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The role of dietary patterns in osteoporosis- related outcomes in older adults

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‘The research associated with this thesis abides by the international and Australian codes on human and animal experimentation, the guidelines by the Australian Government's Office of the Gene Technology Regulator and the rulings of the Safety, Ethics and Institutional Biosafety Committees of the University. Ethnic Approval No EC00337’.

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List of abbreviations

ABS	Australian Bureau of Statistics
AUD	Australian dollar
β	Beta coefficient
BMC	Bone mineral content
BMD	Bone mineral density
BMI	Body mass index
BUA	Broadband ultrasound attenuation
CA	Cluster analysis
CCVFFQ	Cancer Council Victoria food frequency questionnaire
CI	Confidence interval
CT	Computerised tomography
DALY	Disability-adjusted life year
dB	Decibel units
DPA	Dual photon absorptiometer
DXA	Dual-energy x-ray absorptiometry
FA	Factor analysis
FD	Food diary
FFQ	Food frequency questionnaire
FN	Femoral neck
H	Healthy
HR	Hazard ratio
HRT	Hormone replacement therapy
IEO	Index of education and occupation

IER	Index of economic resources
IRSAD	Index of Relative Socioeconomic Advantage and Disadvantage
KJ	Kilojoule
KMO	Kaiser-Meyer-Olkin
LS	Lumbar spine
MRI	Magnetic resonance imaging
NA	Not available/not applicable
OR	Odds ratio
P	P value
PCA	Principal component analysis
PLS	Partial least-squares
PPA	Physiological profile assessment
PQCT	Peripheral quantitative computerised tomography
Q	Quintiles/quartiles
RCT	Randomized controlled trial
RR	Risk ratio
RRR	Reduced rank regression
SD	Standard deviation
SEIFA	Socio-Economic Indexes for Areas
SOS	Speed of sound
SPA	Single photon absorptiometer
T	Tertiles
TASOAC	Tasmanian Older Adult Cohort
TB	Total body

List of abbreviations

TBBMC	Total body bone mineral content
TBBMD	Total body bone mineral density
W	Western

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Abstract

Fractures are a major public health issue in older adults and have two major risk factors: low bone mineral density (BMD) and falls. Nutrition plays a critical role in the prevention of these outcomes. Most previous studies have investigated single nutrients, such as calcium and vitamin D but focussing on individual nutrients does not account for the complex interaction between nutrients consumed in the diet, and could result in an inability to detect a small effect from a single nutrient in this context. Consequently, the approach of using dietary patterns to account for the overall effect of diet has been recommended for bone research. Few cohort studies have investigated the associations of dietary patterns with fracture and BMD, and none have investigated the impact of dietary patterns identified using a posterior method on falls or falls risk. Therefore, this thesis aimed to identify the role of such dietary patterns in these osteoporosis-related outcomes in adults (≥ 50 years).

This thesis has two major components: a systematic review synthesising the literature reporting associations between empirically derived dietary patterns with BMD and fracture in healthy adults (≥ 18 years); and a longitudinal study of Tasmanian Older Adult Cohort (TASOAC) identifying dietary patterns, their predictors and their associations with osteoporosis-related outcomes (falls risk, BMD and fracture) in older adults (≥ 50 years).

The systematic review and meta-analysis included 23 observational studies in the systematic review, 21 in the best evidence synthesis and 4 in a meta-analysis. Of these, 12 were cross-sectional, 10 were longitudinal and one was a case-control study. Key findings were:

1. A healthy pattern was associated with an up to 36% lower risk of hip fracture (for all 4 studies, risk ratio (RR) = 0.73 (95% confidence interval (CI) 0.56, 0.96); $I^2 = 95\%$ and RR = 0.64 (95% CI 0.56, 0.73); $I^2=67\%$ in the subgroup of studies in which fracture was ascertained by medical records rather than self-report).
2. There was conflicting evidence for the associations of dietary patterns with BMD at any site, total body bone mineral content and total fractures, and for western diet and hip fracture. However, the evidence was consistent in that there were no detrimental associations between a healthy pattern and BMD at any site, total body bone mineral content and total fractures nor beneficial associations between a western pattern and of these bone outcomes.

The second component was the longitudinal data from TASSOAC (1098 older adults at baseline: mean age 63 years and 51% of women). TASSOAC followed up participants at an average time of 2.6 years (n=875), 5 years (n=768), and 10.7 years (n=567) from baseline. TASSOAC data were used to determine the dietary patterns in this cohort at baseline, generate a score for each pattern and determine the associations of these pattern scores with participants' characteristics and osteoporosis-related outcomes. The key findings were:

1. Four dietary patterns identified were predominantly comprised of: fruit and vegetable pattern (vegetables, fruits, potatoes, breakfast cereals excluding muesli and porridge); animal protein pattern (red and processed meats, fish, poultry); snack pattern (snacks, sweets, nuts, condiments); western pattern (pizzas, hamburgers, meat pies, sweets).
2. Fruit and vegetable and snack pattern scores were lower but western and animal protein pattern scores higher in men and current smokers at baseline. The sex difference in animal protein score increased over time ($p=0.012$). Snack score was positively associated with age and physical activity at baseline ($p<0.008$ for all), but the effect of age lessened over time ($p=0.035$). Animal protein and western scores were negatively associated with age at baseline, but the effect on western scores reduced over time ($p=0.001$). Animal protein scores were lower in retired people. People living in socially disadvantaged areas had higher western scores.
3. Higher baseline fruit and vegetable pattern score was associated with lower falls risk z-score at baseline ($\beta = -0.05$ per standard deviation (SD) (95% CI -0.09, -0.01)). There were no associations of falls risk z-scores with the baseline scores of the other patterns.
4. Femoral neck and hip BMD reduced over time, but the decreases were less for each SD increase in baseline scores of animal protein and western patterns ($p<0.02$ for all). Lumbar spine increased over time and the increase was greater with higher baseline scores of fruit and vegetable, animal protein and western patterns (all $\beta = 0.001$ g/cm²/year/SD of pattern score, all $p<0.02$).

5. Baseline scores of fruit and vegetable and snack patterns were associated with a higher risk of lumbar spine BMD increasing over ten years (RR=1.06 and 1.05 respectively, $p<0.05$).
6. There were no associations between any dietary pattern and incident fractures.

In summary, the data from the systematic review and the analyses in this thesis suggest that current dietary guidelines that recommend adhering to a healthy diet and avoiding a western diet are also appropriate for the optimising bone health and preventing osteoporotic fractures. The results also identified potential target groups for interventions to improve diet quality namely men, smokers, retirees, and those experiencing social disadvantage to inform the targeting of clinical and public health practice and future research. A fruit and vegetable dietary pattern may be beneficial for reducing a proxy measure of falls risk, the falls risk z-score. However, there is still a lack of longitudinal data examining the association of dietary patterns and incident falls. Increases in LS BMD can be a marker of degenerative changes in older adults, so associations of higher scores of fruit and vegetable, western and animal protein patterns with increases in lumbar spine BMD raises the possibility that dietary patterns could be implicated in the development of osteoarthritis.

Future research is needed including:

- Confirmation of any relationship between dietary patterns and falls in prospective studies measuring incident falls.
- Studies to investigate the effect of nutrition on osteoarthritis of the spine, and potentially at other sites.
- Randomized control trials to confirm whether improving diet quality can improve bone density and reduce falls and fractures, though these are likely to be costly and logistically challenging.

Chapter 1: Introduction

1.1 Fracture in older adults

1.1.1 The prevalence of fracture, major consequences and economic burden

Fracture is a major public health issue in older adults causing physical disability and reducing quality of life ⁽¹⁾. Moreover, it increases the risk of premature death, morbidity, hospitalization, and the burden on healthcare services ⁽²⁻⁴⁾. Most elderly people having fractures require health care services (e.g. hospitals, nursing homes or home health care), and many of them have to deal with long-term limitations of physical function ⁽⁵⁾. Mortality in the first three months after hip fracture is markedly increased in older people with a hazard ratio (HR) of 5.75 (95% confidence interval (CI) 4.94, 6.67) in women and 7.95 (6.13, 10.30) in men ⁽⁶⁾.

Osteoporotic fractures, also known as fragility or low-trauma fractures, result from trauma equivalent to a fall from a standing height or less ⁽⁷⁾. The most common sites of osteoporotic fractures are the hip, spine, and distal forearm ⁽⁸⁾. In the year 2000, 9 million older adults (aged over 50 years) worldwide were diagnosed with osteoporotic fractures ⁽⁹⁾. In particular, hip fractures account for a major part of health care expenditure and mortality in the elderly people ⁽¹⁰⁾. The incidence of hip fractures worldwide was 1.66 million in 1990 and this was predicted to increase to 6.26 million in 2050 ⁽¹¹⁾.

Fracture is also a major health problem in older adults in Australia ⁽¹²⁻¹⁴⁾ with one fracture-related hospitalisation occurring every 3.6 minutes ⁽¹⁵⁾. This figure is estimated to reduce to 2.9 minutes by 2022 ⁽¹⁵⁾. In 2015-16, there were 50,900 hospitalisations related to hip fracture (9 in 10 had hip fracture recorded as the

principal diagnosis)⁽¹⁶⁾. Moreover, the lifetime risk of fracture is substantial in Australian older adults, with a range of 27% to 29% for men and 42% to 56% for women⁽¹⁷⁾.

In 2012, the total direct and indirect costs of fractures was \$1.925 billion (AUD)⁽¹⁵⁾. This cost included hospitalization, ambulance services, rehabilitation, nursing home, community services, outpatient services, pharmaceutical fracture management, vitamin D and calcium supplements, informal care, and productivity loss. The treatment for fractures is very expensive. For example, the average cost for each partial joint replacement in the treatment of hip fractures is \$15,500-19,500 (AUD)⁽¹⁸⁾. The total direct and indirect annual costs of hip fracture are estimated to increase from \$829 million in 2013 to \$1.27 billion in 2022 (AUD)⁽¹⁵⁾.

The substantial burden of osteoporotic fractures on individuals and the health system indicates a need to reduce contributing risk factors⁽¹⁹⁾. Two major risk factors: low bone mineral density (BMD) and falls are considered in the following section of this thesis.

1.1.2 Two major fracture risk factors: low bone mineral density and falls

Low bone mineral density and associated risk factors

Low BMD is one of the major risk factors contributing to an increased risk of fracture in older adults⁽²⁰⁾. For example, in pooled data from two longitudinal studies of 14,017 American older adults (mean age over 73 years for both low and high-trauma fracture groups), a one standard deviation decrease in total hip BMD was associated with a higher risk of both low and high trauma fractures in women

(HR= 1.49 (95% CI 1.42, 1.57) and 1.45 (1.23, 1.72), respectively) and men (1.69 (1.49, 1.91) and 1.54 (1.20, 1.96), respectively) ⁽²¹⁾.

Worldwide, the prevalence of low BMD in older adults (≥ 50 years) nearly doubled from 0.12% in 1990 to 0.21% in 2010 ⁽²²⁾. Moreover, the global death and disability-adjusted life year (DALY) attributed to fractures due to low BMD, was estimated to increase from 103,000 and 3,125,000 in 1990 to 188,000 and 5,216,000 in 2010 respectively ⁽²²⁾. In 2012, there were about 4.7 million Australians with osteoporosis or osteopenia, and this is predicted to increase to 6.2 million in 2022 ⁽¹⁵⁾. The proportion of women aged 70 years and over with low BMD was greater than that of same-age men (odds ratio (OR) = 2.25 (95% CI 1.95, 2.61)) ⁽²³⁾.

There is strong evidence that older age, being a current smoker, low weight or weight loss and previous fracture are important risk factors for low BMD ⁽²⁴⁻²⁶⁾. These risk factors contribute to an increased risk of fractures through their influence on BMD. In a meta-analysis of 10 prospective cohorts of 59,232 participants (mean age 62.8 years), being a current smoker was associated with a higher risk of hip fracture compared with being a non-smoker (risk ratio (RR) = 1.84 (95% CI 1.52, 2.22)) ⁽²⁷⁾. Low BMD explained about 45% of the risk of overall fractures associated with current smoking and 23% of hip fractures ⁽²⁷⁾. Weak or inconsistent evidence exists linking other risk factors for low BMD to fracture including; family history of fracture/osteoporosis, physical inactivity, low calcium intake, muscle weakness, and high alcohol consumption (men) ^(24, 26). The role of nutrition in maintaining BMD is discussed in detail in Section 1.2.

Falls and associated risk factors

Falls are another important factor leading to an increased risk of fracture in older people (≥ 50 years) ⁽²⁸⁾. In one study of 832 older patients (mean age 79.7 years), more than 75% of hip fractures were attributed to falls whilst they were standing or walking ⁽²⁹⁾. Annually, the incidence of falls in people aged over 65 years is about 33%, and rising to 50% in those aged over 80 years ⁽³⁰⁾. Generally, older women have higher fall rates than men regardless of age ⁽³¹⁾. Similarly, Australian women had higher rates of fall injury than men in all age groups, with the highest rate being in women aged 95 years and over (16,820 cases/100,000 population) in 2014-15 ⁽³²⁾.

Beyond fracture, falls account for 40% of all injury-related deaths (although this rate varies across countries and populations) ⁽³³⁾. The fall mortality rate for older Americans (≥ 65 years) is 36.8/100000 population compared with the Canadian fatality rate for the same age group of 9.4/10000 population ⁽³³⁾. Treatment of fall-related injuries is costly. Worldwide, the total fall-related cost per inhabitant ranged from \$113 in Europe to \$547 in the USA ⁽³⁴⁾. In Australia, the total cost of falls to the health care system in people aged 65 years and over was \$86.4 million (AUD) in 2001-2002, and was predicted to increase to \$181 million (AUD) by 2021 ⁽³⁵⁾.

Major risk factors of falls in older adults are impaired balance and gait, advancing age, cognitive decline, visual impairment, and history of previous falls ⁽³⁶⁾. Other risk factors ^(37, 38) include limitation of physical activity, physical disability, disability relating to instrumental activities of daily living, low education, no use of walking aids, depression, rheumatic disease, dizziness and vertigo, Parkinson

disease, poor health status, fear of falling and medication use (e.g. antihypertensive drugs, sedatives and hypnotics, antidepressant and benzodiazepines).

Low BMD and falls are the major factors contributing to the probability of fracture in older adults. Good nutrition with a well-balanced diet rich in calcium, vitamin D and other nutrients, is essential to minimize the impact of these two factors ⁽³⁹⁾. Therefore, the influence of diet and nutrition on improving bone health and mitigating the risk of falls, is discussed in detail below.

1.2 Diet as a modifiable factor for improving bone health (fracture and BMD) and preventing falls in older adults

A balanced diet promotes strong and healthy bones at every stage of life ⁽⁴⁰⁾. For example, it helps to build peak bone mass in childhood and adolescence, which reduces osteoporosis later in life as well as maintaining bone mass and strength in adults ^(1, 41-43). Therefore, ensuring good nutrition to optimise bone health throughout life is important. This thesis emphasises the role of nutrition and bone health in older adults who are a higher risk population for osteoporosis, falls and fracture.

1.2.1 Key nutrients and food items for improving bone health (fractures and BMD) and/or the prevention of falls in older people

Nutrition has a potentially important role in maintaining bone health and prevention of falls. However, current guidelines for osteoporosis prevention and bone health focus mainly on the individual nutrients of calcium and vitamin D, for which there

is the greatest evidence. The numerous randomized control trials (RCT) in this area and even meta-analyses can be conflicting. Two meta-analyses, one of 11 RCT of 31,022 older adults (≥ 65 years) ⁽⁴⁴⁾ and 51 RCT of 12,000 older people aged 50 years and over ⁽⁴⁵⁾ showed a beneficial effect of vitamin D/calcium supplementation on bone outcomes, but others ^(46, 47) have shown no effect of these supplements on musculoskeletal health including fracture, BMD, or fall outcomes. If benefits do exist, their magnitude is likely to be low (e.g. vitamin D may reduce the risk of any nonvertebral fracture by 7-14% reduction ⁽⁴⁴⁾ and calcium supplements result in 0.7-1.8% increase of BMD ⁽⁴⁵⁾). Current Australian guidelines recommend against the routine use of supplements in non-institutionalised elderly people ⁽⁴⁸⁾. Furthermore, observational evidence also suggests that dietary calcium (as distinct from calcium supplements) has little, if any effect on fracture risk ⁽⁴⁹⁾.

The importance of other single nutrients to bone health is less clear. Protein intake has been extensively studied but the extent to which this influences bone health is nonetheless controversial. In a systematic review of 16 RCT and 20 cohort studies, there was moderate evidence that higher vs lower protein intake may be beneficial for lumbar spine (LS) BMD (net percentage change= 0.52% (95% CI 0.06%, 0.97%)), but no effect on the femoral neck (FN), total hip, or whole body ⁽⁵⁰⁾. However, a recent systematic review of 127 papers showed little benefit of increasing protein intake (around 0.8–1.3g/kg/day) for bone health in healthy adults ⁽⁵¹⁾.

For other less well-studied nutrients, such as phosphorus, B-group vitamins and vitamin A, the evidence base remains limited and often inconsistent. A recent review of dietary phosphorus intake ⁽⁵²⁾ demonstrated both the small amount of evidence and its inconsistency, finding no relationships of dietary phosphorus with BMD, bone mineral content (BMC), or osteoporosis in cross-sectional studies of American and Korean populations but a 9% increase in fracture risk for each increase of 100 mg/d in dietary phosphorus in a Brazilian cohort study ⁽⁵²⁾. Bailey et al reported a small significant effect of vitamin B12 on risk of fracture (RR=0.96 (95 % CI 0.92, 1.00) but no effect on BMD ⁽⁵³⁾. The different types of vitamin A have conflicting results, such as a high intake of excess retinol may be detrimental to bone health but there is no evidence for the association between β -carotene intake and osteoporosis-related fractures ⁽⁵⁴⁾.

Potential mechanisms by which nutrients could maintaining bone structures are described in the next section 1.2.2. Given the limited evidence for clinically important effects of individual nutrients and food types, a different approach is needed to determine what role diet has in improving bone health and reducing falls risk. Studies that investigate the influence of individual key nutrients are limited in that they do not account for the impact of a complete diet, or the interaction of multiple nutrients. These limitations are considered in Section 1.2.3 below.

1.2.2 Potential mechanism by which nutrients could influence bone health

Nutrients could influence fractures through effects on bone, and effects on falls via influencing muscle strength and balance.

The effects of nutrients on bone cells including stem cells, osteoblast and osteoclasts are complex, potentially both promoting bone formation and enhancing the bone breakdown ⁽⁵⁵⁾. Nutrient intakes could prevent bone loss and modulate the activity of calcium, vitamin D, or parathyroid hormone. Nutrient intake also influences cellular energetics by binding nutrients into the cell or elevating nutrients relating to hormones (e.g. insulin or insulin-like growth factor 1). For example, vitamin D regulates calcium absorption/serum calcium level that influences the mineralization and differentiation of osteoblasts and reduces the phosphate synthesis from bones ⁽⁵⁶⁾.

Inflammation relates to bone health ⁽⁵⁷⁾ and there is a link between diet and inflammation. Certain pro-inflammatory cytokines involve the process of bone remodelling and pathogenesis of bone diseases ⁽⁵⁸⁾. Specifically, interleukin-6 promotes osteoclast differentiation and activation, and interleukin-1 relates to bone resorption linked to the accelerated bone loss in both idiopathic and postmenopausal osteoporosis. A raised nutrient (e.g. fruits, vegetables, fibre, or omega-3 fatty acids) in the post-prandial state closely relates to increasing circulation of proinflammatory cytokines, recruits neutrophils and oxidative stress ⁽⁵⁹⁾. Vitamin D is associated with oxidative stress and inflammation ⁽⁶⁰⁾. A pooled analysis of 9 RCTs of 838 participants showed that whole grains reduced systemic inflammatory (standardized mean difference (SMD= 0.16 (95% CI 0.02, 0.30)) ⁽⁶¹⁾.

The balance of nutrition is the key factor for maintaining muscle mass and strength, which helps to reduce falls risk resulting in fractures ⁽⁶²⁾. A cohort study of 686 older adults found that there was a significantly positive association between a

change in 25-hydroxyvitamin D and baseline muscle parameters including % appendicular lean mass ($\beta = 1.70$ (95% CI 0.47, 2.93)), leg strength ($\beta = 8.88$ (95% CI 0.98, 16.78)) and leg muscle quality ($\beta = 0.49$ (95% CI 0.03, 0.95))⁽⁶³⁾. Another cohort study of 791 elderly people showed that men consumed the unhealthy dietary pattern named “High Red Meat” had worse hand grip strength than those eating “Low Meat” ($\beta = -1.70$ (Standard error= 0.86))⁽⁶⁴⁾.

1.2.3 Limitations of single nutrient studies in medical research

The limitations of studies that focus on single nutrient analysis have been increasingly acknowledged in nutritional epidemiology. For example, as people generally consume multiple foods, analyses of single nutrients on health outcomes may not provide an accurate picture of diet and its impact on health⁽⁶⁵⁾. While there are limitations and controversies around the evidence for the roles of single nutrients in bone health described above, it is unlikely that the effects of any one nutrient on bone will be independent of other dietary components. For example, vitamin D is one of main factors contributing to a regulation of the blood calcium level⁽⁶⁶⁾ and vitamin D deficiency leads to lower calcium absorption⁽⁶⁷⁾. The effects of dietary protein on bone may be promoted by an adequate calcium intake⁽⁶⁸⁾. Calcium intake also relates to maintaining magnesium and vice versa⁽⁶⁹⁾.

It is difficult to account for the interaction among nutrients or food items or detect small effects from studies of single nutrients⁽⁷⁰⁾. In addition, substitution effects are commonly seen in changes in diet behaviours, when one component of the diet changes, so will others⁽⁷¹⁾. This makes estimating associations of individual foods or nutrients almost infeasible. Analysis that can assess the synergistic or cumulative

effect of different nutrients or foods could provide greater insights into the role of diet in health. Dietary pattern analysis is one such approach which has been recommended as an alternative method to single nutrient analysis to assess the association of a diet with health outcomes in the past few decades ^(70, 72).

1.2.4 Dietary pattern analysis

Definition and advantages of dietary pattern analysis

A dietary pattern is defined as the quantities, proportions, variety or combination of different foods, drinks, and nutrients in diets, and the frequency with which they are habitually consumed ^(71, 73, 74).

Conceptually, dietary patterns provide a whole picture of the association of overall diet with health outcomes because they account for all foods or nutrients and their inter-correlations in the analysis ⁽⁷⁴⁾. For this reason, pattern analysis may result in greater correlations between diet and health outcomes compared with analysing single components of a pattern. In addition, dietary patterns could be useful as a covariate variable to determine whether a specific nutrient is independent of the overall diet ⁽⁷²⁾. Dietary patterns are also helpful in the development of food-based dietary guidelines ⁽⁷⁵⁾. People eat multiple foods that combine a variety of nutrients; therefore, results of dietary pattern analysis are more applicable and translate more readily into public health practice. Dietary recommendations based on eating or dietary patterns are also more accessible and easier to understand than those for single nutrients, making their guidelines easier to adopt.

Approaches to assessing dietary patterns

There are two ways to derive dietary patterns in a given population: using nutrition theory or knowledge (a priori method for defined patterns), or using statistical methods (a posteriori/empirical method for exploratory patterns) ⁽⁷⁰⁾.

In an a priori approach, dietary indices or scores based on current dietary guidelines quantify the adherence of participants to specific patterns, for example, the Healthy Eating Index, Diet Quality Index, Healthy Diet Index, or Mediterranean diet score, with higher scores indicating higher adherence ⁽⁷⁶⁾. There are many factors that should be considered in creating an index score including; the variables to be measured, their cut-off values, and how to score them ⁽⁷⁶⁾. In addition, dietary patterns deriving from a priori approach, normally include different dietary variables or different weighting of those variables. This results in indexes that lead to different definitions of healthy behaviour ⁽⁷⁰⁾.

In contrast, an empirical or a posteriori approach reflects the current dietary data of a given population using statistical methods (e.g. factor analysis, principal component analysis, cluster analysis, and reduced rank regression) ^(70, 76, 77). Principal component analysis produces a linear combination of dietary intake variables to maximize total variance, whereas factor analysis focuses on shared variance ⁽⁷⁶⁾. For cluster analysis, participants having a similar diet are classified into the same cluster using the mean values for food groups ⁽⁷⁷⁾. Reduced rank regression creates a linear combination of dietary intake variables that maximizes the variance of response variables ^(76, 77).

Both priori and posteriori/empirical approaches are useful in deriving dietary patterns. A priori approach creating index variables is usually quantified and provides an overall measure of dietary quality, however, there are various definitions of healthy patterns based on indexes ⁽⁷⁰⁾. Meanwhile, an empirical approach describes the existing dietary patterns in the population ⁽⁷⁷⁾. Therefore, the selection of an approach to assessing dietary patterns depends on the aims of the specific research questions being asked. In this thesis, an empirical approach was chosen because we aimed to identify the existing dietary patterns of Tasmanian older adults without any prior theory about their patterns.

1.3 Dietary patterns using an empirical approach and osteoporosis outcomes in older adults

1.3.1 Major dietary patterns in older adults

Dietary patterns derived using an empirical approach in older adults vary considerably in the existing literature. However, there are two common types of dietary patterns that can be broadly termed as healthy and western. Other patterns that are less commonly reported include snack, animal protein, and traditional dietary patterns.

Healthy and western dietary patterns are the most common and are to a large extent comparable across studies, as they are usually comprised of similar major food items. A healthy dietary pattern (variously named healthy ⁽⁷⁸⁻⁸²⁾, prudent ⁽⁸³⁻⁸⁶⁾, more healthful ⁽⁸⁷⁾, health-conscious ⁽⁸⁸⁾, nutrient-dense ⁽⁸⁹⁾, fruits, vegetables, and cereals ⁽⁹⁰⁾, dairy and fruits ⁽⁹¹⁾, fruits, vegetables, and dairy ⁽⁹²⁾, Lebanese pattern

⁽⁹³⁾, vegetable and fruit ⁽⁹⁴⁾, factor 1 ⁽⁹⁵⁾ and pattern 4 ⁽⁹⁶⁾) is mainly composed of fruits, vegetables, whole grains, fish, or nuts. A western dietary pattern (termed western ^(78, 79, 83-87, 93), unhealthy ⁽⁸⁰⁾, processed pattern ^(81, 88), energy-dense ⁽⁸⁹⁾, meat ⁽⁹⁷⁾, meat and sweet-baked products ⁽⁹⁰⁾, meats, alcohol, and sugar ⁽⁹¹⁾, high fat ⁽⁸²⁾, sweet, animal fat and low meat ⁽⁹²⁾, factor 3 ⁽⁹⁵⁾ and pattern 1 ⁽⁹⁶⁾) is predominantly characterized by a high intake of red and processed meats, refined grains, sweets, fast foods or take away foods.

Although there are fewer studies exploring an animal protein pattern and snack dietary pattern in older adults, there are also some similar major components of food items for these dietary patterns. For example, an animal protein dietary pattern (titled meat-fish ⁽⁹⁴⁾, high protein ⁽⁸⁰⁾ and high protein/alcohol ⁽⁹³⁾) is characterised by high consumption of red/processed meats, poultry and fish. A snack dietary pattern (labelled snacks-drinks-milk products ⁽⁹⁴⁾, snack food ⁽⁸¹⁾ and pattern 6 ⁽⁹⁶⁾) is mainly composed of snacks, coffee and nuts.

Unlike the previously mentioned patterns, there are large variations in ‘traditional’ diets depending on the cultural norms of the studied populations. Examples of traditional patterns from different countries with their constituent foods include:

- Brazilian comprised of vegetables, beans, chicken, rice and olive oil ⁽⁹⁸⁾;
- French of vegetables, butter, bread, potatoes, milk and stock ⁽⁷⁸⁾;
- Lebanese of vegetables, fruits, legumes, bulgur, nuts and seeds ⁽⁹³⁾;
- Iranian of whole grains, pickles, hydrogenated oil, animal fat and salt ⁽⁸⁰⁾;
- Chinese - herbal tea, double-stewed soup, animal organ meat, processed meat and fish and low intake of soybeans and dark-coloured vegetables ⁽⁸²⁾;

- Dutch - meat, potatoes, fat and low intake of soy products ⁽⁸⁸⁾;
- The ‘traditional’ Japanese pattern of miso soup, rice and natto ⁽⁹⁷⁾.

Thus, unlike healthy, western, animal protein and snack patterns, these are not readily comparable across studies. Their potential effects on health outcomes may well be very different and despite the shared terminology of “traditional” are probably best considered as individual, separate patterns rather than as a category of similar patterns.

Understanding the major factors associated with different types of dietary patterns can help to design and target interventions to improve diet quality and to improve bone health outcomes as outlined in 1.3.2 to 1.3.4 below.

1.3.2 Factors associated with dietary patterns in older people

Given the potential importance of dietary patterns for musculoskeletal health outcomes of older adults (see Sections 1.3.3 and 1.3.4), it is important to identify factors associated with those patterns that could enable the targeting of intervention programs. Healthy, western, animal protein and snack dietary patterns were comparable across studies, therefore factors associated with these patterns are described here.

Previous studies (1 cohort ⁽⁷⁹⁾ and 7 cross-sectional ^(78, 80, 83, 87, 93, 94, 96)) identified many factors that contribute to the diversity of dietary patterns in elderly people such as socioeconomic status (e.g. age, sex, body mass index (BMI), education,

marital status, religion, income, occupation and family size), and lifestyle factors (e.g. smoking and physical activity).

A healthy dietary pattern (termed healthy⁽⁷⁸⁻⁸⁰⁾, prudent⁽⁸³⁾, vegetable and fruit⁽⁹⁴⁾, Lebanese pattern⁽⁹³⁾, and more healthful⁽⁸⁷⁾) has consistently been shown to be positively associated with higher education^(78-80, 83, 87, 93, 94), higher income^(80, 87) and being a woman^(79, 87, 93). In contrast, there were inconsistent results for the associations of a healthy dietary pattern with age, BMI, physical activity and smoking status. For example, there were positive associations between a healthy dietary pattern and older age in Norwegian⁽⁸³⁾ and Iranian⁽⁸⁰⁾ studies in comparison to a negative relationship of these variables in a French study (women)⁽⁷⁸⁾ or no association in other studies^(87, 93). Similarly, a healthy diet was negatively associated with current smokers (men) in a French study⁽⁷⁸⁾ but positively associated with current smokers at baseline in an Irish study⁽⁷⁹⁾.

Western dietary pattern (titled western^(78, 79, 83, 87, 93) and unhealthy⁽⁸⁰⁾) was associated with being a man^(79, 93). There were inconsistent findings for the associations of a western dietary pattern with age, education, BMI, physical activity and smoking in previous studies. A western dietary pattern was positively associated with older age in a Norwegian study⁽⁸³⁾, but negatively associated with older age in a French study⁽⁷⁸⁾ or not associated with age in others^(79, 80, 87, 93). A western diet was associated with lower education in some studies^(79, 83, 93) vs absent in other studies^(78, 80). Similarly, less physical activity^(83, 93) was related to a western pattern but there were no associations of these variables in other studies^(79, 87).

An animal protein dietary pattern (named meat-fish ⁽⁹⁴⁾, high protein ⁽⁸⁰⁾ and high protein/alcohol ⁽⁹³⁾) was consistently not associated with age ^(80, 93, 94), marital status ^(80, 93) and smoking status ^(93, 94). There was conflicting evidence for the relationship of an animal protein dietary pattern with education, alcohol consumption and physical activity. An animal protein pattern was negatively associated with education in Chinese men ⁽⁹⁴⁾ compared with absent in Iranian ⁽⁸⁰⁾ or positive in Lebanese ⁽⁹³⁾. A positive relationship was found between alcohol intake and an animal protein pattern in one study ⁽⁹³⁾ vs no association in another study (women) ⁽⁹⁴⁾. Physical activity was negatively associated with an animal protein pattern in Chinese women, but not for men ⁽⁹⁴⁾.

A snack dietary pattern (labelled snacks-drinks-milk products ⁽⁹⁴⁾ and pattern 6 ⁽⁹⁶⁾) was not associated with physical activity ^(94, 96). However, there were inconsistent results for the associations of a snack dietary pattern with age, education, and smoking status. A snack diet was not associated with age in a Chinese study ⁽⁹⁴⁾ vs a positive association of these variables in an Iranian study ⁽⁹⁶⁾. There was a positive relationship of a snack dietary pattern with education and current smoking in Chan et al study ⁽⁹⁴⁾ vs absent in Karamati et al study ⁽⁹⁶⁾.

Of the studies mentioned above, only one was longitudinal ⁽⁷⁹⁾ assessing the changes in dietary patterns in older adults, using a latent analysis. This study found that 49% of participants remained stable in their healthy and western dietary patterns (33% in healthy and 16% in western) over ten years. Being a man and less-educated was more likely to result in dietary stability in the western class; compared to being a woman, well-educated and a current smoker (baseline) in the healthy

class. Further longitudinal studies to clarify factors associated with changes in dietary patterns in older people are therefore important, and this is addressed by the study described in Chapter 5 of this thesis.

In summary, there is consistent evidence of the association of western dietary patterns with being a man; healthy dietary patterns with higher education, higher income and being a woman. However, there were conflicting results for the associations of healthy and western dietary patterns and other characteristics of older adults (e.g. age, BMI, smoking and physical activity) that mostly came from cross-sectional studies. Consistently, there were no associations of an animal protein pattern with age, marital status, and smoking status. Similarly, no association was found between a snack diet and physical activity. While the current literature provides some guidance for potentially targeting dietary interventions, the lack of longitudinal data and the inconsistencies in cross-sectional data suggest that further research is needed.

1.3.3 Associations between dietary patterns, fractures, and BMD in older people

Although previous studies ^(81, 82, 84-86, 88-92, 96, 97, 99-116) have examined the associations of dietary patterns with fracture and BMD in adults, the minority are cohort studies ^(84, 86, 88, 89, 92, 97, 99) and there are no intervention studies relating to elderly people aged 50 years and over. Importantly, the studies have conflicting findings. For example, a healthy dietary pattern (e.g. high consumption of fruits, vegetables, whole grains and fish) was positively associated with BMD in some studies ^(86, 88, 92, 100, 109), compared with no such associations in other studies ^{(81, 103,}

¹⁰⁶). Therefore, a systematic review and meta-analysis was undertaken as the first component of this thesis which aimed to; determine whether empirically derived dietary patterns are associated with BMD and fracture in healthy adults, and identify gaps in the current literature. The study is reported in full in chapter 3 of this thesis.

1.3.4 Associations between dietary patterns and falls in older adults

Although falls that lead to increased mortality and morbidity are frequent in older adults ^(117, 118) and poor nutrition is one of the important risk factors for falls ⁽¹¹⁹⁾, no previous studies have used an empirical approach to examine the association between dietary patterns and the risk of falls in these populations. However, several previous studies have reported inconsistent results for the association between dietary patterns and major risk factors for falls in older adults, for example, muscle weakness, sarcopenia/frailty, cognitive problem and gait/balance problems (Section 6.4 of Chapter 6 for more detail). Given these findings support a potential relationship between dietary patterns and a range of falls risk factors, an association between dietary patterns with falls risk is likely. The gap in the literature highlights an urgent need for further studies that investigate these associations in older people, an evidence gap addressed in Chapter 6 of this thesis.

1.4 Conclusion

Dietary pattern analysis is recommended as an approach that assesses the whole diet and its relationship with health outcomes. The comparable patterns identified in older adults include healthy-, western-, animal protein- and snack- type dietary patterns. In older adults, there are similar major food items for healthy (e.g. high consumption of fruits, vegetables, whole grains, fish and nuts) and western dietary patterns (e.g. high intake of red and processed meats, refined grains, sweets and fast foods). An animal protein dietary pattern was mainly composed of meats, poultry and fish, and a snack dietary pattern was predominated by a high intake of snacks, nuts and coffee.

For factors associated with dietary patterns in older people, a healthy diet was associated with being a woman, having higher education and greater income; and a western pattern was associated with being a man. There were inconsistent results from the observational studies (mostly cross-sectional) for the associations between healthy and western dietary patterns and other characteristics such as age, BMI, smoking and physical activity. Consistently, there were no associations of an animal protein pattern with age, marital status, and smoking status. Similarly, no association was found between a snack diet and physical activity. While the current literature provides some guidance for potentially targeting dietary interventions, the lack of longitudinal data and the inconsistencies in cross-sectional data suggest that further research with longitudinal studies is needed.

