1.7)	4.5 (2.3)	<0.001
Polyunsaturated fat (g/d), mean (SD)	16.2 (7.0)	14.9 (6.8)	15.3 (5.8)	18.6 (7.7)	<0.001	13.4 (6.7)	15.7 (5.8)	19.5 (7.0)	<0.001
Saturated fat (g/d), mean (SD)	28.6 (12.0)	27.5 (13.7)	27.4 (10.1)	30.8 (11.9)	<0.001	20.3 (6.5)	27.4 (6.9)	37.5 (13.9)	<0.001
Sodium (mg/d), mean (SD)	2354.3 (905.1)	2077.5 (753.5)	2296.2 (793.0)	2689.4 (1037.8)	<0.001	1655.4 (467.0)	2249.3 (510.8)	3119.4 (940.5)	<0.001
Cholesterol (mg/d), mean (SD)	277.6 (118.4)	253.8 (99.4)	268.3 (97.2)	310.9 (145.4)	<0.001	212.1 (75.2)	268.7 (81.7)	348.5 (141.8)	<0.001
Fat (g/d), mean (SD)	88.5 (30.3)	81.2 (27.6)	85.4 (26.2)	99.0 (33.7)	<0.001	70.0 (23.7)	85.2 (21.4)	109.4 (30.6)	<0.001
Carbohydrates (g/d), mean (SD)	210.1 (93.1)	173.9 (69.0)	204.1 (90.3)	252.3 (99.8)	<0.001	163.6 (66.3)	207.8 (96.4)	256.4 (88.9)	<0.001
Energy from food (kj/d), mean (SD)	8665.4 (2611.3)	7509.5 (2184.1)	8405.9 (2193.0)	10082.3 (2747.2)	<0.001	6818.7 (1814.1)	8435.1 (1834.0)	10640.2 (2534.4)	<0.001
Fibre (g/d), mean (SD)	28.4 (11.2)	19.9 (6.7)	27.2 (7.8)	37.9 (10.4)	<0.001	24.9 (9.5)	28.2 (11.1)	31.8 (11.6)	<0.001

Supplementary Table 8.2 Food and nutrient intake across tertiles of dietary patterns derived by partial least-squares

Factor	Partial least-squares															
N	Factor 1				Factor 2				Factor 3				Factor 4			
	T1	T2	T3	*P* value	T1	T2	T3	*P* value	T1	T2	T3	*P* value	T1	T2	T3	*P* value
Foods																
High fat dairy (g/d), mean (SD)	175.4 (222.7)	62.3 (136.2)	30.3 (108.1)	<0.001	45.0 (109.6)	72.8 (151.1)	150.2 (225.1)	<0.001	186.8 (234.1)	67.5 (129.6)	13.7 (64.1)	<0.001	206.1 (242.1)	39.9 (90.5)	21.9 (62.9)	<0.001
Medium fat dairy (g/d), mean (SD)	110.8 (136.1)	253.0 (194.0)	423.5 (238.1)	<0.001	333.7 (249.7)	264.4 (223.0)	189.3 (198.7)	<0.001	149.6 (165.4)	215.3 (187.5)	422.5 (242.5)	<0.001	244.6 (251.6)	299.8 (234.7)	243.1 (203.9)	<0.001
Soft drinks (g/d), mean (SD)	275.6 (430.3)	150.7 (243.1)	122.7 (227.5)	<0.001	229.8 (415.5)	167.1 (268.7)	152.2 (247.0)	0.001	190.1 (381.2)	169.4 (263.6)	189.5 (307.0)	0.590	141.9 (286.0)	178.4 (278.7)	228.7 (382.1)	<0.001
Processed meat (g/d), mean (SD)	30.2 (26.1)	22.5 (21.1)	19.9 (18.5)	<0.001	22.7 (20.7)	23.2 (19.6)	26.8 (26.5)	0.021	26.7 (25.1)	21.4 (18.7)	24.6 (22.9)	0.004	17.3 (16.6)	21.8 (19.2)	33.5 (27.2)	<0.001
High fiber cereal (g/d), mean (SD)	1.4 (5.7)	1.7 (7.0)	3.5 (9.8)	<0.001	2.2 (7.5)	2.1 (8.0)	2.4 (7.7)	0.89	2.2 (7.9)	1.8 (7.0)	2.6 (8.3)	0.350	2.5 (8.0)	2.3 (8.3)	1.8 (6.8)	0.41
Take away foods (g/d), mean (SD)	45.3 (39.2)	31.5 (25.6)	24.7 (22.1)	<0.001	35.8 (35.2)	32.2 (28.2)	33.6 (29.3)	0.26	35.9 (33.6)	33.1 (31.2)	32.4 (28.2)	0.240	25.9 (21.1)	31.0 (24.3)	44.7 (40.9)	<0.001
Citrus fruit (g/d), mean (SD)	12.7 (21.3)	21.0 (32.5)	28.1 (32.9)	<0.001	25.5 (34.7)	21.6 (32.5)	14.7 (19.8)	<0.001	27.0 (36.1)	20.4 (28.9)	14.4 (22.2)	<0.001	19.8 (29.1)	21.5 (29.1)	20.4 (31.9)	0.72
Fruity vegetables (g/d), mean (SD)	71.3 (47.9)	109.6 (57.2)	166.5 (72.4)	<0.001	121.9 (76.3)	109.9 (66.3)	115.6 (71.6)	0.065	149.8 (82.0)	110.6 (62.1)	87.1 (53.1)	<0.001	87.8 (55.4)	115.6 (62.7)	144.0 (82.7)	<0.001
Other fruits (g/d), mean (SD)	164.4 (118.4)	211.8 (129.8)	292.4 (197.1)	<0.001	269.1 (200.2)	208.7 (126.3)	190.8 (136.8)	<0.001	283.7 (206.9)	210.9 (129.9)	173.9 (110.3)	<0.001	209.2 (140.6)	224.3 (173.5)	235.0 (167.1)	0.078
Root vegetables (g/d), mean (SD)	9.7 (8.7)	14.0 (11.8)	22.7 (15.2)	<0.001	16.5 (13.3)	14.8 (12.8)	15.1 (13.8)	0.16	20.7 (16.2)	14.9 (11.8)	10.8 (9.0)	<0.001	11.4 (10.4)	16.1 (13.2)	18.9 (14.9)	<0.001
Root vegetables (g/d), mean (SD)	9.7 (8.7)	14.0 (11.8)	22.7 (15.2)	<0.001	16.5 (13.3)	14.8 (12.8)	15.1 (13.8)	0.16	20.7 (16.2)	14.9 (11.8)	10.8 (9.0)	<0.001	11.4 (10.4)	16.1 (13.2)	18.9 (14.9)	<0.001
Leafy vegetables (g/d), mean (SD)	14.7 (15.0)	23.3 (20.8)	41.4 (32.6)	<0.001	24.6 (27.0)	25.7 (24.6)	29.1 (27.3)	0.042	37.9 (33.7)	22.7 (18.9)	18.8 (19.9)	<0.001	22.5 (25.0)	25.7 (23.5)	31.2 (29.5)	<0.001
High fiber bread (g/d), mean (SD)	52.2 (49.1)	58.5 (42.9)	60.0 (40.8)	0.033	66.7 (48.3)	56.7 (42.5)	47.2 (40.1)	<0.001	68.4 (50.6)	54.1 (40.5)	48.1 (39.1)	<0.001	56.3 (44.9)	56.0 (43.1)	58.2 (45.6)	0.75
Cabbages (g/d), mean (SD)	20.7 (17.8)	30.3 (24.1)	53.2 (37.1)	<0.001	34.8 (30.4)	31.2 (25.5)	38.2 (35.1)	0.006	46.8 (37.6)	31.9 (26.8)	25.5 (21.5)	<0.001	29.1 (26.8)	33.9 (27.2)	41.1 (36.1)	<0.001
Leguems (g/d), mean (SD)	26.4 (36.7)	35.2 (55.0)	54.8 (104.5)	<0.001	43.0 (96.9)	32.2 (49.9)	41.1 (61.4)	0.082	58.9 (104.3)	30.7 (50.5)	26.6 (40.8)	<0.001	35.2 (56.1)	33.0 (48.0)	48.1 (100.6)	0.006
Nutrients																
Protein (g/d), mean (SD)	88.9 (32.7)	90.2 (29.5)	104.3 (37.3)	<0.001	91.8 (26.9)	88.9 (26.7)	103.3 (44.4)	<0.001	102.4 (34.7)	87.1 (26.7)	93.9 (37.9)	<0.001	81.5 (25.8)	90.5 (23.2)	112.6 (42.5)	<0.001
Calcium (mg/d), mean (SD)	744.0 (283.8)	826.7 (286.2)	1064.1 (328.4)	<0.001	974.5 (341.2)	837.6 (311.8)	819.0 (311.0)	<0.001	914.1 (294.8)	772.6 (302.7)	949.1 (360.0)	<0.001	912.1 (325.9)	858.5 (322.8)	863.9 (337.2)	0.045