The observational studies (mainly cross-sectional) showed conflicting findings for the associations of dietary patterns with BMD and fracture in adults and a systematic review addressing this is therefore needed, as is further longitudinal data. No previous studies have investigated the association between dietary patterns using an empirical method and falls in elderly people, which is a major evidence gap. The remainder of this thesis reports on studies performed to address these gaps.

1.5 Structure of thesis

The introduction to this thesis (Chapter 1) has described the major health problems in older adults of fracture, low BMD and falls, focussing on the prevalence, major consequences, and economic burden of these outcomes. It describes the role of nutrition in these outcomes and highlights the evidence gaps addressed by this thesis. Chapter 2 describes the research questions of the thesis. Chapter 3 is a systematic review and meta-analysis to determine the association of dietary patterns with fractures and BMD in adults. Chapter 4 provides the detailed methodology of the Tasmanian Older Adult Cohort study and the statistical methodology used for two original studies of this thesis (Chapters 5 and 6).

Chapter 5 is an original study examining the association between dietary patterns with socio-demographic and lifestyle factors in Tasmanian older adults. Chapter 6 examines the longitudinal associations of dietary patterns with falls risk, BMD, and fracture in older adults. Finally, the key findings and implications for future research are summarized in Chapter 7.

Chapter 2: Research questions

Fracture prevention is a major public health issue in older adults and can be addressed by improving two major risk factors of fracture (low bone mineral density and falls)⁽⁸⁾. Diet is an important modifiable factor that could help to reduce the occurrence of fracture and/or the risk factors associated with fracture^(120, 121). However, studies that rely upon the analysis of single foods or individual nutrients appear to show small effects. It is proposed that this approach cannot capture the impact of a whole diet, as people consume multiple foods/nutrients⁽⁷⁰⁾. Dietary pattern analysis is an alternative approach that is recommended as it accounts for the complexities of an overall diet and interactions between different foods⁽⁷⁰⁾. There are limited longitudinal studies investigating the associations between dietary patterns with bone health in older adults⁽¹¹⁴⁻¹¹⁶⁾. More importantly, no previous studies have examined the association between dietary patterns using an empirical approach and falls risk.

To fill these evidence gaps, this research aimed to investigate dietary patterns and their associations with falls risk, bone mineral density, and fracture in older adults. The specific research questions addressed are given below.

The first research question of this thesis was addressed by a systematic review with meta-analysis:

Question 1: Which (if any) dietary patterns are associated with bone mineral density and fracture in the existing literature?

Questions 2-5 were addressed using data from the Tasmanian Older Adult Cohort (TASOAC) Study. The TASOAC study is a population-based cohort study originally aimed at investigating associations between osteoarthritis and osteoporosis and lifestyle, genetic and biochemical factors. At baseline (2002-2004), 1098 participants aged 50 years and over were recruited and followed over a period of more than ten years (n=567).

Question 2: What dietary patterns can be empirically derived and scored from a food frequency questionnaire in a population-based sample of older Tasmanian adults?

Question 3: Do the scores for these patterns change over time?

Question 4: Which participants' socio-demographic characteristics (age, sex, occupation, education, and area-level socioeconomic status) and lifestyle factors (smoking and physical activity), are associated with dietary pattern scores over time?

Question 5: Are dietary patterns longitudinally associated with falls risk, bone mineral density and/or fracture in a population-based cohort of older Tasmanian adults?

Chapter 3: Associations of dietary patterns with bone mineral density and fractures in adults: a systematic review and meta-analysis

This chapter was the first systematic review of the associations of dietary patterns with bone outcomes at specific sites, including bone mineral density (hip, lumbar spine, femoral neck, forearm, total body bone mineral density), total body bone mineral content and fracture (hip, total fracture) in adults aged ≥ 18 years. This paper was completed in 2018.

3.1 Introduction

Optimizing bone mineral density (BMD) throughout the life-course is one of the main strategies to reduce the risk of osteoporosis and osteoporotic fractures ⁽³⁹⁾. Nutrition plays a vital role in this, but most research has focused on the role of single nutrients or food items. However, there are high correlations between individual nutrients and food items as they are consumed together in the diet and potentially interact in complex ways ⁽⁹⁶⁾. Taking a dietary pattern approach may address these limitations ⁽⁹⁶⁾ as well as potentially provide evidence that is easier to translate into practice ⁽⁷⁵⁾. In the past two decades, increasing attention has been paid to dietary pattern analysis to examine the role of overall diet as compared to the traditional analysis of using single nutrient or food items ⁽⁷⁰⁾. Approaches to identify dietary patterns can use scoring systems that assess how well a population's dietary intake conforms to pre-defined dietary patterns, for example, the Healthy Diet Index ⁽¹²²⁾ or the Healthy Eating Index ⁽¹²³⁾. An alternative method determines dietary patterns using approaches such as factor analysis ⁽¹²⁴⁾ that identify dietary patterns empirically, without using a priori definitions or constructs ⁽⁷⁰⁾.

Individual studies investigating associations of dietary patterns with bone density and fractures have to date provided conflicting results. For example, McNaughton et al found that an energy-dense pattern characterized by refined cereals, soft drinks, fried potatoes, processed meat, and take away foods was negatively associated with total body bone mineral content (TBBMC) in 527 Australian women aged 18 to 65 years ⁽¹⁰⁴⁾. While this pattern was similar to a fast food and

soda pattern (high consumption of pizza and hamburgers, French fries, soda and coffee, and sweet fruit juice) identified in study of 1818 Korean healthy adults (mean age 46.4 years)⁽¹⁰⁸⁾, in the latter study, there was no association between this pattern and BMD. Similarly for fractures, a healthy dietary pattern (high consumption of fruits and vegetables) was negatively associated with hip fracture risk in 581 pairs of cases and controls of Chinese people aged 55 to 80 years⁽⁸²⁾ while in a USA cohort of 74,540 post-menopausal women and 38,305 men aged over 50 years consuming a similar prudent dietary pattern (characterized by high intake of fruits, vegetables, poultry, and whole grains) was not associated with the risk of hip fracture⁽⁸⁴⁾. A scoping review⁽¹¹⁴⁾ describing studies assessing associations of dietary patterns with a range of bone outcomes confirms this inconsistency, with different patterns of associations being seen for similar outcomes in different studies.

Because of these inconsistencies, a robust systematic synthesis of studies examining associations of dietary patterns and bone outcomes is needed that examines evidence separately for different clinically important fracture and bone density sites. The latter is important as fracture risk factors differ for different sites⁽¹²⁵⁾, as do the costs and sequelae of fractures⁽¹²⁶⁾. Failing to examine fractures or bone mineral density/content outcomes by sites is a significant limitation of the only systematic review⁽¹¹⁵⁾ addressing this issue. Therefore, we undertook a systematic review aiming to determine whether empirically derived dietary patterns are associated with bone density and fracture outcomes at key clinically important sites, namely the hip, lumbar spine, and forearm in healthy adults.

3.2 Materials and methods

This review was prospectively registered on the PROSPERO (the International prospective register of systematic reviews - Registration number CRD42017071676).

3.2.1 Literature search and register

We searched the electronic bibliographical databases Medline and Embase via OVID, CENTRAL (Cochrane) and Proquest: theses and dissertations from their inception to 12/5/2017 using key words relating to dietary patterns, BMD, and fracture. We limited the search to adults, English language, and human subjects. The full search strategy for each database is given in **Appendix 3-1**.

3.2.2 Selection criteria

Types of studies and participants

We included quantitative studies of any design, including cross-sectional studies, case-control studies, cohort studies, randomized and non-randomized controlled trial (RCT), quasi-experimental study designs or pre-post intervention studies reporting associations between dietary patterns and bone density outcomes and/or fractures. Studies were included if they were published in English, as full text and were peer-reviewed, and if participants were healthy adults aged 18 and over. We excluded studies that focused on adults with diseases or on medications affecting bone metabolism such as (but not limited to) coeliac disease or users of corticosteroids. We also excluded duplicate publications of the same study.

Types of exposure

We included studies assessing dietary patterns as exposures using an empirical (posteriori) approach such as factor analysis, principal component analysis, cluster analysis, reduced rank regression, or partial least-squares that were based on a dietary intake measurement using a validated method such as 24-hour recall, food diary, or validated food frequency questionnaire (FFQ) ⁽⁷⁰⁾. Dietary pattern scores could be calculated using any method including non-refined methods (sum score by a factor, sum score – above a cut-off, sum score – standardized variables, and weighted sum score) and refined methods (regression score, Bartlett score, and Anderson-Rubin score) ⁽¹²⁷⁾.

Types of outcomes

Studies were included if they measured bone density and/or fractures. For bone density, we included studies that measured areal or volumetric BMD, or bone mineral content (BMC) using dual-energy x-ray absorptiometry (DXA), single-photon absorptiometry, dual-photon absorptiometry, peripheral quantitative computerised tomography, or broadband ultrasound attenuation and ultrasonic speed of sound by quantitative ultrasound. Studies had to measure at least one of the following sites: femoral neck (FN), total hip, total body (TB), lumbar spine (LS), proximal or distal forearm. Studies that reported total fracture and/or hip, distal forearm, or radius and clinical (symptomatic), or radiological vertebral fracture fractures were included. For all except radiological vertebral fracture, we accepted self-reported outcomes if radiological confirmation was not available.

Radiological vertebral fracture could be assessed by computed tomography, X-ray, DXA-based vertebral morphometry or magnetic resonance imaging.

3.2.3 Study selection and data extraction

Two authors (HHN and FW) independently screened the titles and abstracts of potential articles against the inclusion and exclusion criteria, and further assessed the full text if it was unclear whether a study should be excluded. Disagreements were resolved by consensus. Two authors (HHN and JKM) independently extracted the following data using a standardised data extraction form:

- Study characteristics: title, author, study design, study time (duration or what date the study was done), sample size and source population (where participants were recruited).
- Participant characteristics: age, sex, ethnicity, potential confounders, country, criteria for inclusion and exclusion.
- Method of measuring dietary intake, including a number of food items and food groups
- Methods for determining dietary patterns, description of patterns and method to calculate diet scores.
- Sites, methods, and time points of measurement of bone mineral density and/or fracture.
- Methods (including any adjustment for potential confounders) used to test for associations between outcomes and exposures and their results. For the meta-analysis, we selected the included studies which had similar dietary patterns and BMD/fracture sites. In this process, we contacted study authors

to request unpublished data. However, for some studies, there were insufficient data for meta-analysis for all sites of BMD and total fracture, due to uncontactable authors, lack of relevant data, and insufficient similar studies.

3.2.4 Assessment of methodological quality of included studies

HHN and JKM independently assessed the methodological quality of included studies using an approach developed for observational studies on musculoskeletal topics⁽¹²⁸⁾ that can be modified for a specific topic, as we have previously done^(129, 130). This approach has criteria assessing both the internal validity and informativeness of each study as given in Part A of **Appendix 3-2**. The number of criteria used for each study depended on the outcome measures - 19, 20 and 22 criteria were used if the study measured BMD, fracture or both respectively. Each criterion was assessed according to four categories: adequate if the study met the criterion (+), inadequate if the study did not meet the criterion (-), unclear (?), and not applicable (NA). The full list of criteria is in **Appendix 3-2 – Part B**. A methodological quality assessment score was calculated by summing the number of criteria met (+), divided by the applicable number of criteria, multiplied by 100 to generate a percentage. We considered studies with a methodological assessment score $\geq 60\%$ as being high quality⁽¹²⁸⁾.

3.2.5 Data synthesis

For each included study, we used tables to summarise key study and participant characteristics (**Table 3-1**), methods of assessing dietary patterns and bone outcomes (**Table 3-2**) and key methods and results of tests of associations between dietary patterns and bone outcomes (**Tables 3-3** and **3-4**). Because a priori we expected there would be substantial clinical and methodological heterogeneity in the included studies, our first step was to consider from these tables whether the studies reporting data for each outcome were acceptably similar for meta-analysis to be possible and best evidence synthesis to be appropriate. A major consideration in this was judging the extent to which different dietary patterns were sufficiently similar to each other. This was undertaken by consensus between four authors (HHN, TW, FW, WHO), one of whom is a professor of nutritional epidemiology (WHO), by examining the composition of all the published dietary patterns in each study (as summarised in **Table 3-2**). There were two categories of dietary patterns with the most consistently observed similarities in their composition, which we grouped under the umbrella terms of healthy and western patterns as the closest reflection of their content though they were named differently across studies (see **Table 3-2** for details). The healthy group of patterns was characterised by high consumption of fruits, vegetables, whole grain, nuts, legumes and fish and the western group of patterns by high consumption of meats, processed meats, sweets including cakes or desserts, fats/oils, soft drinks and take away foods. There were relevant data available for meta-analysis for only one outcome and exposure (hip fracture and healthy pattern). There were insufficient data to perform meta-analyses

for the associations of dietary patterns with BMD at any site, TBBMC and total fracture.

A best evidence synthesis for both healthy and western dietary patterns was possible and performed for each bone density site (FN, total hip, LS, TB and forearm BMD and TBBMC). Similarly, the approach of best evidence synthesis was applied to hip fracture and western pattern, and total fracture and both healthy and western patterns. The levels of evidence were classified into five categories according to the criteria of Liewense et al ⁽¹²⁸⁾. Evidence was considered strong if there were consistent findings in multiple high-quality cohort studies; moderate if the general consistent findings were shown in a single high-quality cohort study and ≥ 2 high-quality case-control studies, or ≥ 3 high-quality case-control studies; limited if consistent findings were shown in a single cohort study, 1 or 2 case-control studies, or multiple cross-sectional studies; conflicting if fewer than 75% of studies had consistent findings and as no evidence if no studies were found.

For the meta-analysis of healthy dietary pattern and hip fracture, we used the number of events and the total number of participants in the highest vs the lowest categories of this pattern scores (variously tertiles, quartiles, quintiles) to estimate the pooled risk ratio (RR) and 95% confidence interval (CI), using random-effects modelling. We performed a subgroup analysis by method for measuring fracture (confirmed by medical record vs. self-report). The heterogeneity of the included studies was assessed using I-square (I^2). Review Manager software version 5.3 (The Nordic Cochrane Centre, Copenhagen) was used for meta-analysis.

3.3 Results

3.3.1 Characteristics of included studies

From 1750 potential articles, 23 studies were included in the systematic review (**Figure 3-1**) but 21 were included in the best evidence synthesis as two studies did not identify dietary patterns comparable to healthy or western patterns to enable such synthesis. The characteristics of studies and their participants are given in **Table 3-1**. Sample sizes ranged from 154 ⁽⁹⁶⁾ to 112,845 ⁽⁸⁴⁾. Over half of studies were conducted in western countries ^(81, 84, 85, 88-90, 92, 101-104, 106, 110) and focused on older adults ^(81, 82, 84, 85, 88-92, 96, 97, 99). Seven studies reported results for both sexes combined ^(82, 85, 88, 92, 97, 107, 109), 8 studies reported separate result for each sex ^(82, 84, 89, 90, 102, 106-108) and 10 studies were in women only ^(81, 91, 96, 99-101, 103-105, 110). All studies were considered high quality with methodological quality assessment scores ranging from 68.4% ⁽¹⁰²⁾ to 93.3% ^(96, 104). Only 4 studies ^(89, 97, 101, 102) had a score of <75%. There were 12 cross-sectional studies (52.2%) ^(81, 85, 90, 91, 96, 100, 101, 103, 104, 106, 108, 109), 10 cohort studies (43.5%) ^(84, 88, 89, 92, 97, 99, 102, 105, 107, 110) and one case-control study (4.3%) ⁽⁸²⁾.

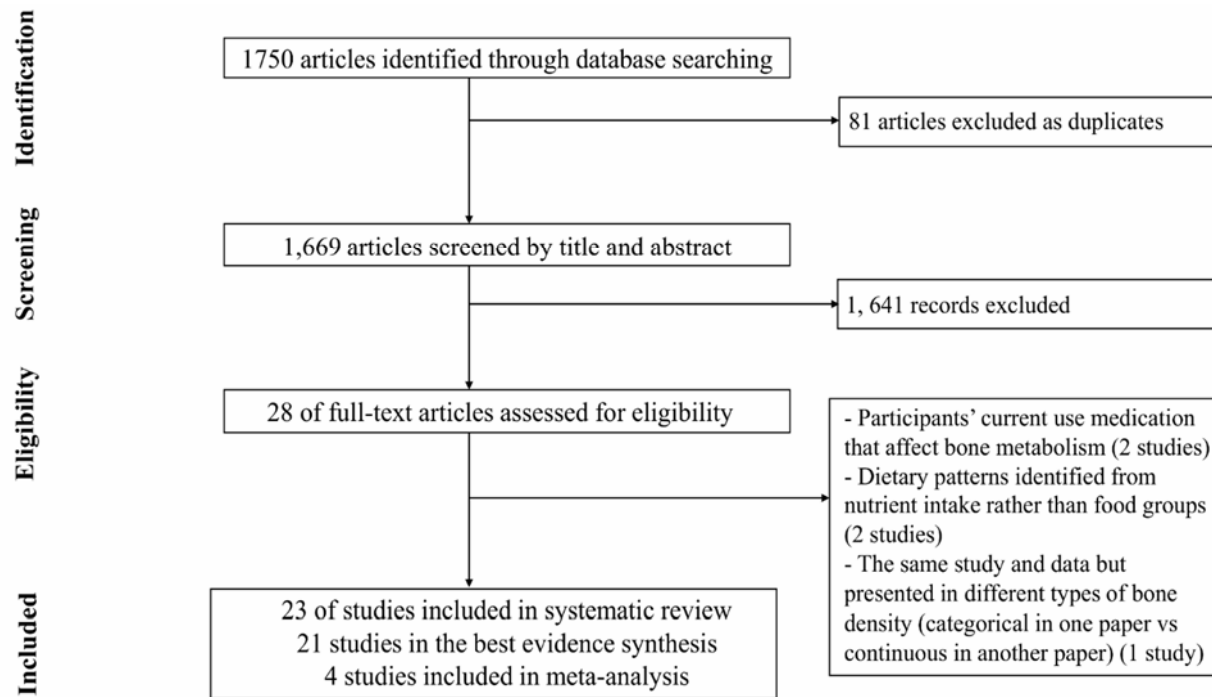


Figure 3-1: Flow chart of studies included in the systematic review and meta-analysis.

Table 3-1: Characteristics of studies and participants

<i>Author Country Year</i>	<i>Sample size</i>	<i>Study design</i>	<i>Age (yr)^a</i>	<i>Sex N (%)</i>	<i>Setting</i>	<i>Inclusion and/or exclusion criteria^b</i>	<i>Percentage of quality score</i>
Tucker USA 2002 ⁽⁹⁰⁾	907	Cross- sectional	Men 75.1 (4.9); women 75.3 (4.8) Range 69-93	Men 345 (38), women 562 (62)	Population- based	In the original cohort (the Framingham Heart Study in 1948), participants aged 28–62 years were selected as a population-based random sample of households in Framingham, Massachusetts. The current study was a cross-sectional analysis of data obtained from 1988-1989, among participants who completed BMD measurement, nutrition questionnaire and other relevant questionnaires.	80.0
Okubo Japan 2006 ⁽¹⁰⁰⁾	291	Cross- sectional	46.4 (3.7) Range 40-55	Women only	Community -based	The original cohort was a national community-based study of farm-women adults aged 20-78 years (2000-2003). This study was conducted in 5 districts located in the north end of Kyushu and Honshu Islands. The current study was restricted to women aged 40-55 years who completed diet questionnaire, BMD measurement and other relevant questionnaires. They had no history of taking medications or any conditions that may affect bone or calcium metabolism.	86.7
Kontogianni Greece 2009 ⁽¹⁰¹⁾	196	Cross- sectional	Premenopausal 38 (8.7), postmenopausal 56.7 (6.4) Not report age range	Women only	Community -based	Women who did not have medications or medical treatment that could influence BMD, having diabetic or weight-reducing diet, and no exposure with HRT for menopausal. They completed nutrition questionnaire, BMD measurement and other questionnaires.	73.3

Langsetmo Canada 2010 ⁽¹⁰²⁾	6539	Cohort	Men 58.8 (13.5), women 61.2 (12.2) ≥25, not report age range	Men 1928 (29.5), women 4611 (70.5)	Population- based	Participants (the Canadian Multicentre Osteoporosis Study) were ≥25 years old at enrollment in 1995 (baseline) and followed up for five years (2000-2002), lived within a 50-kilometre radius of one of nine Canadian cities (St John's, Halifax, Quebec City, Toronto, Hamilton, Kingston, Saskatoon, Calgary, and Vancouver) and were able to converse in English, French, or Chinese (Toronto or Vancouver). They completed the food frequency questionnaire with ≤10 missing responses, BMD assessment and potential confounders.	68.4
Monma Japan 2010 ⁽⁹⁷⁾	877	Cohort	Fall-related fracture 82.3 (5.9) and non-fall related fracture 79.1 (4.6) ≥70, not report age range	Fall-related fracture: men 8 (28.6), women 20 (71.4); non-fall related fracture: men 380 (44.8), women 469 (55.2)	Population based	Participants were aged over 70 years and living in the Tsurugaya area of Sendai in Japan in 2002. They completed dietary questionnaire, fracture and other data and scored higher than 18 in the Mini Mental State Examination. They were followed up for their incidence of fall-related fracture until the end of July 2006.	70.0
Fairweather- Tait UK 2011 ⁽¹⁰³⁾	2464	Cross- sectional	56.3 (11.9) Not report age range	Women only	National- based	The healthy twins were enlisted in the national register between 1993 and 2004. They were postmenopausal women (UK residents) without metabolic disorders, but completed dietary intake or require its modification and BMD measurement, and brought up together and lived apart in adult life.	81.3

Hardcastle Scotland 2011 ⁽⁸¹⁾	3236	Cross-sectional	55.1 (2.2) Range 50-59	Women only	Population-based	Participants from a population-based screening program for osteoporosis fracture risk, involving 5119 women aged 45-54 years, who had the first visit from 1990 to 1994. The present study was a cross-sectional study of participants, who completed diet and bone density measurement, provided urine and non-fasted blood samples and other information (1997-1999).	86.7
Langsetmo Canada 2011 ⁽⁸⁹⁾	5188	Cohort	Men 64.6 (10.0), women 67.6 (8.6) ≥50, not report age range	Men 1649 (31.8), women 3539 (68.2)	Population-based	Participants from the Canadian Multicentre Osteoporosis Study who were postmenopausal women and men aged ≥ 50 years were recruited at the baseline (1997-1999) and followed up for 8 years (2005-2007). They completed a diet questionnaire with ≤10 missing responses.	70.0
McNaughton Australia 2011 ⁽¹⁰⁴⁾	527	Cross-sectional	Pattern 1 [Q5 33.2 (9.6); Q1 43.6 (8.7)] Range 18-65	Women only	Community-based	Twin pairs of the Australian Twin Registry who resided in Melbourne and surrounding areas of Victoria (1991-2001). Participants completed BMD data, dietary intake and other data. Exclusions: excessively extended period (>10 months) between food data collection and physical measurements, or potentially underreported dietary intake (a ratio of the mean of 4-d energy intake/basal metabolic rate <0.8).	93.3
Karamati Iran 2012 ⁽⁹⁶⁾	154	Cross-sectional	60 (8.4) Range 50-85	Women only	Community-based	Menopausal women aged 50-85 years who had BMD measurement and completed general questionnaires including diet (winter 2011). They were not following a specific diet, did not consumption of alcohol or drugs (except for antiresorptive medications) that affect bone metabolism and did not have diagnosed endocrine, gastrointestinal, rheumatoid and renal disorders.	93.3

Park Korea 2012 ⁽¹⁰⁵⁾	1464	Cohort	Traditional pattern [Q5: 58.2 (6.6); Q1: 59.4 (6.8)] Range 40-69	Women only	Community -based	The Korean Genome and Epidemiology Study recruited postmenopausal women from a rural (Ansung) and urban (Ansan) area, who completed questionnaires including nutrition and BMD measurement in May 2001 (baseline), followed up to February 2003. Participants were excluded for: reported daily energy intake lower or higher than 2 standard deviations (< 347.0 kcal or > 3204.6 kcal) from the mean value; early menopause prior to 40 years; on insulin therapy, HRT or thyroid drugs.	77.8
Whittle Ireland 2012 ⁽¹⁰⁶⁾	489	Cross- sectional	Men 22.4 (1.6), women 22.8 (1.7) Range 20-25	Men 251 (51.3), women 238 (48.7)	Post- primary schools	The original cohort study (the Young Heart Project) began from 1989 to 1990 with participants aged 12-15 years from post-primary schools. The present study was based on phase three (1997-1999). They completed BMD measurement, dietary and other relevant data.	86.7
Shin Korea 2013 ⁽⁹¹⁾	3735	Cross- sectional	64.1 (9.5) Not report age range	Women only	National- based	The Korean National Health and Nutrition Examination Survey was originally conducted in 1998. The present study was based on a cross-sectional data collected during 2008 to 2010. Women who completed health interview, nutrition, and BMD measurement. People with implausibly low or high daily energy intakes (< 2,092 or > 20,920 kJ/d) were excluded.	86.7
Zeng China 2013 ⁽⁸²⁾	1162	Case control	Cases 71 (6.7), control group 70.9 (6.7) Range 55-80	Men 296 (25.5), women 866 (74.5)	Hospital and community	Case-control study conducted 2009-2012 in Guangdong Province, China. Eligible cases were newly diagnosed with hip fractures (within 2 weeks) according to their medical records and confirmed by X-ray image; aged between 55 and 80 years; and had lived in Guangdong Province more than 10 years. They completed a structured questionnaire. For each case, 1 matched control was recruited according to age (within 3 years) and gender, with the	87.5

<p>same inclusion and exclusion criteria applied. Controls came from:1) apparently healthy community residents in the same cities; and 2) inpatients hospitalized for less than 1 week with influenza, pneumonia, benign ophthalmic or otorhinolaryngological tumor, acute surgical disease, or a cataract in 1 eye. Participants were excluded if they had: 1) high-energy fractures or pathological fractures; 2) dietary habits that had changed significantly within the previous 5 years; 3) chronic disease such as diabetes, cardiovascular disease, cancer, cognitive disorder, liver cirrhosis, thyroid disorder, renal failure, or chronic diarrhea; 4) currently used certain medications such as exogenous estrogens, thiazine, or corticosteroids; 5) poor vision.</p>							
Dai Singapore 2014 ⁽¹⁰⁷⁾	63,154	Cohort	Vegetable-fruit-soy pattern in men [Q5: 55.9 (7.8); Q1: 57.7 (8.2)] and women [Q5: 55.3 (7.8); Q1:57.9 (8.4)] Range 45-74	Men 27,913 (44.2), women 35,241 (55.8)	Population based	<p>The Singapore Chinese Health Study recruited participants (aged 45-74 years) from 2 major dialect groups (Hokkiens and Cantonese), who originated from Fujian and Guangdong provinces in Southern China, respectively (April 1993 to December 1998), and they were followed up until 31 December 2010. All participants resided in government housing estates. They completed a diet questionnaire, fracture and relevant data.</p>	90.0
Chen China 2015 ⁽⁹⁹⁾	282	Cohort	56.1 (3.8) Range 50-65	Women only	Community health center	<p>Participants were aged between 50 and 65 years and lived in Harbin for at least 5 years in 2009 (baseline) and were followed up to 2011. They completed diet data, BMD measurement and relevant questionnaires. Participants were excluded if they: 1) had disorders of calcium metabolism/ calcium absorption, or bone; 2) had gastrointestinal disease, coronary heart, stroke, diabetes, cancer, thyroid or parathyroid disease, chronic liver disease or chronic kidney disease; 3) suffered from ovarian surgery, premenopausal</p>	82.4

						hysterectomy, gastric resection and thyroidectomy; 4) used estrogen at the time of the study or had taken drugs (not specified) for a month or more; 5) and were likely to migrate.	
Fung USA 2015 ⁽⁸⁴⁾	112,845	Cohort	Prudent pattern of women [Q5: 54, Q1: 53]; men [Q5: 58, Q1: 56] ≥50, not report age range	Men 38,305 (33.9), women 74,540 (66.1)	Not clear	The Nurses' Health Study was originally conducted in 1976 with women aged 30-55 years and the Health Professionals Follow-up Study began in 1986 with men aged 40-75 years. For the present study, women were postmenopausal in 1980 and followed up until 2010; Men were recruited in 1986 or when they reached 50 years and followed up until 2012. Participants completed medical history, dietary questionnaire and lifestyle information. They were excluded at entry if they did not have the most recent dietary assessment, had previously reported a hip fracture or diagnosis of cancer or osteoporosis, or were non-Caucasian (<3%).	75.0
Shin Korea 2015 ⁽¹⁰⁸⁾	1818	Cross-sectional	46.4 (12.3) ≥30, not report age range	Men 716 (39.4), women 1102 (60.6)	Community-based	The original study (the Healthy Twin Cohort Study) was conducted in 2005 with participants (aged ≥ 30 years) who visited study centers in Seoul or Pusan, Korean. The present study was from 1 July 2009 to 31 January 2012. Participants completed a questionnaire, health examinations and a nutrition survey. They were excluded if they had implausibly low or high daily energy intakes (< 500 or 5000 kcal per day) and did not have BMD measurements.	86.7
De Jonge Netherland 2016 ⁽⁸⁸⁾	5144	Cohort	Traditional pattern [median (range) T3: 66 (61-72), T1: 67 (61-74)]	Men in traditional pattern: T3 (59), T2 (38), T1 (26)	Population-based	Participants were aged 55 years and over at baseline (1989-1993) and living in Ommoord district of Rotterdam (the Rotterdam Study), followed up to 2002-2004. They were included when they completed both diet data and BMD measurement. Participants were	78.9

			≥55, not report age range			excluded due to suspected dementia, unreliable dietary intake data defined by the dietician and for logistical reasons.	
Denova-Gutierrez Mexico 2016 ⁽¹⁰⁹⁾	6915	Cross-sectional	Prudent pattern [Q5: 53.7 (9.7), Q1: 51.6 (9.4)] Range 20-80	Men 1948 (28.2), women 4967 (71.8)	Health and academic institutions	Participants and their relatives aged 20 to 80 years from three health and academic institutions in Morelos and other Mexico states were included in 2004 (the Health Workers Cohort Study). They were excluded if they had >10 % blank items on their food intake information, or daily energy intake values outside of 600–7000 kcal/day, incomplete BMD data or for other important covariates (tobacco, BMI, use of supplement, and estrogen use for women).	86.7
De Jonge Netherland 2017 ⁽⁹²⁾	4028	Cohort	Median (range) in men 66 (61-72); women 66 (61-73) ≥55, not report age range	Men 1705 (42.3), women 2323 (57.7)	Population-based	Participants were aged 55 years and over at baseline (1989-1993) who were living in Ommoord district of Rotterdam (the Rotterdam Study), followed up to December 2012. They completed diet data, BMD measurement, fracture and other relevant questionnaires.	77.3
Melaku Australia 2017 ⁽⁸⁵⁾	1182	Cross-sectional	Median (range) 62 (56-69) ≥50, not report age range	Men 545 (46), women 637 (54)	Community-based	The North West Adelaide Health Study was originally conducted from 1999 to 2003 (baseline). The present study was of participants (aged ≥50 years) who completed both bone mass measurement (2004-2006) and dietary data (2008-2010).	75.0
Warensjo Sweden 2017 ⁽¹¹⁰⁾	56,736	Cohort	Healthy pattern [Quartile 4: 52 (9), Quartile 1: 54 (10)] Not report age range	Women only	Community-based	The Swedish Mammography Cohort was established in 1987-1990 (baseline), followed up to December 2014. All women born between 1914 and 1948 and residing in two Swedish counties were included. They completed a questionnaire including diet, fracture	80.0

and relevant data. Participants were excluded if the national registration number was missing, the questionnaire had not been dated, energy intakes were implausible (± 3 SD from the mean value of the ln-transformed energy intake), had prior cancer diagnosis (except non-melanoma skin cancer) or more than 10 of the food groups missing.

^a Age: Mean (SD) unless otherwise stated. Q (quintile), T (tertile);

^b BMD (bone mineral density), HRT (hormone replacement therapy), BMI (body mass index).

The methods of measurement of dietary pattern, BMD and fracture are given in **Table 3-2**. Diet was mostly measured using FFQ ^(81, 82, 84, 85, 88-90, 92, 96, 97, 99, 100, 102, 103, 105, 107, 109, 110) and dietary patterns were generally identified by principal component analysis ^(81, 82, 84, 85, 88, 91, 96, 101, 103-110). Dietary pattern scores were mostly calculated using the weighted sum score method ^(81, 82, 88, 91, 96, 97, 100, 104-106, 109, 110). The two types of patterns with the most consistently observed similarities in their compositions were healthy patterns (variously termed healthy dietary pattern ^(81, 82, 100, 106, 110), health conscious ⁽⁸⁸⁾, prudent dietary pattern ^(84, 85, 109), traditional pattern ⁽¹⁰⁵⁾, nutrient dense ^(89, 102), fruit-vegetable ⁽¹⁰³⁾, fruit-vegetable-cereal ⁽⁹⁰⁾, vegetable-fruit-soy ⁽¹⁰⁷⁾, fruit-vegetable-dairy ⁽⁹²⁾, dairy-fruit ⁽⁹¹⁾, fruit-milk-whole grain ⁽¹⁰⁸⁾, pattern 3 ⁽¹⁰⁴⁾ and pattern 4 ⁽⁹⁶⁾) and western patterns (named western dietary pattern ^(84, 85, 100, 105, 110), energy dense ^(89, 102), processed food pattern ^(81, 88), refined food pattern ^(106, 109), meat pattern ⁽⁹⁷⁾, meat-baked product ⁽⁹⁰⁾, eggs-meat-flour ⁽¹⁰⁸⁾, meat-dim-sum ⁽¹⁰⁷⁾, meat-alcohol-sugar ⁽⁹¹⁾, sweets-animal fat-low meat ⁽⁹²⁾, high fat ⁽⁸²⁾ and pattern 1 ^(96, 104)). The healthy patterns were predominantly composed of fruits, vegetables, whole grain, nuts, legumes and fish. The western patterns were mainly characterized by high consumption of meats, processed meats, sweets, fats/oils, soft drinks, and take-away foods.

Table 3-2: Measurement of dietary pattern, bone mineral density and fracture

<i>Author Country Year</i>	<i>Method of dietary intake^a</i>	<i>Food items/ Food groups^b</i>	<i>Method of identifying dietary pattern^c</i>	<i>Method of calculating diet score</i>	<i>Number of dietary pattern (% variance)^d</i>	<i>Definition of dietary patterns*</i>	<i>Outcome measurement^e</i>	<i>Sites of outcome^f</i>
Tucker USA 2002 ⁽⁹⁰⁾	FFQ	126/34	CA	K mean	6 (NA)	1) Meat, dairy, and bread pattern: high consumption of meat, poultry, fish, milk and dairy products, and bread and less from sweet baked products. 2) Meat and baked product pattern (W): high intake of meats, processed meats , and moderately sweet baked products. 3) Sweet baked product pattern: high intake of sweet baked products, including cakes, pies, doughnuts, and cookies and a low intake of fruit, vegetables, bread, and cereal. 4) Alcohol pattern: high intake of alcohol. 5) Candy pattern: high candy intake. 6) Fruit, vegetables, and cereal pattern (H): high intake of fruits and vegetables , <i>breakfast cereal</i> and the lowest intake of red and processed meats and of candy and soft drinks.	BMD: SPA, DPA	FN, trochanter, wards, and radius
Okubo Japan 2006 ⁽¹⁰⁰⁾	FFQ	147/30	FA	Weighted sum score	4 (29.7)	1) Healthy pattern (H): high consumption of green and white vegetables , <i>mushrooms</i> , fish and shellfish, fruits , processed fish, <i>seaweed</i> , and <i>soy products</i> .	BMD: DXA	Forearm (distal sites of radius and ulna)

						<p>2) Western pattern (W): high consumption of fats and oils, meats, processed meats, and <i>seasoning</i>.</p> <p>3) Japanese traditional pattern: high consumption of rice, miso soup and soy products.</p> <p>4) Beverage and meats pattern: high consumption of coffee, soft drinks, dairy products, sugary foods, and meats.</p>		
Kontogianni Greece 2009 ⁽¹⁰¹⁾	3-days FD	Not clear/15	PCA	Not clear	10 (80.0)	<p>1) Pattern 1: high intake of dairy, cereals, red meat and olive oil.</p> <p>2) Pattern 2: rich in vegetables, fruits and olive oil.</p> <p>3) Pattern 3: high consumption of fish and olive oil and low intake of red meat and products.</p> <p>4) Pattern 4: high consumption of poultry and nuts and low intake of red meat and red meat products.</p> <p>5) Pattern 5: high in alcohol consumption.</p> <p>6) Pattern 6: legume consumption.</p> <p>7) Pattern 7: sweets consumption.</p> <p>8) Pattern 8: fruit drink consumption.</p> <p>9) Pattern 9: coffee consumption.</p> <p>10) Pattern 10: soft drink consumption.</p>	BMD: DXA	LS
Langsetmo Canada 2010 ⁽¹⁰²⁾	FFQ	69/34	FA	Not clear	2 (17.1)	<p>1) Nutrient dense (H): high intake of fruits, vegetables, and whole grains, fish, cheese, pasta, nuts, legumes.</p> <p>2) Energy dense (W): high consumption of soft drinks, potato chips and French fries, certain meats (hamburger, hot dog, lunch meat, smoked meat, bacon, and sausage), and certain desserts (doughnuts, chocolate, ice cream).</p>	BMD: DXA	FN

Monma Japan 2010 ⁽⁹⁷⁾	FFQ	75/27	FA	Weighted sum score	3 (30.0)	1) Vegetable pattern: high consumption of vegetables, seaweeds, mushrooms, soy products and salt. 2) Meat pattern (W): rich in meats (chicken, pork and beef), processed meats (ham, sausage, liver paste) and <i>seafood</i> (squid, octopus, shrimp, lobster and shellfish). 3) Traditional Japanese pattern: high intake of rice, miso soup intake and mildly loaded with Natto.	Fracture: Insurance claim records (medical record)	Any fractures, except traumatic fracture such as traffic accidents
Fairweather- Tait UK 2011 ⁽¹⁰³⁾	FFQ	131/NA	PCA	Standardized sum score	5 (NA)	1) Traditional English pattern (food groups not specified). 2) High alcohol pattern (food groups not specified). 3) Dieting pattern (food groups not specified). 4) Fruit and vegetable pattern (H) (food groups not specified). 5) Low-meat pattern (food groups not specified).	BMD: DXA	FN, hip, LS
Hardcastle Scotland 2011 ⁽⁸¹⁾	FFQ	98/35	PCA	Weighted sum score	5 (26.0)	1) Healthy diet (H): high loadings of fruits, vegetables, rice/pasta, white meat, oily fish and <i>dairy products</i> (excluding milks), and negative loading with processed foods (biscuits, confectionery and processed meats). 2) Bread and butter diet: high intake of bread and fats or oils and negative for red meats and spirits. 3) Processed food pattern (W): rich in processed foods (biscuits, confectionary and processed meats), cakes and desserts , and <i>negative loadings with fats/oils and breads</i> . 4) Fish and chips diet: high loadings of fish, fish dishes, potatoes, bread and fats or oils. 5) Snack food diet: rich in confectionery, crisps or nuts and sauces.	BMD: DXA	FN, LS

Langsetmo Canada 2011 ⁽⁸⁹⁾	FFQ	69/34	FA	Not clear	2 (17.1)	1) Nutrient dense (H): high intake of fruits, vegetables, and whole grains, fish, cheese, pasta, nuts, legumes. 2) Energy dense (W): high consumption of soft drinks, potato chips and French fries , certain meats (hamburger, hot dog, lunch meat, smoked meat, bacon, and sausage), and certain desserts (doughnuts, chocolate, ice cream).	Fracture: Self-report	Total low-trauma fractures
McNaughton Australia 2011 ⁽¹⁰⁴⁾	4-days FD	NA/46	PCA	Weighted sum score	5 (NA)	1) Pattern 1 (W): high consumption of <i>refined cereals, soft drinks, fried potatoes, sausages and processed meats, vegetable oils, beer, and take-away foods and low intake of soy products, other vegetables and vegetable dishes, tea and coffee, fruit, and wholegrain.</i> 2) Pattern 2: high intake of vegetables (potatoes, carrot, peas, and beans, brassica vegetables, zucchini, and squash), red meat, butter, and cream and negative loadings for pasta and pasta dishes and take-away foods. 3) Pattern 3 (H): high loadings of leafy vegetables , <i>tomato and tomato products, milk and yogurt (<1% fat), fruits, cheese, eggs, and fish and low intake of cakes, biscuits, and other baked sweet products, butter, and cream.</i> 4) Pattern 4: rich in legumes, seafood, seeds and nuts, wine, rice and rice dishes, and other vegetables and vegetable dishes and negative loadings with bacon and ham. 5) Pattern 5: high consumption of chocolate, confectionary, and added sugar, fruit drinks and cordials, and dairy milk and yogurt (>1% fat) and low consumption	BMD: DXA	Hip, LS

						of fruit and vegetable juices, poultry, wine, spirits, and other alcoholic beverages.		
Karamati Iran 2012 ⁽⁹⁶⁾	FFQ	168/25	PCA	Weighted sum score	6 (48.3)	<p>1) Pattern 1 (W): high consumption of <i>high-fat dairy products, organ meats, red or processed meats and non-refined cereals</i>.</p> <p>2) Pattern 2: rich in French fries, mayonnaise, sweets and desserts, and vegetable oils.</p> <p>3) Pattern 3: high intake of hydrogenated fats, pickles, eggs and soft drinks.</p> <p>4) Pattern 4 (H): rich in vegetables, <i>low-fat dairy products, fruits and fruit juices, legumes and fish, and low intakes of salt</i>.</p> <p>5) Pattern 5: high loadings of condiment, potatoes and low refined cereals content.</p> <p>6) Pattern 6: high intake of snacks, tea and coffee, poultry and nuts.</p>	BMD: DXA	FN, LS
Park Korea 2012 ⁽¹⁰⁵⁾	FFQ	103/18	PCA	Weighted sum score	3 (33.9)	<p>1) Traditional dietary pattern (H): high loadings of <i>rice, kimchi, vegetables, and fruits</i>.</p> <p>2) Dairy dietary pattern: rich in milk, dairy products, and green tea.</p> <p>3) Western dietary pattern (W): high consumption of <i>noodles, breads, sugar, fat, potatoes, meats, eggs, fish and sea foods, coffee and carbonated beverages</i>.</p>	BMD: SOS	Radius shaft and mid-tibia
Whittle Ireland 2012 ⁽¹⁰⁶⁾	7-days FD	Over 1000/31	PCA	Weighted sum score	Men: 4 (29.4), women: 4 (28.0)	1) Healthy dietary pattern (men and women) (H): high positive loadings for fruits, vegetables, brown bread, rice	BMD: DXA	FN, LS

						<p><i>and pasta and negative loadings for white bread, chips and meat dishes.</i></p> <p>2) Traditional dietary pattern (men and women): high consumption of white bread, fats and hot drinks and loaded negatively for soft drinks.</p> <p>3) Social dietary pattern (men and women): alcohol consumption.</p> <p>4) Refined dietary pattern (men) (W): rich in puddings (cakes), <i>crisps, chips, confectionery, chocolate, meats, condiments</i> and soft drinks.</p> <p>5) Nuts and meat pattern (women): high loadings of nuts, chocolate, red meat, meat dishes and poultry.</p>		
Shin Korea 2013 ⁽⁹¹⁾	24-hour recall	NA/20	PCA	Weighted sum score	4 (30.9)	<p>1) Meat, alcohol and sugar dietary pattern (W): high loadings for oils, <i>starch syrup</i> and sugar, meats and its products, <i>alcohol and a negative loading for legumes</i>.</p> <p>2) Vegetables and soya sauce pattern: high intake of vegetables and mushrooms, soya sauce and red pepper, garlic and onion, legumes and white rice.</p> <p>3) White rice, kimchi and seaweed dietary pattern: high loadings for white rice, seaweed, kimchi, and fish and shellfish but negative loadings for whole grains, potatoes, eggs, and noodles and dumplings.</p> <p>4) Dairy and fruit pattern (H): rich in legumes, <i>milk and dairy foods, flour and bread</i>, fruits and nuts.</p>	BMD: DXA	FN, LS
Zeng China 2013 ⁽⁸²⁾	FFQ	79/30	PCA	Weighted sum score	4 (26.7)	<p>1) Healthy dietary pattern (H): high intake of fruits, vegetables, <i>eggs</i>, and freshwater fish.</p>	Fracture: Medical record	Hip

						<p>2) Prudent dietary pattern: high loadings of nuts, mushrooms, algae, sea foods, and white vegetables and a low intake of grains (mainly refined).</p> <p>3) Traditional pattern: rich in Chinese herbal tea, Chinese double-stewed soup, processed meat and fish, animal organ meat, and a low intake of soybeans and related products, other soy, and darkly colored vegetables.</p> <p>4) High-fat dietary pattern (W): high consumption of red meats, <i>poultry with the skin</i>, <i>animal organ meat</i>, and cooking oil and a low intake of <i>nuts</i>, <i>poultry without the skin</i>, and <i>mushrooms and algae</i>.</p>		
Dai Singapore 2014 ⁽¹⁰⁷⁾	FFQ	165/NA	PCA	Unweighted sum of standardized frequencies	2 (NA)	<p>1) Vegetable-fruit-soy pattern (H): high loadings of vegetables, fruits, and <i>soy foods</i>.</p> <p>2) Meat-dim-sum pattern (W): rich in red/processed meats, <i>sodium</i> and <i>refined starchy foods</i>.</p>	Fracture: Surgical or medical records	Hip
Chen China 2015 ⁽⁹⁹⁾	FFQ	80/13	FA	Not available	6 (64.6)	<p>1) Pattern 2: high intake of rice, cooked wheaten food, fried food, and other grains and little intake of fruits.</p> <p>2) Pattern 3: rich in milk and little intake of root vegetables.</p> <p>3) The other dietary patterns were not mentioned.</p>	BMD: DXA	Hip, LS, total body
Fung USA 2015 ⁽⁸⁴⁾	FFQ	130/38	PCA	Standardized sum score	2 (Not available)	<p>1) Prudent pattern (H): high intake of fruits, vegetables, whole grains, <i>poultry</i>, and <i>low-fat dairy products</i>.</p> <p>2) Western pattern (W): high consumption of red and processed meats, <i>refined grains</i>, sweets and desserts, and <i>full fat dairy products</i>.</p>	Fracture: Self- report	Hip

Shin Korea 2015 ⁽¹⁰⁸⁾	3-days FD	NA/22	PCA	Not clear	4 (31.1)	<p>1) Rice and kimchi dietary pattern: high consumption of white rice, kimchi, garlic and onions, fish and shellfish, legumes, vegetables and mushrooms and with low consumption of bread and snacks.</p> <p>2) Eggs, meat and flour pattern (W): high loadings of oil and <i>seasoning, eggs, processed meats, meats</i> and <i>poultry, noodles and dumplings and bread and snacks</i>.</p> <p>3) Fruit, milk and whole grains pattern (H): rich in fruits, potatoes, whole grains, dairy foods, vegetables and mushrooms and nuts and <i>negative loadings for meat and poultry and noodles and dumplings</i>.</p> <p>4) Fast food and soda pattern: high intake of pizza and hamburgers, French fries, soda, coffee and sweet fruit juice.</p>	BMD: DXA	LS, total body, whole arm, whole leg, whole pelvis
De Jonge Netherland 2016 ⁽⁸⁸⁾	FFQ	170/28	PCA	Weighted sum score	3 (19.0)	<p>1) Health-conscious dietary pattern (H): high intake of fruits and vegetables, poultry, fish and <i>alcohol and low intake of sweets</i>.</p> <p>2) Traditional dietary pattern: high consumption of potatoes, meat and fat and low intake of soy products.</p> <p>3) Processed dietary pattern (W): rich in processed meats, eggs, animal fats and oils, refined grain, alcohol, potatoes, soups and sauces, mixed dishes like pizza, and <i>low intake of fruit and yoghurt</i>.</p>	BMD: DXA	FN
Denova-Gutierrez Mexico 2016 ⁽¹⁰⁹⁾	FFQ	116/22	PCA	Weighted sum score	3 (26.1)	<p>1) Prudent dietary pattern (H): rich in fresh vegetables, fruits, tomato, oils, legumes, fish, and whole grains and <i>negatively on refined grains, soft drinks, and other sweetened beverages</i>.</p>	BMD: DXA	Hip, LS, total body

De Jonge Netherland 2017 ⁽⁹²⁾	FFQ	170/28	RRR	Standardized sum score	2 (17.3)	2) Dairy and fish pattern: high intake of fish and other seafood, dairy foods, whole grains, and milk and negative loadings for corn tortillas and Mexican food, legumes, and refined grains.	BMD: DXA	Proximal femur
						3) Refined foods (W): high loadings of red meats, fats, sugar and sweets, soft drinks, eggs, refined grains, and alcoholic beverages and negative loadings for milk and fresh fruit.		
						1) Fruit, vegetables and dairy pattern (H): high intake of fruits, vegetables, milk, and yogurt , and low factor loadings for sweets and animal fats.	Fracture: Report of general practitioners	Hip, all osteoporotic fractures
						2) Sweets, animal fat and low meat pattern (W): rich in refined grains, sweets , animal fats , and porridge, and low factor loadings for soy, meats , and poultry intake.		
Melaku Australia 2017 ⁽⁸⁵⁾	FFQ	NA/39	PCA, RRR, PLS	The continues factor score (the linear functions of food groups)	PCA: 2 (16.7), PLS: 4 (21.1), RRR: 4 (14)	1) Prudent pattern (PCA, PLS, or RRR) (H): high intake of medium fat dairy, vegetables, fruits, legumes and fish , and low intake of soft drinks, processed meat and take away foods.	BMD: DXA	Total body
						2) Western pattern (PCA) (W): rich in processed meat, take away foods, white bread, red meats and soft drinks and low intake of dairy products and nuts. Western pattern (PLS, RRR): high consumption of animal foods (poultry, eggs, red and processed meat, fish and high fat dairy) and low intake of medium fat dairy, fruit and nuts.		

Warensjö Sweden 2017 ⁽¹¹⁰⁾	FFQ	67 in 1987 and 96 in 1997/31	PCA	Weighted sum score	4 (25.0)	<p>3) Dairy pattern (PLS, RRR): high intake of dairy products; however, a slight difference in food groups was identified using PLS and RRR.</p> <p>4) Vegetables and fruit pattern (PLS, RRR): low intake of dairy products and high consumption of vegetables</p>	Fracture: Individual linkage to the Swedish National Patient Registry (medical record)	Hip
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^a Method of dietary intake: FFQ (food frequency questionnaire), FD (food diary).

^b Food items (number of different foods assessed by dietary questionnaires), food groups (number of food items grouped for identifying dietary patterns), NA (not available).

^c Method of identifying dietary pattern: FA (factor analysis), PCA (principal component analysis), RRR (reduced-rank regression), PLS (partial least-squares), CA (cluster analysis).

^d % variance (the percentage of variance explained by all dietary patterns for each study); NA (not available).

*W: western pattern, H: healthy pattern. These healthy and western dietary patterns with various names were used in the best evidence synthesis and meta-analysis due to the similar common food items across studies. The matched major components of these dietary patterns are bolded and those of different items italicized.

^e Outcome measurement: BMD (bone mineral density), DXA (dual-energy x-ray absorptiometry), SOS (speed of sound), SPA (single-photon absorptiometer), DPA (dual-photon absorptiometer).

^f FN (femoral neck), LS (lumbar spine).

Dual-energy X-ray absorptiometry (**Table 3-2**) was the most common method used to measure BMD ^(81, 85, 88, 91, 92, 96, 99-104, 106, 108, 109), with LS ^(81, 91, 96, 99, 101, 103, 104, 106, 108, 109), FN ^(81, 88, 90, 91, 96, 102, 103, 106) and hip ^(99, 103, 104, 109) as the most commonly measured sites. Fractures were mainly assessed from medical records ^(82, 92, 97, 107, 110) and hip fracture ^(82, 84, 92, 107, 110) was the most common site measured.

3.3.2 Bone density outcomes

For each bone density outcome, the evidence for associations with both healthy and with western patterns was conflicting. The results of individual studies are summarised in **Table 3-3**.

Table 3-3: Findings of the association between dietary pattern scores and bone density

Author Country Year	Nature dietary pattern score	Nature of BMD	Variables for which analysis adjusted ^a	Findings ^b	
				Healthy dietary pattern*	Western dietary pattern*
Hip BMD (g/cm ²)					
Fairweather-Tait UK 2011 ⁽¹⁰³⁾	Continuous	Continuous	Age, BMI, smoking, physical activity, and age squared.	No association between a fruit-vegetable dietary pattern score and hip BMD (β= 0.027 (95% CI -0.015, 0.068) for one SD increase in score).	NA
McNaughton Australia 2011 ⁽¹⁰⁴⁾	Categorical (quintile)	Continuous	Age, height, physical activity, education, smoking, energy intake, sport, walking and calcium intake.	No association between the score of dietary pattern 3 and hip BMD (β= - 0.0006 (95% CI -0.0025, 0.0013) per quintile increase in score).	No association between the score of dietary pattern 1 and hip BMD (β= 0.0013 (95% CI -0.0008, 0.0033) per quintile increase in score).
Denova-Gutierrez Mexico 2016 ⁽¹⁰⁹⁾	Categorical (quintile)	Binary (low vs normal/high BMD)**	Age, sex, BMI, height, smoking, physical activity, energy intake and multivitamin use. For women with additional adjustment for age of menarche, estrogen use, parity and menopause.	Participants in the highest vs the lowest quintile of a prudent pattern score had lower odds of low hip BMD (OR= 0.71 (95% CI 0.44. 0.97)).	Participants in the highest (vs the lowest) quintile score of a refined food pattern had greater odds of low hip BMD (OR= 1.91 (95% CI 1.19, 3.04)).
LS BMD (g/cm ²)					
Fairweather-Tait UK 2011 ⁽¹⁰³⁾	Continuous	Continuous	Age, BMI, smoking, physical activity, and age squared.	No association between a fruit-vegetable dietary pattern score and LS BMD (β= 0.022 (95% CI -0.029, 0.073) for one SD increase in score).	NA

Hardcastle Scotland 2011 ⁽⁸¹⁾	Continuous	Continuous	Age, weight, height, smoking, physical activity, HRT, menopausal status and social deprivation.	A healthy diet score was not associated with LS BMD (results not reported).	One unit increase in a processed food diet score was negatively associated with LS BMD ($\beta = -0.008$ (95% CI -0.013, -0.003)).
McNaughton Australia 2011 ⁽¹⁰⁴⁾	Categorical (quintile)	Continuous	Age, height, physical activity, education, smoking, energy intake, sport, walking and calcium intake.	No association between the score of dietary pattern 3 and LS BMD ($\beta = -0.0004$ (95% CI -0.0022, 0.0015) per quintile increase in score).	No association between the score of dietary pattern 1 and LS BMD ($\beta = -0.0010$ (95% CI -0.0029, 0.0009) per quintile increase in score).
Karamati Iran 2012 ⁽⁹⁶⁾	Categorical (binary)	Binary (below vs above median of BMD)	Age, BMI, education, smoking, physical activity, energy intake, fragility fracture history, history of HRT, supplement intake, anti-resorptive drug use, parity and age at menarche.	No association between the score of dietary pattern 4 and LS BMD (OR= 0.72 (95% CI 0.35, 1.50)).	Women with higher scores of dietary pattern 1 were more likely to have LS BMD below the median (OR=2.29 (95% CI 1.05, 4.96)) compared to those with lower scores.
Whittle Ireland 2012 ⁽¹⁰⁶⁾	Categorical (quintile)	Continuous	Age, BMI, smoking, physical activity, energy intake and father's social class.	No association between a healthy dietary pattern score and LS BMD in men (mean Q5=1.251 vs Q1=1.220, $p = 0.184$) or women (mean Q5=1.219 vs Q1=1.193, $p = 0.295$)	No association between a refined dietary pattern score and LS BMD in men (mean Q5= 1.249 vs Q1=1.259, $p = 0.856$). Women did not have this dietary pattern.
Shin Korea 2013 ⁽⁹¹⁾	Categorical (quintile)	Binary (Incident osteoporosis)	Age, BMI, smoking, alcohol intake, moderate physical activity, energy intake, parathyroid hormone, serum 25-hydroxyvitamin D, supplement use and oral contraceptive use.	Participants in the highest (vs the lowest) quintile score of a dairy-fruit dietary pattern had a lower risk of osteoporosis defined by LS BMD (OR= 0.47 (95% CI 0.34, 0.65)).	No association between a meat-alcohol-sugar dietary pattern score and osteoporosis at LS (OR= 0.78 (95% CI 0.57, 1.07)).

Shin Korea 2015 ⁽¹⁰⁸⁾	Continuous	Continuous	Age, body size, smoking, alcohol consumption, physical activity, energy intake, family structure and twins and menopausal status (women only).	One unit increase in a fruit-milk-whole grains dietary pattern score was positively associated with LS BMD in men ($\beta = 0.016$ (95% CI 0.005, 0.027)), but not women ($\beta = 0.008$ (95% CI -0.001, 0.016)).	No association between one unit increase in an eggs-meat-flour dietary pattern score and LS BMD in either men ($\beta = 0.000$ (95% CI -0.011, 0.011)) or women ($\beta = -0.005$ (95% CI -0.015, 0.004)).
Denova-Gutierrez Mexico 2016 ⁽¹⁰⁹⁾	Categorical (quintile)	Binary (low vs normal/high BMD**	Age, sex, BMI, height, smoking, physical activity, energy intake and multivitamin use, For women with additional adjustment for age of menarche, estrogen use, parity and menopause.	Participants in the highest (vs the lowest) quintile score of a prudent pattern had lower odds of low LS BMD (OR=0.80 (95% CI 0.68, 0.94)).	Participants in the highest (vs the lowest) quintile of a refined food pattern had greater odds of low LS BMD (OR=1.61 (95% CI 1.06, 2.45)).
<i>FN BMD (g/cm²)</i> Tucker USA 2002 ⁽⁹⁰⁾	Categorical (6 clusters)	Continuous	Age, height, BMI, smoking, physical activity, energy intake, vitamin D and calcium supplement use, estrogen use (women only) and season.	Greatest FN BMD was found in a fruit-vegetable-cereal group in men but not for women compared with the other groups (meat-dairy-bread; meat-baked products; sweet-baked products; alcohol and candy groups). Effect size not reported.	No association between a meat-baked products group and FN BMD in women or men compared with the other groups (meat-dairy-bread; sweet-baked products; alcohol; candy; fruit-vegetable groups). Effect size not reported.
Langsetmo Canada 2010 ⁽¹⁰²⁾	Continuous	Continuous	BMI	For men 25-49 years old, each SD increase in a nutrient-dense pattern score was associated with a FN BMD increase of 0.012 (95% CI 0.002, 0.022). Results for the other groups (men 50+,	Each SD increase in energy-dense pattern score was associated with a FN BMD decrease of 0.009 (95% CI 0.002, 0.016) for men 50+ years old and 0.004 (95% CI 0.000, 0.008) for postmenopausal women. Results for

				premenopausal and postmenopausal women) not reported.	the other groups (men aged 25-49 years and premenopausal women) not reported.
Fairweather-Tait UK 2011 ⁽¹⁰³⁾	Continuous	Continuous	Age, BMI, smoking, physical activity, and age squared.	No association between a fruit-vegetable dietary pattern score and FN BMD ($\beta=0.017$ (95% CI -0.032, 0.065) per SD increase in score).	NA
Hardcastle Scotland 2011 ⁽⁸¹⁾	Continuous	Continuous	Age, weight, height, smoking, physical activity, HRT, menopausal status and social deprivation.	A healthy diet score was not associated with FN BMD (results not reported).	One unit increase in a processed food diet score was negatively associated with FN BMD ($\beta= -0.009$ (95% CI -0.013, -0.004)).
Karamati Iran 2012 ⁽⁹⁶⁾	Categorical (binary)	Binary (below vs above median of BMD)	Age, BMI, education, smoking, physical activity, energy intake, fragility fracture history, history of HRT, supplement intake, anti-resorptive drug use, parity and age at menarche.	No association between the score of dietary pattern 4 and FN BMD (OR= 0.90 (95% CI 0.44, 1.86)).	No association between the score of dietary pattern 1 and FN BMD (OR= 1.84 (95% CI 0.87, 3.88)).
Whittle Ireland 2012 ⁽¹⁰⁶⁾	Categorical (quintile)	Continuous	Age, BMI, smoking, physical activity, energy intake and father's social class.	No association between a healthy dietary pattern score and FN BMD in men (mean Q5=1.132 vs Q1=1.121, $p=0.537$) and women (mean Q5=1.026 vs Q1=1.045, $p=0.757$).	No association between a refined dietary pattern score and FN BMD in men (mean Q5=1.143 vs Q1=1.139, $p=0.970$). Women did not have the refined pattern.

Shin Korea 2013 ⁽⁹¹⁾	Categorical (quintile)	Binary (Incident osteoporosis)	Age, BMI, smoking, alcohol intake, moderate physical activity, energy intake, parathyroid hormone, serum 25-hydroxyvitamin D, supplement use and oral contraceptive use.	No association between a dairy-fruit dietary pattern and osteoporosis at FN (OR= 0.80 (95% CI 0.54, 1.19)).	No association between a meat-alcohol-sugar dietary pattern score and osteoporosis risk at FN (OR= 0.89 (95% CI 0.60, 1.31)).
De Jonge Netherland 2016 ⁽⁸⁸⁾	Continuous	Continuous	Age, sex, smoking, physical activity, energy intake, socioeconomic status, prevalent type 2 diabetes mellitus at baseline, use of lipid lowering drugs and adherence to other dietary patterns.	Positive association between a healthy conscious pattern score and FN BMD (β = 0.06 (95% CI 0.03, 0.08) per SD increase in score).	Negative association between a processed pattern score and FN BMD (β = -0.03 (95% CI -0.06, -0.01) per SD increase in score).
<i>Forearm BMD (g/cm²)</i>					
Tucker USA 2002 ⁽⁹⁰⁾	Categorical (6 clusters)	Continuous	Age, height, BMI, smoking, physical activity, energy intake, vitamin D and calcium supplement use, estrogen use (women only) and season.	Radius BMD was higher in a fruits-vegetable-cereal group compared with other groups (meat-dairy-bread; meat-baked products; sweet-baked products; alcohol and candy groups) in men and women (except alcohol group). The authors did not report the effect size.	No association between radius BMD and a meat-baked product group in men or women. The authors did not report the effect size.
Okubo Japan 2006 ⁽¹⁰⁰⁾	Categorical (quintile)	Continuous	Age, BMI, smoking, fracture history, HRT, calcium and multivitamin supplements, grasping power (as an indicator of physical activity), age at menarche and parity.	A healthy pattern score was positively associated with BMD at forearm (mean Q5=0.498 vs Q1=0.476, $p<0.05$).	No association was found between a western diet score and BMD at forearm (mean Q5= 0.482 vs Q1=0.501, $p= 0.08$).

Park Korea 2012 ⁽¹⁰⁵⁾	Categorical (quintile)	Binary (Incident osteoporosis)	Age, passive smoking, exercise and residual area.	The highest vs the lowest quintile of a traditional dietary pattern score was associated with higher risk of osteoporosis incidence at radius but this was not statistically significant (RR= 1.46 (95% CI 1.00, 2.13)).	The highest vs the lowest quintile of a western dietary pattern score was associated with higher incidence of osteoporosis at radius (RR= 1.46 (95% CI 1.02, 2.10)).
<i>TBBMD (g/cm²)</i>					
Shin Korea 2015 ⁽¹⁰⁸⁾	Continuous	Continuous	Age, body size, smoking, alcohol consumption, physical activity, energy intake, family structure and twins and menopausal status (women only).	One unit increase in the fruit-milk- whole grains dietary pattern score was positively associated with TBBMD in both men (β = 0.017 (95% CI 0.008, 0.027)) and women (β = 0.007 (95% CI 0.000, 0.015)).	No association between one unit increase in an eggs-meat-flour dietary pattern score and TBBMD in either men (β = 0.009 (95% CI - 0.001, 0.019)) or women (β = 0.004 (95% CI -0.005, 0.013)).
Denova- Gutierrez Mexico 2016 ⁽¹⁰⁹⁾	Categorical (quintile)	Binary (low vs normal/high BMD**	Age, sex, BMI, height, smoking, physical activity, energy intake and multivitamin use, For women with additional adjustment for age of menarche, estrogen use, parity and menopause.	No association between a prudent pattern score and TBBMD (OR= 0.83 (95% CI 0.63, 1.07)).	Participants in the highest (vs the lowest) quintile score of a refined food pattern had greater odds of low TBBMD (OR= 1.74 (95% CI 1.10, 2.76)).
Melaku Australia 2017 ⁽⁸⁵⁾	Categorical (tertile)	Continuous	Age, sex, BMI, marital status, income, smoking, alcohol intake, energy intake, health literacy, leisure-time and job- related physical activity levels, chronic conditions.	No association between a prudent dietary pattern score and TBBMD in the PCA (β = 4.25 (95% CI -13.74, 22.24)) and PLS (β =13.71 (95% CI -2.95, 30.37)) methods. For the RRR method, the highest vs the lowest tertile of a prudent dietary pattern score was positively associated TBBMD (β = 26.99	No association between TBBMD and one unit increase in the western dietary pattern score using the PCA (β = -8.45 (95% CI -29.46, 12.56), PLS (β = -0.72 (95% CI -16.88, 15.44) or RRR methods (β = -8.26 (95% CI -24.31, 7.78)).

(95% CI 10.94, 43.04) for one unit increase in score).					
TBBMC (g) McNaughton Australia 2011 ⁽¹⁰⁴⁾	Categorical (quintile)	Continuous	Age, height, physical activity, education, smoking, energy intake, sport, walking and calcium intake.	No association between the score of pattern 3 and TBBMC ($\beta = 4.72$ (95% CI -6.77, 16.22) per quintile increase in score).	One quintile increase in the dietary pattern 1 score was negatively associated with TBBMC ($\beta = -15.37$ (95% CI -27.41, -3.34)).
Melaku Australia 2017 ⁽⁸⁵⁾	Categorical (tertile)	Continuous	Age, sex, BMI, marital status, income, smoking, alcohol intake, energy intake, health literacy, leisure-time and job-related physical activity levels, chronic conditions.	No association between a prudent dietary pattern score and TBBMC in the PCA ($\beta = -6.30$ (95% CI -65.40, 52.81)) and PLS ($\beta = 28.95$ (95% CI -25.96, 83.85)) methods. For the RRR method, the highest vs the lowest tertile of a prudent dietary pattern score was positively associated TBBMC ($\beta = 69.65$ (95% CI 16.67, 122.63) for one unit increase in score).	No association between one unit increase in the western dietary pattern score and TBBMC in the PCA ($\beta = 7.04$ (95% CI -62.01, 76.10), PLS ($\beta = 15.38$ (95% CI -37.71, 68.48) and RRR methods ($\beta = 16.03$ (95% CI -36.68, 68.74)).

^a BMI (body mass index), HRT (hormone replacement therapy).

^b BMD (bone mineral density), TBBMD (total body bone mineral density), BMC (bone mineral content), TBBMC (total body bone mineral content), LS (lumbar spine), FN (femoral neck), Q (quintile), β (beta coefficient), OR (odds ratio), CI (confidence interval), NA (not applicable), PCA (principal component analysis), PLS (partial least-squares), RRR (reduced-rank regression).

* Healthy and western dietary patterns were renamed from the original studies.

** Low BMD (osteopenia/osteoporosis) was defined as ≤ -1.0 T-score.

Healthy dietary pattern score was positively associated with BMD at the hip⁽¹⁰⁹⁾, LS^(91, 109), FN^(88, 102), forearm^(90, 100) and TB⁽¹⁰⁸⁾ in some studies but was not associated with BMD at the hip^(103, 104), LS^(81, 96, 103, 104, 106), FN^(81, 91, 96, 103, 106), forearm⁽¹⁰⁵⁾, and TB⁽¹⁰⁹⁾ and TBBMC⁽¹⁰⁴⁾ in others. There were mixed results in two studies (LS⁽¹⁰⁸⁾ and FN⁽⁹⁰⁾) showing a positive association of healthy pattern score with BMD in men but no association in women. Another study⁽⁸⁵⁾ of TBBMD and TBBMC outcomes showed a positive association with a healthy dietary pattern in the reduced-rank regression method but no association was found in either the principal component or partial least-squares analyses. There were no negative associations between healthy pattern score and any bone density outcomes.

For the western dietary pattern, there was a negative association with BMD (hip⁽¹⁰⁹⁾, LS^(81, 96, 109), FN^(81, 88, 102), forearm⁽¹⁰⁵⁾ and TB⁽¹⁰⁹⁾) and TBBMC⁽¹⁰⁴⁾ in some studies but there was no association with BMD (hip⁽¹⁰⁴⁾, LS^(91, 104, 106, 108), FN^(90, 91, 96, 106), forearm^(90, 100) and TB^(85, 108)) and TBBMC⁽⁸⁵⁾ in others. There were no beneficial associations of western pattern scores with bone density outcomes.

3.3.3 Fractures

The findings of individual studies for fracture outcomes are given in **Table 3-4** and the characteristics of these studies ^(82, 84, 89, 92, 97, 107, 110) are given in **Table 3-1**. Over 70% of studies reporting fracture outcomes focused on older adults ^(82, 84, 89, 92, 97) and over half reported results for both sexes combined ^(82, 92, 97, 107). All studies had high-quality scores ($\geq 70\%$). There were insufficient data for pre-specified subgroup analyses by age, sex, and study quality score. The healthy patterns of these studies were mainly characterised by high consumption of fruits, vegetables and fish and the western patterns were mainly characterized by red meats, processed meats and sweets.

Of four studies included in the meta-analysis, two studies were of older adults ^(82, 84) and two included both younger and older adults ^(107, 110). Two studies ^(82, 107) reported results for both sexes combined, three studies ^(82, 84, 107) for each sex separately and one for women only ⁽¹¹⁰⁾. A meta-analysis of data from these studies reporting associations between the lowest vs the highest categories (tertiles, quartiles, or quintiles) of healthy dietary pattern score and hip fracture ^(82, 84, 107, 110) demonstrated a reduced risk of hip fracture with higher healthy dietary pattern scores (RR= 0.73 (95% CI 0.56, 0.96)) (**Figure 3-2**). Heterogeneity was high ($I^2=95\%$, $p<0.05$).

There were sufficient data only for best evidence synthesis to examine associations of western pattern with hip and total fracture, and healthy pattern with total fracture. There was conflicting evidence for detrimental associations between western dietary pattern and both hip and total fracture and a beneficial association between

healthy pattern and total fracture. Western pattern score was associated with higher hip fracture risk in three studies ^(82, 92, 110) but there were no associations in two other studies ^(84, 107). Similarly, one study ⁽⁹²⁾ reported a detrimental association between the western pattern and total fracture while there were no associations in two other studies ^(89, 97). The risk of total fracture was lower with higher healthy dietary pattern score in one study ⁽⁹²⁾ while another study reported mixed results with a reduced risk of low-trauma fractures in women but no association in men ⁽⁸⁹⁾. There were no detrimental associations between a healthy pattern score and fracture nor beneficial associations between the western pattern and fracture in any study.