Factor N	Partial least-squares															
	Factor 1				Factor 2				Factor 3				Factor 4			
	T1	T2	T3	*P* value	T1	T2	T3	*P* value	T1	T2	T3	*P* value	T1	T2	T3	*P* value
Potassium (mg/d), mean (SD)	3261.5 (1179.0)	3775.0 (1251.3)	4717.8 (1514.1)	<0.001	4233.4 (1570.3)	3702.4 (1369.9)	3812.6 (1348.1)	<0.001	4552.9 (1466.2)	3587.8 (1275.0)	3616.5 (1399.4)	<0.001	3626.9 (1387.8)	3825.3 (1400.5)	4331.6 (1483.6)	<0.001
Vitamin D (mcg/d), mean (SD)	4.1 (2.3)	3.2 (1.7)	3.2 (1.8)	<0.001	2.8 (1.4)	3.2 (1.7)	4.5 (2.5)	<0.001	4.7 (2.4)	3.2 (1.5)	2.6 (1.3)	<0.001	4.1 (2.4)	3.0 (1.5)	3.3 (1.9)	<0.001
Polyunsaturated fat (g/d), mean (SD)	17.2 (7.4)	15.3 (6.4)	16.2 (7.0)	0.001	17.3 (7.3)	15.5 (6.4)	15.9 (7.1)	<0.001	18.8 (7.4)	15.1 (6.5)	14.8 (6.3)	<0.001	14.5 (6.6)	15.6 (6.4)	18.8 (7.3)	<0.001
Saturated fat (g/d), mean (SD)	32.2 (14.6)	26.8 (10.2)	26.7 (10.0)	<0.001	30.5 (13.7)	26.5 (10.0)	28.6 (11.8)	<0.001	33.6 (14.1)	26.0 (9.3)	26.0 (10.6)	<0.001	26.4 (13.7)	26.0 (8.7)	33.5 (11.7)	<0.001
Sodium (mg/d), mean (SD)	2437.1 (958.0)	2246.6 (851.3)	2381.2 (895.7)	0.012	2491.8 (914.6)	2221.2 (782.4)	2346.8 (991.4)	<0.001	2713.0 (1001.5)	2138.4 (725.7)	2210.2 (857.1)	<0.001	1962.3 (682.8)	2229.6 (639.9)	2903.1 (1071.2)	<0.001
Cholesterol (mg/d), mean (SD)	289.0 (117.5)	263.5 (107.0)	280.6 (128.7)	0.010	250.6 (96.4)	258.7 (90.9)	326.3 (147.1)	<0.001	311.2 (129.1)	257.6 (96.0)	264.0 (120.5)	<0.001	254.1 (110.0)	259.5 (89.6)	321.7 (139.7)	<0.001
Fat (g/d), mean (SD)	94.2 (31.5)	84.6 (28.2)	86.8 (30.3)	<0.001	92.9 (29.9)	83.0 (27.1)	89.6 (32.8)	<0.001	102.6 (30.5)	82.2 (26.5)	80.7 (28.6)	<0.001	79.2 (28.1)	83.0 (24.1)	104.3 (32.1)	<0.001
Carbohydrates (g/d), mean (SD)	199.8 (79.8)	204.3 (91.6)	226.3 (104.2)	<0.001	250.2 (107.0)	199.8 (84.0)	178.0 (67.4)	<0.001	244.3 (91.9)	193.2 (85.8)	192.7 (91.9)	<0.001	194.2 (92.5)	204.8 (95.3)	232.6 (87.0)	<0.001
Energy from food incl fibre (kj/d), mean (SD)	8646.0 (2706.5)	8317.4 (2464.6)	9036.4 (2616.6)	<0.001	9425.4 (2529.9)	8177.4 (2323.6)	8364.0 (2798.4)	<0.001	9966.4 (2540.6)	8006.9 (2252.8)	8017.8 (2531.4)	<0.001	7798.0 (2330.4)	8268.2 (2192.6)	10007.0 (2770.0)	<0.001
Fibre (g/d), mean (SD)	22.9 (8.7)	27.5 (9.7)	34.6 (11.6)	<0.001	31.9 (12.3)	27.0 (10.1)	26.0 (10.0)	<0.001	34.5 (11.3)	26.5 (9.6)	24.0 (9.7)	<0.001	25.5 (10.5)	28.0 (10.7)	31.9 (11.4)	<0.001

ANOVA was used to test the mean difference across tertiles. SD – standard deviation; T1 – tertile 1 (lowest adherence); T2 – tertile 2; T3 – tertile 3 (highest adherence)

Supplementary Table 8.3 Food and nutrient intake across tetiles of dietary patterns derived by reduced-rank regression

	Reduced-rank regression															
	Factor 1				Factor 2				Factor 3				Factor 4			
	T1	T2	T3	*P*	T1	T2	T3	*P*	T1	T2	T3	*P*	T1	T2	T3	*P*
Foods																
High fat dairy (g/d), mean (SD)	82.2 (134.2)	101.6 (185.5)	84.3 (197.0)	0.23	8.2 (41.0)	36.1 (72.3)	223.8 (238.7)	<0.001	22.1 (66.1)	48.3 (109.7)	197.6 (238.9)	<0.001	70.6 (167.3)	96.9 (176.8)	100.5 (178.0)	0.031
Medium fat dairy (g/d), mean (SD)	111.7 (112.5)	209.4 (153.3)	466.3 (242.1)	<0.001	393.5 (242.3)	243.2 (196.1)	150.7 (186.4)	<0.001	236.4 (200.5)	275.2 (216.7)	275.8 (271.7)	0.024	370.3 (260.9)	238.3 (213.0)	178.9 (171.2)	<0.001
Soft drinks (g/d), mean (SD)	246.9 (405.4)	160.8 (226.6)	141.4 (295.4)	<0.001	181.8 (322.3)	171.9 (262.2)	195.3 (369.3)	0.59	190.1 (325.8)	174.0 (250.9)	185.0 (374.2)	0.77	222.9 (361.7)	165.5 (259.8)	160.7 (329.4)	0.010
Processed meat (g/d), mean (SD)	27.7 (25.0)	22.9 (20.7)	22.1 (21.2)	<0.001	21.7 (19.7)	23.0 (20.1)	28.0 (26.6)	<0.001	28.0 (25.7)	24.2 (21.1)	20.5 (19.7)	<0.001	29.1 (26.0)	20.9 (17.5)	22.7 (22.4)	<0.001
High fiber cereal (g/d), mean (SD)	1.6 (6.6)	2.0 (7.5)	3.0 (8.8)	0.036	2.8 (8.5)	2.1 (7.9)	1.7 (6.7)	0.12	2.2 (8.0)	1.7 (6.4)	2.7 (8.6)	0.18	1.8 (6.8)	2.3 (7.6)	2.6 (8.6)	0.35
Take away foods (g/d), mean (SD)	41.2 (37.8)	31.6 (26.0)	28.7 (26.7)	<0.001	31.9 (30.4)	32.8 (30.7)	36.9 (31.8)	0.053	38.5 (38.3)	33.2 (28.2)	29.7 (24.5)	<0.001	38.7 (33.6)	33.0 (30.6)	29.8 (28.2)	<0.001
Citrus fruit (g/d), mean (SD)	17.0 (27.0)	20.8 (30.4)	24.0 (32.2)	0.004	25.3 (34.0)	19.4 (29.2)	17.1 (25.9)	<0.001	17.7 (27.3)	21.9 (31.2)	22.2 (31.3)	0.062	15.7 (25.7)	19.7 (30.1)	26.3 (33.0)	<0.001
Fruity vegetables (g/d), mean (SD)	100.9 (68.6)	106.5 (60.1)	140.0 (78.8)	<0.001	135.2 (76.7)	108.4 (63.0)	103.7 (70.6)	<0.001	126.3 (74.5)	115.3 (69.0)	105.8 (70.0)	<0.001	91.2 (62.3)	103.9 (60.1)	152.3 (76.5)	<0.001
Other fruits (g/d), mean (SD)	210.4 (151.2)	210.0 (165.8)	248.1 (163.8)	<0.001	269.7 (201.3)	199.4 (115.6)	199.4 (144.7)	<0.001	204.2 (141.6)	221.6 (142.2)	242.8 (192.6)	0.003	179.5 (119.4)	201.9 (122.4)	287.1 (206.0)	<0.001
Root vegetables (g/d), mean (SD)	13.4 (12.4)	14.5 (12.2)	18.5 (14.7)	<0.001	18.6 (14.7)	14.0 (11.7)	13.9 (12.8)	<0.001	17.2 (14.4)	15.3 (12.9)	14.0 (12.4)	0.003	12.2 (10.5)	13.5 (10.7)	20.7 (16.3)	<0.001
Root vegetables (g/d), mean (SD)	13.4 (12.4)	14.5 (12.2)	18.5 (14.7)	<0.001	18.6 (14.7)	14.0 (11.7)	13.9 (12.8)	<0.001	17.2 (14.4)	15.3 (12.9)	14.0 (12.4)	0.003	12.2 (10.5)	13.5 (10.7)	20.7 (16.3)	<0.001
Leafy vegetables (g/d), mean (SD)	20.3 (20.5)	24.7 (25.2)	34.4 (30.6)	<0.001	30.8 (30.3)	23.8 (20.9)	24.8 (26.7)	<0.001	28.0 (25.1)	26.3 (26.7)	25.1 (27.2)	0.32	19.1 (21.3)	21.6 (18.5)	38.6 (32.8)	<0.001
High fibre bread (g/d), mean (SD)	62.8 (50.9)	53.3 (41.8)	54.5 (39.4)	0.005	57.7 (44.7)	56.7 (39.5)	56.2 (48.9)	0.89	50.9 (41.7)	54.8 (39.1)	64.9 (50.7)	<0.001	62.0 (49.1)	56.5 (42.5)	52.1 (41.0)	0.007
Cabbages (g/d), mean (SD)	27.3 (24.6)	32.3 (29.2)	44.5 (34.9)	<0.001	39.4 (33.4)	32.8 (28.8)	32.1 (29.3)	0.001	40.8 (35.2)	31.7 (27.5)	31.7 (28.0)	<0.001	25.5 (22.0)	30.3 (25.0)	48.4 (37.8)	<0.001
Legumes (g/d), mean (SD)	34.5 (51.3)	37.4 (91.2)	44.4 (68.6)	0.14	46.5 (99.9)	29.5 (41.4)	40.3 (62.2)	0.004	44.0 (97.3)	32.6 (47.2)	39.7 (62.8)	0.081	28.6 (42.3)	34.0 (52.1)	53.7 (104.2)	<0.001
Nutrients																
Protein (g/d), mean (SD)	88.2 (28.9)	91.0 (31.1)	104.7 (39.2)	<0.001	94.0 (25.7)	87.6 (26.3)	102.6 (45.9)	<0.001	108.3 (44.0)	89.7 (25.6)	86.9 (26.6)	<0.001	101.9 (39.0)	88.6 (26.8)	93.7 (34.4)	<0.001
Calcium (mg/d), mean (SD)	702.4 (252.8)	817.1 (277.6)	1129.3 (297.0)	<0.001	997.1 (337.9)	776.1 (300.8)	858.8 (307.1)	<0.001	774.7 (318.4)	845.3 (306.1)	1004.8 (320.9)	<0.001	987.3 (335.5)	830.6 (319.3)	828.7 (309.8)	<0.001

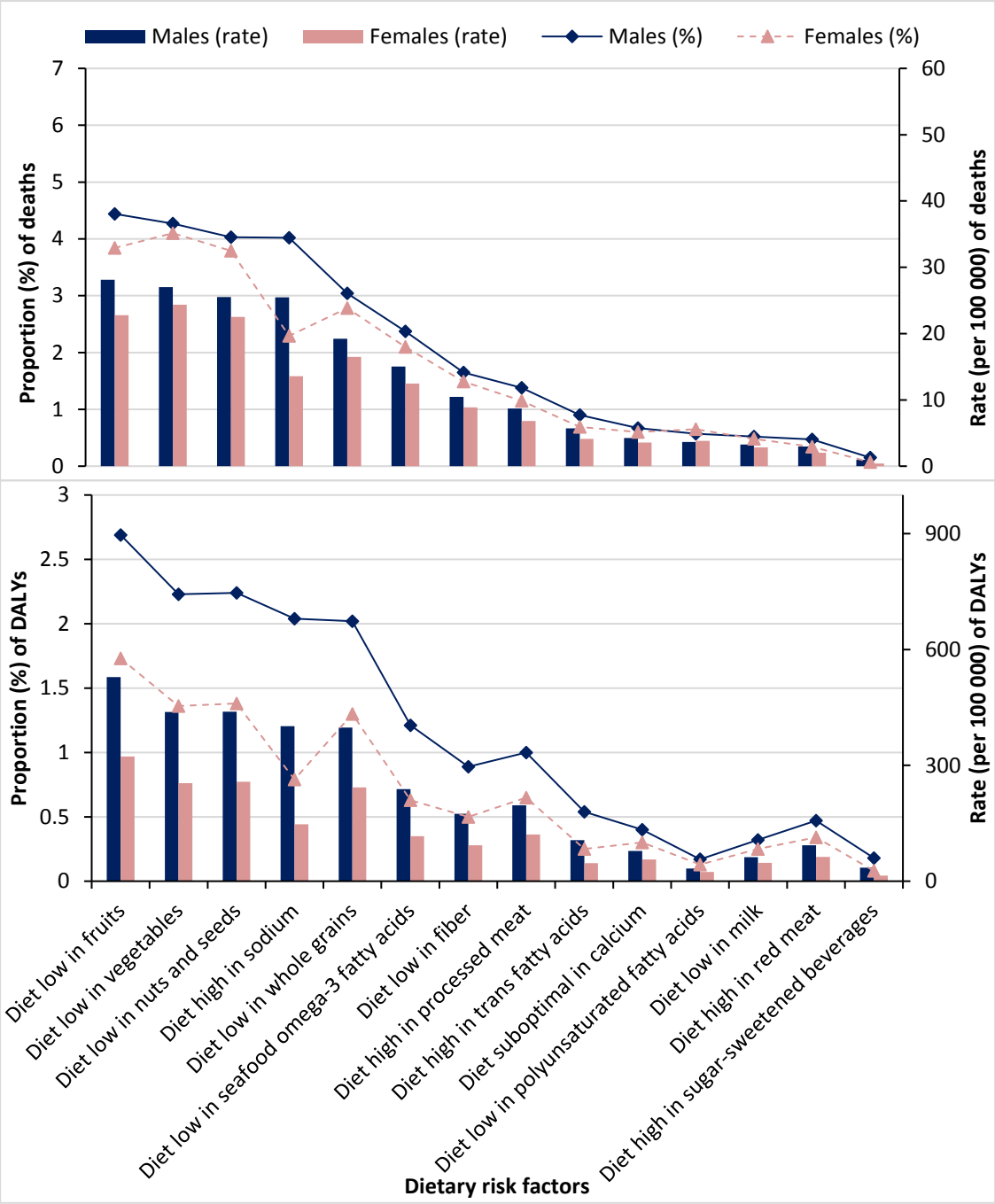
	Reduced-rank regression															
	Factor 1				Factor 2				Factor 3				Factor 4			
	T1	T2	T3	*P*	T1	T2	T3	*P*	T1	T2	T3	*P*	T1	T2	T3	*P*
Potassium (mg/d), mean (SD)	3590.5 (1463.1)	3745.1 (1307.6)	4450.1 (1438.1)	<0.001	4437.0 (1600.1)	3521.5 (1126.5)	3780.3 (1431.3)	<0.001	3942.5 (1405.4)	3778.3 (1341.3)	4041.0 (1585.9)	0.038	3600.0 (1119.3)	3633.9 (1349.4)	4494.0 (1635.6)	<0.001
Vitamin D (mcg/d), mean (SD)	3.3 (1.7)	3.5 (1.9)	3.7 (2.3)	0.012	2.4 (1.1)	2.9 (1.2)	5.4 (2.3)	<0.001	3.3 (2.0)	3.1 (1.5)	4.1 (2.3)	<0.001	3.4 (1.9)	3.3 (1.8)	3.8 (2.2)	0.004
Polyunsaturated fat (g/d), mean (SD)	17.5 (7.1)	15.4 (6.6)	15.7 (7.0)	<0.001	16.1 (7.1)	15.3 (5.7)	17.4 (7.9)	<0.001	16.8 (7.4)	15.9 (6.4)	16.1 (7.2)	0.22	17.4 (7.3)	15.6 (6.5)	15.9 (7.0)	0.001
Saturated fat (g/d), mean (SD)	30.8 (14.0)	27.2 (10.9)	27.6 (10.5)	<0.001	27.6 (10.1)	26.1 (12.5)	32.3 (12.7)	<0.001	28.7 (12.2)	26.7 (9.2)	30.2 (14.0)	<0.001	31.5 (12.2)	27.2 (10.1)	27.3 (13.2)	<0.001
Sodium (mg/d), mean (SD)	2476.5 (897.0)	2216.7 (852.6)	2365.2 (947.7)	<0.001	2385.6 (898.9)	2193.9 (747.4)	2496.2 (1036.3)	<0.001	2527.7 (1054.8)	2272.9 (762.2)	2280.2 (871.3)	<0.001	2546.4 (914.6)	2170.9 (749.8)	2364.8 (998.8)	<0.001
Cholesterol (mg/d), mean (SD)	270.8 (111.0)	271.9 (107.6)	290.8 (134.7)	0.035	249.8 (91.5)	256.6 (89.9)	332.0 (150.5)	<0.001	317.4 (141.6)	262.3 (94.0)	257.4 (108.6)	<0.001	302.7 (138.8)	268.9 (99.9)	263.8 (112.1)	<0.001
Fat (g/d), mean (SD)	94.6 (30.5)	84.3 (29.0)	86.3 (30.3)	<0.001	86.9 (29.2)	82.1 (24.6)	97.3 (34.8)	<0.001	92.1 (33.6)	84.9 (26.0)	88.9 (30.7)	0.005	95.4 (33.4)	84.6 (26.6)	86.2 (29.8)	<0.001
Carbohydrates (g/d), mean (SD)	225.5 (103.5)	195.0 (86.7)	209.2 (85.0)	<0.001	243.2 (116.8)	189.5 (69.6)	195.8 (73.7)	<0.001	190.4 (71.7)	205.0 (88.6)	232.9 (108.5)	<0.001	205.9 (61.5)	196.9 (87.9)	227.1 (116.4)	<0.001
Energy from food including fibre (kj/d), mean (SD)	9026.1 (2636.4)	8201.1 (2564.6)	8756.9 (2568.2)	<0.001	9103.7 (2534.7)	7958.1 (2169.7)	8954.5 (2962.3)	<0.001	8745.7 (2887.2)	8348.4 (2297.3)	8909.7 (2620.6)	0.008	9011.0 (2635.5)	8205.7 (2307.3)	8814.0 (2809.6)	<0.001
Fibre (g/d), mean (SD)	27.8 (11.4)	27.1 (11.0)	30.2 (10.9)	<0.001	32.6 (12.6)	25.9 (8.7)	26.2 (10.5)	<0.001	27.9 (10.7)	27.6 (10.0)	29.5 (12.5)	0.039	25.0 (8.3)	26.3 (10.0)	33.4 (12.7)	<0.001

Supplementary Table 8.4 Pearson correlation coefficients among response variables

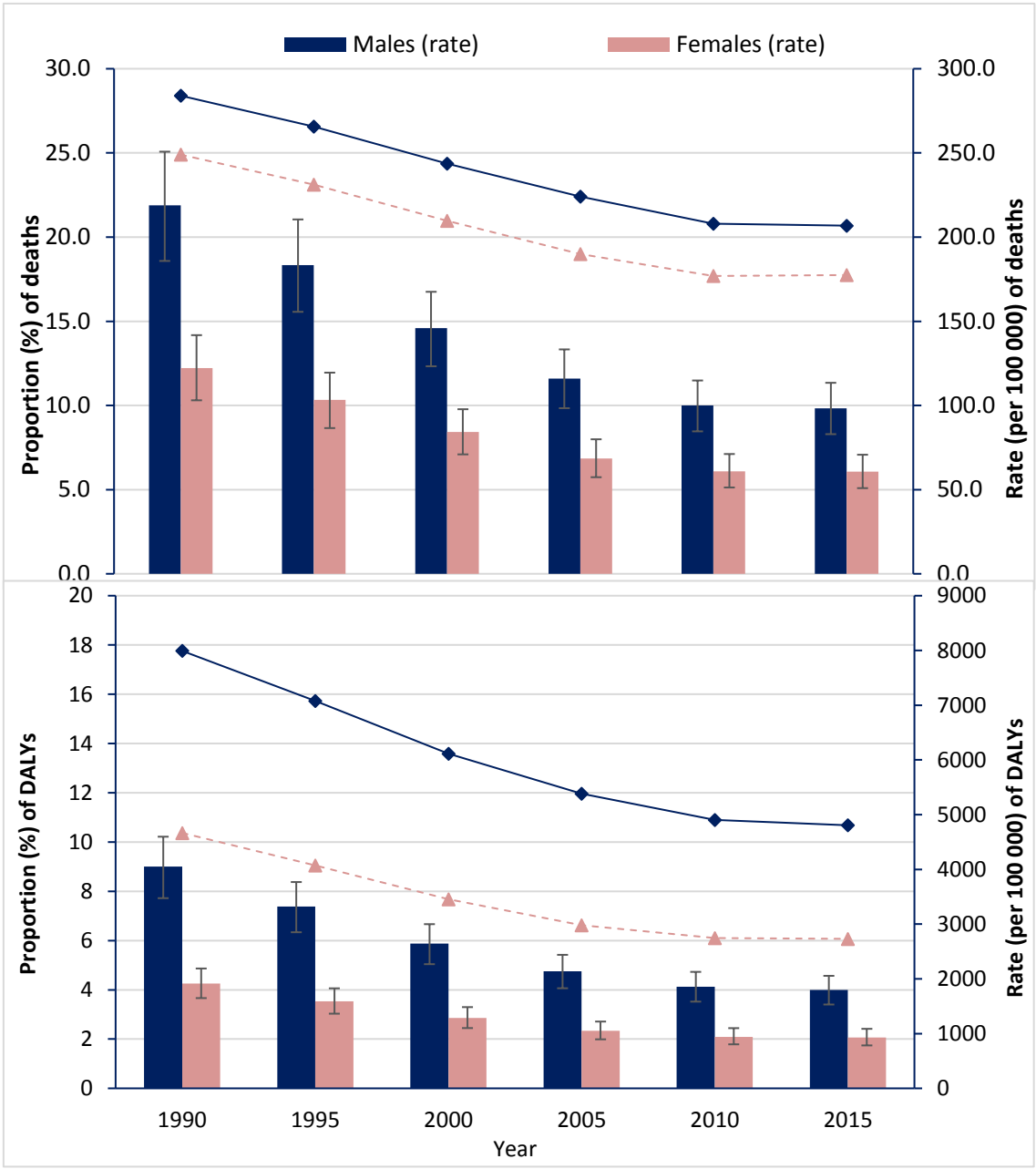
Response variables	Energy from protein	Calcium density	Potassium density	Vitamin D density
Energy from protein (%/day)	1.00	0.28**	0.28**	0.15**
Calcium density(mg/day/Kcal)		1.00	0.43**	0.10*
Potassium density(mg/day/Kcal)			1.00	-0.06*
Vitamin D density(ng/day/Kcal)				1.00