Table 3-4: Findings of the association between dietary pattern scores and fractures

<i>Author Country Year</i>	<i>Nature of dietary pattern score</i>	<i>Nature of fractures</i>	<i>Variables for which analysis adjusted^a</i>	<i>Findings^b</i>	
				<i>Healthy dietary pattern*</i>	<i>Western dietary pattern*</i>
<i>Hip fractures</i>					
Zeng China 2013 ⁽⁸²⁾	Categorical (tertile)	Binary (case vs control)	BMI, income, education, smoking, alcohol drinking, tea drinking, physical activity, daily energy intake, family history of fractures, calcium supplement use, multivitamin use and house orientation.	The highest (vs the lowest) tertile of a healthy dietary pattern score was associated with lower risk of hip fracture (OR= 0.42 (95% CI 0.24, 0.73)).	The highest (vs the lowest) tertile for a high-fat dietary pattern score was associated with higher risk of hip fracture (OR= 2.25 (95% CI 1.38, 3.69)).
Dai Singapore 2014 ⁽¹⁰⁷⁾	Categorical (quintile)	Incident fractures	Age, sex, BMI, education, smoking, physical activity, energy intake, year of recruitment, dialect group, HRT use and menopausal status (women only), and history of diabetes mellitus and stroke.	Being in the highest quintile of vegetable-fruit-soy dietary pattern score was associated with lower risk of hip fracture (HR= 0.66 (95% CI 0.55, 0.78)) compared in the lowest quintile.	A meat-dim-sum dietary pattern score was not associated with hip fracture risk (HR= 1.15 (95% CI 0.95, 1.40)).
Fung USA 2015 ⁽⁸⁴⁾	Categorical (quintile)	Incident fractures	Age, BMI, smoking, physical activity, energy intake, thiazides, lasix, anti- inflammatory steroids, calcium and	No association between a prudent dietary pattern score and risk of hip fractures in either women (RR=1.14	No association between a western dietary pattern score and risk of hip fractures in either women (RR=1.05

			multivitamin supplements postmenopausal hormone use (women).	(95% CI 0.96, 1.36)) or men (RR= 0.86 (95% CI 0.64, 1.16)).	(95% CI 0.87, 1.26)) or men (RR= 1.03 (95% CI 0.73, 1.46)).
De Jonge Netherland 2017 ⁽⁹²⁾	Continuous (z-score)	Incident fractures	Age, sex, body weight, height, energy intake, vitamin D, season of vitamin D measurement and use of lipid-lowering drugs.	A fruit-vegetable-dairy dietary pattern score was associated with lower hazards of hip fractures (HR=0.81 (95% CI 0.70, 0.93))	A sweets-animal fat-low meat pattern score was associated with higher hazards of hip fractures (HR=1.14 (95% CI 1.05, 1.23)).
Warensjo Sweden 2017 ⁽¹¹⁰⁾	Categorical (quartile)	Incident fractures	Age, height, BMI, education, smoking, physical activity, energy intake, living alone, previous fracture, calcium, multi-vitamin use, postmenopausal status and Charlson's comorbidity index.	Participants in the highest compared to the lowest quartile of a healthy dietary pattern score had lower hip fracture rate (HR= 0.57 (95% CI 0.52, 0.62)).	Participants in the highest vs the lowest quartile of a western dietary pattern score had a higher risk of hip fracture (HR= 1.22 (95% CI 1.10, 1.34)).
Total fractures					
Monma Japan 2010 ⁽⁹⁷⁾	Categorical (tertile)	Incident fractures	Age, sex, BMI, energy intake and fall experience in previous 6 months.	Not applicable	No association between the highest vs the lowest tertile of the meat diet score and fall-related fractures (HR= 0.36 (95% CI 0.12, 1.06)).
Langsetmo Canada 2011 ⁽⁸⁹⁾	Continuous (z-score)	Incident fractures	BMI, smoking, bone mineral density, falls, prior fracture, comorbidities, milk consumption, and supplements (vitamin D and calcium). For women only, education, alcohol use, physical activity, diagnosis of osteoporosis, anti-resorptive use, and sedentary hours were adjusted for.	A nutrient-dense diet score was associated with a reduced risk of low-trauma fracture in women (HR= 0.86 (95% CI 0.76, 0.98)). No association in men (HR= 0.83 (95% CI 0.64, 1.08)).	No association between an energy-dense diet score and low-trauma fractures in either women (HR= 1.01 (95% CI 0.89, 1.15)) or men (HR= 1.06 (95% CI 0.82, 1.37))

De Jonge Netherland 2017 ⁽⁹²⁾	Continuous (z-score)	Incident fractures	Age, sex, body weight, height, energy intake, vitamin D, season of vitamin D measurement and use of lipid-lowering drugs.	A fruit-vegetable-dairy dietary pattern score was associated with lower hazards of osteoporotic fractures (HR= 0.92 (95% CI 0.89, 0.96)).	A sweets-animal fat-low meat pattern score was associated with higher hazards of osteoporotic fractures (HR= 1.12 (95% CI 1.07, 1.16)).
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^a BMI (body mass index), HRT (hormone replacement therapy).

^b OR (odds ratio), HR (hazard ratio), RR (relative risk), CI (confidence interval).

* Healthy and western dietary patterns were renamed from the original studies.

Study	Highest level		Lowest level		Weight	Risk ratio M-H, Random 95% CI
	Events	Total	Events	Total		
Zeng 2013	132	326	266	459	24.5%	0.70 [0.60, 0.81]
Dai 2014	240	12631	438	12631	24.4%	0.55 [0.47, 0.64]
Fung 2015	480	22569	433	22569	25.1%	1.11 [0.97, 1.26]
Warensjö 2017	1002	14184	1501	14184	26.0%	0.67 [0.62, 0.72]
Total (95% CI)		49710		49843	100.0%	0.73 [0.56, 0.96]
Total events	1854		2638			
Heterogeneity: $\tau^2 = 0.07$; $\chi^2 = 59.03$, $df = 3$ ($P < 0.00001$); $I^2 = 95\%$						
Test for overall effect: $Z = 2.26$ ($P = 0.02$)						

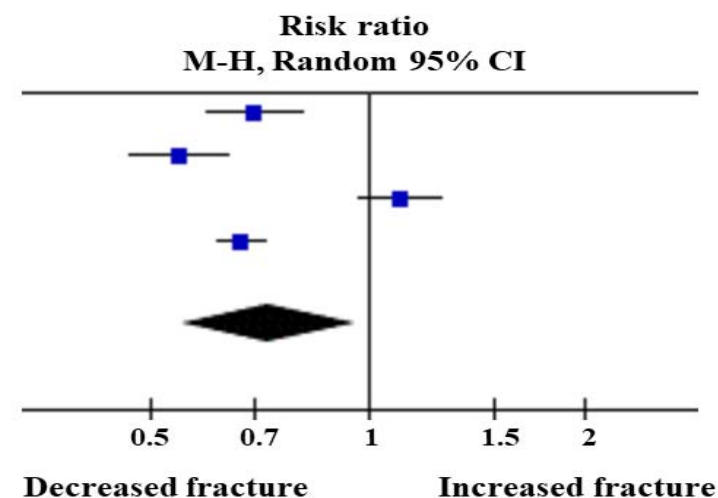


Figure 3-2: Forest plot of the association between healthy dietary pattern and hip fracture.

3.4 Discussion

This systematic review is the first to provide a robust site-specific synthesis of the evidence for the associations of empirically derived dietary patterns and site-specific bone density and fracture outcomes. Evidence was synthesised for two types of dietary patterns that most frequently shared content across studies, termed the healthy (fruits, vegetables, whole grain, nuts, legumes and fish) and western (meats, processed meats, sweets, fats/oils, soft drinks, and take-away foods). Best evidence synthesis was performed for most outcomes as meta-analysis was not possible. This assessed evidence supporting beneficial effects of a healthy diet on bone density and detrimental effects of a western diet on both bone density and fracture outcomes was conflicting. However, studies consistently failed to demonstrate any detrimental effect of a healthy pattern, nor any beneficial effects of a western pattern on bone outcomes. Our meta-analysis based on a small number of large studies demonstrated a beneficial association between healthy dietary patterns and hip fracture in adults. These results suggest that having a healthy diet and avoiding a western dietary pattern may be beneficial for bone health overall, and more importantly, having a healthy dietary pattern may help reduce the risk of hip fracture. However, given the heterogeneity and limited data for hip fracture, and the inconsistency of evidence for other outcomes, RCT of interventions to improve dietary patterns are needed to definitively assess the effects of such improvements on bone health. Nonetheless, the current observational evidence suggests that it is reasonable to incorporate dietary advice to consume a diet, high in fruits, vegetables, nuts, fish, whole grain and legumes and low in red meats, processed meats, fats, sweets, take away foods and soft drinks into

recommendations for promoting bone health, particularly given the known wide-ranging health benefits of improving diet quality for the prevention and management of a range of chronic diseases.

Our study makes an important contribution to understanding the potential benefits of improving diet quality for bone health as it is the first systematic review that examines outcomes separately for different fracture and bone density sites. The latter is a particularly important consideration, as fracture risk factors ⁽¹²⁵⁾ differ for different sites, as do the costs and sequelae of fractures ⁽¹²⁶⁾. Nutritional influences could come into play differently at different sites, for example through effects on BMI, weight, muscles strength and diabetes ^(125, 131) and could modulate these risk factors ^(54, 62, 132). Combining fracture sites together could dilute associations of dietary patterns with fractures at specific sites ⁽¹²⁵⁾. Site-specific data are necessary to assess the potential clinical, public health and health economic benefits of any potential intervention and are an important component of any economic modelling ⁽¹³³⁾.

A key finding of the current study comes from the meta-analysis, suggesting that a healthy dietary pattern was associated with reduced risk of hip fracture, by as much as 36%. This is a very substantial effect of both clinical and public health importance. It is comparable with the effect size observed in a recent RCT determining the effect of zoledronate on reducing risk of fracture among 2000 older New Zealand women with osteopenia (aged ≥ 65 years) ⁽¹³⁴⁾. Participants who received 5mg zoledronate at 18-month intervals had lower risk of non-vertebral fragility fracture (hazard ratio (HR)= 0.66 (95% CI 0.51, 0.85)) and hip fracture

(HR= 0.66 (95% CI 0.27, 1.16)) compared to placebo. It is also comparable to the effects of other bisphosphonates for hip fracture prevention ⁽¹³⁵⁾.

The lack of site-specific analyses for either bone density or fracture is a limitation of a recent systematic review ⁽¹¹⁵⁾. This pooled fracture data from three cohort studies without separately analysing different sites or specifying which fracture sites were included in the analysed data. Using this approach, a lower risk of fracture (site(s) unspecified) in the highest compared to the lowest categories of a healthy dietary pattern (odds ratio (OR)= 0.81 (95% CI 0.69, 0.95)) ⁽¹¹⁵⁾ was observed in men, but no such effect in women. This contrasts with our data for hip fracture which suggests that a healthy diet may be important in both sexes for the prevention of this costly and damaging major osteoporotic fracture. The same systematic review pooled dichotomous bone density outcomes of BMD and BMC together, regardless of site. Bone density was dichotomized as low or not low without specifying the definitions used to define this in each analysis. In three separate analyses pooling data from (1) two cross-sectional studies in adults aged 20-50 years and (2) two cohort studies and (3) three cross-sectional studies in adults aged ≥ 50 years there were reductions in the odds of having low BMD/BMC in the highest compared to the lowest category of a healthy dietary pattern (OR ranging from 0.52 to 0.61). From the same pooled studies, being in the highest category of a western pattern was only deleterious in cross-sectional studies in adults ≥ 50 years (OR 1.93), not in other analyses. While these data broadly support the potential benefits and detriments of healthy and western diet patterns respectively, the results from this analysis approach are difficult to interpret clinically.

Our results suggest that promoting adherence to a healthy dietary pattern and avoiding a western dietary pattern could be a prominent and major part of advice for promoting bone health in adults. Importantly, advice to consume a diet, high in fruits, vegetables, nuts, fish, whole grain and legumes and low in red meats, processed meats, fats, sweets, take away foods and soft drinks are already embedded in dietary recommendations around the world, including the US ⁽¹³⁶⁾, UK ⁽¹³⁷⁾ and Australia ⁽¹³⁸⁾. This is in recognition of the fact that the impact of poor diet quality on health globally is immense. As just one example, the Global Burden of Disease study determined that in 2016, suboptimal diet was the second-leading risk factor for deaths and disability-adjusted life year (DALY) globally, accounting for 18.8% (16.0–21.7) of all deaths and 9.6% (8.2–11.1) of all DALY ⁽¹³⁹⁾. We recognize that the evidence in our review comes solely from observational studies, and thus must be interpreted with caution. RCT of behavioural interventions of sufficient scale to measure fracture outcomes will be large and logistically challenging, as seen in one of the few such trials for cardiovascular outcomes ⁽¹⁴⁰⁾ so this is likely to remain an evidence gap for some time. Thus, given the wide-ranging potential health benefits of the advice we propose and our evidence suggesting substantial potential benefits of a healthy dietary pattern for bone health, and a lack of evidence for detrimental impacts, it seems reasonable and warranted to implement this health promotion advice now.

Calcium and vitamin D play key roles in bone metabolism and feature prominently in advice for improving bone health. However, the effects of vitamin D and calcium supplements on fracture appear minimal - a recent meta-analysis of 33 RCT in 51,145 adults aged 50 years and over demonstrated no effects of supplementation

by vitamin D, calcium, or vitamin D and calcium in combination on fracture ⁽⁴⁶⁾. Similarly, while calcium-rich foods such as dairy products also include other nutrients that are potentially important for bone health such as protein, and absorption of calcium from foods may differ from absorption from supplements. There is little consistent evidence for an association between dietary intake of calcium or dairy intake and risk of fracture ⁽⁴⁹⁾. Effects of dietary calcium and calcium supplements on BMD also appear modest ⁽¹⁴¹⁾. Dairy foods were not a consistent feature of the patterns comprising the healthy or western groups of patterns in our analysis. Thus, while our findings do not negate the need for awareness of the role of adequate calcium intake and vitamin D status for bone health, given the potential for much larger effects to come from addressing diet in a more wholistic way, consideration could be given to changing the relative emphasis of providing single nutrient advice around calcium and vitamin D compared to advising improving diet quality more generally ^(75, 136-138).

Strengths and limitations

The major strength of this study is the use of meta-analysis where it was possible and a structured best evidence synthesis approach otherwise, which together result in assembling the strongest evidence from the available data.

This systematic review also has limitations:

A major limitation comes from the nature of the available data, which for the most part was cross-sectional, thus prone to bias and not able to be used to determine causation. This is the case even though all studies were considered high quality for

their design, exceeding the pre-specified quality score of 60%. There were some characteristics leading to their lower quality scores than the other studies, for example, not prospective cohort/RCT study design, lack of duration of the study reported, insufficient description of characteristics of participants at baseline and so on. Moreover, there was unclear some information relating to the percentage of withdrawals $\leq 20\%$, information about completers vs withdrawals, the response rate of participants and known characteristics of responders and non-responders comparable, or description of an appropriate method for dealing with missing data. In general, most information was related to poor reporting of details of participants and participant flow, which could be addressed in future studies. The adherence to STROBE guidelines could enhance this. To more confidently attribute causation and accurately determine the true effect of improving diet on bone outcomes, better evidence from longitudinal studies and RCT would be desirable. RCT of behavioural interventions of sufficient scale to measure fracture outcomes will be large and logistically challenging so this is likely to remain an evidence gap for some time.

The lack of comparability in analytical approaches and measurement of outcomes and exposures limited our meta-analysis to the single outcome of hip fracture, and to two major categories of dietary patterns. However, while hip fracture data came from few studies, these studies were mostly very large (there were over 25000 participants in the analyses of three out of four studies). The small number of studies meant that we were unable to meaningfully examine sources of heterogeneity in the meta-analysis, so despite the large numbers of participants, the results should still be treated with some caution.

The evidence for all the outcomes assessed by best evidence synthesis was also conflicting. This is not surprising, given the diversity in study populations and methodologies used and the variation in the exact food items making up the healthy and western type patterns in each study. For example, most but not all studies used FFQs to measure dietary intake. FFQs are useful because they measure usual intake over the previous 12 months and are easy to use in large epidemiological studies compared to methods like weighed food records or 24-hour recall ⁽¹⁴²⁾. In determining dietary patterns and scores, different methodological decisions were made, such as in the number of factors extracted (median of 4, range 2 to 10) and the methods used for calculating factor scores, reflecting the lack of a gold standard approach ⁽¹⁴³⁾. Nonetheless, it is reassuring that there is consistency with regards to the lack of any evidence for possible detrimental bone outcomes from recommending either promoting a healthy diet pattern or advising avoidance of a western pattern.

We could not include in our syntheses or meta-analysis dietary patterns which appeared in only small numbers of studies, such as patterns traditional in specific cultural contexts e.g. Japanese ^(97, 100) and English traditional ⁽¹⁰³⁾ or with major emphasis on culturally specific food components (e.g. white rice, kimchi and seaweed pattern in a Korean population ⁽⁹¹⁾). We therefore cannot rule out that other patterns could affect bone health. This review may be subject to language bias due to the inclusion of only articles in English.

Lastly, selective reporting and publication bias are potential issues in any meta-analysis of observational studies as, unlike for RCT, there is no repository of study protocols or expectation of pre-publication of protocols. We made every effort to minimise this by identifying any study that reported fracture outcomes regardless of whether or not they published usable results and by approaching study authors for unpublished data. Because of the small number of studies, it is difficult to meaningfully assess potential publication bias. However, it is reassuring that the results of the only study with hip fracture outcomes which was not included in the meta-analysis is consistent with the meta-analysis findings namely, a reduction in the hazard ratio for hip fracture with increasing fruit-vegetable-dairy dietary pattern score ⁽⁹²⁾.

3.5 Conclusion

In conclusion, the best evidence synthesis supports a beneficial effect of a healthy diet on bone density and detrimental effects of a western diet on both bone density and fracture outcomes as conflicting, but no studies to date demonstrated any detrimental effect of a healthy pattern, nor any beneficial effects of a western pattern on bone outcomes. The meta-analysis was based on a small number of observational studies but demonstrated a beneficial association between healthy dietary patterns and hip fracture in adults. Thus, the current observational evidence suggests that it is reasonable to incorporate existing population health recommendations for a healthy diet into recommendations for promoting bone health, especially given the known wide-ranging health benefits of improving diet quality for the prevention and management of a range of chronic diseases.

3.6 Postscript

Two other systematic reviews ^(115, 116) have been recently published on this topic. The paper of Denova-Gutiérrez et al ⁽¹¹⁵⁾ is cited in our paper as it was published after the analyses were completed but during the drafting of the thesis chapter at the end of 2018. The second paper of Fabiani et al ⁽¹¹⁶⁾ was published in 2019 after the completion of this thesis chapter. The characteristics of these two systematic reviews and ours are described and compared in **Table 3-5**.

Table 3-5: Characteristics of three systematic reviews of the associations of dietary patterns and bone outcomes

<i>Contents</i>	<i>Denova-Gutiérrez et al paper ⁽¹¹⁵⁾</i>	<i>Our systematic review</i>	<i>Fabiani et al paper ⁽¹¹⁶⁾</i>
1/ PROSPERO Registration	No	Yes (CRD42017071676)	No
- Date of literature search	- Searched articles up to May 2018	- 12 May 2017	- Searched articles up to March 2018
- Date of publication/completion	- 5 December 2018	- 28 May 2019	- 17 January 2019
2/ Inclusion criteria			
- Age of participants	- Not limited (children to older adults)	- Adults aged ≥ 18 years	- Not limited (children to older adults)
- Study design	- Observational studies	- Quantitative studies of any design	- Observational studies
- Methods used to identify dietary patterns	- Any empirical approach ^a	- Any empirical approach ^a	- Any empirical approach ^a
- Methods used to measure bone outcomes ^b	- Not specified.	- Bone density (DXA, SPA, DPA, PQCT, BUA and SOS. Radiological vertebral fracture (CT, X-ray, DXA-based vertebral morphometry or MRI); other fractures (self-report or radiological confirmation).	- Not specified.
3/ Study quality assessment	The GRADEpro ⁽¹⁴⁴⁾ : high to very low	A specific tool for musculoskeletal topics ⁽¹²⁸⁻¹³⁰⁾ : scoring as percentage (over 60% as high quality)	The New-castle-Ottawa scale ⁽¹⁴⁵⁾ : 9 full score (over 7 as high quality)
4/ Method of data synthesis			
a/ Meta-analysis			
- Exposure comparison: The highest vs the lowest categories (dichotomy, tertile, quartile, quintile) of dietary patterns	- Yes (prudent/healthy, western/unhealthy)	- Yes (healthy)	- Yes (healthy, meat/western, milk/dairy)

Outcomes			
- Low BMD ^c	- Site not specified	- Not applicable	- Femur, LS, TBBMD
- Fracture	- Site not specified	- Hip	- Hip, any site
b/ Systematic review			
- Method of evidence synthesis	- Descriptive	- The best evidence synthesis ⁽¹²⁸⁻¹³⁰⁾	- Not done
Outcomes			
- BMD ^c	- Site not specified	- FN, hip, TBBMD, LS, forearm, TBBMC	- Not applicable
- Fracture	- Site not specified	- Total fracture, hip	- Not applicable
5/ Results			
a/ Participants (age)	175,060 participants (≥6 years)	279,333 participants (≥18 years)	276,624 participants (≥10 years)
b/ Study design	31 studies in systematic review (18 cohort, 1 case-control, 12 cross-sectional); 12 studies in meta-analysis	23 studies in systematic review (10 cohort, 1 case-control, 12 cross-sectional); 4 studies in meta-analysis	20 studies in meta-analysis (9 cohort, 1 case-control, 10 cross-sectional)
c/ Meta-analysis			
- Low bone density ^c	(-) for the highest vs the lowest category of a healthy/prudent pattern (OR 0.49-0.61, p<0.02) for both sexes-all ages. (+) for the highest vs the lowest category of a western/unhealthy pattern (OR 1.53-1.93, p<0.01) for both sexes-older adults.	- Not applicable	(-) for the highest vs the lowest category of a healthy pattern (OR=0.70, 95% CI 0.51, 0.96), and (+) for the highest vs the lowest category of a meat/western pattern (OR=1.50, 95% CI 1.01, 2.22) at TBBMD for both sexes-all ages. (-) for the highest vs the lowest level of a milk/dairy pattern (OR=0.50, 95% CI 0.38, 0.66) at LS for both sexes-all ages.

- Fracture risk ^c	(-) for the highest vs the lowest category of a healthy/prudent pattern (OR=0.81, 95% CI 0.69, 0.95) for older men. (+) for the highest vs the lowest category of a western/unhealthy pattern (OR=1.10, 95% CI 1.02, 1.19) for older men.	(-) for the highest vs the lowest level of a healthy pattern (RR=0.73, 95% CI 0.56, 0.96) at hip fracture for both sexes-adults.	(-) for the highest vs the lowest level of a healthy pattern (OR=0.71, 95% CI 0.55, 0.91), and (+) for the highest vs the lowest level of a meat/western pattern (OR=1.15, 95% CI 1.05, 1.25) at hip fracture for both sexes-all ages.
d/ Systematic review			
- Bone density	- Conflicting evidence	- Conflicting evidence	- Not applicable
- Fracture risk	- Conflicting evidence	- Conflicting evidence	- Not applicable

^a An empirical approach: e.g. factor analysis, cluster analysis and reduced rank regression.

^b BMD: bone mineral density; BMC: bone mineral content; DXA: dual-energy x-ray absorptiometry; SPA: single photon absorptiometry; DPA: dual photon absorptiometry; PQCT: peripheral quantitative computerised tomography; BUA: broadband ultrasound attenuation; SOS: speed of sound; CT: computed tomography; MRI: magnetic resonance imaging.

^c LS: lumbar spine; FN: femoral neck; TBBMD: total body bone mineral density; TBBMC: total body bone mineral content; OR: odds ratio; RR: risk ratio; CI: confidence interval; (+): positive association; (-): negative association.

Low BMD defined as osteopenia ($-2.5 < T \text{ score} < -1$ or $-2 < Z \text{ score} < -1$) and osteoporosis ($T \text{ score} \leq -2.5$ or $Z \text{ score} \leq -2$) in Fabiani et al paper, but not in Denova et al paper.

The three reviews share some characteristics. All included a very large number of participants and the risk of bias was assessed using the validated tools. They all assessed the associations of dietary patterns that were determined using an empirical approach with bone density and fracture outcomes, and all were limited by being mainly based on cross-sectional studies, thus limiting ability to attribute causation. Healthy and western diets were the major dietary patterns in meta-analyses and none of the reviews examined other dietary patterns relating to culture (e.g. the traditional English pattern or Japanese pattern) as data were limited, so the effects of cultural food choices on bone health remain unclear. However, there are also some important differences between the reviews.

It is clinically important to examine the effect of dietary patterns on different sites of fracture/bone density because fracture risk factors differ for different sites ⁽¹²⁵⁾ as do the fracture's cost and its pathological condition ⁽¹²⁶⁾. Our paper and Fabiani et al paper ⁽¹¹⁶⁾ assessed specific sites of bone outcomes but the other review pooled data from different sites ⁽¹¹⁵⁾, reducing the clinical interpretability of its results.

The different reviews made other different decisions with regards to pooling data. Unlike in the other two reviews, we chose not to pool BMD outcomes and total fracture as we considered that the included studies reported insufficient and incomparable data for specific sites of these outcomes. We instead selected the best evidence synthesis at each clinically important site to optimise the available evidence. While Denova ⁽¹¹⁵⁾ and Fabiani ⁽¹¹⁶⁾ pooled BMD outcomes, the data did not allow pooling of BMD as a continuous variable, but as a category termed 'low' the definition of which varied across the different studies in the reviews. Moreover,

Fabiani's primary analysis pooled BMD across sites ⁽¹¹⁶⁾, and when they stratified their analyses by sites of femur, LS, and whole body. The results were inconsistent with a statistically significant effect only being seen at the whole body. These results are complicated to interpret for clinical guidelines.

Nonetheless, despite the different approaches to data synthesis the conclusions coming from the three reviews are similar, and their results similarly support the contention that promoting adherence to a healthy dietary pattern and avoiding a western dietary pattern could be greater emphasised in dietary guidelines and recommendations to improve bone outcomes. However, there is a lack of longitudinal studies investigating associations between the continuous scores of these dietary patterns and bone outcomes in these literature reviews, a gap which is addressed in Chapter 6 of this thesis.

This chapter was published in the Australian Journal of General Practice. Nguyen, H., Wu, F., Makin, J., Oddy, W., Wills, K., Jones, G., & Winzenberg, T. (2021). Associations of dietary patterns with bone density and fractures in adults. Aust J Gen Pract, 50, 394-401 (see **Appendix 3-3**).

**Chapter 4: Methodology of Tasmanian Older Adult
Cohort (TASOAC) study**

4.1 Introduction

The methods for this thesis are for the most part fully described in the appropriate chapters. Chapter 3, Section 3.2 outlines the methods used in the systematic review. The sections below provide greater detail about the Tasmanian Older Adult Cohort (TASOAC) study and the key variables measured.

4.2 Participants and sample size

The TASOAC Study was established to investigate the risk factors associated with the development and progression of osteoarthritis and osteoporosis in older adults (146-148). At baseline (from April 2002 to September 2004), 1098 participants aged 50 years and over were randomly recruited from the electoral roll in Southern Tasmania. Participants were excluded if they were or had been institutionalized or had any contraindication to magnetic resonance imaging. They were followed up over a period of more than ten years. The number of participants in Study 1 (Chapter 5) and Study 2 (Chapter 6) differ as they used different exposures and outcomes. Study 1 includes three phases of dietary pattern scores as the main outcomes and baseline predictors (age, sex, education, employment, smoking, and physical activity). Study 2 has bone mineral density, falls risk, and incident fracture over ten years as main outcomes; and baseline dietary pattern scores, age, sex, and body mass index as exposures. The TASOAC study was approved by the Tasmanian Health and Medical Human Research Ethics Committee, and all participants signed the consent form.

4.3 Outcome measurements

All outcomes were measured at baseline (2002-2004) and followed up for an average time of 2.6, 5, and 10.7 years.

4.3.1 Fracture

A self-reported questionnaire was used to identify participants' fractures. While this may be subject to recall bias, fractures are major life events and recall inaccuracy is unlikely ⁽¹⁴⁹⁾. Furthermore, this approach has been validated with radiologic reports and medical records in older adults ⁽¹⁵⁰⁾. Radiological confirmation was not available in our data. Participants were asked to list any fractures they had by location (e.g. left thumb, right wrist, or leg). Fracture data was then recorded in two categories including binary variable (yes/no). Participants having at least one new fracture since the baseline were coded as "1" and those without any incident fracture as "0" ⁽¹⁴⁹⁾.

4.3.2 Bone mineral density (BMD) (g/cm²)

Dual-energy X-ray absorptiometry (DXA) was used to measure BMD (g/cm²) at the whole body, total hip and lumbar spine (LS), using a Hologic Delphi densitometer (Hologic, Waltham, MA, USA) ⁽¹⁵¹⁾. The Hologic densitometer was calibrated automatically using a spine phantom with a longitudinal coefficient variation of 0.39 % ^(152, 153). Participants were excluded from the DXA scan if their weight was over 130 kg ⁽¹⁵¹⁾.

4.3.3 Falls risk z-score

The validated Physiological Profile Assessment (Prince of Wales Medical Research Institute, Sydney, Australia) was used to assess the falls risk in older adults as described in previous studies ^(149, 154, 155). Falls risk was calculated from results in five domains, that is, edge contrast sensitivity (vision), reaction time of hand, proprioception, knee extension strength, and sway/balance test. The total falls risk scores were then standardized into a z-score, with a higher z-score indicating a higher risk of falls in older adults ^(154, 155). Detailed information about the assessment of these measurements is described below ⁽¹⁵⁶⁾:

- Edge contrast sensitivity (decibel units: dB, where $1 \text{ dB} = -10\log_{10} \text{ contrast}$): This measurement was assessed using the Melbourne Edge test from twenty circular patches (**Figure 4-1**). Participants were asked to look at an unprotected photo and the circles one at a time on the big chart. Within plenty of time, they described which way that the line went through the circle to select the correct match for each one from the small card. The measure of contrast sensitivity was measured as decibel units. A score of 1 to 15 is considered as poor contrast vision compared with fair (16-19), good (20-23) and excellent vision (24).

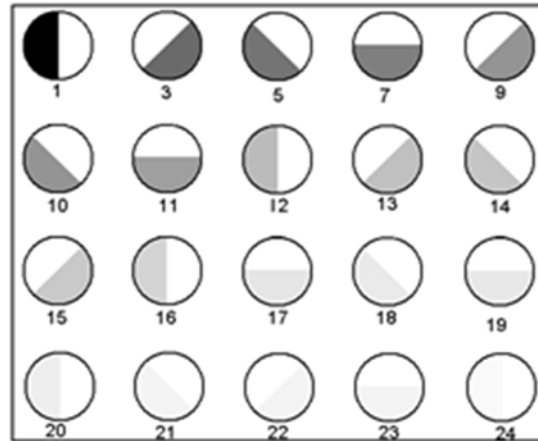


Figure 4-1: Edge contrast sensitivity test

- Reaction time of hand (milliseconds): Light as the stimulus and the hand as the response were used to measure participants' reaction time (**Figure 4-2**). When a light came on, participants pressed the button as fast as they could (20 times in total, with the first 10 times for practice, followed by 10 times of experimental measurement). The reaction time was measured in milliseconds, with poor reaction recorded as 300+, fair (250-300), good (200-250), and excellent (<200).

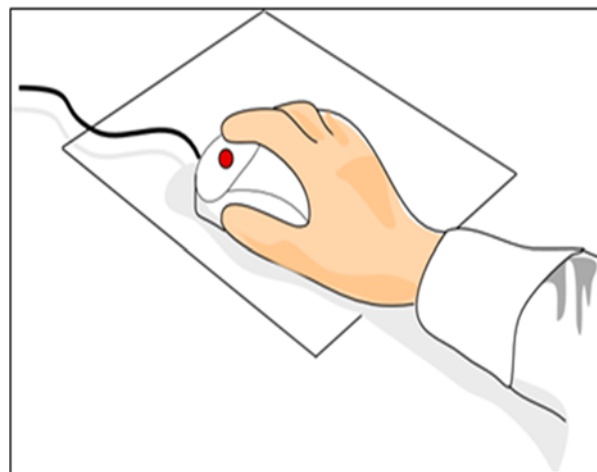


Figure 4-2: Reaction time-hand test

- Proprioception (degrees): The proprioception test was used to measure how well participants could judge the position and movement of their body segments (**Figure 4-3**). In this test, participants were asked to close their eyes and put the big toe of each foot in the same position but on opposite sides of a vertical acrylic sheet. The differences between matching toes were assessed as degrees with three levels including poor ($>4^{\circ}$), fair ($1-3^{\circ}$), and good ($<1^{\circ}$).

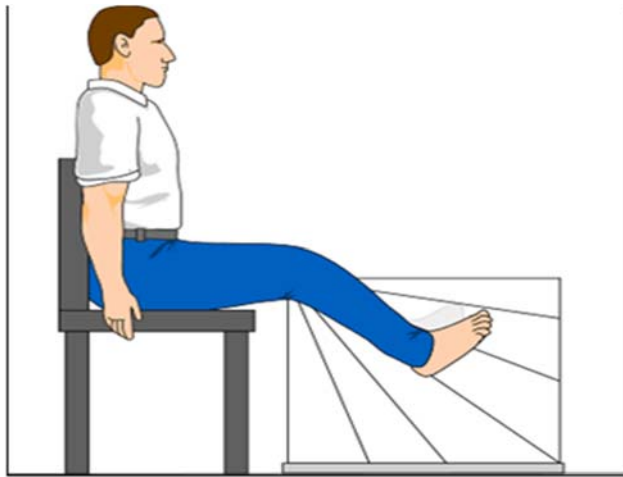


Figure 4-3: A proprioception test

- Knee extension strength (quadriceps): This test was used to measure the strength of the knee muscle group in the dominant leg, using a dynamometer. Participants were asked to sit up straight on a tall chair (**Figure 4-4**) with their hip and knees at 90 degrees and a strap tied below the end of the calf muscle. Participants held on to the chair for support and attempted to pull against the strap as strong as they could. Three trials were

conducted, and the greatest force measurement was recorded. There were four levels of knee extension strength: poor (<15), fair (15-20), good (20-30), and excellent (>30).

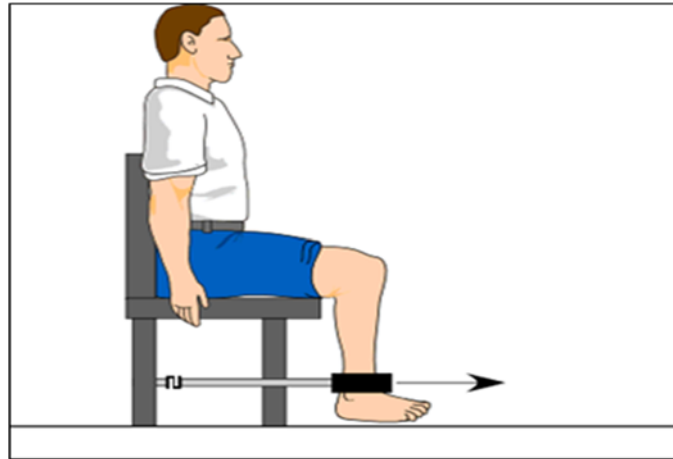


Figure 4-4: Knee extension strength test

- Body sway (meter): The sway or balance test was used to measure the displacement of the body at waist level (**Figure 4-5**). A sway-meter device consisting of a 40cm long rod was attached to participants by a firm belt. The rod extended posteriorly, with a vertically mounted pen at its end. The pen was used to record the sway of participants on a sheet of millimetre graph paper fastened to the top of an adjustable height table. The test was performed with the eyes open on a piece of foam rubber (15cm thick) and participants attempted to stand as still as they could for 30 seconds. The total sway path was measured as the length of the sway path in millimetres (mm), with poor sway (>1300), fair (800-1300), good (400-800), and excellent (<400). The total sway was converted into meters (m) for further analysis.

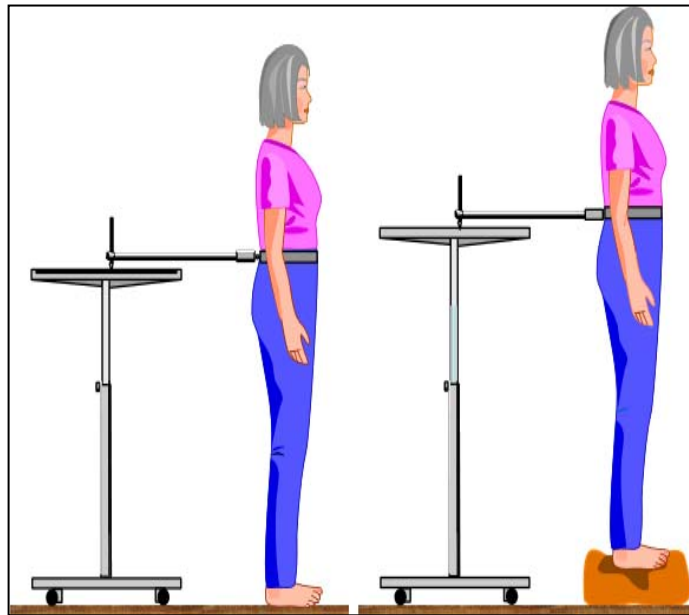


Figure 4-5: A body sway test

4.4 Food frequency questionnaire

Dietary intakes, including beverages, were measured at baseline (2002-2004) and followed up for an average time of 2.6 and 5 years, using the Cancer Council Victoria food frequency questionnaire (CCVFFQ) which covers 101 food items across 33 food groups ⁽¹⁵⁷⁾ (**Appendices 4-1 – 4-2**). The CCVFFQ assessed the eating habits of participants over a 12-month period. Nutrient intake was calculated using NUTTAB95 food composition data. This instrument is divided into four sections as described in Section 6.2 of Chapter 6.