* $P < 0.05$; ** $P < 0.001$

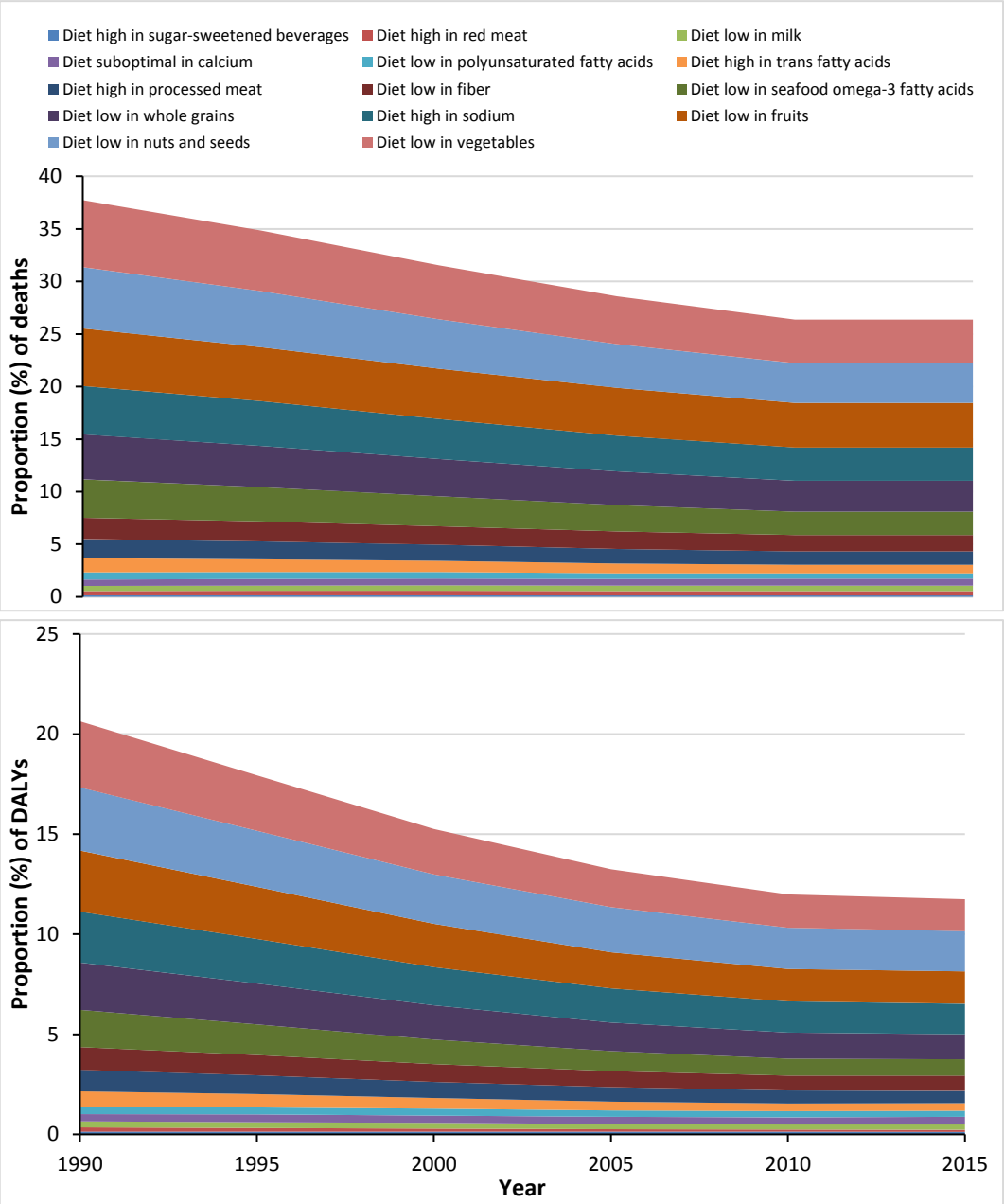
Appendix II – Supplementary Figures



Supplementary Figure 4.1 Burden of disease (deaths and disability-adjusted life years (DALYs)) associated with specific dietary risks and proportion of contribution to the non-communicable disease burden by sex in Australia, 2015



Supplementary Figure 4.2 Age-standardized burden of disease (deaths and disability-adjusted life years (DALYs)) associated with dietary risks and relative contribution to the non-communicable disease burden by sex in Australia, between 1990 and 2015



Supplementary Figure 4.3 Age-standardized burden of non-communicable diseases (deaths and disability-adjusted life years (DALYs)) associated with specific dietary risks between 1990 and 2015 in Australia

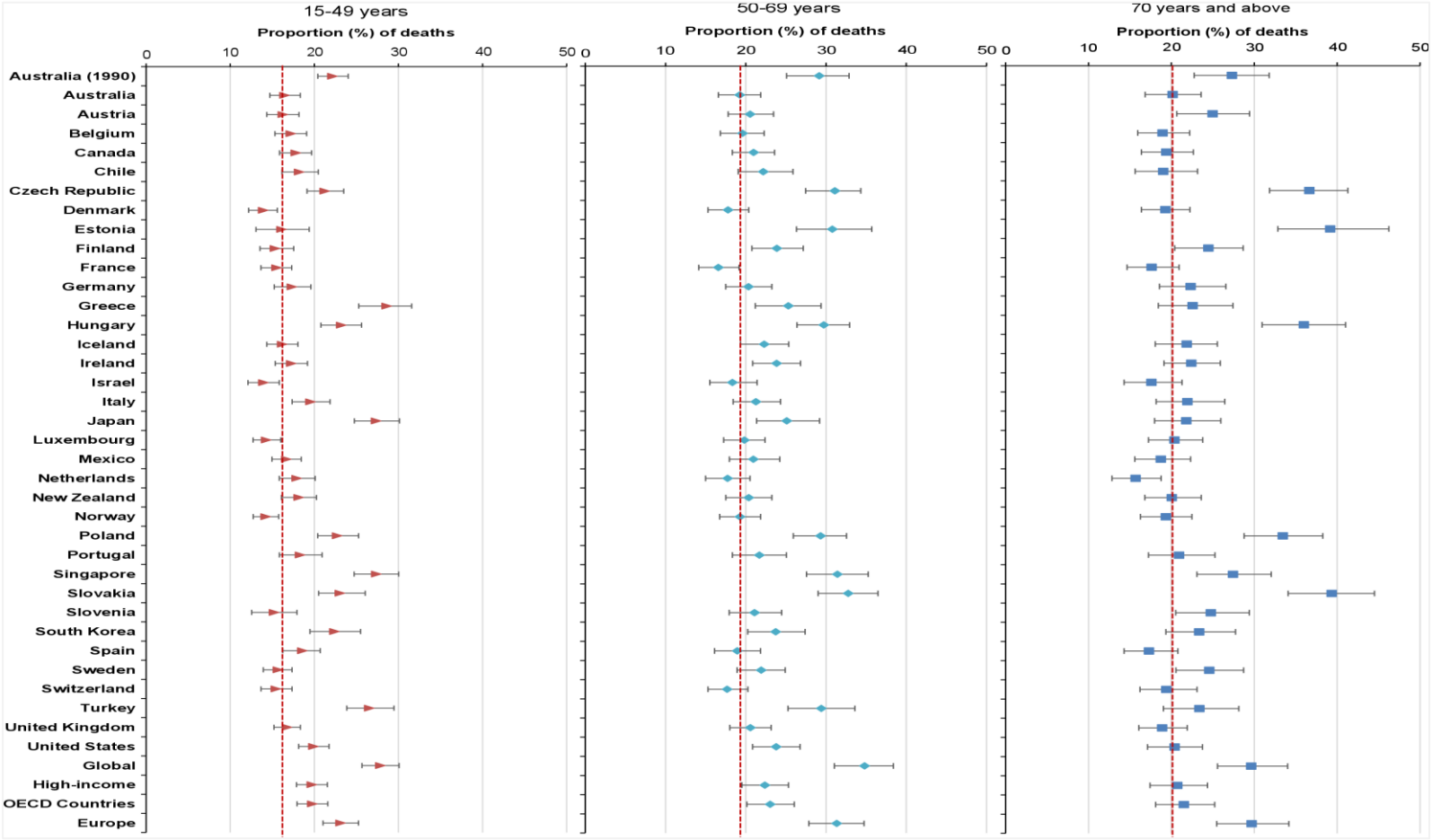
[The sum of percentages in rows exceeds the total for all dietary risk factors combined because overlap between various risk factors.]

		Death														DALY												
Country		Diet low in fruits	Diet low in vegetables	Diet low in nuts and seeds	Diet high in sodium	Diet low in whole grains	Diet low in seafood omega-3 fatty acids	Diet low in fibre	Diet high in processed meat	Diet high in trans fatty acids	Diet suboptimal in calcium	Diet low in polyunsaturated fatty acids	Diet low in milk	Diet high in red meat	Diet high in sugar-sweetened beverages	Diet low in fruits	Diet low in nuts and seeds	Diet low in vegetables	Diet low in whole grains	Diet high in sodium	Diet low in seafood omega-3 fatty acids	Diet high in processed meat	Diet low in fibre	Diet high in red meat	Diet high in trans fatty acids	Diet suboptimal in calcium	Diet low in milk	Diet high in sugar-sweetened beverages	Diet low in polyunsaturated fatty acids
Australia	%	4.2	4.1	3.8	3.1	2.9	2.2	1.5	1.3	0.8	0.7	0.5	0.5	0.4	0.1	2.0	1.6	1.6	1.5	1.3	0.8	0.8	0.6	0.4	0.4	0.3	0.3	0.1	0.1
	Rank	1	2	3	4	5	6	7	8	9	10	11	12	13	14	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Austria	%	3.8	4.9	4.0	5.7	4.2	3.3	1.4	2.0	0.8	0.6	1.2	0.4	0.3	0.1	2.0	1.7	2.1	2.2	2.3	1.4	1.2	0.6	0.3	0.3	0.3	0.2	0.1	0.4
	Rank	5	2	4	1	3	6	8	7	10	11	9	12	13	14	4	5	3	2	1	6	7	8	11	10	11	13	14	9
Belgium	%	4.7	3.8	3.5	3.2	3.6	2.4	1.2	1.5	0.6	0.6	0.3	0.5	0.2	0.1	2.7	1.8	1.8	2.1	1.5	1.1	1.1	0.6	0.2	0.3	0.3	0.3	0.1	0.1
	Rank	1	2	4	5	3	6	8	7	10	9	12	11	13	14	1	4	3	2	5	6	6	8	12	10	9	11	13	14
Canada	%	3.7	3.5	3.9	3.5	3.5	2.2	1.2	1.5	1.4	0.6	1.3	0.5	0.3	0.2	2.1	1.9	1.6	2.1	1.6	0.9	1.0	0.6	0.3	0.7	0.3	0.3	0.2	0.5
	Rank	2	3	1	3	3	6	10	7	8	11	9	12	13	14	2	3	4	1	4	7	6	9	12	8	11	13	14	10
Chile	%	4.8	3.4	3.6	3.9	4.9	1.8	0.9	1.2	0.5	0.6	0.6	0.4	0.2	0.1	3.0	2.1	1.8	3.2	1.9	0.9	0.9	0.4	0.2	0.3	0.3	0.2	0.1	0.4
	Rank	2	5	4	3	1	6	8	7	11	10	9	12	13	14	2	3	5	1	4	6	7	9	13	11	10	12	14	8
Czech Republic	%	6.5	7.2	7.0	8.2	8.4	4.4	2.1	2.6	1.5	0.7	2.9	0.6	0.3	0.1	3.8	3.6	3.6	4.8	4.3	2.1	1.8	1.0	0.3	0.9	0.4	0.4	0.1	1.2
	Rank	5	3	4	2	1	6	9	8	10	11	7	12	13	14	3	4	5	1	2	6	7	9	13	10	11	12	14	8
Denmark	%	4.3	3.8	3.4	2.8	3.6	2.2	1.1	1.6	0.4	0.5	0.7	0.5	0.3	0.1	2.4	1.6	1.7	2.1	1.3	0.9	1.1	0.5	0.3	0.2	0.2	0.3	0.1	0.2
	Rank	1	2	4	5	3	6	8	7	12	11	9	10	13	14	1	4	3	2	5	7	6	8	9	13	11	10	14	12
Estonia	%	6.5	6.9	6.9	10.6	9.3	4.6	1.2	2.3	0.9	0.3	2.1	0.3	0.1	0.0	3.8	3.3	3.4	5.2	5.2	2.1	1.5	0.5	0.2	0.5	0.2	0.2	0.0	0.8
	Rank	5	3	4	1	2	6	9	7	10	11	8	12	13	14	3	5	4	1	2	6	7	9	11	9	11	11	14	8
Finland	%	4.5	5.5	5.5	5.3	4.2	3.2	1.2	2.0	0.6	0.2	1.5	0.3	0.1	0.1	2.4	2.6	2.5	2.3	2.4	1.4	1.3	0.5	0.2	0.3	0.1	0.1	0.1	0.5
	Rank	4	1	2	3	5	6	9	7	10	12	8	11	13	14	3	1	2	5	3	6	7	9	11	10	13	12	14	8
France	%	3.9	3.1	3.1	2.9	3.2	2.0	1.4	1.3	0.3	0.7	0.3	0.7	0.3	0.0	2.2	1.5	1.4	1.8	1.3	0.9	0.8	0.6	0.2	0.2	0.3	0.3	0.0	0.1
	Rank	1	3	4	5	2	6	7	8	12	9	11	9	13	14	1	3	4	2	5	6	7	8	11	12	10	9	14	13
Germany	%	4.5	4.8	4.2	4.1	2.3	3.3	1.3	2.0	0.7	0.5	0.8	0.5	0.3	0.1	2.5	1.9	2.2	1.3	1.8	1.4	1.3	0.6	0.2	0.3	0.3	0.3	0.1	0.2
	Rank	2	1	3	4	6	5	8	7	10	11	9	12	13	14	1	3	2	7	4	5	6	8	13	9	10	11	14	12
Greece	%	4.0	3.3	4.4	5.2	5.5	4.0	1.3	1.6	0.7	0.4	1.2	0.4	0.2	0.1	2.3	2.4	1.7	3.3	2.4	2.1	1.1	0.7	0.2	0.4	0.2	0.2	0.1	0.5
	Rank	5	6	3	2	1	4	8	7	10	11	9	12	13	14	4	3	6	1	2	5	7	8	13	10	11	11	14	9
Hungary	%	6.5	6.2	6.7	8.9	9.3	4.2	1.6	2.2	1.1	0.8	1.4	0.6	0.2	0.1	4.3	3.8	3.5	6.0	4.9	2.2	1.7	0.9	0.3	0.7	0.5	0.4	0.1	0.5
	Rank	4	5	3	2	1	6	8	7	10	11	9	12	13	14	3	4	5	1	2	6	7	8	13	9	11	12	14	10
Iceland	%	4.4	5.6	5.4	3.5	3.2	2.6	1.9	1.8	1.2	0.3	0.1	0.3	0.2	0.1	2.1	2.3	2.3	1.6	1.4	1.0	1.0	0.8	0.2	0.5	0.1	0.2	0.1	0.0
	Rank	3	1	2	4	5	6	7	8	9	11	14	10	12	13	3	1	2	4	5	7	6	8	10	9	12	11	13	14
Ireland	%	4.7	4.9	5.1	3.6	4.2	3.1	1.5	1.9	0.4	0.6	1.2	0.5	0.2	0.1	2.4	2.4	2.1	2.2	1.5	1.3	1.1	0.6	0.2	0.2	0.3	0.3	0.1	0.4
	Rank	3	2	1	5	4	6	8	7	12	10	9	11	13	14	1	2	4	3	5	6	7	8	12	13	10	11	14	9
Israel	%	3.1	2.3	2.7	3.8	4.6	1.7	0.7	1.2	0.3	0.6	0.7	0.6	0.1	0.1	1.8	1.3	1.0	2.7	1.6	0.7	0.8	0.3	0.1	0.1	0.3	0.3	0.1	0.2
	Rank	3	5	4	2	1	6	8	7	12	10	9	11	14	13	2	4	5	1	3	7	6	8	14	12	8	10	12	11
Italy	%	3.4	3.2	3.6	5.7	6.0	2.5	1.1	1.6	0.3	0.6	0.7	0.5	0.3	0.0	1.9	1.7	1.4	3.2	2.4	1.1	1.1	0.5	0.3	0.1	0.3	0.3	0.0	0.2
	Rank	4	5	3	2	1	6	8	7	12	10	9	11	12	14	3	4	5	1	2	6	7	8	11	13	9	10	14	12
Japan	%	5.5	3.0	2.9	7.6	5.6	1.9	1.5	0.8	0.3	1.0	0.4	0.8	0.1	0.1	3.1	1.6	1.5	3.4	3.5	0.8	0.6	0.7	0.1	0.2	0.5	0.4	0.1	0.2
	Rank	3	4	5	1	2	6	7	10	12	8	11	9	13	14	3	4	5	2	1	6	8	7	13	12	9	10	14	11
Luxembourg	%	2.9	4.0	3.6	3.9	3.6	2.3	2.7	1.5	0.5	1.2	1.0	0.5	0.3	0.1	1.5	1.7	1.7	2.0	1.6	0.9	1.0	1.1	0.3	0.2	0.5	0.2	0.1	0.3
	Rank	5	1	3	2	4	7	6	8	12	9	10	11	13	14	5	2	3	1	4	8	7	6	10	13	9	12	14	11
Mexico	%	4.0	3.9	5.3	2.5	1.8	2.5	0.3	0.9	1.9	0.3	1.0	0.2	0.3	0.7	2.9	3.5	2.1	1.4	1.3	1.3	0.8	0.2	0.4	1.2	0.2	0.1	0.7	0.6
	Rank	2	3	1	5	7	4	11	9	6	13	8	14	11	10	2	1	3	4	5	6	8	13	11	7	12	14	9	10
Netherlands	%	3.7	3.3	2.9	3.2	2.6	2.0	0.9	1.4	0.9	0.2	0.4	0.3	0.2	0.1	2.2	1.5	1.6	1.6	1.5	0.9	1.0	0.4	0.2	0.4	0.1	0.1	0.1	0.1