The CCVFFQ has been validated against seven-day weighed food records. There were close relationships between CCVFFQ and this method in terms of energy-adjusted, log-transformed, and daily adjusted nutrient intake, with the correlation coefficients ranging from 0.28 (vitamin A) to 0.78 (carbohydrate) ⁽¹⁵⁸⁾. However, there was a poorer association of these methods in retinol intake.

For the validity of the food group intakes of the FFQ ⁽¹⁵⁹⁾, the range of correlation coefficients was from 0.03 (liquid oil) to 0.77 (simple sugars) for men, and 0.12 (snacks) to 0.79 (simple sugars) for women. Snacks and desserts were marked as the highest percentage of agreement in men (60.6%). Meanwhile, tea and coffee obtained the highest rate of agreement in women (62.9%).

Scores were calculated adjusting for energy intake and these adjusted scores were used in the analysis. The FFQ consisting of a structured food list and a frequency response section that measures participant's dietary intake over 12 months. It is used to conduct repeated measures due to low participant burden, therefore, it is usually used to capture long-term variation in diets ⁽¹⁶⁰⁾. It indicates that the FFQ usually has lower within-person variation than other dietary assessment methods (e.g. 24h-recalls or dietary records) because of assessing long-term dietary intake which is the exposure of etiological interest for most diseases ⁽¹⁶⁰⁾. As the critical analysis was of dietary pattern scores as an exposure to examine effects on bone outcomes (Chapter 6), we did not analyse the within-person variation due to its limitations.

4.5 Other factors

The other factors relating to socio-demographic (age, sex, education, employment status and socio-economic indexes for areas), anthropometrics (height, weight and body mass index) and lifestyle factors (smoking and physical activity), were described in detail in Section 5.2 of Chapter 5.

4.6 Medical history and medication

A self-reported questionnaire was used to record participants' medical history and medication. For medical history, participants were asked to answer a question, "Have you ever been diagnosed by a doctor as having any of the following diseases?" Disease options of diabetes, heart attack, hypertension, thrombosis, asthma, bronchitis or emphysema, osteoporosis, hyperthyroidism, hypothyroidism, and rheumatoid arthritis were given. They were coded as binary variables (yes/no).

Respondents also listed any prescription and over the counter medication they had taken in the last two weeks, including dosage and frequency. The medications were then classified into major groups for further analysis such as hormone replacement therapy, corticosteroid, bisphosphonates or denosumab, vitamin D, calcium, antihypertensive drugs, psychotropic drugs, and opioids. These were also coded as binary variables (yes/no).

4.7 Statistical analysis

The statistical methods used in each paper are provided in the relevant chapters. The methods for identifying dietary patterns and calculating diet scores are described in Section 5.2 of Chapter 5. The associations between dietary pattern scores with socio-demographic and lifestyle factors are also given at Section 5.2 of Chapter 5. The associations between dietary pattern scores and osteoporosis-related outcomes are illustrated in Section 6.2 of Chapter 6.

Chapter 5: A longitudinal cohort study of dietary patterns and their associations with socio-demographic and lifestyle factors in older adults

The previous Chapter 4 describes the methodology of the Tasmanian Older Adult Cohort (TASOAC) Study used in this Chapter and Chapter 6. This Chapter addresses research questions 2-4 of this thesis, reporting the identification of dietary patterns and investigating the association between dietary patterns with socio-demographic factors (age, sex, employment, education, and area-level socioeconomic status) and lifestyle factors (smoking and physical activity) in Tasmanian older adults.

The results from the initial analyses addressing these research questions published in the European Journal of Clinical Nutrition 2018 (<https://doi.org/10.1038/s41430-018-0264-1>). However, after publication, I discovered a data analysis error in generating food groups used in the exploratory factor analysis identifying the dietary patterns for this paper. This led to the original publication being retracted (see **Appendix 5-1**)⁽¹⁶¹⁾. Nguyen HH, Wu F, Oddy WH, Wills K, Brennan-Olsen SL, Jones G, et al. Longitudinal associations of dietary patterns with sociodemographic and lifestyle factors in older adults: the TASOAC study. Eur J Clin Nutr. 2020. The new publication is attached in **Appendix 5-2**.

5.1 Introduction

The global burden of chronic diseases is substantial in older adults and is increasing with rapid population ageing worldwide ⁽¹⁶²⁾. Nutrition has an important role in the prevention of many chronic diseases ⁽¹⁶³⁾, with two of the top ten leading causes of the global burden of disease being a diet low in fruits and diet high in sodium ⁽¹⁶⁴⁾. However, until recently, nutritional research has mostly examined the association of single or a few nutrients or foods with disease outcomes, which ignores the inter-correlation between multiple nutrients and foods, as they are consumed in practice ⁽⁷⁰⁾. Determining dietary patterns is an alternative approach used to examine the whole diet and identify the simultaneous effects of multiple dietary components ⁽¹⁶⁵⁾. Scoring systems have been used to assess how well a population's dietary intake conforms to pre-defined dietary patterns, for example, a Mediterranean Diet Score and a Healthy Diet Index ⁽¹²²⁾, and the Healthy Eating Index ⁽¹²³⁾. An alternative method is to determine dietary patterns using a posteriori approaches such as factor analysis that identify dietary patterns without using a priori definitions or constructs ⁽⁷⁰⁾.

There are few studies of posteriori-derived dietary patterns and their associations with demographic, socio-economic, and lifestyle factors in elderly people ^(78-80, 83, 87, 93-95). Most are cross-sectional and their results are inconsistent. For example, both western and prudent dietary patterns were positively associated with age in older Norwegian women ⁽⁸³⁾, but negatively associated with age in an elderly French population ⁽⁷⁸⁾ and a fruit and vegetable dietary pattern was positively associated with age in Chinese men but not women ⁽⁹⁴⁾. The single longitudinal

study ⁽⁷⁹⁾ identified dietary patterns using latent class analysis in Irish older adults at two-time points over 10 years. At both times, men were more likely to adopt a western dietary pattern compared with women, but individuals with lower education were more likely to have a western dietary pattern at 10 years but not at baseline.

Given the limitations of current data, we therefore aimed to identify dietary patterns in a population-based sample of older adults, and investigate the longitudinal associations of socio-demographic and lifestyle factors with dietary scores calculated for each pattern.

5.2 Materials and methods

This is a corrected analysis of a published paper ⁽¹⁶⁶⁾ that was retracted due to a data analysis error ⁽¹⁶¹⁾.

5.2.1 Participants and sample size

The Tasmanian Older Adult Cohort (TASOAC) Study was established to investigate relationships between osteoarthritis and lifestyle, genetic, and biochemical factors. At baseline, 1098 participants (50–80 years) were randomly recruited from the electoral roll in Southern Tasmania. Dietary intakes were assessed at baseline in 2002, 2.6 years, and 5 years after study enrolment. The study was approved by the Tasmanian Health and Medical Research Ethics Committee. All participants provided written informed consent.

5.2.2 Dietary intakes

Dietary intakes including beverages were assessed using the Cancer Council of Victoria Food Frequency Questionnaire (CCV-FFQ) ⁽¹⁵⁷⁾. The CCVFFQ includes both a frequency component and portion size of food items, from which food intake is calculated as grams per day. The questionnaire estimates intake over the previous 12 months from 101 food items. The CCV-FFQ has been validated against 7-day weighed food records and the Commonwealth Scientific and Industrial Research Organization FFQ ⁽¹⁶⁷⁾.

Scores were calculated adjusting for energy intake and these adjusted scores were used in the analysis. The FFQ consisting of a structured food list and a frequency response section that measures participant's dietary intake over 12 months. It is used to conduct repeated measures due to low participant burden, therefore, it is usually used to capture long-term variation in diets ⁽¹⁶⁰⁾. It indicates that the FFQ usually has lower within-person variation than other dietary assessment methods (e.g. 24h-recalls or dietary records) because of assessing long-term dietary intake which is the exposure of etiological interest for most diseases ⁽¹⁶⁰⁾. As the critical analysis was of dietary pattern scores as an exposure to examine effects on bone outcomes (Chapter 6), we did not analyse the within-person variation due to its limitations.

5.2.3 Socio-demographic and lifestyle factors

Weight was measured using Seca Delta scales (Delta Model 707; Seca, Hamburg, Germany) ⁽¹⁶⁸⁾ and height by stadiometer ⁽¹⁶⁹⁾. BMI was calculated (weight (kg)/height (m)²). Date of birth, sex, education level (highest attained), and employment and smoking status were assessed by questionnaire. Education was categorized into primary (no formal qualifications/ school or intermediate certificate), secondary (higher school or leaving certificate/ trade/ apprenticeship), and tertiary (certificate/ diploma/ university degree/ higher university degree), and employment status into employed (employed or self-employed either full- or part-time), unemployed (home duties/ student/ sole parent pension/ disability pension/ unemployed), and retired.

To assess area-level socio-economic status, each participant's residential address was matched to the corresponding Australian Bureau of Statistics (ABS) Census Collection District. ABS software (ABS, Canberra, Australia) was used to determine the Socio-Economic Indexes for Areas (SEIFA) value from the 2001 census for each participant ⁽¹⁷⁰⁾. SEIFA is a collection of four separate indices, each constructed from different variables, which summarizes the characteristics of residents within an area (~250 households), thereby providing a single measure to rank the level of advantage and/or disadvantage at the area level, not of the individual person. For this study, we used the three SEIFA that are equivalized for both advantage and disadvantage: the Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD), the Index of Education and Occupation (IEO), and the Economic Resources (IER) ^(170, 171). The IRSAD is an aggregate of variables

including, but not limited to, household income, car ownership, the number of one parent families, and educational attainment. Similarly, the IEO includes the proportion of employed individuals within the area, educational attainment, and if employed, the type of occupation held. The IER measures area-based household income, markers of dwelling size, and car ownership. For each of IRSAD, IEO and IER, quartile cut-points were based on the 2001 Tasmanian population ⁽¹⁷¹⁾. We used the lowest quartile to indicate the most socially disadvantaged group and dichotomised the cohort using this cut-point.

Smoking status was categorized as currently smoking (smoking ≥ 7 cigarettes/week for at least 3 months), being a former smoker or being a never smoker. Physical activity was measured as steps per day using a pedometer as previously reported ⁽¹⁷²⁾. Briefly, participants wore a pedometer at least 5 days (≥ 8 h/day) at their waist band or belt. Participants were asked to report the duration of wear, reasons for not wearing the pedometer, and other issues that may have influenced the pedometer data.

5.2.4 Statistical analysis

The 101 food items, measured from the CCV-FFQ as grams per day of intake were collapsed into 33 food groups using previously published groupings for this questionnaire ⁽¹⁵⁷⁾ (**Appendix 4-2**). The food groups were used to identify dietary patterns using exploratory factor analysis. We used principal factor extraction with varimax rotation so that factors were uncorrelated ⁽¹⁷³⁾. We used the Kaiser–Meyer–Olkin (KMO) test to assess sampling adequacy ⁽¹⁷⁴⁾. The number of factors selected were based on established criteria ⁽¹⁷⁵⁾. First, we selected factors according to the

Kaiser rule (considering selection of factors only with an eigenvalue >1). Next, we examined the scree plot of eigenvalues of each factor and identified five potential factors with eigenvalues above the point at which the scree plot slope most markedly changed (**Appendix 5-3**). We then examined the variance explained by these factors and their interpretability before selecting the final clinically interpretable dietary patterns.

A cut-off point of 0.2 for factor loadings was used to select food groups to be included for the generation of dietary pattern scores ⁽¹⁵⁷⁾. For each pattern, scores were calculated by summing intakes of food groups weighted by their loading on each respective pattern. To assess changes in food intake across the three study time points, we applied the baseline dietary factor loadings to generate scores at each time point. We adjusted the dietary pattern scores by total energy intake (i.e., scores per 1000 kilojoules) and these energy-adjusted dietary pattern scores were used in further analyses. Associations between energy-adjusted dietary pattern scores and participants' socio-demographic and lifestyle characteristics were investigated using linear mixed-effects models. Separate models were fitted for each socio-demographic exposure of interest. Each model included fixed effect terms for time (in years) and the exposure, with an interaction term for time and exposure. The interaction term estimates the additional change in dietary pattern score per year associated with a unit increase in exposure. A random intercept was specified for each participant to account for individual differences in baseline dietary patterns, and the correlation between the repeated measures was modelled using an exponential covariance structure. Variables were retained for the multivariable model based on significant baseline association ($p < 0.05$) or interaction term

($p < 0.2$), or clinical importance. Stata software version 14 (StataCorp, College Station, Texas, USA) was used for data analysis⁽¹⁷⁶⁾. Associations were considered statistically significant at a two tailed p -value < 0.05 .

5.3 Results

Participant flow through the study is shown in **Figure 5-1**. Of 1098 participants who completed the food frequency questionnaire at baseline, 766 remained at 5 years. Baseline characteristics of participants are given in **Table 5-1**. Their mean age was 63 years and 51% were women.

Four dietary patterns were identified which we labeled fruit and vegetable, animal protein, snack and western dietary patterns based on the key food groups of which they were composed (**Table 5-2**). The KMO was 0.71, indicating sufficient common variance for factor analysis. The proportion of variance explained by each dietary pattern was 6.67%, 6.26%, 5.10% and 5.06%, respectively. The fruit and vegetable pattern was predominantly composed of vegetables, fruits, potatoes, and breakfast cereals other than those grouped as whole grains (i.e. excluding muesli and porridge); the animal protein pattern of red and processed meats, fish and poultry; the snack pattern of snacks, sweets, condiments and nuts; and the western dietary pattern of pizza, hamburgers, meat pies and sweets. The mean (standard deviation) and range of the baseline energy-adjusted scores (score per 1000KJ) was 23.4 (9.7) and 2 to 68 for the fruit and vegetable pattern, 23.4 (8.2) and 4 to 69 for the animal protein pattern, 18.7 (7.9) and 2 to 52 for the snack pattern, 7.9 (3.3) and 1 to 26 for the western dietary.

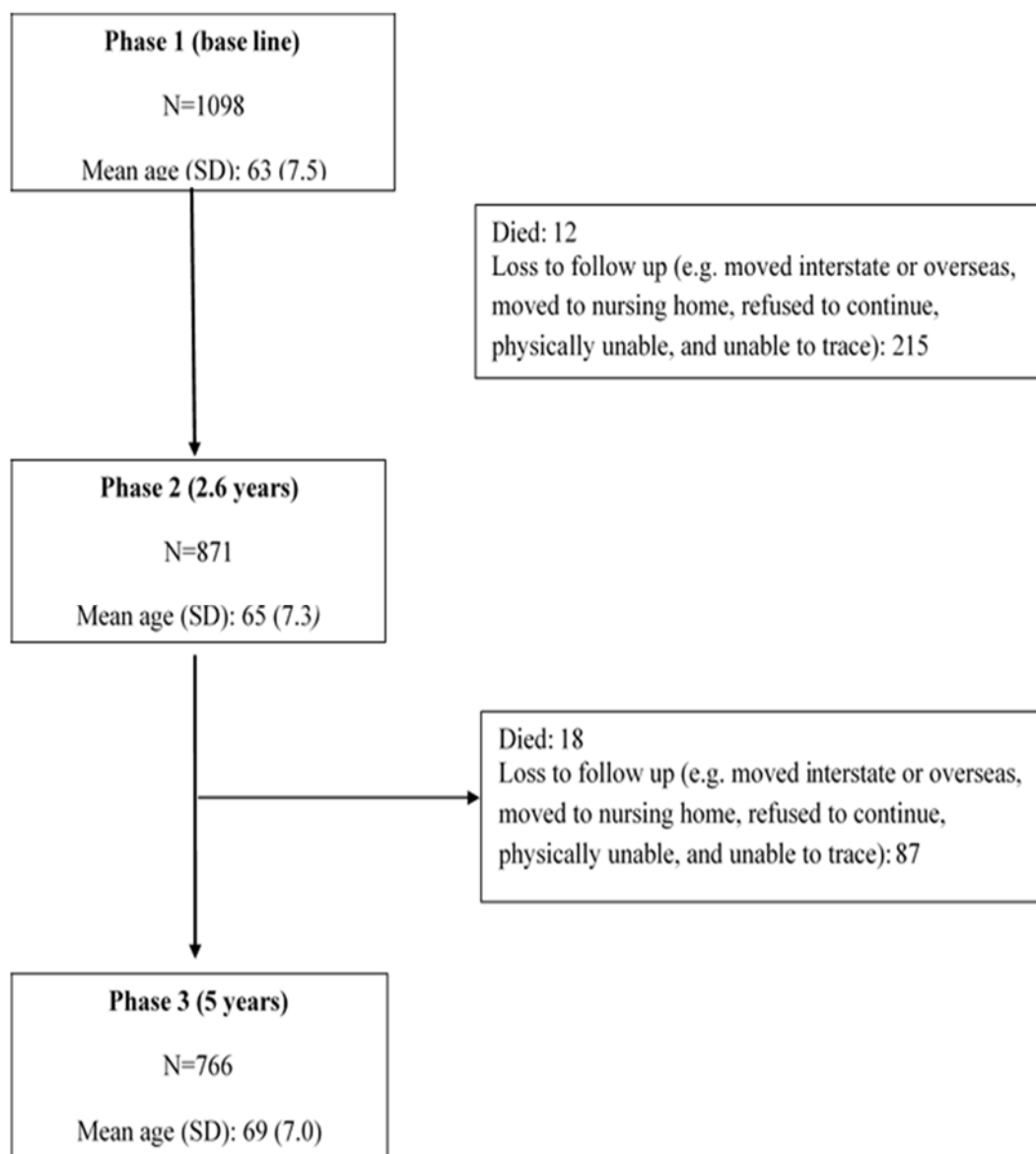


Figure 5-1: Flow of participants through the study

Table 5-1: Characteristics of participants at baseline

<i>Characteristics</i>	<i>N = 1098^a</i>
Age (years), mean (SD)	63.0 (7.5)
Women, n (%)	562 (51.2)
Body mass index (kg/m ²), mean (SD)	27.9 (4.8)
Education, n (%)	
Primary	398 (36.2)
Secondary	358 (32.6)
Tertiary	341 (31.1)
Employment status, n (%)	
Employed	432 (39.3)
Unemployed	248 (22.6)
Retired	418 (38.1)
Smoking status, n (%)	
Never	542 (49.4)
Former	423 (38.5)
Current	131 (11.9)
Physical activity (steps/day), mean (SD)	8617 (3356)
Energy intake (KJ), mean (SD)	7669 (2835)

^a Missing data: education (n=1); smoking status (n=2); physical activity (n=50); SD standard deviation, KJ kilojoules.

Table 5-2: Factor loadings for the three major dietary patterns identified by exploratory factor analysis^a

<i>Food groups</i>	<i>Fruit and vegetable</i>	<i>Animal protein</i>	<i>Snack</i>	<i>Western</i>
Green leafy vegetables	0.54		0.21	
Fruits	0.28		0.38	
Cruciferous vegetables	0.73			
Potatoes	0.58			
Dark-yellow vegetables	0.79			
Other vegetables*	0.36	0.22		
Other breakfast cereals**	0.26		0.45	
Fish		0.53		
Chips		0.22		
Processed meats		0.28		0.28
Red meats		0.65		
Poultry		0.78		
Refined grain		0.40		0.22
Sweets		0.23	0.49	0.36
Condiments		0.30	0.36	
Fruit juice		0.39		
Pizzas				0.55
Hamburgers				0.63
Meat pies				0.71
Nuts			0.45	
Snacks			0.67	
Variance explained (%)^b	6.67	6.26	5.10	5.06

^a Only factor loadings ≥ 0.2 are presented (factor loading shows the correlation between food items and these dietary patterns).

^b Gives the proportion of variance accounted for each factor.

* Other vegetables: celery, mushrooms, capsicum, beetroot and onion.

** Other breakfast cereals: all bran, branflakes, weet bix, and cornflakes

Unadjusted and multivariable models of the associations between energy-adjusted dietary pattern scores and participants socio-demographic characteristics and health behaviours are presented in **Tables 5-3 and 5-4** respectively.

In both unadjusted and adjusted analyses, older age was associated with lower animal protein and western pattern scores at baseline, with a significant age-time interaction for western pattern scores, such that the effect of age decreased over time (β (95% confidence interval (CI)) = 0.01 (0.004, 0.02) unit per 1000KJ per year for age-time interaction for both models) (See **Figure 5-2A**). Older age was associated with higher snack pattern scores at baseline only in the adjusted model, also with a reduction in the effect of age over time (-0.02 (-0.03, -0.001) unit per 1000KJ per year for age-time interaction) (**Figure 5-2B**).

Being a man was associated with lower fruit and vegetable and snack patterns scores, but higher animal protein and western scores at baseline in both unadjusted and adjusted models. The sex difference in animal protein pattern score increased over time (0.32 (0.11, 0.52) and 0.27 (0.06, 0.48) unit per 1000KJ per year, respectively) (**Figure 5-2C**), but there were no other sex-time interactions.

There were no associations between education and dietary pattern scores in either unadjusted and adjusted analyses, except that people with primary vs tertiary education had slightly greater decrease in western pattern scores over time in the adjusted model (-0.10 (-0.20, -0.004) unit per 1000KJ per year) (**Figure 5-2D**). Being retired vs employed was associated with lower baseline animal protein pattern scores (-2.50 (-3.57, -1.44) and -1.87 (-3.01, -0.72 unit per 1000KJ in unadjusted and adjusted models respectively) but with no interaction with time.

Energy-adjusted fruit and vegetable and animal protein pattern scores were not associated with any of the three SEIFA indices in either adjusted or unadjusted analyses (data not shown). Residing in a socially disadvantaged area (vs. advantaged), as determined by the IRSAD, was associated with lower baseline snack pattern scores (-1.80 (-3.00, -0.60) unit per 1000KJ) but higher baseline western pattern scores (0.52 (0.01, 1.04) unit per 1000KJ), with no time interactions. Similar small baseline differences were observed using the IER and IEO (data not shown).

In both unadjusted and adjusted models, being a current smoker was associated with higher animal protein and western pattern scores but lower fruit and vegetable and snack pattern scores at baseline, and being more physically active was associated with higher baseline snack pattern scores (0.15 (0.01, 0.29) and 0.24 (0.11, 0.37) unit per 1000KJ, respectively). There were no significant interactions with time for these variables.

Table 5-3: Unadjusted models of the associations between dietary pattern scores and participants' characteristics

<i>Variables^a</i>	<i>Fruit and vegetable</i> <i>β (95% CI)*</i>	<i>Animal protein</i> <i>β (95% CI)*</i>	<i>Snack</i> <i>β (95% CI)*</i>	<i>Western</i> <i>β (95% CI)*</i>
Age				
Time	0.93 (-0.06, 1.91)	-0.78 (-1.68, 0.13)	1.03 (0.22, 1.85)	-0.77 (-1.13, -0.42)
Age (years)	0.05 (-0.03, 0.12)	-0.14 (-0.20, -0.08)	0.05 (-0.01, 0.11)	-0.07 (-0.10, -0.05)
Age by time (years)	-0.01 (-0.03, 0.004)	0.01 (-0.01, 0.02)	-0.01 (-0.03, 0.0003)	0.01 (0.004, 0.02)
Sex				
Time	0.22 (0.06, 0.38)	-0.38 (-0.53, -0.23)	0.29 (0.16, 0.42)	-0.19 (-0.25, -0.13)
Women	Reference	Reference	Reference	Reference
Men	-3.98 (-5.09, -2.87)	1.08 (0.14, 2.02)	-2.53 (-3.43, -1.63)	1.00 (0.63, 1.37)
Sex by time (years)				
Women	Reference	Reference	Reference	Reference
Men	0.06 (-0.16, 0.29)	0.32 (0.11, 0.52)	-0.10 (-0.28, 0.09)	0.04 (-0.04, 0.12)
Education				
Time	0.20 (0.01, 0.40)	-0.17 (-0.35, 0.01)	0.29 (0.12, 0.45)	-0.13 (-0.20, -0.06)
Tertiary	Reference	Reference	Reference	Reference
Secondary	-0.33 (-1.75, 1.08)	-0.11 (-1.29, 1.07)	-0.58 (-1.73, 0.57)	0.37 (-0.10, 0.85)
Primary	1.31 (-0.08, 2.69)	-0.29 (-1.45, 0.86)	-0.41 (-1.53, 0.71)	0.25 (-0.21, 0.71)

Education by time (years)				
Tertiary	Reference	Reference	Reference	Reference
Secondary	0.14 (-0.14, 0.42)	-0.003 (-0.26, 0.25)	-0.01 (-0.24, 0.22)	-0.001 (-0.10, 0.10)
Primary	0.01 (-0.27, 0.28)	-0.15 (-0.41, 0.10)	-0.14 (-0.36, 0.09)	-0.09 (-0.19, 0.01)
Employment status				
Time	0.33 (0.16, 0.50)	-0.25 (-0.41, -0.10)	0.35 (0.21, 0.49)	-0.21 (-0.27, -0.14)
Employed	Reference	Reference	Reference	Reference
Unemployed	2.14 (0.65, 3.64)	-1.81 (-3.04, -0.57)	0.52 (-0.68, 1.73)	-0.69 (-1.18, -0.19)
Retired	0.72 (-0.56, 2.01)	-2.50 (-3.57, -1.44)	0.56 (-0.49, 1.60)	-0.84 (-1.26, -0.41)
Employment by time (years)				
Employed	Reference	Reference	Reference	Reference
Unemployed	-0.21 (-0.51, 0.09)	0.03 (-0.25, 0.30)	-0.20 (-0.45, 0.05)	0.02 (-0.09, 0.12)
Retired	-0.08 (-0.34, 0.17)	0.06 (-0.17, 0.30)	-0.21 (-0.42, 0.002)	0.10 (0.01, 0.19)
Smoking status				
Time	0.20 (0.04, 0.36)	-0.29 (-0.43, -0.14)	0.25 (0.12, 0.38)	-0.15 (-0.21, -0.09)
Never	Reference	Reference	Reference	Reference
Former	-0.78 (-1.99, 0.42)	0.90 (-0.11, 1.91)	-0.82 (-1.79, 0.15)	0.35 (-0.05, 0.76)
Current	-4.43 (-6.24, -2.61)	2.79 (1.27, 4.30)	-4.37 (-5.83, -2.91)	1.89 (1.29, 2.50)

Smoking by time (years)				
Never	Reference	Reference	Reference	Reference
Former	0.13 (-0.11, 0.37)	0.11 (-0.12, 0.33)	-0.02 (-0.22, 0.18)	-0.01 (-0.10, 0.07)
Current	0.01 (-0.36, 0.37)	0.27 (-0.07, 0.61)	-0.09 (-0.39, 0.22)	-0.06 (-0.19, 0.08)
Physical activity				
Time	0.22 (-0.10, 0.55)	0.01 (-0.29, 0.31)	0.11 (-0.16, 0.38)	-0.07 (-0.19, 0.05)
Physical activity (1000 steps/day)	0.02 (-0.15, 0.19)	0.04 (-0.10, 0.19)	0.15 (0.01, 0.29)	0.05 (-0.004, 0.11)
Physical activity by time (years)	0.003 (-0.03, 0.04)	-0.03 (-0.06, 0.01)	0.01 (-0.01, 0.04)	-0.01 (-0.02, 0.003)

^a Each variable was adjusted for other variables in the column.

* The energy-adjusted dietary pattern score, that is dietary pattern score per 1000 kJ energy intake

The bold number indicates statistically significant (p<0.05).

CI, confidence interval.

Table 5-4: Adjusted linear mixed-effects models for the association between participants' characteristics at baseline and change in dietary pattern scores during follow-up in the TASOAC study

<i>Variables^a</i>	<i>Fruit and vegetable</i> <i>β (95% CI)*</i>	<i>Animal protein</i> <i>β (95% CI)*</i>	<i>Snack</i> <i>β (95% CI)*</i>	<i>Western</i> <i>β (95% CI)*</i>
Time	0.26 (0.14, 0.37)	-0.36 (-0.51, -0.22)	1.16 (0.29, 2.03)	-0.76 (-1.15, -0.38)
Age (years)	0.02 (-0.05, 0.09)	-0.08 (-0.15, -0.002)	0.09 (0.02, 0.15)	-0.07 (-0.10, -0.05)
Age by time (years)			-0.02 (-0.03, -0.001)	0.01 (0.004, 0.02)
Sex				
Women	Reference	Reference	Reference	Reference
Men	-3.76 (-4.77, -2.74)	1.12 (0.11, 2.12)	-2.89 (-3.72, -2.06)	1.06 (0.73, 1.40)
Sex by time (years)				
Women		Reference		
Men		0.27 (0.06, 0.48)		
Education				
Tertiary				Reference
Secondary				0.30 (-0.15, 0.75)
Primary				0.43 (-0.01, 0.88)

Education by time (years)

Tertiary	Reference
Secondary	0.001 (-0.10, 0.10)
Primary	-0.10 (-0.20, -0.004)

Employment status

Employed	Reference
Unemployed	-1.12 (-2.40, 0.16)
Retired	-1.87 (-3.01, -0.72)

Smoking status

Never	Reference	Reference	Reference	Reference
Former	0.16 (-0.93, 1.25)	1.05 (0.16, 1.95)	-0.22 (-1.09, 0.66)	0.14 (-0.22, 0.49)
Current	-3.78 (-5.39, -2.16)	3.01 (1.52, 4.49)	-3.68 (-5.06, -2.30)	1.47 (0.90, 2.04)

Physical activity (1000 steps/day)	-0.14 (-0.28, 0.001)	0.24 (0.11, 0.37)
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^a Each variable was adjusted for other variables in the column.

The blank spaces indicated that variables were not included in the model. We selected potential variables in the models depending on the significant baseline ($p < 0.05$), significant interaction ($p < 0.2$) and clinical meaning.

* The energy-adjusted dietary pattern score, that is dietary pattern score per 1000 kJ energy intake.

The bold number indicates statistically significant ($p < 0.05$).

CI, confidence interval.

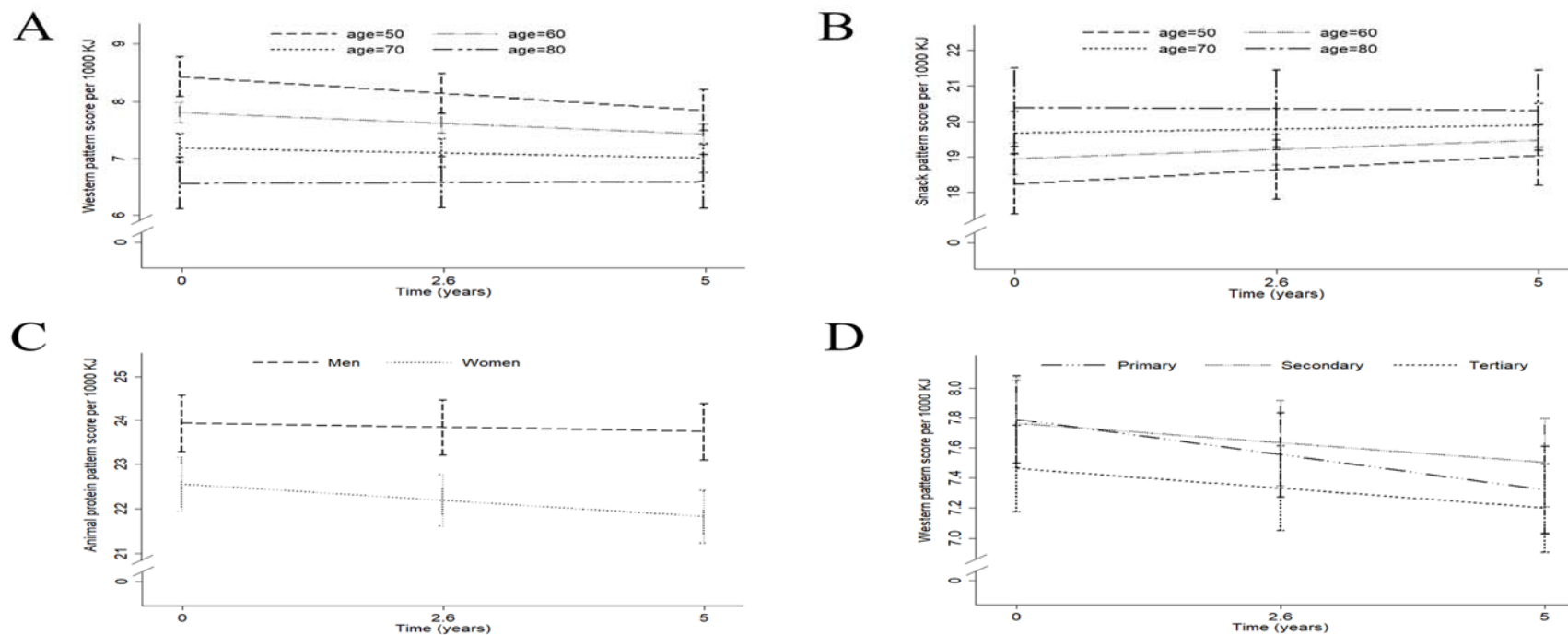


Figure 5-2: Changes in dietary pattern scores over time by age (a, b), sex (c) and education (d) from the adjusted models.

The 95% confidence intervals of all dietary pattern scores at each time point are shown. The range of baseline age of participants was 50 to 80 and we selected four examples of age values, such as 50, 60, 70, and 80 to show in this figure.

5.4 Discussion

This is the first study in older adults examining longitudinal changes in posteriori-derived dietary pattern scores and their associations with socio-demographic and lifestyle factors. The four distinct dietary patterns that were identified (fruit and vegetable, animal protein, snack and western) are broadly similar to patterns reported in other studies of older adults. Men and current smokers had higher energy-adjusted scores for diets that potentially have adverse health effects, specifically the animal protein and western patterns as well as lower scores for the potentially beneficial fruit and vegetable pattern. Retired people also had lower animal protein scores, and those residing in a socio-economically disadvantaged area had higher western pattern scores. Being a man, smoking status and socioeconomic disadvantage are also risk factors for many chronic diseases to which poor nutrition may contribute, so these data help to identify suitable groups to target for interventions to improve diet quality in older adults.

Although the exact food groups comprising dietary patterns differ across studies, the fruit and vegetable, animal protein and western dietary patterns in our study contained a core of similar food groups to healthy, high protein and unhealthy patterns described in other studies of older adults ^(78-80, 83, 87, 93, 94) and particularly in Australian people ^(95, 157). Such patterns have a variety of labels, for example, fruits and vegetables were major components of the pattern we termed the fruit and vegetable pattern, and also of patterns titled healthy ⁽⁷⁸⁻⁸⁰⁾, prudent ^(83, 157), more healthful ⁽⁸⁷⁾, vegetables-fruits ⁽⁹⁴⁾, Lebanese ⁽⁹³⁾ and factor 1 ⁽⁹⁵⁾. Similarly, our western dietary pattern shared content of red/processed meats, refined grain,

sweets or take away foods with others variously named western ^(78, 79, 83, 87, 93, 157), unhealthy ⁽⁸⁰⁾ and factor 3 ⁽⁹⁵⁾. Lastly, high protein diets like the animal protein pattern in our study and high protein/alcohol ⁽⁹³⁾, high protein ⁽⁸⁰⁾ and meat-fish pattern ⁽⁹⁴⁾ in other studies have poultry, fish, red/processed meats in common. Nonetheless, there were also differences in the content of these patterns in different populations – for instance, our animal protein pattern also included refined grains, while another included whole grains ⁽⁸⁰⁾. The similarities mean that there is potential value in comparing predictors of patterns, but the differences will likely contribute to a degree of inconsistency across studies in different populations.

Our findings that the healthy fruit and vegetable pattern score was lower and western pattern scores higher in men and current smokers are consistent with other studies ^(78, 79, 83, 87, 93, 95). Compared to women and non-smokers, men and smokers are at increased risk for heart disease, cancer, lower respiratory disease, stroke and diabetes which contribute to the top six leading causes of death among men in the United States ⁽¹⁷⁷⁾. Consequently, they should be an important target population for nutritional intervention programs. People residing in areas that are socioeconomically disadvantaged are also more likely to consume a western dietary pattern and are another target group for intervention. This result is consistent with a systematic review that higher socio-economic status or living in urban areas was associated with a healthier dietary pattern ⁽¹⁷⁸⁾.