	Rank	1	2	4	3	5	6	8	7	9	12	10	11	13	14	1	4	3	2	5	7	6	9	10	8	12	11	14	13
New Zealand	%	4.0	3.9	4.6	2.9	1.5	2.7	1.5	1.7	0.8	1.0	0.4	0.8	0.4	0.0	2.1	2.2	1.7	0.9	1.2	1.1	1.2	0.7	0.4	0.4	0.5	0.4	0.0	0.1
	Rank	2	3	1	4	8	5	7	6	10	9	12	11	12	14	2	1	3	7	4	6	5	8	12	10	9	11	14	13
Norway	%	3.8	4.4	3.9	2.4	3.5	2.6	1.3	1.8	0.3	0.6	0.5	0.6	0.2	0.1	2.0	1.8	1.8	1.9	1.0	1.0	1.2	0.5	0.2	0.1	0.3	0.3	0.1	0.1
	Rank	3	1	2	6	4	5	8	7	12	9	11	10	13	14	1	4	3	2	7	6	5	8	11	12	9	9	14	12
Poland	%	5.7	5.2	6.6	8.7	8.0	4.3	1.0	2.5	1.1	0.7	2.0	0.5	0.2	0.0	3.6	3.6	2.8	4.9	4.8	2.1	1.8	0.5	0.3	0.7	0.4	0.3	0.0	0.9
	Rank	4	5	3	1	2	6	10	7	9	11	8	12	13	14	3	3	5	1	2	6	7	10	13	9	11	12	14	8
Portugal	%	4.5	3.2	3.0	5.7	4.1	1.9	0.9	1.5	0.3	0.8	0.9	0.6	0.3	0.0	2.6	1.6	1.5	2.4	2.6	0.8	1.1	0.4	0.3	0.2	0.4	0.3	0.0	0.3
	Rank	2	4	5	1	3	6	8	7	12	10	9	11	13	14	2	4	5	3	1	7	6	8	12	13	9	10	14	11
Singapore	%	4.7	5.0	4.7	9.6	6.5	3.2	1.3	1.4	0.8	1.2	2.1	0.9	0.0	0.0	2.7	2.5	2.6	3.9	4.6	1.6	0.9	0.6	0.0	0.5	0.6	0.5	0.0	0.9
	Rank	5	3	4	1	2	6	9	8	12	10	7	11	13	13	3	5	4	2	1	6	7	9	13	12	10	11	13	7
Slovakia	%	6.3	7.3	7.5	9.1	9.0	5.1	2.2	2.8	1.6	0.8	2.8	0.7	0.2	0.2	3.8	3.8	3.7	5.3	4.9	2.5	1.9	1.1	0.2	1.0	0.5	0.4	0.3	1.2
	Rank	5	4	3	1	2	6	9	8	10	11	7	12	14	13	4	3	5	1	2	6	7	9	14	10	11	12	13	8.0
Slovenia	%	3.3	4.5	3.8	6.3	5.7	2.7	1.0	1.9	0.6	0.6	1.1	0.6	0.3	0.1	1.9	1.9	2.1	3.2	2.9	1.1	1.3	0.4	0.3	0.4	0.3	0.3	0.1	0.4
	Rank	5	3	4	1	2	6	9	7	10	11	8	12	13	14	5	4	3	1	2	7	6	8	11	10	13	12	14	9
South Korea	%	5.6	1.9	2.7	8.4	5.9	1.5	1.0	0.8	0.3	0.8	0.3	0.6	0.2	0.0	3.4	1.6	1.0	3.9	4.1	0.6	0.7	0.5	0.2	0.2	0.4	0.4	0.0	0.2
	Rank	3	5	4	1	2	6	7	8	12	9	11	10	13	14	3	4	5	2	1	7	6	8	11	13	9	10	14	12.0
Spain	%	3.6	2.7	2.6	4.0	3.3	2.0	1.0	1.6	0.3	0.8	0.8	0.6	0.3	0.1	2.1	1.3	1.3	2.0	1.9	0.9	1.1	0.5	0.3	0.2	0.4	0.3	0.1	0.3
	Rank	2	4	5	1	3	6	8	7	13	9	9	11	12	14	1	4	5	2	3	7	6	8	11	13	9	10	14	12
Sweden	%	3.8	5.3	4.7	6.1	5.0	3.1	1.5	1.0	0.0	0.4	1.0	0.4	0.2	0.1	2.0	2.1	2.2	2.7	2.5	1.2	0.6	0.6	0.3	0.0	0.2	0.2	0.1	0.3
	Rank	5	2	4	1	3	6	7	8	14	10	9	11	12	13	5	4	3	1	2	6	7	8	10	14	11	11	13	9
Switzerland	%	3.8	4.0	2.9	3.2	3.5	2.7	1.6	1.5	0.7	0.5	0.9	0.4	0.2	0.0	1.8	1.1	1.6	1.7	1.3	1.0	0.8	0.6	0.2	0.3	0.2	0.2	0.0	0.2
	Rank	2	1	5	4	3	6	7	8	10	11	9	12	13	14	1	5	3	2	4	6	7	8	12	9	11	12	14	10
Turkey	%	5.1	2.6	4.2	7.3	6.4	3.7	0.5	0.9	0.6	0.4	1.5	0.3	0.0	0.2	3.2	2.4	1.4	4.3	3.4	1.8	0.7	0.3	0.0	0.4	0.2	0.2	0.2	1.0
	Rank	3	6	4	1	2	5	10	8	9	11	7	12	14	13	3	4	6	1	2	5	8	10	14	9	11	13	12	7
United Kingdom	%	4.3	3.9	3.8	3.2	4.1	2.4	1.0	1.3	0.9	0.5	0.9	0.5	0.2	0.1	2.4	2.0	2.0	2.4	1.6	1.2	0.8	0.5	0.1	0.5	0.3	0.2	0.1	0.3
	Rank	1	3	4	5	2	6	8	7	9	11	10	12	13	14	1	3	4	2	5	6	7	8	13	8	11	12	14	10
United States	%	4.5	4.1	4.4	3.6	4.2	2.4	1.6	1.8	1.6	0.5	0.4	0.4	0.3	0.4	2.8	2.5	2.1	2.8	1.8	1.2	1.5	0.8	0.4	0.9	0.2	0.2	0.4	0.1
	%	1	4	2	5	3	6	9	7	8	10	11	12	14	13	2	3	4	1	5	7	6	9	11	8	12	13	10	14
OECD Countries	%	4.5	3.8	4	4.78	4.4	2.6	1.3	1.5	0.9	0.6	0.8	0.5	0.2	0.2	2.7	1.9	2.2	2.2	2.7	1.2	0.6	1.13	0.6	0.3	0.3	0.3	0.3	0.2
	Rank	2	5	4	1	3	6	8	7	9	11	10	12	13	14	2	5	4	3	1	6	8	7	9	11	10	12	12	14
Global	%	7.2	4.9	5.3	10.4	7.7	3.7	1.0	1.4	1.1	0.4	1.0	0.3	0.1	0.1	5	3.1	3.4	5.9	5.5	2.2	0.6	1.0	0.8	0.2	0.6	0.2	0.1	0.1
	Rank	3	5	4	1	2	6	10	7	8	11	9	12	13	14	3	5	4	1	2	6	9	7	8	11	9	12	13	14
High-income	%	4.5	3.8	3.8	4.52	4.3	2.4	1.36	1.54	0.85	0.6	0.61	0.52	0.25	0.17	2.6	1.8	2	2.1	2.6	1.1	0.7	1.1	0.5	0.3	0.2	0.3	0.3	0.2
	Rank	2	5	4	1	3	6	8	7	9	11	10	12	13	14	2	5	4	3	1	7	8	6	9	10	13	11	11	14
Europe	%	6.4	5.8	5.9	6.5	7.8	4.1	1.3	2.2	0.8	0.5	1.9	0.4	0.2	0.1	4	3.2	3.3	3.5	4.9	2.2	0.7	1.5	0.5	0.3	1.0	0.2	0.2	0.1
	Rank	3	5	4	2	1	6	9	7	10	11	8	12	13	14	2	5	4	3	1	6	9	7	10	11	8	12	13	14

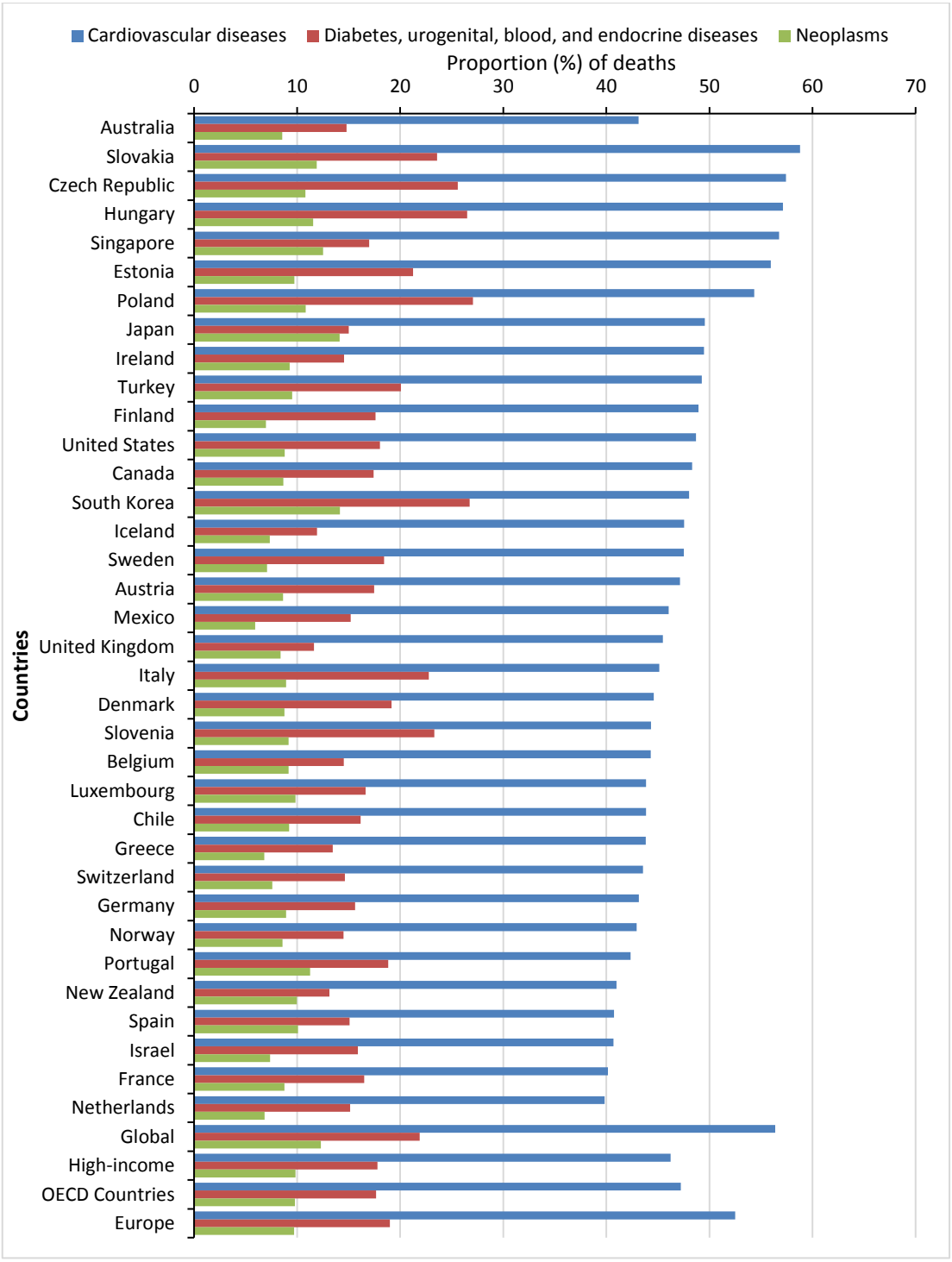
Supplementary Figure 4.4 Age-standardized burden of non-communicable diseases (expressed as percentage of deaths and disability-adjusted life years) associated with specific dietary risks and their rank of relative contribution in respective OECD countries in 2015

[Gradient of the colour represents the ranking of specific dietary risks (deep red shows high ranked dietary risks contributing to a high burden of NCDs in respective countries). The sum of percentages in rows exceeds the total for all dietary risk factors combined because of an overlap between various risk factors. 0% represents very low proportion. OECD – Organization for Economic Cooperation and Development]