Dietary patterns play an important role in contributing to human health. According to the World Health Organization, fruits and vegetables are the key components of healthy dietary patterns that reduce the risk of non-communicable diseases ⁽¹⁷⁹⁾.

Conversely, a western dietary pattern is one of the main factors that contributes to many chronic illness and health problems ^(180, 181). The impacts of high intakes of an animal protein and/or snack pattern are less clear. Generally, animal proteins are important foods for improving the human diet, but a high intake of red meats or processed meats has been associated with several chronic diseases ⁽¹⁸²⁾. The contribution of snack food for people with health problems is still debatable due to the variation of snack food patterns across studies ⁽¹⁸³⁾.

Studies of associations of dietary pattern scores with other socio-demographic characteristics and lifestyle factors in older adults are less consistent. For example, older age was negatively associated with western pattern scores in our study and also in a French study ⁽⁷⁸⁾ compared with other studies report positive ⁽⁸³⁾ or no association ^(79, 87, 93). Snack pattern scores were positively associated with age in our study but not in a Chinese population ⁽⁹⁴⁾. Associations of education with animal protein scores have variously been negative in men ⁽⁹⁴⁾, or positive ⁽⁹³⁾ or absent ⁽⁸⁰⁾ as in our study. No association was found between healthy pattern score and physical activity in ours and an Irish study ⁽⁷⁹⁾ compared with positive associations reported in other studies ^(83, 93). These conflicting results could be explained by variations in study design and methods used to identify dietary patterns and calculate diet score. For example, most previous studies were cross-sectional ^(83, 87, 93, 94) only our study and one other reporting longitudinal data ⁽⁷⁹⁾. Even though both were longitudinal studies, a latent class analysis was used to identify dietary patterns in the Irish study ⁽⁷⁹⁾, which may account for the differing results ⁽¹⁸⁴⁾. Different methodological decisions made to identify dietary patterns, such as the

number of factors extracted (median of 4, range 2 to 10) and the methods used for calculating factor scores, reflecting the lack of a gold standard approach ⁽¹⁴³⁾.

Being retired was associated with lower scores of animal protein pattern in our study but no previous studies ^(80, 93, 94) have investigated the association of an animal dietary protein and employment status. This is a potentially important problem. Although high intakes of animal protein may have detrimental effects, equally the nearly 50% of older American adults who did not meet recommended levels of protein intake had more functional limitations ⁽¹⁸⁵⁾. A lower protein intake also relates to many health problems such as acute and chronic diseases in the elderly ^(186, 187). It is therefore likely that content of advice addressing protein intake will need to be tailored according to whether a person's intake is potentially too high or too low.

Study strengths and limitations

Strengths of our study include that it provides novel information about longitudinal changes in dietary pattern scores and their associations with characteristics of older people from a large, population-based sample. The CCVFFQ was applied to estimate dietary intake due to its low cost, ease of use, and ability to be self-administered ⁽¹⁴²⁾. Potential limitations should be acknowledged. By their nature, a posteriori-derived dietary patterns vary across studies, limiting the ability to directly compare results of different studies. The fruit and vegetable, animal protein, and western dietary patterns we identified were largely similar to those in previous studies, suggesting that it is reasonable to compare findings for these dietary patterns. Missing data are an inherent issue of any longitudinal study,

however, missing data of predictors/exposures in our study were very low (<5%) reducing the risk of biased results. Moreover, we used linear mixed-effects model to utilize all available data to minimize the impact of missing data.

For both baseline and over 5 years, people with low energy intake have lower mean scores of fruit and vegetable, animal protein, snack and western patterns compared with the normal group. It may be related to their illness. The number of participants with low/high energy intake is very small and there is no difference between BMI and energy intake. Moreover, there is a little different coefficient but no change for significant associations of participant's characteristics with energy-adjusted dietary pattern scores (all cases vs dropping low/high energy intake). See **Appendix 5-4** for more detail. Therefore, the dropping low/high energy intake did not influence our results.

5.5 Conclusion

In conclusion, we identified four dietary patterns among Tasmanian older adults, namely fruit and vegetable, animal protein, snack and western dietary patterns. Men, smokers, retired people, and those living in areas of socioeconomic disadvantage are potential target groups for nutrition interventions to encourage improved intakes of healthier foods in older adults.

Chapter 6: Associations between dietary patterns and osteoporosis-related outcomes in older adults: a longitudinal study

Chapter 5 reported the dietary patterns identified in Tasmanian older adults, and the sociodemographic factors associated with the different patterns that may help with targeting dietary interventions to people at higher risk of poorer quality diets. This Chapter aimed to examine the longitudinal associations of dietary patterns with other health outcomes (falls risk, BMD, and fracture) in this population, addressing a gap in the literature as described in Chapter 3. Nguyen HH, Wu F, Oddy WH, Wills K, Winzenberg T, Jones G. Associations between dietary patterns and osteoporosis-related outcomes in older adults: a longitudinal study. *Eur J Clin Nutr.* 2020. The publication is put in **Appendix 6-1**.

6.1 Introduction

Fractures are a major public health issue in adults fifty years or older⁽⁸⁴⁾, with more than 8.9 million osteoporotic fractures occurring annually worldwide⁽¹⁸⁸⁾. Fractures lead to many severe health consequences, such as increased mortality and reduced quality of life⁽¹⁸⁹⁾. The annual economic burden due to incident fractures is substantial, estimated to be about US\$17 billion in 2005 and is predicted to increase by nearly 50% by the year 2025⁽¹⁹⁰⁾. Low bone mineral density (BMD) and falls are two major risk factors for fractures in older people^(191, 192). Therefore, preventing low BMD and reducing falls risk are critically important for the prevention of fractures in older adults.

Diet is considered an important modifiable risk factor for bone quality and fracture risk⁽⁵⁴⁾. There is evidence that single nutrients or food items (e.g., calcium, vitamin D, phosphorus, magnesium, fruit and vegetables) could influence bone health⁽⁵⁴⁾. However, the approach of examining a single nutrient or food item is limited because it does not account for the high correlation between individual nutrients and food items and the fact they are consumed together in the diet⁽⁷⁰⁾. Taking a dietary pattern approach may address this issue⁽⁷⁷⁾. There are two ways to derive dietary patterns: the a priori approach using nutrition theory/knowledge and the a posteriori approach using statistical methods⁽⁷⁰⁾. The a priori method creates index variables that are usually quantified to provide an overall measure of dietary quality. However, there are various definitions of healthy patterns based on different indices⁽⁷⁰⁾. The a posteriori method, by contrast, describes existing dietary patterns in the population⁽⁷⁷⁾.

No previous study has examined dietary patterns using the a posteriori method and falls risk in older adults and there are limited longitudinal studies examining BMD (86, 88, 99) and fracture (84, 89, 92) in the elderly. These studies suggest that dietary patterns could play a key role in bone health, although results are inconsistent. Specifically, a healthy dietary pattern was protective for bone health in three cohort studies (86, 88, 92) but there were no such associations in Canadian (men) (89) and Americans (84). Given the conflicting data and the lack of evidence around falls risk, further research is required. We therefore aimed to describe the association of dietary pattern z-scores with osteoporosis-related outcomes of falls risk z-scores, BMD, and incident fracture in a population-based cohort of Tasmanian older adults.

6.2 Materials and methods

6.2.1 Participants

Participants (N=1098, aged ≥ 50 years) were from the Tasmanian Older Adult Cohort (TASOAC) study. The detailed study design is published elsewhere (147). Briefly, participants aged 50 years and older were randomly recruited using the electoral roll in Southern Tasmania and assessed at baseline and at an average of 2.6, 5 and 10.7 years later. People in whom magnetic resonance imaging was contraindicated and those who were institutionalized were excluded. The study was approved by the Tasmanian Health and Medical Research Ethics Committee. All participants gave written informed consent.

6.2.2 Dietary intake at baseline and the identification of dietary patterns

The Cancer Council Victoria food frequency questionnaire (CCVFFQ) including 101 food items was used to estimate participants' dietary intake by asking about their usual eating habits over the last 12 months ⁽¹⁵⁷⁾. Briefly, this instrument includes four sections ascertaining: 1) the frequency of consumption of 101 specific foods (cereal foods, sweets and snacks; dairy products, meat and fish; fruit; and vegetables); 2) the frequency of drinking beverages such as beer, wine, and/or spirits; 3) the usual portion size of potatoes, vegetables, steak, and meat/vegetable casserole; and 4) the type of bread (e.g. whole meal), milk (e.g. reduced fat), spread (e.g. butter) usually consumed. This self-report questionnaire has been validated against the Commonwealth Scientific and Industrial Research Organization FFQ and weighed food records ⁽¹⁶⁷⁾. We converted all dietary intakes of foods and drinks to grams per day for our analysis. Energy intake (KJ) was calculated from this CCVFFQ by Australian food composition tables ⁽¹⁹³⁾.

We classified the 101 food and drink items into 33 food groups as previously done ⁽¹⁵⁷⁾ (**Appendix 4-2**). Exploratory factor analysis with a varimax rotation was used to identify dietary patterns ⁽¹⁵⁷⁾. The number of dietary patterns was determined based on the following criteria: the Kaiser rule (Eigenvalues >1), the elbow of scree plot, variance explained by each pattern, as well as interpretation and meaning of each pattern ⁽¹⁷⁵⁾. Four dietary patterns were identified (**Table 5-2**): a fruit and vegetable pattern characterized by high consumption of fruits, potatoes, vegetables, breakfast cereals excluding muesli and porridge; an animal protein pattern composed of fish, poultry, red and processed meats; a snack pattern of snacks,

sweets, nuts and condiments; and a western pattern of hamburgers, meat pies, pizzas and sweets. The percentage variance explained by each dietary pattern was 6.67%, 6.26%, 5.10% and 5.06%, respectively. Scores for each dietary pattern were calculated for each participant as the sum of the intake of each food group weighted by their factor loadings (≥ 0.20)⁽¹⁵⁷⁾. Dietary pattern scores were standardized to z-scores to enable comparison of associations among dietary patterns.

6.2.3 Falls risk z-score

We calculated fall risk z-scores at baseline, 2.6, 5 and 10.7 years using the short form of the physiological profile assessment (Prince of Wales Medical Research Institute, Sydney, Australia)⁽¹⁴⁹⁾. This assessment has five domains: edge contrast sensitivity, hand reaction time, proprioception (position sense), knee extension, and sway test and is a valid and reliable tool for falls risk assessment in older adults⁽¹⁴⁹⁾. The falls risk z-scores using these tests were assessed for each participant at each time point, with a higher score indicating a higher risk of falls⁽¹⁹⁴⁾.

6.2.4 Bone mineral density (BMD) (g/cm²)

We used dual-energy X-ray absorptiometry (Hologic, Waltham, MA, USA)⁽¹⁴⁷⁾ to measure BMD of femoral neck (FN), hip, and lumbar spine (LS) at baseline, 2.6, 5 and 10.7 years. The Hologic densitometer was calibrated automatically using the internal software system and the longitudinal coefficient of variation for BMD was 0.39%⁽¹⁹⁴⁾.

6.2.5 Fracture

We used a self-administered questionnaire, that has been validated with radiologic reports and medical records in older adults ⁽¹⁵⁰⁾ at baseline, 2.6, 5 and 10.7 years to collect fracture data over 10 years as described previously ⁽¹⁴⁹⁾. Participants listed any fractures they had since their previous visit and the site of each fracture. We coded participants who experienced at least one fracture as ‘1’ and those without incident fracture as ‘0’.

6.2.6 Other baseline explanatory factors

Body mass index (BMI) was calculated as weight (kg) measured by Seca Delta scales (Delta Model 707; Seca, Hamburg, Germany) ⁽¹⁴⁷⁾ divided by squared height (m²) measured by stadiometer. We used a self-reported questionnaire to obtain information about age (years), sex, education (primary, secondary and tertiary), smoking status (never smoked, former or current smoker), medical history (yes/no), and current use of medications (yes/no) affecting bone metabolism. We measured physical activity as steps per day using a validated Omron pedometer (HJ-003 & HJ-102, Omron Healthcare, Kyoto, Japan) and Yamax pedometer (SW-200, Yamax USA, San Antonio, Texas, USA) as previous study reported ⁽¹⁶⁹⁾. There was a strong linear correlation of the estimates of these pedometers ($r=0.88$) although the mean steps of Omron pedometer were 10% higher than Yamax pedometer. Participants were guided to wear a pedometer at least 5 days/week (≥ 8 hours/day) and report the duration of wear and any problem relating to this data collection.

6.2.7 Statistical analysis

We report the baseline characteristics of participants as mean (standard deviation (SD)) or frequency (%) for continuous and categorical variables respectively. Linear mixed-effects models were used to estimate the association of baseline dietary pattern z-scores with falls risk z-score and BMD. Each model included fixed effect terms for time (years since baseline) and dietary pattern score, and an interaction term for dietary pattern score with time. The interaction term estimates the additional change in the outcome per year associated with a one SD increase in dietary pattern score at baseline. A random intercept was specified for each participant to account for individual differences in baseline dietary patterns, and the correlation between the repeated measurements over time was modelled using an exponential residual variance-covariance structure. When this model would not converge we specified an independent variance-covariance structure with cluster-robust standard errors that allow for correlation among the repeated observations on an individual.

Log-binomial regression models were used to estimate association of baseline dietary pattern z-scores with the risk of fracture and category of change in LS BMD over ten years. Participants were coded as “0” if their LS BMD did not change or decreased over 10 years and “1” if their LS BMD increased. This categorization was performed because LS BMD increased over time, suggesting an effect of lumbar spinal degenerative disease in older adults ⁽¹⁹⁵⁾. Participants with increasing LS BMD over ten years are more likely to have degenerative spine conditions and so this variable was used as a proxy for LS degenerative status.

All models were adjusted for the baseline age, sex and BMI to account for potential confounding of the association between dietary pattern z-scores and outcomes (falls risk, BMD and fracture). We additionally assessed potential confounding by energy intake, physical activity, medication and medical history but as there was no evidence of confounding by these variables, they were not included in the adjusted models. The retained variables depended on the p-value showing a significant association at baseline ($p < 0.05$), or the p-values of the interaction term ($p < 0.2$), or clinical importance. We also examined the magnitude of coefficients for dietary patterns when we added each potential confounder. We retained the variable if the coefficient from the model changed by more than 10%.

Missing baseline data for the linear mixed models were imputed using the method of chained equations, assuming data were missing at random ⁽¹⁹⁶⁾. The imputation model included four phases of BMD (FN, hip and LS) and falls risk z-score; baseline education, physical activity, smoking status and all variables from the analytical models. Fifty imputed datasets were created and the estimates from the multiple imputed datasets were combined into an overall estimate using Rubin's rules ⁽¹⁹⁷⁾. Missing data in the log-binomial models for fracture were accounted for using inverse probability weighting as previously described ⁽¹⁹⁸⁾. The following baseline variables were used to calculate predicted probability of being observed for each participant: age, sex, physical activity, smoking status and medication; and a binary variable indicating if any fracture had been observed during the ten-year study period.

Evidence for the role of obesity or overweight on bone health is inconsistent ⁽¹⁹⁹⁾. For example, a recent Mendelian Randomization Study found that there was a positive association between BMD and BMI in men, but not for postmenopausal women ⁽²⁰⁰⁾. Moreover, the loss of muscle mass in older adults may indicate that the prediction of body fat using BMI to determine whether obesity causes changes in bone mass is less accurate ⁽¹⁹⁹⁾. As the relationship between obesity and bone health is not clear, we considered the possibility of BMI being on the causal pathway rather than a confounder and so performed sensitivity analyses comparing models with and without adjusting for BMI. There were only small variations in estimated coefficients and no changes in statistical inference (**Appendix 6-2** and **Table 6-4**). Results may not be generalisable to people weighting over 130 kg as they were excluded from the TASOAC study.

As a positive relationship between a western dietary pattern and obesity/overweight ⁽²⁰¹⁾ may contribute to an increase in LS BMD, we also specifically examined the association between BMI-adjusted western pattern scores and LS BMD. The association of dietary pattern z-scores with falls risk z-scores, BMD and fracture were also estimated using unweighted data of complete cases as sensitivity analyses. All analyses were conducted using the Stata software version 14 (StataCorp, College Station, Texas, USA) ⁽¹⁷⁶⁾. A two-tailed p-value < 0.05 was considered statistically significant.

6.3 Results

Of 1098 participants at baseline, 567 (52%) were retained at 10.7 years (**Figure 6-1**). Participant characteristics at baseline are presented in **Table 6-1**. Mean age was 63.0 years (SD=7.5), and 51% were women. People lost to follow up over ten years had higher falls risk and lower physical activity at baseline (**Table 6-1** and **Appendix 6-3**).

On average, falls risk z-score was estimated to increase by 0.04 (95% confidence interval (CI) 0.04, 0.05) SD per year. There was a negative (beneficial) association between the fruit and vegetable dietary pattern z-score and falls risk z-score at baseline -0.05 (95% CI -0.09, -0.01) but no interaction with time (**Table 6-2**). There were no associations between falls risk z-score and any other dietary patterns.

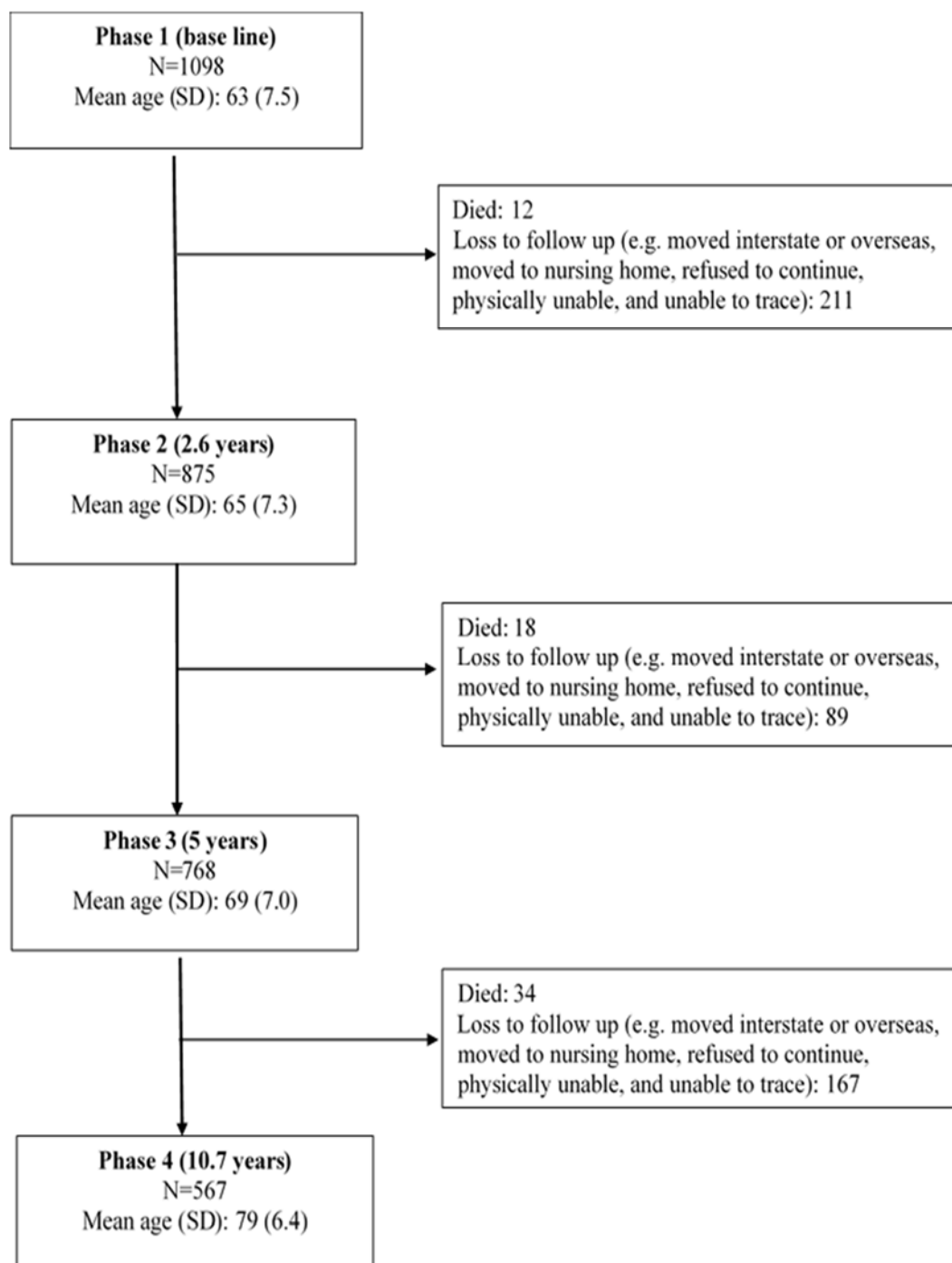


Figure 6-1: Flow of participants through the study

Table 6-1: Baseline characteristics of the completers and participants who lost to follow up over ten years in the Tasmanian Older Adult Cohort (TASOAC) Study

<i>Variables</i>	<i>Total sample^a (n=1098)</i>	<i>Retained a ten years^a (n=567)</i>
Age (year)	63 (7.5)	61 (6.6)
Women, N (%)	562 (51.2)	284 (50.1)
Body mass index (kg/m ²)	27.9 (4.8)	27.6 (4.4)
Physical activity (steps/day) ^b	8617 (3356)	9171 (3261)
Energy intake (KJ)	7669 (2835)	7764 (2677)
Fruit and vegetable pattern raw score ^c	170.5 (75.8)	168.9 (70.0)
Animal protein pattern raw score ^c	184.4 (114.3)	186.8 (113.0)
Snack pattern raw score ^c	140.7 (72.8)	139.2 (68.7)
Western pattern raw score ^c	62.3 (41.4)	64.7 (39.9)
Femoral neck BMD (g/cm ²) ^b	0.766 (0.125)	0.776 (0.118)
Hip BMD (g/cm ²) ^b	0.966 (0.156)	0.979 (0.144)
Lumbar spine BMD (g/cm ²) ^b	1.012 (0.174)	1.015 (0.163)
Falls risk z-score ^b	0.185 (0.853)	0.029 (0.758)

KJ kilojoules.

BMD bone mineral density.

^a Values are mean (standard deviation) unless otherwise specified.

^b Missing data: physical activity (n=50), femoral neck BMD (n=5), hip BMD (n=5), lumbar spine BMD (n=6), falls risk z-score (n=8).

^c The range of raw scores for each dietary pattern was 18 to 585 for the fruit and vegetable pattern, 15 to 1250 for the animal protein pattern, 7 to 476 for the snack pattern, and 4 to 381 for the western pattern.

Table 6-2: Linear mixed-effects model for the association between dietary pattern z-scores and falls risk z-scores

	<i>Falls risk z-score</i> <i>β (95% CI)^a</i>
Time (per year)	0.04 (0.04, 0.05)
Fruit and vegetable pattern	
Fruit and vegetable pattern z-scores (per SD) at baseline	-0.05 (-0.09, -0.01)
Fruit and vegetable pattern z-scores (SD) by time (per year)	-0.0003 (-0.01, 0.01)
Animal protein pattern	
Animal protein pattern z-scores (per SD) at baseline	0.01 (-0.03, 0.05)
Animal protein pattern z-scores by time (per year)	-0.003 (-0.01, 0.004)
Snack pattern	
Snack pattern z-scores (per SD) at baseline	-0.03 (-0.07, 0.01)
Snack pattern z-scores by time (per year)	-0.01 (-0.01, 0.002)
Western pattern	
Western pattern z-scores (per SD) at baseline	0.03 (-0.01, 0.07)
Western pattern z-scores by time (per year)	-0.004 (-0.01, 0.002)

β, beta coefficient.

SD, standard deviation.

CI, confidence interval.

Bold denotes statistical significance, p<0.05.

^a Adjusted for age, sex and body mass index at baseline.

There were no associations between any dietary pattern z-scores and FN or hip BMD at baseline (**Table 6-3**). BMD was estimated to reduce by 0.002 (95% CI -0.002, -0.001) g/cm² per annum at the FN, and by 0.004 (95% CI -0.004, -0.003) g/cm² per annum at the hip. The changes in FN and hip BMD were lower over time for every one SD increase in baseline animal protein, and western dietary pattern z-scores (p<0.02 for all). LS BMD increased by 0.001 (95% CI 0.001, 0.002) g/cm² annually. The change in LS BMD was 0.001 g/cm² greater per year for every one SD increase in baseline fruit and vegetable, animal protein and western pattern z-scores (p<0.02 for all) (**Table 6-3**). The association between BMI-adjusted western pattern score LS BMD was similar to that with unadjusted score, with little difference in the estimated coefficient and no change in statistical inference (**Appendix 6-4**). We also compared models for bone density outcomes with and without adjustment for BMI, and there were only small variations in estimated coefficients and no changes in statistical inference (see **Table 6-4**). Baseline scores of fruit and vegetable and snack patterns were associated with a higher risk of LS BMD increasing over ten years (p<0.05 for all) (**Table 6-5**).

There were 259 (45.7%) people having fractures during the follow-up phase. However, there was no evidence for any associations between risk of fracture and baseline scores of any of the dietary patterns before or after adjustment for confounders (**Table 6-6**).

All results for the associations of dietary patterns with falls risk, BMD and fracture were similar for complete case analyses (data not shown) with only small variations in estimated coefficients and no changes in statistical inference.

Table 6-3: Linear mixed-effects model for the association between dietary pattern z-scores and bone mineral density (BMD) (g/cm²)

	<i>Femoral neck BMD</i>	<i>Hip BMD</i>	<i>Lumbar spine BMD</i>
	<i>β (95% CI)^a</i>	<i>β (95% CI)^a</i>	<i>β (95% CI)^a</i>
Time (per year)	-0.002 (-0.002, -0.001)	-0.004 (-0.004, -0.003)	0.001 (0.001, 0.002)
Fruit and vegetable pattern			
Fruit and vegetable pattern z-scores (per SD) at baseline	0.002 (-0.005, 0.008)	0.005 (-0.002, 0.013)	0.009 (-0.001, 0.019)
Fruit and vegetable pattern z-scores (SD) by time (per year)	0.0001 (-0.0004, 0.001)	-0.00001 (-0.001, 0.001)	0.001 (0.0001, 0.001)
Animal protein pattern			
Animal protein pattern z-scores (per SD) at baseline	-0.001 (-0.008, 0.006)	-0.004 (-0.012, 0.004)	-0.001 (-0.011, 0.008)
Animal protein pattern z-scores by time (per year)	0.001 (0.0001, 0.001)	0.001 (0.0004, 0.001)	0.001 (0.001, 0.002)
Snack pattern			
Snack pattern z-scores (per SD) at baseline	0.004 (-0.002, 0.011)	0.007 (-0.001, 0.014)	0.011 (0.001, 0.021)
Snack pattern z-scores by time (per year)	0.0003 (-0.0002, 0.001)	0.0001 (-0.0004, 0.001)	0.0003 (-0.0002, 0.001)
Western pattern			
Western pattern z-scores (per SD) at baseline	-0.001 (-0.008, 0.006)	-0.007 (-0.015, 0.002)	-0.007 (-0.017, 0.003)
Western pattern z-scores by time (per year)	0.001 (0.0001, 0.001)	0.001 (0.0004, 0.002)	0.001 (0.0001, 0.001)

β, beta coefficient; SD, standard deviation; CI, confidence interval.

Bold denotes statistical significance, p<0.05.

^a Adjusted for age, sex and body mass index at baseline.

Table 6-4: Compared models for bone density outcomes (BMD) (g/cm²) with and without adjustment for BMI

	<i>Femoral neck BMD</i>		<i>Hip BMD</i>		<i>Lumbar spine BMD</i>	
	<i>β (p value)^a</i>	<i>β (p value)^b</i>	<i>β (p value)^a</i>	<i>β (p value)^b</i>	<i>β (p value)^a</i>	<i>β (p value)^b</i>
Time (per year)	-0.002 (0.000)	-0.002 (0.000)	-0.004 (0.000)	-0.004 (0.000)	0.001 (0.000)	0.001 (0.000)
Fruit and vegetable (FV) pattern						
FV pattern z-scores (per SD) at baseline	0.002 (0.551)	0.002 (0.612)	0.006 (0.180)	0.005 (0.191)	0.009 (0.067)	0.009 (0.079)
FV pattern z-scores (SD) by time (per year)	0.0001 (0.777)	0.0001 (0.746)	-0.00001 (0.970)	-0.00001 (0.979)	0.001 (0.016)	0.001 (0.016)
Animal protein (AP) pattern						
AP pattern z-scores (per SD) at baseline	0.001 (0.705)	-0.001 (0.799)	0.001 (0.903)	-0.004 (0.352)	0.001 (0.767)	-0.001 (0.798)
AP pattern z-scores by time (per year)	0.001 (0.013)	0.001 (0.014)	0.001 (0.000)	0.001 (0.000)	0.001 (0.000)	0.001 (0.000)
Snack pattern						
Snack pattern z-scores (per SD) at baseline	0.003 (0.367)	0.004 (0.208)	0.005 (0.254)	0.007 (0.073)	0.010 (0.064)	0.011 (0.039)
Snack pattern z-scores by time (per year)	0.0003 (0.301)	0.0003 (0.274)	0.0001 (0.648)	0.0001 (0.585)	0.0003 (0.278)	0.0003 (0.259)
Western pattern						
Western pattern z-scores (per SD) at baseline	-0.001 (0.813)	-0.001 (0.843)	-0.007 (0.132)	-0.007 (0.110)	-0.007 (0.199)	-0.007 (0.182)
Western pattern z-scores by time (per year)	0.001 (0.017)	0.001 (0.017)	0.001 (0.000)	0.001 (0.000)	0.001 (0.018)	0.001 (0.017)

β, beta coefficient; SD, standard deviation; CI, confidence interval. Bold denotes statistical significance, p<0.05.

^a Adjusted for age and sex at baseline.

^b Adjusted for age, sex and body mass index at baseline.

Table 6-5: Log binomial regression model for the association between dietary pattern z-scores and category of change in lumbar spine bone mineral density (LS BMD) over ten years

	LS BMD*	
	<i>Unadjusted model</i>	<i>Adjusted model</i>
	<i>RR (95% CI)</i>	<i>RR (95% CI)^a</i>
Fruit and vegetable pattern z-scores	1.16 (1.14, 1.18)	1.06 (1.03, 1.09)
Animal protein pattern z-scores	1.06 (1.05, 1.07)	1.01 (0.94, 1.09)
Snack pattern z-scores	1.13 (1.06, 1.21)	1.05 (1.00, 1.11)
Western pattern z-scores	1.08 (1.07, 1.10)	1.00 (0.93, 1.06)

RR, relative risk.

CI, confidence interval. BMD: bone mineral density.

^a Adjusted for age, sex and body mass index at baseline.

* The LS BMD is coded as a binary variable representing category of change in LS BMD over ten years: each person was coded as '0' if their LS BMD did not change/decreased LS (reference) or '1' if their LS BMD increased.

Table 6-6: Log binomial regression model for the association between dietary pattern z-scores and incident fracture

	Incident fracture	
	<i>Unadjusted model</i>	<i>Adjusted model</i>
	<i>RR (95% CI)</i>	<i>RR (95% CI)^a</i>
Fruit and vegetable pattern z-scores	0.91 (0.77, 1.07)	0.92 (0.78, 1.08)
Animal protein pattern z-scores	1.00 (0.86, 1.15)	1.13 (0.99, 1.28)
Snack pattern z-scores	0.90 (0.76, 1.06)	0.91 (0.76, 1.08)
Western pattern z-scores	0.95 (0.81, 1.11)	1.09 (0.94, 1.27)

RR, relative risk.

CI, confidence interval.

^a Adjusted for age, sex and body mass index at baseline.

6.4 Discussion

This longitudinal study identified several osteoporosis-related outcomes that could be influenced by dietary patterns, including for the first time, falls risk. A fruit and vegetable dietary pattern could be beneficial for falls risk and intake of an animal protein or a western pattern could be beneficial for reducing losses in FN and hip BMD. Higher intake of fruit and vegetable, animal protein, and western patterns could add to gains in LS BMD over time, but the clinical interpretation of this is unclear as LS BMD can increase with degenerative change in older people. There were no associations of any dietary pattern z-scores with incident fractures, so these modest effects on falls and BMD did not appear to translate into an improved fracture risk.

A novel finding of our study is that a higher intake of foods comprising a fruit and vegetable (healthy) dietary pattern could be helpful for a 5% reduction of falls risk in older adults. The potential importance of a healthy dietary pattern in reducing falls has been largely ignored in elderly people, with no previous studies reporting associations of dietary patterns using the a posteriori method with falls risk. However, our data is consistent with studies that have examined the associations of dietary patterns with major falls risk factors. In these other studies, higher scores of a healthy pattern (termed healthy ⁽²⁰²⁾, prudent ⁽²⁰³⁾, Mediterranean ^(204, 205), seafood and vegetable ⁽²⁰⁶⁾ and mushroom, vegetable and fruit ⁽²⁰⁷⁾) were associated with a lower risk of frailty ^(202, 203), sarcopenia ⁽²⁰⁴⁾ (a condition characterized by the loss of skeletal muscle mass and strength due to ageing) ⁽²⁰⁸⁾, cognitive impairment ^(206, 207) and faster gait speed ⁽²⁰⁵⁾.

Our study is the first longitudinal study examining the association of an animal protein pattern using the a posteriori method with BMD in older people, finding a positive association between an animal protein pattern and FN BMD. In contrast, cross-sectional studies ^(90, 96) have found no associations of dietary protein patterns (termed meat, dairy and bread pattern ⁽⁹⁰⁾ and pattern 1 ⁽⁹⁶⁾) and FN BMD. Similarly, there was a positive association between animal protein pattern and LS BMD in our study but a negative relationship of these variables in another study ⁽⁹⁶⁾. The inconsistent results could be explained by the study design mentioned above but also the different food components of the patterns. While our study shared similar major food items such as red/processed meat, poultry, and fish with the other studies ^(90, 96), dairy products were included in the patterns of these two studies^(90, 96) but not in ours. As there are a limited number of studies examining the role of dietary protein patterns on bone health, there is a need for more longitudinal or intervention studies investigating this issue in elderly people to clarify our results.

There is also conflicting evidence for the associations of other dietary patterns with BMD (3 cohort ^(86, 88, 99) and 6 cross-sectional ^(81, 85, 90-92, 96)) and fracture (4 cohort ^(84, 89, 92, 97), 1 case-control ⁽⁸²⁾ and 1 cross-sectional ⁽¹¹³⁾) in older people. For example, a higher score of healthy patterns (variously named healthy ⁽⁸¹⁾, fruit, vegetable and cereal ⁽⁹⁰⁾, health-conscious ⁽⁸⁸⁾, dairy and fruit ⁽⁹¹⁾, and dietary pattern 4 ⁽⁹⁶⁾) was positively associated with FN BMD in two studies ^(88, 90) compared with no association in our longitudinal study and others ^(81, 91, 96). A negative association of a snack pattern score with both FN and LS BMD was found in a Scottish study ⁽⁸¹⁾ in comparison to no association of these variables in our Australian study and an Iranian study (dietary pattern 6) ⁽⁹⁶⁾. A western pattern (titled western ⁽⁸⁴⁾, sweet,

animal fat and low meat ⁽⁹²⁾, high fat ⁽⁸²⁾ and energy-dense ⁽⁸⁹⁾) has been associated with an increased risk of fracture in two studies ^(82, 92) but not in ours and other studies ^(84, 89). These inconsistent results could be explained by factors such as differences in study design mentioned above, methods used to calculate diet scores, and variations in the foods composing dietary patterns across studies. Standardized dietary pattern scores were used in ours and other studies ^(88, 89, 92) compared with unstandardized scores ⁽⁸¹⁾, mean scores ⁽⁹⁰⁾, and category scores (two levels ⁽⁹⁶⁾, tertiles ⁽⁸²⁾ and quintiles ^(84, 91)). A healthy pattern is mainly composed of fruits and vegetables among studies, but there are still some different items such as sweet-based products and red meats ⁽⁹⁰⁾, soups and sauces ⁽⁸⁸⁾, and rice/pasta ⁽⁸¹⁾. Snacks and nuts are the major food components in a snack food pattern, however, we have included other different food groups, for instance, tea and coffee ⁽⁹⁶⁾ and fruits and cereals in our study. A western pattern is characterized by high consumption of red/processed meats and sweet products, but differs in other foods including whole grains ⁽⁹²⁾, pulses and soups ⁽⁸¹⁾.