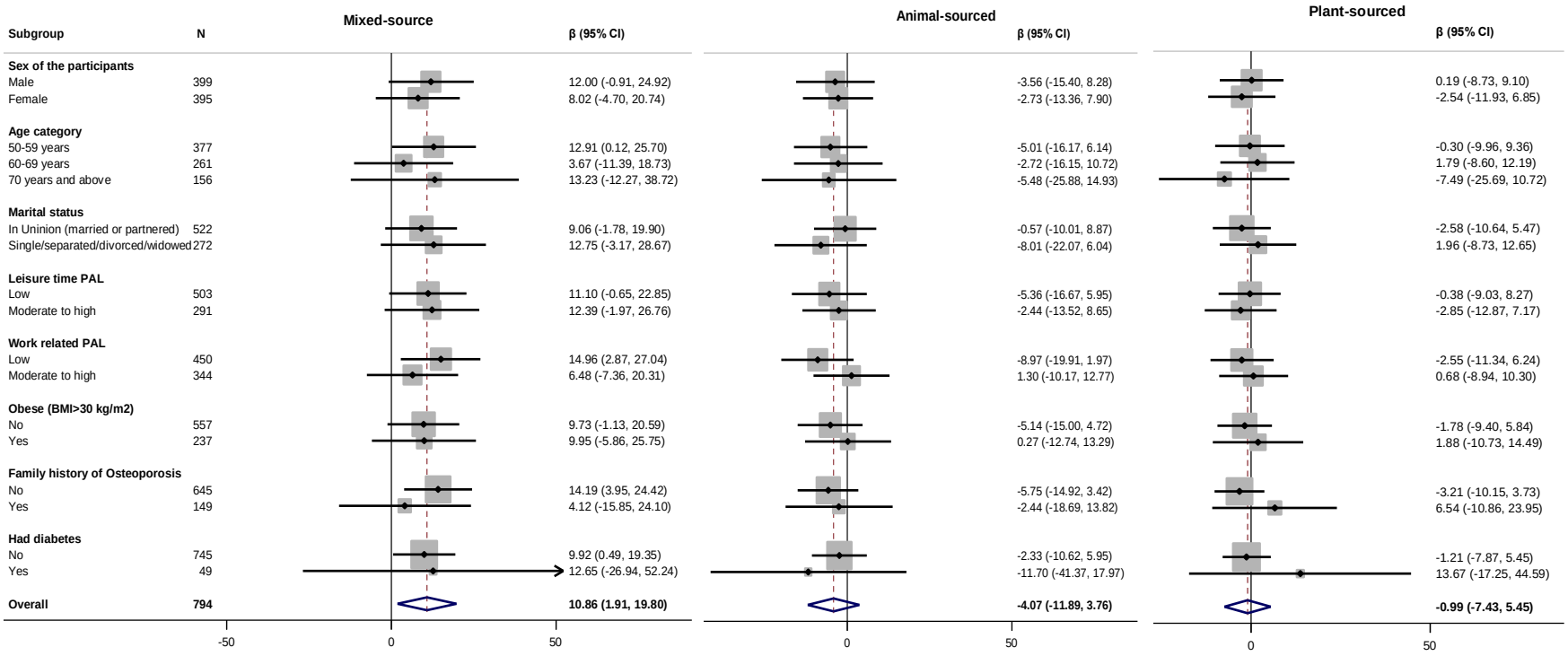
Supplementary Figure 4.5 Age-specific burden of non-communicable diseases (expressed as percentage of deaths) associated with dietary risks in 35 countries in 2015

[The vertical red lines show the respective level of burden in Australia in 2015. OECD – Organization for Economic Cooperation and Development]



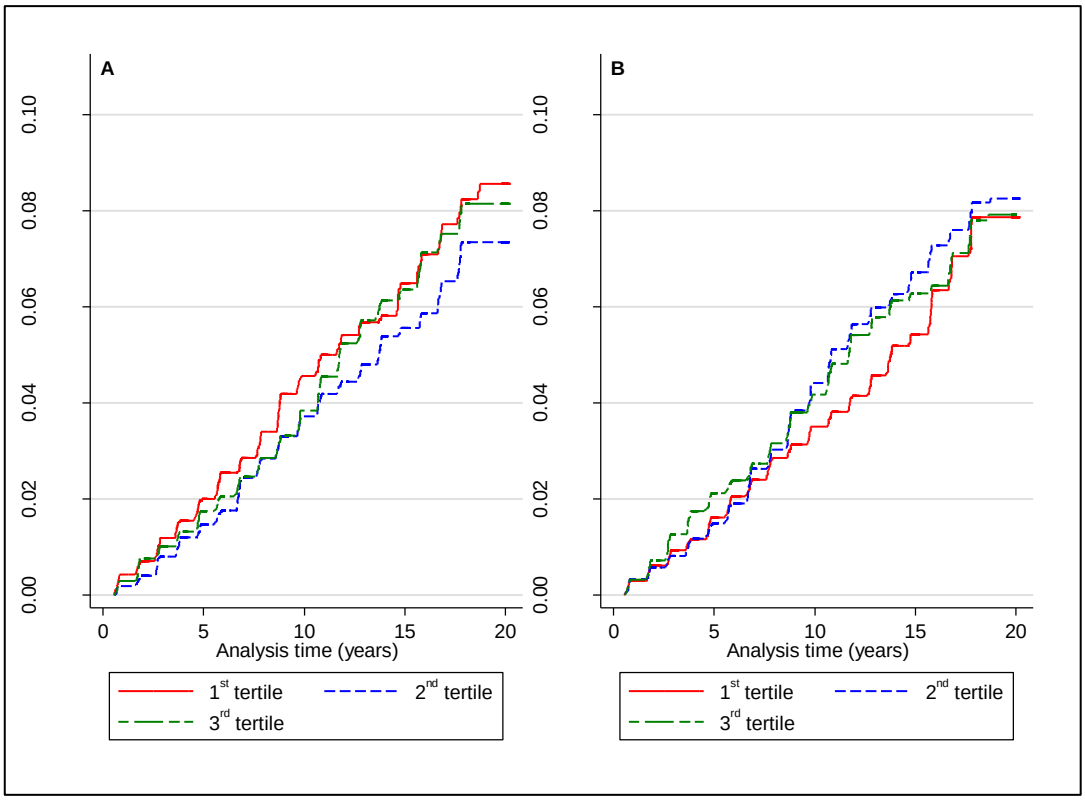
Supplementary Figure 4.6 Age-standardized burden of specific non-communicable disease (expressed as percentage of deaths) associated with dietary risks in 35 countries in 2015

[OECD – Organization for Economic Cooperation and Development]

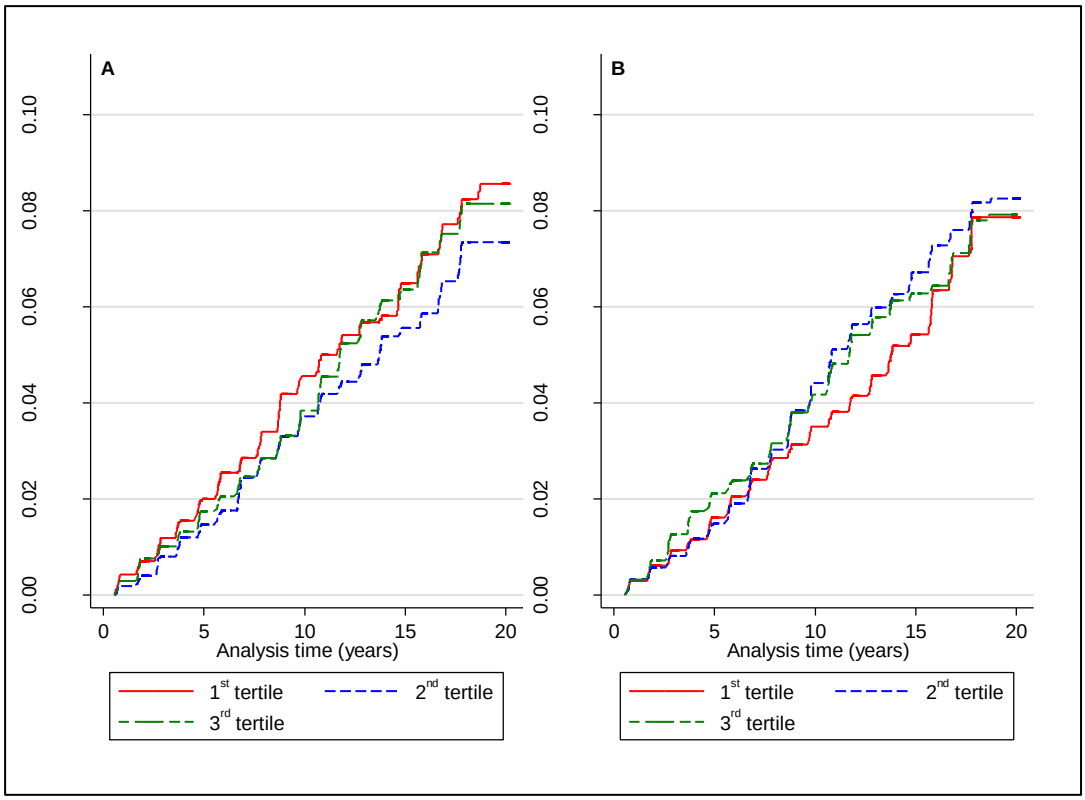


Supplementary Figure 6.1 Subgroup analyses of association (β) [95% confidence interval (CI)] of z scores of nutrient patterns with bone mineral density among adults 50 years and over, the North West Adelaide Health Study

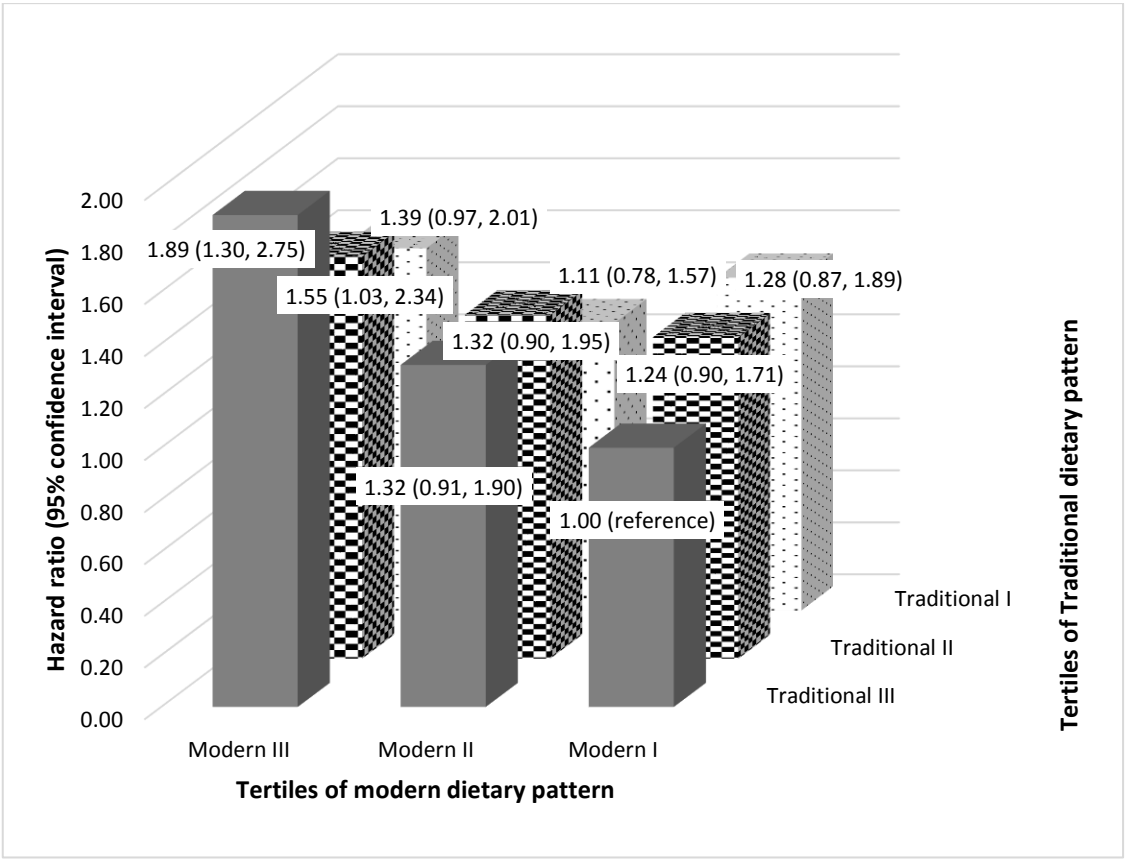
[Results were adjusted for sex and age ,socio-economic and lifestyle factors (smoking, alcohol intake (no/low risk, medium/very high risk), marital status, income, health literacy (limited, adequate), leisure time and job related physical activity levels (low, moderate/high), chronic conditions (diabetes mellitus, family history of osteoporosis and body mass index (continuous)), energy intake (continuous); PAL-Physical Activity level]



Supplementary Figure 7.1 Nelson-Aalen cumulative hazard estimates by tertiles of A) plant-sourced and B) animal-sourced nutrient pattern scores (cumulative average) for study participants aged 18 years and over and both sexes (1991-2011), the China Health and Nutrition Survey

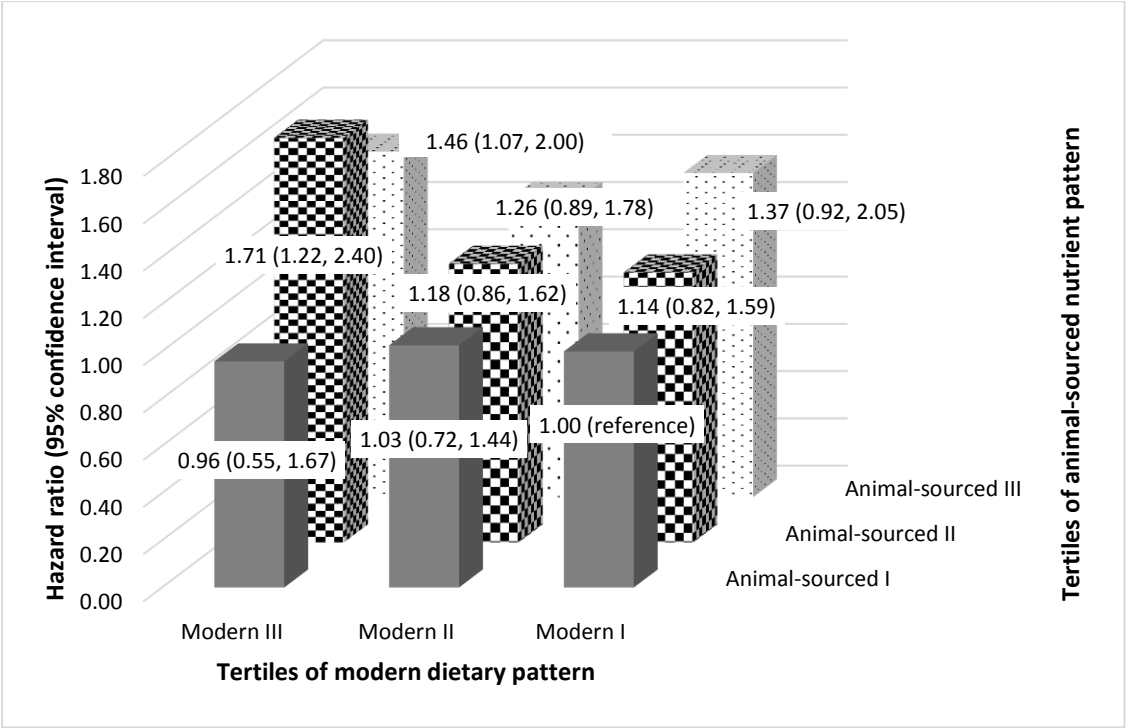


Supplementary Figure 7.2 Nelson-Aalen cumulative hazard estimates by tertiles of A) plant-sourced and B) animal-sourced nutrient pattern scores (cumulative average) for study participants aged 18 years and over and both sexes (1991-2011), the China Health and Nutrition Survey



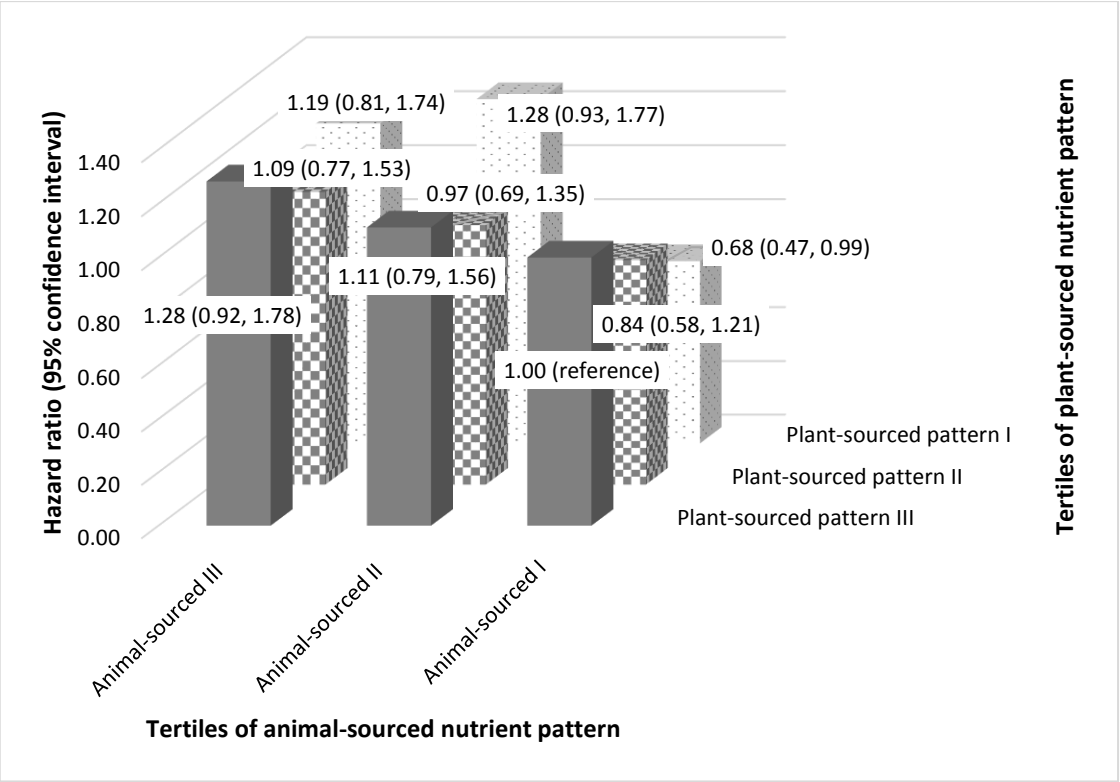
Supplementary Figure 7.3 Multivariable adjusted hazard ratio (HR) [95% confidence interval] of fractures in joint classified participants across nine strata formed with the tertiles of the modern dietary pattern and animal sourced nutrient pattern, the China Health and Nutrition Survey

[Modern I and traditional I were used as references. The model was adjusted for sex, age (continuous), energy intake (continuous), educational status (low, medium and high), income (low, medium and high), alcohol consumption (none, <1, 1-2, 3-4 per week and daily), smoking (non-smoker and current/ex-smoker), residency (rural and urban) and physical activity level (metabolic equivalent task-hours/week, continuous), body-mass index (continuous) and high blood pressure (yes/no). Exposure levels of dietary and nutrient patterns were determined based on cumulative mean]



Supplementary Figure 7.4 Multivariable adjusted hazard ratio (HR) [95% confidence interval] of fractures in joint classified participants across nine strata formed with the tertiles of the modern dietary pattern and animal sourced nutrient pattern, the China Health and Nutrition Survey

[Modern I and animal-sourced I were used as references. The model was adjusted for sex, age (continuous), energy intake (continuous), educational status (low, medium and high), income (low, medium and high), alcohol consumption (none, <1, 1-2, 3-4 per week and daily), smoking (non-smoker and current/ex-smoker), residency (rural and urban) and physical activity level (metabolic equivalent task-hours/week, continuous), body-mass index (continuous) and high blood pressure (yes/no). Exposure levels of dietary and nutrient patterns were determined based on cumulative mean]



Supplementary Figure 7.5 Multivariable adjusted hazard ratio (HR) [95% confidence interval] of fractures in joint classified participants across nine strata formed with the tertiles of the modern dietary pattern and animal sourced nutrient pattern, the China Health and Nutrition Survey

[Plant-sourced I and animal-sourced I were used as references. The model was adjusted for sex, age (continuous), energy intake (continuous), educational status (low, medium and high), income (low, medium and high), alcohol consumption (none, <1, 1-2, 3-4 per week and daily), smoking (non-smoker and current/ex-smoker), residency (rural and urban) and physical activity level (metabolic equivalent task-hours/week, continuous), body-mass index (continuous) and high blood pressure (yes/no). Exposure levels of dietary and nutrient patterns were determined based on cumulative mean]