In our cohort, LS BMD increased over ten years, suggesting a role for degenerative change of the lumbar spine that may lead to misinterpretation of BMD in older adults ⁽²⁰⁹⁾. Higher scores of the fruit and vegetable, animal protein, and western dietary pattern were all associated with increases in LS BMD suggesting these findings may be osteoarthritis rather than osteoporosis as we would expect BMD to decrease over time in those without osteoarthritis. Therefore, the clinical interpretation of our findings is difficult – increasing LS BMD may be beneficial if some of the increase is due to slowing of age-related bone loss, but detrimental if due to accelerated degenerative change. This, and the modest magnitude of the

BMD associations in this study, may explain why the BMD effects seen did not translate to reductions in fracture. There is a lack of studies investigating the potential role of nutrition in slowing down the in LS BMD diagnosed using lateral scans ⁽²¹⁰⁾, therefore, this issue needs to be investigated in future research.

It was inconsistent evidence for the role of obesity or overweight on bone health ⁽¹⁹⁹⁾. For example, a recent Mendelian Randomization Study found that there was a positive association between BMD and BMI in men, but not for postmenopausal women ⁽²⁰⁰⁾. Moreover, the loss of muscle mass in older adults may indicate that the prediction of body fat using BMI to determine whether obesity causes changes in bone mass is less accurate ⁽¹⁹⁹⁾. However, our results were similar regardless of whether we adjusted for BMI. We also ran two models with and without adjustment for BMI, and there were only small variations in estimated coefficients and no changes in statistical inference.

Study strengths and limitations

In our study, we provide new findings regarding dietary pattern scores and falls risk, BMD, and incident fractures in a large population-based cohort study of older adults. The study does have limitations. The variation of dietary patterns derived across studies is a barrier to directly comparing results of different studies, although our dietary patterns are similar to others reported in the literature in terms of major food items. We had missing data as in all longitudinal studies. However, multiple imputation and inverse probability weighting methods were used to take missing data into account and the results were largely similar to those using complete-case analysis, suggesting a minor impact of missing data on our findings. Results may

not be generalisable to people with weights over 130 kg as they were excluded from the TASOAC study.

The accuracy of a self-report fracture has been demonstrated for several important osteoporotic fractures (e.g. hip, wrist, or humerus) ⁽¹⁵⁰⁾. However, a high false-positive rate occurred at the spine due to pain caused by spinal osteoarthritis, degenerative disc disease, or skeletal irregularities ⁽²¹¹⁾. Our data did not have enough number of fractures by sites, so we used the number of total fractures for our current analysis. However, there were a small number of vertebral fractures (5/875 of phase 2, 7/768 of phase 3, 9/567 of phase 4). It is unlikely to bias our results.

A self-report FFQ was popularly used to measure dietary intake over 12 months due to low cost and time-saving in previous epidemiology studies although it recalls bias and requires the evaluated accuracy for designing the questionnaire ⁽¹⁴²⁾. Our FFQ is validated. We did not use it to categorise people but use scores as the continuous variables. Therefore, it is unlikely to have the potential error impacting our results.

Analysis by spine BMD change: There are not enough cases to analyse results separately for individuals who displayed an increase in spine BMD over time (n=309).

6.5 Conclusion

In conclusion, a fruit and vegetable dietary pattern may be beneficial for reducing falls risk. The associations of dietary patterns and BMD are modest in magnitude and did not translate into an improved fracture risk. Associations between diet and LS BMD may reflect osteoarthritis rather than osteoporosis.

**Chapter 7: Summary of findings and future
directions**

7.1 Summary of findings

Fracture is a major public health issue in older adults ⁽²¹²⁾ due to the substantial economic burden they place on health care services, rehabilitation, and community services. Low bone mineral density (BMD) and falls are the two major risk factors for fractures ⁽¹⁹⁾; therefore, focusing on the prevention of these factors may, in turn, reduce the incidence of fractures.

Diet is an important modifiable factor for maintaining bone health and preventing falls, and dietary pattern analysis is a promising approach in the current nutritional epidemiology when investigating the role of overall diet in improving health outcomes ⁽⁷⁰⁾. Limited longitudinal research has been done to examine the association between dietary patterns and musculoskeletal health in older adults and the findings remain controversial.

Chapter 3 reports the findings of a systematic review and meta-analysis to synthesize current evidence of the associations of dietary patterns with fractures and BMD in healthy adults from 23 observational studies (6 cohort studies in older adults ^(84, 88, 89, 92, 97, 99)). This review showed strong evidence for a beneficial association between healthy dietary pattern and hip fracture (pooled risk ratio (RR) = 0.73: 95% confidence interval (CI) 0.56, 0.96, $I^2 = 95\%$). There were inconsistent findings for associations between a) western diet and hip fracture, b) any dietary pattern and total fracture, or c) any dietary pattern with all sites of BMD and total body bone mineral content (TBBMC). However, no studies demonstrated either a beneficial effect of western patterns or a detrimental effect of healthy patterns on bone health. These results suggest that a healthy diet may be beneficial for reducing

the occurrence of hip fracture. However, the inconsistent findings mentioned above need further investigations, particularly by high quality longitudinal or intervention studies.

Chapter 5 and 6 examined the longitudinal associations of dietary patterns with sociodemographic characteristics, lifestyle factors and osteoporosis-related outcomes (falls risk, BMD, and fracture) in the Tasmanian Older Adult Cohort (TASOAC) study. The main findings are summarised below:

Four dietary patterns were identified, comprised predominantly of the following food groups: fruit and vegetable pattern (vegetables, fruits, potatoes, breakfast cereals excluding muesli and porridge); animal protein pattern (red and processed meats, fish, poultry); snack pattern (snacks, sweets, nuts and condiments); and western dietary pattern (pizzas, hamburgers, meat pies, and sweets).

Men and current smokers had lower baseline fruit and vegetable and snack pattern scores but higher baseline western and animal protein pattern scores. There was an increasing difference in animal protein pattern score by genders over time ($\beta = 0.27$ (95% CI 0.06, 0.48) unit per 1000KJ per year). There were positive associations between snack pattern score and age and physical activity, but the effect of age was reduced over time by 0.02 (95% CI -0.03, -0.001) unit per 1000KJ per year. Higher baseline scores of the animal protein and western patterns were negatively associated with age, but the effect of age on the western scores was less over time by 0.01 (95% CI 0.004, 0.02) unit per 1000KJ per year. Being retired was associated with lower baseline scores of animal protein pattern and people living in socially disadvantaged areas had higher baseline western pattern scores.

Fall risk z-score increased over time but this increase was reduced annually for each standard deviation (SD) increase in baseline fruit and vegetable pattern scores ($\beta = -0.05$ (95% CI -0.09, -0.01)). There were no associations of fall risk z-scores with other dietary patterns.

Femoral neck (FN) and hip BMD reduced over time ($\beta = -0.002$ (95% CI -0.002, -0.001) and $\beta = -0.004$ (95% CI -0.004, -0.003) g/cm² per annum, respectively), and the changes in FN and hip BMD were less for each SD increase in baseline animal protein and western pattern z-scores. Lumbar spine (LS) BMD increased over time by 0.001 (95% CI 0.001, 0.002) g/cm² annually), and this change in LS was positively associated with higher baseline scores of fruit and vegetable, animal protein, and western patterns.

People with higher baseline scores of fruit and vegetable and snack patterns were more likely to have an increase in LS BMD rather than a decrease or no change (RR for increase = 1.06 (95% CI 1.03, 1.09) and RR=1.05 (95% CI 1.00, 1.11), respectively).

There was no association between an incident fracture and any dietary pattern.

In summary, existing literature suggests that a healthy dietary pattern may be beneficial to the prevention of hip fracture but the impacts of other dietary patterns on fracture and BMD are unclear. The substantial heterogeneity suggests this needs further examination. In support of this, the analysis from TASOAC showed that a fruit and vegetable (healthy) dietary pattern may be associated with a reduced falls risk in older adults. However, in the TASOAC cohort, associations of dietary

patterns and BMD were modest in magnitude and did not translate into an improved fracture risk. Associations between diet and LS BMD may reflect osteoarthritis rather than osteoporosis. Being men, current smokers, retirees, and people residing in a disadvantaged area had higher baseline scores of the unhealthy patterns (western and/or animal protein).

7.2 Implications and future directions

7.2.1 Implications

By summarising existing evidence from the best synthesis and meta-analysis of Chapter 3 (multiple cohort ^(84, 88, 89, 92, 97, 102, 105, 107, 110) and case-control studies ⁽⁸²⁾) and analysing TASOAC study (Chapter 5 and 6), the current observational studies suggest that eating a healthy diet and avoiding western dietary pattern is unlikely to be detrimental to BMD/fracture, and in particular that a healthy dietary pattern (that is a diet, high in fruits, vegetables, nuts, fish, whole grain and legumes and low in red meats, processed meats, fats, sweets, take away foods and soft drinks) may be beneficial for the prevention of hip fracture (Chapter 3) and for falls risk (Chapter 6). Importantly, the fruit and vegetable dietary pattern (healthy pattern) identified using the principal-component factor estimation method closely is very consistent with current Australian guidelines which advises high intake of fruits, vegetables and grain (cereal) foods ⁽¹³⁸⁾. Therefore, it seems reasonable to recommend the healthy dietary pattern in dietary guidelines for maintaining bone health, especially given the known wide-ranging health benefits of improving diet quality for the prevention of other chronic diseases.

Additionally, the unhealthy patterns (animal protein pattern having a high intake of red/ processed meats and a western pattern having a high consumption of pizzas, hamburgers, meat pies, and sweets) were associated with being a man, a current smoker, retiree and those experiencing social disadvantage in older adults (Chapter 5). These may therefore be the appropriate target groups for nutritional intervention programs to improve bone health and a broad range of diet-related outcomes, such as cardiovascular diseases. This information may also help to develop dietary guidelines or recommendations for ‘high-risk’ population groups to encourage the adoption of a healthy diet. Such messages might include emphasising the need to reduce consumption of processed and takeaway foods and increase consumption of fruit and vegetables, but strategies to overcome potential practical difficulties in the uptake of this advice also require consideration. The barrier to adopt the healthy eating may involve the cost of healthy foods, the meal sizes for the whole family, the habit to eat foods away from home, food environment barriers and geographic isolation, and difficulty avoiding unhealthy food at community venues ⁽²¹³⁾. Additionally, there are further factors that challenge nutritional status older adults such as reduced energy expenditure, physiological change (e.g. hormonal, cytokines, taste/smell) and pathological change (medical, social, psychological) ⁽²¹⁴⁾. These also pose hurdles that would need to be overcome in any intervention program.

7.2.2 Future directions

7.2.2.1 Issues requiring further research

Substantial heterogeneity in observational studies

Substantial heterogeneity ($I^2=95\%$) was noted in the meta-analysis of the association of a healthy dietary pattern with hip fracture (Chapter 3) highlighting a requirement for a careful examination of the sources of heterogeneity. Such an examination may shed new light on: a) the identification of subgroups with specific characteristics, for whom improving healthy or reducing unhealthy dietary patterns may have a larger role in improving bone health, and b) important clinical or methodological differences that may reduce the comparability between dietary pattern studies, which could also inform the design of future studies.

The heterogeneity was significantly reduced to 67% in the subgroup analysis of which fracture ascertained by a medical examination (Chapter 3), however, this investigation of potential heterogeneity is by nature exploratory, and in turn these results should be interpreted with caution ⁽²¹⁵⁾. Further investigation of the heterogeneity by other characteristics was not feasible in this systematic review due to the limited number of studies currently available (e.g., age, sex, ethnic, country and study design), but will be warranted as more studies become available.

The conflicting findings of the relationship between dietary patterns and bone outcomes

The conflicting findings of the relationship between dietary patterns and all sites of BMD, TBBMC and total fracture that are solely based on the cross-sectional studies (Chapter 3) suggest that further research is needed to resolve the question of what effect dietary patterns may have on these outcomes. RCT of interventions would be needed to definitively assess the effect of having a high intake of a healthy dietary pattern and low intake of a western dietary pattern on bone health. However, such intervention studies may be logistically difficult as seen in previous clinical trials ⁽²¹⁶⁾. Such RCTs are limited and have mainly been conducted for cardiovascular outcomes ⁽¹⁴⁰⁾. In the absence of such RCTs, more cohort studies could help clarify the associations between dietary patterns and these bone outcomes in elderly people. The research method of Mendelian randomisation using genetic variants as natural experiments could also help to explore the causal relationship between modifiable risk factors and these outcomes in the observational studies ⁽²¹⁷⁾. Such studies would provide stronger evidence to support dietary recommendations for bone health.

Potential for dietary patterns to impact on osteoarthritis

An increase in lumbar spine BMD relating to the degenerative spine disease in older adults that may reflect osteoarthritis rather than osteoporosis (Chapter 6). However, there were no previous studies examining the association between dietary patterns and the slowing down of degenerative spine progression diagnosed using Lumbar X-rays which include a full series of standing anterior-posterior pelvis and lateral

flexion-extension views ⁽²¹⁰⁾, so this needs to be investigated in future cohort/RCT research. Moreover, these studies also need to clarify the effect of dietary patterns in osteoarthritis treatment, not just of single nutrients as previously done ⁽²¹⁸⁾.

Dietary patterns and falls

Importantly, data from the TASOAC for the first time showed that a higher fruit and vegetable (healthy) dietary pattern score was associated with lower falls risk z-score in older adults (Chapter 6). However, the Physiological Profile Assessment does not directly measure the incidence of falls (which was not measured in TASOAC study) and there were no previous studies examining the association between dietary patterns and incident falls in elderly people. Prospective data for the incidence of falls is required to confirm the association between dietary patterns and falls risk in older people. In addition, the combination of nutrition and physical activity is recommended to maintain muscle strength ⁽¹³⁸⁾, which is an important contributor to improving balance and reducing falls ⁽²¹⁹⁾. Therefore, future clinical trials may need to consider important co-interventions for the prevention of falls.

7.2.2.2 Methodological consideration for future research

FFQ used to measure dietary intakes

Methodological factors are critically important when conducting, interpreting, and comparing findings of dietary pattern studies. Most previous studies in adults used food frequency questionnaires (FFQs) to assess dietary intake (Chapter 3). This method may be suitable for epidemiological studies but is subject to recall bias and requires accurate evaluation of developed questionnaires ⁽¹⁴²⁾. Additionally, there

are variations across and within the FFQs used in these studies in terms of food items and food groups. All these factors could contribute to the differences in dietary pattern components observed and may have also reduced comparability across studies. Consequently, future research should consider better methods for measuring dietary intakes, such as the combined methods of FFQ and 24h record to measure dietary intake ⁽²²⁰⁾.

The statistical methods used to derive dietary patterns

The various statistical methods used to derive dietary patterns could also contribute to the inconsistent associations discovered between dietary patterns and bone outcomes ⁽⁸⁵⁾. Most studies used a single method (e.g. principal component analysis, cluster analysis or factor analysis) to identify dietary patterns in the literature (Chapter 3). Depending on the research questions (as discussed in Chapter 1.2.3), a specific method could be more appropriate based on its strengths and limitations. Therefore, there is no one-size-fits-all method for identifying dietary patterns and the application of different methods between studies should be considered when comparing their results. Future studies should consider ways to reduce heterogeneity sources and improve comparability across studies thereby better clarifying the role of dietary patterns on reducing fracture risk. Use of different methods might also add different aspects to our knowledge. Selection of the method to identify dietary patterns relates to the purpose of analysis. Factor analysis method was used to derive dietary pattern in our research, in order to explore dietary patterns without making a priori assumptions ⁽⁷⁰⁾, but for example, reduced rank regression (RRR) derives dietary patterns that may contribute to disease risk through specified causal pathways ⁽⁷⁷⁾. Therefore, this RRR method

may help to explain better understanding for the effects of diet on the development of diseases in future research ⁽²²¹⁾.

An alternative to using self-reported dietary intake is to use patterns of nutritional biomarkers. Dietary intake from a self-reported questionnaire is prone to be bias or loss of power seen in nutritional epidemiology in comparison to an error reduction for diet using biomarkers ⁽²²²⁾. Nutritional biomarkers provide a more accurate measure of nutrient status compared with dietary intake ⁽²²³⁾. Nutritional biomarkers could also be used to categorise individuals into certain patterns of nutrient intake. They could also be used to verify adherence/non-adherence to predetermined diet scores ⁽²²⁴⁾. Such biomarkers can be measured in different biological samples (e.g. plasma, urine, serum) as indicators of nutritional status relating to intake or metabolism of dietary constituents ⁽²²⁵⁾. For example, plasma alkylresorcinols levels relate to whole-grain food consumption and carotenoids to fruit and vegetable intake.

The associations of dietary patterns and fractures identified from medical records

A healthy pattern score was associated with a 36% reduced risk of hip fracture in the subgroup analysis of which studies ascertained fractures using a medical record vs self-report (Chapter 3) compared to a 27% reduction overall. A self-reported questionnaire was used to identify participants' fractures given in Chapter 6 because radiological confirmation was not available in our data. It may be subject to recall bias, so ascertainment of fractures from medical records rather than self-

report may be more accurate ⁽¹⁵⁰⁾ and in future research this approach is recommended.

The associations of dietary patterns and physical activity

Physical activity was associated with higher snack pattern score, but no other dietary patterns in our longitudinal data (Chapter 5). However, physical activity was assessed using a pedometer which does not measure the intensity of physical activities compared with an accelerometer ⁽²²⁶⁾. Given the wide availability and acceptability of accelerometer devices, it is therefore suggested that future research should examine the relationship between dietary patterns with different intensities of physical activity using an accelerometer.

7.2.2.3 What messages could be targeted and to whom

Low consumption of a healthy diet (fruit and vegetable pattern) and high intake of a western dietary pattern were found in men and current smokers. The retired participants had a low intake of animal protein pattern and people living in socially disadvantaged areas had a high consumption of the western diet. For Australian dietary guideline, it may recommend the consumption of the fruit and vegetable or healthy dietary pattern and avoiding western dietary pattern to improve bone health for older adults. Men, smokers, retirees and those experiencing social disadvantage are the target population for the intervention program due to a lower score of the healthy dietary pattern (Chapter 5). However, there are some factors that may influence their practical difficulty to adopt certain dietary patterns. Factors that challenge nutritional status in older adults are a reduced energy expenditure,

physiological change (e.g. hormonal, cytokines, taste/smell) and pathological change (medical, social, psychological) ⁽²¹⁴⁾. Moreover, malnutrition may contribute to the development of clinical syndromes or chronic diseases including sarcopenia, frailty and osteoporosis in the elderly ⁽²²⁷⁾. Therefore, the future RCTs for improving bone health should consider these issues to make a better intervention for older adults.

7.2.2.4 Conclusion

In summary, a healthy dietary pattern may be beneficial in the prevention of hip fracture, but more studies are needed to clarify the potential heterogeneity sources that have the greatest impact on this outcome. RCTs would be the best study design to confirm the associations of dietary patterns and these bone outcomes, but they are very costly and difficult to perform. Carefully designed cohort studies might help fill this gap, to examine the associations of dietary patterns with BMD, TBBMC, the incidence of falls, total fracture, or any specific site of fractures. These should be carefully conducted taking into consideration important methodological factors including more accurate methods of assessing dietary intake and fracture outcomes.

Appendices

Appendix 3-1: Search methods for identification of studies

We searched the electronic bibliographical databases Medline and Embase via OVID, CENTRAL (Cochrane) and Proquest: theses and dissertations with key words relating to dietary patterns, bone mineral density, and fracture. We limited the search to adults, English language and human subjects. The full search strategy for each database is given below.

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>
Date Run: 12/05/17

- 1 exp feeding behavior/
- 2 "diet* pattern*".tw.
- 3 "diet* factor*".tw.
- 4 "diet* habit*".tw.
- 5 "eat* habit*".tw.
- 6 "eat* behavi?or*".tw.
- 7 "eat* pattern*".tw.
- 8 "food habit*".tw.
- 9 "food pattern*".tw.
- 10 "feed* behavi?or*".tw.
- 11 "feed* pattern*".tw.
- 12 "nutri* pattern*".tw.
- 13 "nutri* habit*".tw.
- 14 or/1-13
- 15 exp bone density/
- 16 "bone densit*".tw.
- 17 "bone mineral densit*".tw.
- 18 "bone density test*".tw.
- 19 BMD.tw.
- 20 "BMD test*".tw.
- 21 "bone loss*".tw.
- 22 "bone mass*".tw.

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- 23 "bone disease*".tw.
- 24 BMC.tw.
- 25 "bone mineral content*".tw.
- 26 exp osteoporosis/
- 27 osteoporo*.tw.
- 28 or/15-27
- 29 exp fracture, bone/
- 30 fracture*.tw.
- 31 "bone fracture*".tw.
- 32 "broken bone*".tw.
- 33 "osteoporo* fracture*".tw.
- 34 exp osteoporotic fractures/
- 35 or/29-34
- 36 28 or 35
- 37 14 and 36
- 38 limit 37 to (english language and humans)
- 39 limit 38 to "all adult (19 plus years)

Database: Ovid Embase <1974 to 2017 May 11>

Date Run: 12/05/17

- 1 exp feeding behavior/
- 2 "diet* pattern*".tw.
- 3 "diet* factor*".tw.
- 4 "diet* habit*".tw.
- 5 "eat* habit*".tw.
- 6 "eat* pattern*".tw.
- 7 "eat* behavi?or*".tw.
- 8 "food habit*".tw.
- 9 "food pattern*".tw.
- 10 "feed* behavi?or*".tw.
- 11 "feed* pattern*".tw.
- 12 "nutri* pattern*".tw.
- 13 "nutri* habit*".tw.
- 14 or/1-13
- 15 exp bone density/
- 16 "bone densit*".tw.

- 17 "bone mineral densit*".tw.
- 18 "bone density test*".tw.
- 19 BMD.tw.
- 20 "BMD test*".tw.
- 21 "bone loss*".tw.
- 22 "bone mass*".tw.
- 23 "bone disease*".tw.
- 24 BMC.tw.
- 25 "bone mineral content*".tw.
- 26 exp osteoporosis/
- 27 osteoporos*.tw.
- 28 exp bone densitometry/
- 29 or/15-28
- 30 exp fracture/
- 31 fracture*.tw.
- 32 "bone fracture*".tw.
- 33 "broken bone*".tw.
- 34 "osteoporo* fracture*".tw.
- 35 exp osteoporotic fractures/
- 36 exp fragility fracture/
- 37 "fragility fracture*".tw.
- 38 or/30-37
- 39 29 or 38
- 40 14 and 39
- 41 limit 40 to (human and english language)
- 42 limit 41 to (adult <18 to 64 years> or aged <65+ years>)

Database: Central (Cochrane)

Date Run: 13/05/17 06:06:41.96

ID	Search Hits
#1	MeSH descriptor: [Feeding Behavior] explode all trees
#2	"diet* pattern*"
#3	"diet* factor*"
#4	"diet* habit*"
#5	"eat* habit*"
#6	"eat* behavi*or*"
#7	"eat* pattern*"
#8	"food* habit*"
#9	"food* pattern*"
#10	"feed* behavi*or*"
#11	"feed* pattern*"
#12	"nutri* pattern*"
#13	"nutri* habit*"
#14	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13
#15	MeSH descriptor: [Bone Density] explode all trees
#16	"bone densit*"
#17	"bone mineral densit*"
#18	"bone density test*"
#19	BMD
#20	"BMD test*"
#21	"bone loss*"
#22	"bone mass*"
#23	"bone disease*"
#24	BMC
#25	"bone mineral content*"
#26	MeSH descriptor: [Osteoporosis] explode all trees
#27	osteoporo*
#28	#15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27
#29	MeSH descriptor: [Fractures, Bone] explode all trees
#30	fracture*
#31	"bone fracture*"
#32	"broken bone*"
#33	"osteoporo* fracture*"
#34	MeSH descriptor: [Osteoporotic Fractures] explode all trees
#35	#29 or #30 or #31 or #32 or #33 or #34
#36	#28 or #35
#37	#14 and #36

Database: Proquest Dissertations & Theses A&I <1927-2017 May 13>

Date Run: 13/05/17 06:06:41.96

("diet* pattern*" OR "diet* factor*" OR "diet* habit*" OR "eat* pattern*" OR "eat* habit*" OR "eat* behavi?or*" OR "food* habit*" OR "food* pattern*" OR "feed* behavi?or*" OR "feed* pattern*" OR "nutri* pattern*" OR "nutri* habit*")
AND (("bone densit*" OR "bone mineral densit*" OR "bone density test*" OR "bmd" OR "bmd test*" OR "bone mineral content*" OR "bmc" OR "bone loss*" OR "bone mass*" OR "bone disease*" OR "osteoporo*") OR ("fracture*" OR "bone fracture*" OR "broken bone*" OR "osteoporo* fracture*"))

Appendix 3-2: The methodological quality assessment of the included studies

The criteria for the methodological quality assessment is given in two parts. Part A lists the criteria and indicates whether each criterion addresses internal validity (V) or informativeness (I) or both. Part B gives the method of scoring each criterion. All items are scored into four categories: + positive (design or conduct adequate); - negative (design or conduct inadequate); ? unclear (item insufficiently described); NA (not applicable). Studies with methodological assessment scores over 60% are considered high quality.

Criteria – Part A	V/I
<i>Study design</i>	
a. Prospective cohort/RCTs study was used	V
b. The percentage of withdrawals $\leq 20\%$	V
c. Information about completers vs withdrawals	I
d. Duration of the study reported (date of start and completion)	I
<i>Study population</i>	
e. Description of relevant inclusion and exclusion criteria for selection of participants	I
f. Selection participants before outcomes (bone mineral status and fracture) assessed	V
g. Nonbiased selection of participants and with exclusion criteria applied equally to all	V
h. Sufficient description of characteristics of participants at baseline	I
i. Response rate of participants $\geq 80\%$ or $\geq 60\%$ and known characteristics of responders and non-responders comparable	I

Assessment of dietary patterns (exposures)

- | | | |
|----|--|---|
| j. | Method used to measure dietary intake is valid | V |
| k. | Dietary intake was measured identically in entire studied population | V |
| l. | An appropriate empirical approach to identify dietary patterns is described | V |
| m. | Description of an appropriate method for calculation of dietary pattern scores | I |

Assessment of bone density (outcome)

- | | | |
|----|---|---|
| n. | An appropriate method of bone density measurement was used and performed according to a standardised protocol | V |
| o. | Bone density measured at clinically relevant sites | I |

Assessment of fracture (outcome)

- | | | |
|----|---|---|
| p. | Protocol described valid method of fracture assessment | V |
| q. | Clinically relevant fracture sites measured | I |
| r. | Method of fracture measurement is identical for entire study population | V |

Analysis and data presentation

- | | | |
|----|--|---|
| s. | Data presented for bone density and/or fracture outcomes | I |
| t. | Appropriate statistical tests used | V |
| u. | Adjusted for key confounders | V |
| v. | Description of an appropriate method for dealing with missing data | I |

V = criterion on validity / precision; I = criterion on informativeness

Specific criteria list for the quality assessment of methodology (see criteria – Part A above)

Criteria – Part B	
<i>Study design</i>	
a.	<p>Adequate if prospective cohort or RCTs was used. Also positive in case of a historical (retrospective) cohort when the determinants were measured before the outcome was determined.</p> <p>Unclear if a historical cohort was used, considering determinants at baseline which were not related to the primary research question for which the cohort was created or in case of ambispective design. Also unclear if insufficient information about trial design and randomisation.</p>
b.	<p>Adequate if the total withdrawal rate $\leq 20\%$.</p> <p>Not applicable if study design was not prospective cohort or RCTs.</p>
c.	<p>Adequate if at least 2 out of 5 following information were described for completers and withdrawals:</p> <ul style="list-style-type: none"> - Age - Sex - BMI - Dietary patterns - Bone mineral status or fracture <p>Not applicable if study design was not prospective cohort or RCTs.</p>
d.	Adequate if the study date of start and completion was described.
<i>Study population</i>	
e.	Adequate if relevant inclusion and exclusion criteria were formulated.
f.	<p>Adequate if the study population was selected before bone mineral density and fracture status were measured.</p> <p>Also adequate if (sub-) groups were selected at a uniform point in the study.</p>
g.	Adequate if participants were selected from the same population (primary study base) and exclusion criteria were equally applied to all participants.
h.	Adequate if bone mineral status or fracture and at least 7 out of 13 items below were presented:

	<ul style="list-style-type: none"> - Age (mean, sd) - Sex - BMI (mean, sd) or height and weight - Smoking status - Physical activity - Energy intake - Medical history - Medication intake - Fall history - Fracture history - Place of recruitment - Sampling frame of source population (identified community, hospital or general population) - Sample size
i.	Adequate if response rate $\geq 80\%$ or $\geq 60\%$ and known characteristics of responders and non-responders sufficiently comparable to suggest minimal selection bias
<i>Assessment of dietary patterns (exposures)</i>	
j.	Adequate if dietary intake using a validated method such as 24-hour recall, diet record or validated food frequency questionnaire.
k.	Adequate if dietary intake was measured in an identical way for the whole studied population.
l.	Adequate if dietary patterns were identified from a validated empirical approach such as factor analysis, principal component analysis, cluster analysis, reduced rank regression or partial least-squares regression.
m.	Adequate if dietary pattern scores were calculated using a valid method such as sum score by factor, weighted sum score, regression score or Bartlett score.
<i>Assessment of bone density (outcome)</i>	
n.	Adequate if an appropriate method of bone density measurement such as Dual Energy X-ray absorptiometry (DXA), Quantitative computed tomography (QCT) or ultrasound was performed identically for each participant following a standardised protocol.
o.	Adequate if bone mineral density was measured at one or more following sites: lumbar spine, total hip, femoral neck, distal radius or forearm and if total body bone mineral content was measured.

<i>Assessment of fracture (outcome)</i>	
p.	Adequate if fracture assessment using a valid method was described. (For radiological vertebral fracture measurement must use CT, X-ray, DXA-based vertebral morphometry or MRI, other fractures must have been confirmed from radiology)
q.	Adequate if fracture was measured at one or more following sites total, hip, distal forearm or radius and clinical (symptomatic) or radiological vertebral fracture.
r.	Adequate if the fracture was measured in an identical way for all studied individuals.
<i>Analysis and data presentation</i>	
s.	Adequate if the results of test of associations between exposures and outcomes are reported, including measures of variance, precision or a p-value.
t.	Adequate if suitable statistical tests were used to measure the association between exposures and outcomes.
u.	Adequate if studies were adjusted at least 4 out of the following confounders such as age, sex, BMI or height or weight, physical activity, energy intake, smoking, menopausal status (in women) and medication affecting bone metabolism.
v.	Adequate if an appropriate method to treat missing data was described. For example, baseline characteristics of those who lost to follow-up and withdrawals was compared; inverse probability or multiple imputation was used. Not applicable if study design was not prospective cohort or RCTs.

Appendix 3-3: Publication paper

Research

Associations of dietary patterns with bone density and fractures in adults

A systematic review and meta-analysis

HH Nguyen, F Wu, JK Makin, WH Oddy, K Wills, G Jones, T Winzenberg

Background and objective

Although nutrition is important to bone health, the impact of different dietary patterns on bone density and fracture is unclear. The aim of this study was to synthesise conflicting evidence from observational studies to determine associations of empirically derived dietary patterns with bone density and fracture in healthy adults.

Methods

A systematic review (PROSPERO CRD42017071676) with meta-analysis where possible (for hip fracture) and otherwise with best-evidence synthesis.

Results

Twenty-one studies were included in the best-evidence synthesis and four in the meta-analysis. Meta-analysis demonstrated a protective association between 'healthy' pattern score and hip fracture (risk ratio 0.73; 95% confidence interval: 0.56, 0.96; $I^2 = 95\%$) for highest compared to lowest 'healthy' pattern score category. In best-evidence synthesis, there was conflicting evidence for associations of both pattern scores with bone density at all sites and total fractures and for 'Western' score and hip fracture. No study reported detrimental effects of 'healthy' patterns, or beneficial effects of 'Western' patterns.

Discussion

The results suggest that general practitioners promoting a 'healthy' dietary pattern is, at worst, unlikely to be detrimental for bone health and, at best, may reduce hip fracture.

NUTRITION PLAYS A VITAL ROLE in optimising bone mineral density (BMD) throughout life to reduce the risk of osteoporosis and osteoporotic fractures.¹ Current Australian dietary recommendations for osteoporosis prevention in general practice are confined to promoting adequate intake of the individual nutrients calcium and protein.² However, individual nutrients and food items are consumed together in the diet and potentially interact in complex ways.³ Dietary patterns can be used to investigate the effects of this on health outcomes³ as well as potentially provide evidence that is easier to translate into practice.⁴ One way of doing this is to identify dietary patterns from dietary intake data using approaches such as factor analysis.⁵

Individual studies investigating associations of empirically derived dietary patterns with bone density and fractures have produced conflicting results.⁶ A robust systematic synthesis of studies is needed that examines evidence separately for different clinically important fracture and bone density sites. The latter is important as fracture risk factors differ for different sites,⁷ as do the costs and sequelae of fractures.⁸ Failing to examine fracture or BMD/content outcomes by site is a significant limitation of one systematic review⁹ addressing this issue. This, and another review,¹⁰ also used risk of 'low BMD' as an outcome, where this was defined in different ways in different populations, making its clinical interpretation difficult, and in one case resulted in excluding information from

relevant studies that did not use this outcome.¹⁰ Therefore, the aim of this systematic review was to determine whether empirically derived dietary patterns are associated with bone density and fracture outcomes at key clinically important sites, namely the hip, lumbar spine and forearm in healthy adults.

Methods

This review was prospectively registered on PROSPERO, the International Prospective Register of Systematic Reviews (Registration number CRD42017071676).

Literature search

The electronic bibliographical databases Medline and Embase were searched via OVID, CENTRAL (Cochrane) and Proquest: theses and dissertations from their inception to 12 May 2017 using key words relating to dietary patterns, BMD and fracture. The search was limited to adults, English language and human subjects. The full search strategy for each database is given in Appendix 1, available online only.

Selection criteria

The study included quantitative observational or intervention studies of any design that reported associations between dietary patterns and bone density outcomes and/or fractures. Studies were included if they were published in English, as full text and

were peer-reviewed, and if participants were adults aged 18 years and over, who did not have diseases and were not taking medications affecting bone metabolism. The researchers included studies that derived dietary patterns using an empirical approach (eg factor analysis, principal component analysis, cluster analysis) on data from a validated dietary intake measurement.¹¹ Dietary pattern scores could be calculated using any method. Studies were included if they measured bone density and/or fractures. For bone density, the researchers included studies that measured areal or volumetric BMD, or bone mineral content (BMC) using dual-energy X-ray absorptiometry (DEXA), single photon absorptiometry, dual photon absorptiometry, peripheral quantitative computed tomography, or broadband ultrasound attenuation and ultrasonic speed of sound by quantitative ultrasonography. Studies had to measure at least one of the following sites: femoral neck, total hip, total body, lumbar spine, proximal or distal forearm. Studies that reported total fracture and/or hip, distal forearm or radius and clinical (symptomatic) or radiological vertebral fracture fractures were included.

Study selection and data extraction

Two authors (HHN and FW) independently screened titles and abstracts of potential articles against the inclusion and exclusion criteria, and further assessed the full text if required. Disagreements were resolved by consensus. Two authors (HHN and JKM) independently extracted the following:

- study characteristics – title, author, study design, study date and duration, sample size and source population
- participant characteristics – age, sex, ethnicity, criteria for inclusion and exclusion
- methods of measuring dietary intake, determining dietary patterns and calculating diet pattern scores
- sites, methods and time points of measurement of BMD and/or fracture
- methods (including any adjustment for potential confounders) used to test for associations between outcomes and exposures and their results.

Assessment of methodological quality of included studies

HHN and JKM independently assessed the methodological quality of included studies using an approach developed for observational studies on musculoskeletal topics¹² that can be modified for a specific topic, as the researchers had previously done.^{13,14} This approach has criteria assessing both the internal validity and informativeness of each study as given in Part A of Appendix 2, available online only. The number of criteria used for each study depended on the outcome measures: 19, 20 and 22 criteria were used if the study measured BMD, fracture or both respectively. For each study, each criterion was assessed as adequate if met (+), inadequate if not met (–), unclear (?) or not applicable (NA). The full list of criteria is included in Part B of Appendix 2, available online only. A quality assessment score was calculated by summing the number of criteria met (+), divided by the applicable number of criteria, multiplied by 100 to generate a percentage. Studies with a methodological assessment score $\geq 60\%$ were considered to be high quality.¹²

Data synthesis

For each included study, tables were used to summarise key study and participant characteristics, methods of assessing dietary patterns and bone outcomes, and key methods and results of tests of associations between dietary patterns and bone outcomes. Because substantial clinical and methodological heterogeneity were expected in the included studies, the first step was to consider from these tables whether the studies reporting data for each outcome were acceptably similar for meta-analysis to be possible or best-evidence synthesis to be appropriate. A major consideration was judging the extent to which different dietary patterns were sufficiently similar to each other. This was undertaken by consensus between four authors (HHN, TW, FW, WHO), one of whom (WHO) is a Professor of Nutritional Epidemiology, by examining the composition of all the published dietary patterns in each study. The two categories of dietary patterns with the most consistently observed similarities were

termed 'healthy' and 'Western' patterns as the closest reflection of their content, though they were named differently across studies (as summarised in Appendix 3, available online only). The 'healthy' group of patterns was characterised by high consumption of fruits, vegetables, wholegrains, nuts, legumes and fish, and the 'Western' group of patterns by high consumption of meats, processed meats, sweets including cakes or desserts, fats/oils, soft drinks and takeaway foods. There were enough data available for meta-analysis for only one outcome and exposure (hip fracture and 'healthy' pattern).

A best-evidence synthesis for both 'healthy' and 'Western' dietary patterns was therefore instead performed for each bone density site (femoral neck, total hip, lumbar spine, total body and forearm BMD and total body bone mineral content [TBBMC]) and total fracture and for 'Western' pattern and hip fracture. The levels of evidence were classified into five categories according to the criteria of Lieveense et al.¹² Evidence was considered strong if there were consistent findings in multiple high-quality cohort studies; moderate if the general consistent findings were shown in a single high-quality cohort study and two or more high-quality case-control studies, or three or more high-quality case-control studies; limited if consistent findings were shown in a single cohort study, one or two case-control studies, or multiple cross-sectional studies; conflicting if fewer than 75% of studies had consistent findings and as no evidence if no studies were found.

The meta-analysis of 'healthy' dietary pattern and hip fracture used the number of events and total number of participants in the highest versus lowest categories of healthy pattern scores (variously tertiles, quartiles and quintiles) to estimate pooled risk ratio (RR) and 95% confidence interval (CI), using random effects modelling. The researchers performed a subgroup analysis by method for measuring fracture (confirmed by medical record versus self-report). Heterogeneity was assessed using I-square (I²). Review Manager (RevMan) software version 5.3 (The Nordic Cochrane Centre, Copenhagen) was used for meta-analysis.

Results

Characteristics of included studies

From 1750 potential articles, 23 studies were included in the systematic review (Figure 1). Two were excluded from the best-evidence synthesis as they did not identify dietary patterns comparable to 'healthy' or 'Western' patterns. The characteristics of all included studies are given in Table 1. There were 12 cross-sectional studies (52.2%),^{3,15-25} 10 cohort studies (43.5%)²⁶⁻³⁵ and one case-control study (4.3%).³⁶ Sample sizes ranged from 154³ to 112,845.³² All studies were considered high quality. Diet was mostly measured using food frequency questionnaires (FFQ)^{3,15,16,18,19,24-36} and dietary patterns were generally identified by principal component analysis.^{3,17-25,29,30,32,34-36} Dietary pattern scores were mostly calculated using the weighted sum score method.^{3,16,19-22,24,27,29,34-36} BMD was most commonly measured by DEXA,^{3,16-26,31,33,34} and lumbar spine,^{3,17-24,31} femoral neck,^{3,15,18,19,21,22,26,34} and hip^{18,20,24,31} were the most commonly measured sites. Fractures were mainly assessed from medical records^{27,30,33,35,36} and hip fracture^{30,32,33,35,36} was the most common site measured.

Bone density outcomes

The results of individual studies are summarised in Table 2. For each bone density outcome, the evidence for associations with both 'healthy' and 'Western' patterns was conflicting. 'Healthy' dietary pattern score was positively associated with BMD in some studies (hip,²⁴ lumbar spine,^{22,24} femoral neck,^{26,34} forearm^{15,16} and total body²³) but not others (hip,^{18,20} lumbar spine,^{3,18-21} femoral neck,^{3,18,19,21,22} forearm,²⁹ total body²⁴ and TBBMC²⁰). In two studies (lumbar spine²³ and femoral neck¹⁵) there were positive associations of 'healthy' pattern score with BMD in men but no association in women. There were no negative associations between 'healthy' pattern score and any bone density outcomes. 'Western' dietary pattern score was negatively associated with BMD in some studies (hip,²⁴ lumbar spine,^{3,19,24} femoral neck,^{19,26,34} forearm²⁹ and total body bone mineral density [TBBMD]²⁴)

and TBBMC²⁰ but had no associations in others (hip,²⁰ lumbar spine,²⁰⁻²³ femoral neck,^{3,15,21,22} forearm,^{15,16} and TBBMD^{23,25} and TBBMC²⁵). There were no beneficial associations of 'Western' pattern scores with bone density outcomes.

Fractures

Seven studies reported fracture outcomes.^{27,28,30,32,33,35,36} Over 70% of studies reporting fracture outcomes focused on older adults^{27,28,32,33,36} and over half reported results for both sexes combined.^{27,30,33,36} The available data made meta-analysis possible only for

associations between lowest versus highest categories (tertiles, quartiles or quintiles) of 'healthy' dietary pattern score and hip fracture.^{20,32,35,36} There was a reduced risk of hip fracture with higher 'healthy' dietary pattern scores (RR 0.73; 95% CI: 0.56, 0.96; Figure 2). Heterogeneity was high ($I^2 = 95\%$, $P < 0.05$). Heterogeneity was reduced and the effect size larger in those studies in which fracture was ascertained from medical records (RR 0.64; 95% CI: 0.56, 0.73; $I^2 = 67\%$).

Best-evidence synthesis was performed to examine associations of 'Western' pattern with hip and total fracture, and

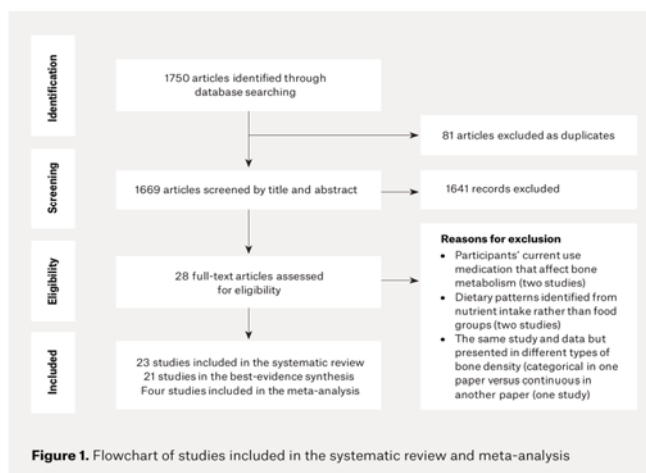


Figure 1. Flowchart of studies included in the systematic review and meta-analysis

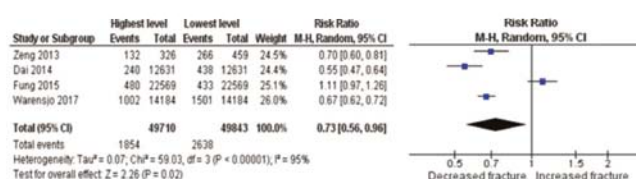


Figure 2. Forest plot of the association between healthy dietary pattern and hip fracture

Table 1. Characteristics of included studies (n = 23)

Characteristic	n (%) ^a
Sample size: median (IQR)	1818 (527–5188)
Study design	
Cross-sectional	12 (52)
Cohort	10 (43)
Case-control	1 (4)
Sex	
Women only	10 (43)
Mixed sexes	13 (57)
Age groups	
Elderly (≥50 years)	12 (52)
Mixed (younger and elderly)	10 (43)
Younger (<50 years)	1 (4)
Method of dietary intake	
Food frequency questionnaire	18 (78)
Food diary	4 (17)
24-hour recall	1 (4)
Method of identifying dietary patterns	
Principal component analysis	15 (65)
Factor analysis	5 (22)
Other ^b	3 (13)
Number of dietary patterns: median (IQR)	4 (3–6)
Method of calculating diet score	
Weighted sum score	12 (52)
Standardised sum score	3 (13)
Other	3 (13)
Not clear/not stated	5 (22)
Outcomes reported	
Bone density	16 (70)
Fracture	6 (26)
Both bone density and fracture	1 (4)
Percentage of quality score: mean (SD)	81.5 (7.3)

^aValues are n (%) unless otherwise specified

^bCluster analysis, reduced rank regression or mixture of methods

IQR, interquartile range; SD, standard deviation

'healthy' pattern with total fracture. Findings of these individual studies are given in Appendix 4, available online only. There was conflicting evidence for detrimental associations between 'Western' dietary pattern and both hip and total fracture and a beneficial association between 'healthy' pattern and total fracture. 'Western' pattern score was associated with higher hip fracture risk in three studies^{33,35,36} but there were no associations in two other studies.^{30,32} Similarly, one study³³ reported a detrimental association between the 'Western' pattern and total fracture while there were no associations in two other studies.^{27,28} The risk of total fracture was lower with higher 'healthy' dietary pattern score in one study³³ while another study reported mixed results with a reduced risk in women but no association in men.²⁸ There were no detrimental associations between a 'healthy' pattern score and fracture, or beneficial associations between the 'Western' pattern and fracture in any study.

Discussion

This systematic review provides a robust site-specific synthesis of the evidence for the associations of empirically derived dietary patterns and site-specific bone density and fracture outcomes. Best-evidence synthesis was performed for most outcomes as meta-analysis was not possible. This assessed evidence supporting beneficial effects of a 'healthy' diet on bone density and detrimental effects of a 'Western' diet on both bone density and fracture outcomes as conflicting. However, studies consistently failed to demonstrate any detrimental effect of a 'healthy' pattern, nor any beneficial effects of a 'Western' pattern on bone outcomes. The meta-analysis demonstrated a beneficial association between 'healthy' dietary patterns and hip fracture in adults. These results suggest that having a 'healthy' diet and avoiding a 'Western' dietary pattern may be beneficial and is unlikely to be detrimental for bone health overall, and importantly, having a 'healthy' dietary pattern could help reduce the risk of hip fracture. In the absence of

Table 2. Associations between healthy-type and Western-type dietary patterns and bone density at different sites in individual studies

Author, year	Findings*	
	'Healthy' dietary pattern	'Western' dietary pattern
Hip bone mineral density (g/cm³)		
Fairweather-Tait, 2011 ¹⁹	No association	NA
McNaughton, 2011 ²⁰	No association	No association
Denova-Gutiérrez, 2016 ²⁴	+ve for low hip BMD ^a (OR 0.71; 95% CI: 0.44, 0.97 for highest vs lowest score quintile)	–ve for low hip BMD ^a (OR 1.91; 95% CI: 1.19, 3.04 for highest vs lowest score quintile)
Lumbar spine bone mineral density (g/cm³)		
Fairweather-Tait, 2011 ¹⁹	No association	NA
Hardcastle, 2011 ¹⁹	No association	–ve (β –0.008; 95% CI: –0.013, –0.003 per unit score)
McNaughton, 2011 ²⁰	No association	No association
Karamati, 2012 ³	No association	–ve for BMD below median (OR 2.29; 95% CI: 1.05, 4.96 for those with higher vs lower score)
Whittle, 2012 ²¹	No association	No association
Shin, 2013 ²²	+ve for osteoporosis at lumbar spine (OR 0.47; 95% CI: 0.34, 0.65 for highest vs lowest quintile of score)	No association
Shin, 2015 ²³	+ve (β 0.016; 95% CI: 0.005, 0.027 per unit score in men) No association in women	No association
Denova-Gutiérrez, 2016 ²⁴	+ve for low lumbar spine BMD ^a (OR 0.80; 95% CI: 0.68, 0.94 for highest vs lowest quintile)	–ve for low lumbar spine BMD ^b (OR 1.61; 95% CI: 1.06, 2.45 for highest vs lowest quintile)
Femoral neck bone mineral density (g/cm³)		
Tucker, 2002 ²⁵	+ve for men: femoral neck BMD greatest in 'fruit, vegetable & cereal' group ^a No association in women	No association
Langsetmo, 2010 ²⁶	+ve for men age 25–49 years (β 0.012; 95% CI: 0.002, 0.022 per SD score) Results for other groups not reported	–ve for men age 50+ years and postmenopausal women (β 0.009 [95% CI: 0.002, 0.016] and 0.004 [95% CI: 0.000, 0.008] per SD score) Others not reported
Fairweather-Tait, 2011 ¹⁹	No association	NA
Hardcastle, 2011 ¹⁹	No association	–ve (β –0.009; 95% CI: –0.013, –0.004 per unit score)
Karamati, 2012 ³	No association	No association
Whittle, 2012 ²¹	No association	No association
Shin, 2013 ²²	No association	No association
De Jonge, 2016 ³⁴	+ve (β 0.06; 95% CI: 0.03, 0.08 per SD score)	–ve (β –0.03; 95% CI: –0.06, –0.01 per SD score)

Table 2. Associations between healthy-type and Western-type dietary patterns and bone density at different sites in individual studies (cont'd)

Author, year	Findings*	
	'Healthy' dietary pattern	'Western' dietary pattern
Total body bone mineral density (g/cm³)		
Shin, 2015 ²³	+ve (β 0.017 [95% CI: 0.008, 0.027] and 0.007 [95% CI: 0.000, 0.015]) per unit score in men and women respectively	No association
Denova-Gutiérrez, 2016 ²⁴	No association	–ve for low TBBMD† (OR 1.74; 95% CI: 1.10, 2.76 for highest vs lowest quintile of score)
Melaku, 2017 ²⁵	+ve (β 0.027; 95% CI: 0.001, 0.043 per tertile score by RRR) No association using PCA or PLS	No association
Forearm bone mineral density (g/cm³)		
Tucker, 2002 ¹⁵	BMD higher in a 'fruits, vegetable and cereal' group† (except alcohol group) in men and women	No association
Okubo, 2006 ¹⁶	+ve (mean of 0.498 vs 0.476 in top vs bottom quintile, <i>P</i> <0.05)	No association
Park, 2012 ²⁹	No association	–ve for osteoporosis (RR 1.46; 95% CI: 1.02, 2.10 for highest vs lowest quintile)
Total body bone mineral content (g)		
McNaughton, 2011 ²⁰	No association	TBBMC (β –15.37 per quintile of score; 95% CI: –27.41, –3.34)
Melaku, 2017 ²⁵	+ve (β 69.65; 95% CI: 16.67, 122.63 per tertile score by RRR) No association using PCA or PLS	No association

*+ve means beneficial association, –ve means detrimental association

†Low defined as *s*–1.0 T-score

‡Compared with other groups ('meat, dairy and bread', 'meat and baked products', 'sweet baked products', 'alcohol and candy groups')

β, beta coefficient; BMC, bone mineral content; BMD, bone mineral density; CI, confidence interval; NA, not applicable; OR, odds ratio; PCA, principal component analysis; PLS, partial least-squares; RR, relative risk; RRR, reduced-rank regression methods of deriving patterns; SD, standard deviation; TBBMD, total body bone mineral density

randomised controlled trials (RCTs), this observational evidence suggests that it is reasonable to incorporate dietary advice to consume a diet high in fruits, vegetables, nuts, fish, wholegrain and legumes and low in red meats, processed meats, fats, sweets, takeaway foods and soft drinks into recommendations for promoting bone health, particularly given the known wide-ranging health benefits of improving diet quality for preventing and managing a range of chronic diseases.

The present study has important differences from previous systematic reviews. Unlike the review of

Denova-Gutiérrez,⁹ it examines bone outcomes separately for different sites. This is important as fracture risk factors⁷ and the costs and sequelae of fractures differ for different sites.⁸ Site-specific data are necessary to assess the potential clinical, public health and health economic³⁷ benefits of any potential intervention. Denova-Gutiérrez et al reported a lower risk of fracture (the site[s] of which were not specified) in the highest compared to lowest categories of 'healthy' dietary pattern (odds ratio [OR] 0.81; 95% CI: 0.69, 0.95) in men, but no effect in women.⁹ This contrasts with the present

data for hip fracture, which suggests that a 'healthy' diet may be important in both sexes for the prevention of this costly and damaging major osteoporotic fracture. Another systematic review¹⁰ only included studies that reported estimates of the risk of being in a 'low' BMD category, rather than associations with BMD as a continuous outcome. This meant that evidence from many studies included in the present review was not considered. Arguably, the review approach used in the present study could be considered to provide a more comprehensive assessment of the available evidence. That second

review¹⁰ reported a risk reduction (OR 0.82) for 'low' BMD when pooling data from all sites but inconsistent associations when analysing site-specific BMD, and subgroups by age and sex.

The findings of the current study that are most relevant to clinical practice are that a 'healthy' dietary pattern was associated with reduced risk of hip fracture, by as much as 36%, and that studies of bone density outcomes were consistent in that none reported detrimental associations of a 'healthy' pattern nor a beneficial association of a 'Western' pattern with BMD. The association with hip fracture is of a substantial magnitude, of both clinical and public health importance. It is comparable with the effect size observed in a recent RCT of zoledronate for hip fracture among older women with osteopaenia (hazard ratio [HR] 0.66; 95% CI: 0.27, 1.16, when compared with placebo)³⁸ and to the effects of other bisphosphonates.³⁹ Results of the present study suggest that promoting the consumption of a diet high in fruits, vegetables, nuts, fish, wholegrains and legumes and low in red meats, processed meats, fats, sweets, takeaway foods and soft drinks could be incorporated into guidelines for promoting bone health in adults. Importantly, there are potential benefits of such dietary changes for many chronic diseases and this advice is already embedded in dietary recommendations around the world, including Australia.⁴⁰ The evidence in the present review comes solely from observational studies, and thus must be interpreted with caution, and RCTs of interventions to improve dietary patterns are needed to definitively assess the effects of dietary changes on bone health. However, RCTs of behavioural interventions with fracture outcomes will be large and logistically challenging, as seen in one of the few such trials for cardiovascular outcomes,⁴¹ so this is likely to remain an evidence gap for some time. Given the wide-ranging potential health benefits of the proposed advice, the evidence suggesting there could be substantial potential benefits of a 'healthy' dietary pattern for hip fracture, and the lack of evidence of any detrimental impacts, it seems reasonable

and warranted to implement this advice for bone health now.

The major strength of this study is the use of meta-analysis where it was possible and a structured best-evidence synthesis approach otherwise, which together result in assembling the strongest and most comprehensive evidence from the available data. This systematic review also has limitations. A major limitation is the cross-sectional nature of most available data, which precludes attribution of causation. To accurately determine the true effect of improving diet on bone outcomes, better evidence from longitudinal studies and RCTs is needed. The lack of comparability in analytical approaches and measurement of outcomes across studies limited the meta-analysis to the single outcome of hip fracture, and to two categories of dietary patterns. The evidence for all the outcomes assessed by best-evidence synthesis was also conflicting. This is not surprising, given the diversity in study design, methods and populations. Nonetheless, it is reassuring that there is consistency with regards to the lack of any evidence for possible detrimental bone outcomes from recommending either promoting a 'healthy' diet pattern or advising avoidance of a 'Western' pattern. Finally, the formal search was completed in 2017. However, the researchers have identified only four other studies reporting dietary patterns similar to those for which data synthesis was performed published since then and they only report bone density outcomes. Like those in the present review, their results are inconsistent⁴²⁻⁴⁵ and they do not materially affect the present results or conclusions.

In conclusion, the current observational evidence suggests that it is reasonable to incorporate existing population health recommendations for a 'healthy' diet into recommendations for promoting bone health, especially given the known wide-ranging health benefits of improving diet quality for the prevention and management of a range of chronic diseases.

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Appendix 4-1: Food frequency questionnaire from the Cancer Council Victoria

Dietary Questionnaire

QUESTIONS ABOUT WHAT YOU USUALLY EAT AND DRINK

INSTRUCTIONS:

This questionnaire is about your **usual** eating habits **over the past 12 months**. Where possible give only **one answer per question** for the type of food you eat **most often**. (If you can't decide which type you have most often, answer for the types you usually eat.)

- Use a soft pencil only, preferably 2B.
- Erase mistakes fully.
- Do not use **any** biro or felt tip pen.
- Make no stray marks.

Please MARK LIKE THIS:
☐ ☐ ☐

Please fill in the date you completed this questionnaire:

DAY	MONTH	YEAR
<input type="checkbox"/>	JAN	<input type="checkbox"/> 2004
<input type="checkbox"/>	FEB	<input type="checkbox"/> 2005
<input type="checkbox"/>	MAR	<input type="checkbox"/> 2006
<input type="checkbox"/>	APR	<input type="checkbox"/> 2007
<input type="checkbox"/>	MAY	<input type="checkbox"/> 2008
<input type="checkbox"/>	JUN	<input type="checkbox"/> 2009
<input type="checkbox"/>	JUL	<input type="checkbox"/> 2010
<input type="checkbox"/>	AUG	<input type="checkbox"/> 2011
<input type="checkbox"/>	SEP	<input type="checkbox"/> 2012
<input type="checkbox"/>	OCT	<input type="checkbox"/> 2013
<input type="checkbox"/>	NOV	<input type="checkbox"/> 2014
<input type="checkbox"/>	DEC	<input type="checkbox"/> 2015

1. How many pieces of fresh fruit do you usually eat per day? (Count 1/2 cup of diced fruit, berries or grapes as one piece.)

☐ I didn't eat fruit

☐ less than 1 piece of fruit per day

☐ 1 piece of fruit per day

☐ 2 pieces of fruit per day

☐ 3 pieces of fruit per day

☐ 4 or more pieces of fruit per day

2. How many different vegetables do you usually eat per day? (Count all types, fresh, frozen or tinned.)

☐ less than 1 vegetable per day

☐ 1 vegetable per day

☐ 2 vegetables per day

☐ 3 vegetables per day

☐ 4 vegetables per day

☐ 5 vegetables per day

☐ 6 or more vegetables per day

3. What type of milk do you usually use?

☐ none

☐ full cream milk

☐ reduced fat milk

☐ skim milk

☐ soya milk

4. How much milk do you usually use per day? (Include flavoured milk and milk added to tea, coffee, cereal, etc.)

☐ none

☐ less than 250 ml (1 large cup or mug)

☐ between 250 and 500 ml (1-2 cups)

☐ between 500 and 750 ml (2-3 cups)

☐ 750 ml (3 cups) or more

5. What type of bread do you usually eat?

☐ I don't eat bread

☐ high fibre white bread

☐ white bread

☐ wholemeal bread

☐ rye bread

☐ multi-grain bread

6. How many slices of bread do you usually eat per day? (Include all types, fresh or toasted and count one bread roll as 2 slices.)

☐ less than 1 slice per day

☐ 1 slice per day

☐ 2 slices per day

☐ 3 slices per day

☐ 4 slices per day

☐ 5-7 slices per day

☐ 8 or more slices per day

7. Which spread do you usually put on bread?

☐ I don't usually use any fat spread

☐ margarine of any kind

☐ polyunsaturated margarine

☐ monounsaturated margarine

☐ butter and margarine blends

☐ butter

8. On average, how many teaspoons of sugar do you usually use per day? (Include sugar taken with tea and coffee and on breakfast cereal, etc.)

☐ none

☐ 1 to 4 teaspoons per day

☐ 5 to 8 teaspoons per day

☐ 9 to 12 teaspoons per day

☐ more than 12 teaspoons per day

9. On average, how many eggs do you usually eat per week?

☐ I don't eat eggs

☐ less than 1 egg per week

☐ 1 to 2 eggs per week

☐ 3 to 5 eggs per week

☐ 6 or more eggs per week

10. What types of cheese do you usually eat?

☐ I don't eat cheese

☐ hard cheeses, e.g. parmesan, romano

☐ firm cheeses, e.g. cheddar, edam

☐ soft cheeses, e.g. camembert, brie

☐ ricotta or cottage cheese

☐ cream cheese

☐ low fat cheese

35045

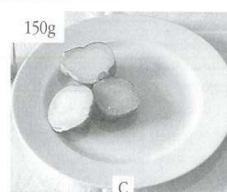
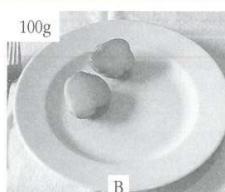
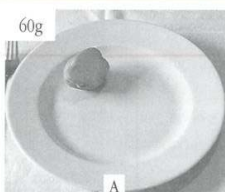
DO NOT WRITE IN THIS AREA.

PERSON 13079

For each food shown on this page, indicate **how much on average you would usually have eaten at main meals during the past 12 months**. When answering each question, think of the **amount** of that food you usually ate, even though you may rarely have eaten the food on its own.

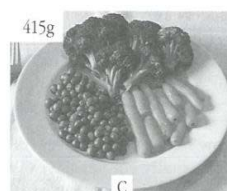
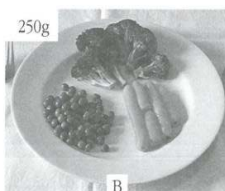
If you usually ate more than one helping, fill in the oval for the serving size closest to the **total amount** you ate.

11. When you ate potato, did you usually eat: ☐ I never ate potato



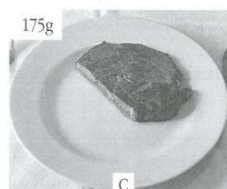
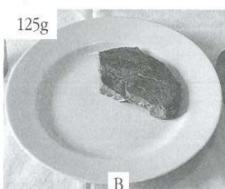
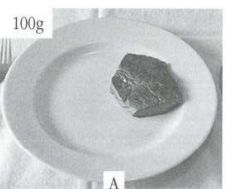
☐ Less than A ☐ A ☐ Between A & B ☐ B ☐ Between B & C ☐ C ☐ More than C

12. When you ate vegetables, did you usually eat: ☐ I never ate vegetables



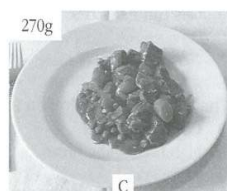
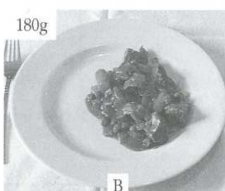
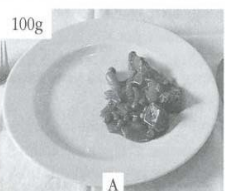
☐ Less than A ☐ A ☐ Between A & B ☐ B ☐ Between B & C ☐ C ☐ More than C

13. When you ate steak, did you usually eat: ☐ I never ate steak



☐ Less than A ☐ A ☐ Between A & B ☐ B ☐ Between B & C ☐ C ☐ More than C

14. When you ate meat or vegetable casserole, did you usually eat: ☐ I never ate casserole



☐ Less than A ☐ A ☐ Between A & B ☐ B ☐ Between B & C ☐ C ☐ More than C

15. Over the last 12 months, on average, *how often* did you eat the following foods? Please completely fill one oval in every line.

Please MARK LIKE THIS: ☐ ☐ ☐ ☐ ☐

NOT LIKE THIS: ☒ ☒ ☒ ☒ ☒

Times You Have Eaten		N E V E R	less than once	1 to 3 times	1 time	2 times	3 to 4 times	5 to 6 times	1 time	2 times	3 or more times
			per month	per week				per day			
CEREAL FOODS, SWEETS & SNACKS											
	All Bran™	A1	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Sultana Bran™, FibrePlus™, Branflakes™	A2	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Weet Bix™, Vita Brits™, Weeties™	A3	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Cornflakes, Nutrigrain™, Special K™	A4	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Porridge	A5	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Muesli	A6	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Rice	A7	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Pasta or noodles (include lasagne)	A8	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Crackers, crispbreads, dry biscuits	A9	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Sweet biscuits	A10	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Cakes, sweet pies, tarts and other sweet pastries	A11	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Meat pies, pasties, quiche and other savoury pastries	A12	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Pizza	A13	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Hamburger with a bun	A14	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Chocolate	A15	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Flavoured milk drink (cocoa, Milo™, etc.)	A16	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Nuts	A17	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Peanut butter or peanut paste	A18	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Corn chips, potato crisps, Twisties™, etc.	A19	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Jam, marmalade, honey or syrups	A20	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Vegemite™, Marmite™ or Promite™	A21	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
DAIRY PRODUCTS, MEAT & FISH											
	Cheese	B1	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Ice-cream	B2	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Yoghurt	B3	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Beef	B4	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Veal	B5	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Chicken	B6	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Lamb	B7	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Pork	B8	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Bacon	B9	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Ham	B10	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Corned beef, luncheon meats or salami	B11	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Sausages or frankfurters	B12	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Fish, steamed, grilled or baked	B13	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Fish, fried (include take-away)	B14	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Fish, tinned (salmon, tuna, sardines, etc.)	B15	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
FRUIT											
	Tinned or frozen fruit (any kind)	C1	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Fruit juice	C2	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Oranges or other citrus fruit	C3	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Apples	C4	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Pears	C5	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Bananas	C6	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Watermelon, rockmelon (cantaloupe), honeydew, etc.	C7	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Pineapple	C8	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Strawberries	C9	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Apricots	C10	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Peaches or nectarines	C11	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Mango or paw paw	C12	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Avocado	C13	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

—

1 bottle wine (750 ml) = 6 glasses

1 bottle of port or sherry (750 ml) = 12 glasses

10

1000

Thank You for completing this questionnaire

1

Appendix 4-2: Food items included in the 33 food groups in the TASOAC study*

Food groups (n=33)	Food items
Processed meats	Bacon, ham, salami, sausage
Red meats	Beef, veal, lamb, pork
Fish	Fish, fried fish, tinned fish
Poultry	Chicken
Meat pies	Meat pies
Hamburgers	Hamburgers
Eggs	Eggs
Butter	Butter, butter and margarine blends
Margarine	Polyunsaturated margarine, monounsaturated margarine, margarine
Low-fat dairy	Skim milk, reduced-fat milk, yoghurt, low-fat cheese
High-fat dairy	Hard cheese, soft cheese, ricotta or cottage cheese, firm cheese, cream cheese, full-cream milk, ice-cream, flavoured milk drink
Whole grains	Muesli, porridge, whole meal bread, multi-grain bread, rye bread
Refined grains	High-fiber, white bread, rice, pasta
Other breakfast cereals	All bran, branflakes, weet bix, cornflakes
Pizza	Pizza
Snacks	Crisps, crackers
Chips	Chips
Sweets	Chocolate, cake, sweet biscuits, sugar
Condiments	Jam, vegemite
Nuts	Nuts, peanut butter
Potatoes	Potatoes
Garlic	Garlic
Other vegetables	Celery, mushrooms, capsicum, beetroot, onion
Legumes	Green beans, peas, other beans, tofu, bean sprouts, soya milk, baked beans
Green leafy vegetables	Spinach, lettuce
Dark-yellow vegetables	Carrots, pumpkin, zucchini, cucumber
Tomatoes	Tomatoes, tomato sauce
Cruciferous vegetables	Broccoli, cauliflower, cabbage
Fruit juice	Fruit juice
Fruit	Avocado, oranges, strawberries, apricots, peaches, mango, apples, pears, bananas, melon, pineapple, tinned fruit
Beer	Light beer, heavy beer
Wine	Red wine, white wine, fortified wines
Spirits	Spirits

* This table based on the paper of Gardener SL et al. Mol Psychiatry. 2015;20(7):860-6.

Appendix 5-1: Retraction Note: Dietary patterns and their associations with socio-demographic and lifestyle factors in Tasmanian older adults: a longitudinal cohort study

Retraction Note to: European Journal of Clinical Nutrition (2019) 73:714–723
<https://doi.org/10.1038/s41430-018-0264-1>

The authors have retracted this article [1] after discovering a major error in the data analysis made when generating the grouped items used in the factor analysis generating the dietary patterns. Because the error is in the foundations of the analysis, it means that the dietary patterns identified were themselves erroneous and their associations with socio-demographic factors are also incorrect. A re-analysis showed up major differences in outcomes when compared with those in [1]. The authors have been given the opportunity to submit a new manuscript for peer review. All authors agree with this retraction.

[1] Hoa H. Nguyen, Feitong Wu, Wendy H. Oddy, Karen Wills, Sharon L. Brennan-Olsen, Graeme Jones & Tania Winzenberg. Dietary patterns and their associations with socio-demographic and lifestyle factors in Tasmanian older adults: a longitudinal cohort study. 2019;73:714–723.

Appendix 5-2: The new publication

European Journal of Clinical Nutrition
https://doi.org/10.1038/s41430-020-00802-4

ARTICLE

Epidemiology



Longitudinal associations of dietary patterns with sociodemographic and lifestyle factors in older adults: the TASOAC study

Hoà H. Nguyen^{1,2} · Feitong Wu¹ · Wendy H. Oddy¹ · Karen Wills¹ · Sharon L. Brennan-Olsen^{3,4,5,6} · Graeme Jones¹ · Tania Winzenberg¹

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Abstract

Background/objectives To derive dietary patterns and examine their longitudinal associations with sociodemographic and lifestyle factors in the Tasmanian Older Adult Cohort.

Subjects/methods This is a corrected analysis of a retracted paper. We followed 1098 adults aged ≥50 years for 5 years. Dietary intake was assessed using a validated food frequency questionnaire. Baseline dietary patterns were identified using exploratory factor analysis and scores at each time point calculated using the weighted sum score method. Associations of energy-adjusted dietary pattern scores with participant characteristics were assessed using linear mixed-effects models.

Results The four dietary patterns identified were: fruit and vegetable (vegetables, potatoes, fruits); animal protein (poultry, red meats, fish); snack (snacks, sweets, nuts); western (meat pies, hamburgers, pizzas). Fruit and vegetable pattern scores were lower in men and current smokers at baseline. Animal protein scores were lower in older and retired people but higher in men and smokers at baseline. The sex difference in animal protein score increased over time ($p = 0.012$). At baseline, snack score was positively associated with age and physical activity, but lower in men and current smokers. The effect of age on snack score lessened over time ($p = 0.035$). Western scores were lower in older people but higher in men, current smokers and those living in disadvantaged areas at baseline. The effect of age on western score reduced over time ($p = 0.001$).

Conclusions The higher scores for healthy and/or lower scores for unhealthy patterns in men, smokers, retirees and those experiencing social disadvantage suggest these could be target groups for interventions to improve diet quality in older adults.

Introduction

The global burden of chronic diseases is substantial in older adults and is increasing with rapid population ageing

worldwide [1]. Nutrition has an important role in the prevention of many chronic diseases [2], with two of the top ten leading causes of the global burden of disease being a diet low in fruits and diet high in sodium [3]. However, until recently, nutritional research has mostly examined the association of single or a few nutrients or foods with disease outcomes, which ignores the inter-correlation between multiple nutrients and foods, as they are consumed in practice [4]. Determining dietary patterns is an alternative

Supplementary information The online version of this article (<https://doi.org/10.1038/s41430-020-00802-4>) contains supplementary material, which is available to authorized users.

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SPRINGER NATURE

approach used to examine the whole diet and identify the combined effects of multiple dietary components [5]. Dietary patterns may be defined based on nutrition theory and/or guidelines or knowledge (a priori method) or by using statistical methods to derive patterns in a given population (a posteriori/empirical approaches) [4]. In the former approach, a predetermined scoring system measures adherence to the proposed pattern, such as the Mediterranean Diet Score, the Healthy Diet Index [6], and the Healthy Eating Index [7]. In the current study, an empirical approach was chosen because we aimed to identify the existing dietary patterns of Tasmanian older adults without holding any prior theory about their patterns.

There are few studies of posteriori-derived dietary patterns and their associations with demographic, socioeconomic, and lifestyle factors in elderly people [8–15]. These studies were mostly cross-sectional [8–14], with only a single longitudinal study [15] of which we are aware. We retracted our previously published longitudinal analysis of associations due to identifying an error in processing the raw data before factor analysis was performed. This had resulted in erroneous patterns being identified. Given the continued need for further longitudinal data, we corrected and reanalyzed our data, aiming to identify dietary patterns in a population-based sample of older adults, and investigate the longitudinal associations of sociodemographic and lifestyle factors with dietary scores calculated for each pattern.

Materials and methods

This is a corrected analysis of a published paper [16] that was retracted due to a data analysis error [17]. An error was made in processing the raw data before factor analysis was performed when collapsing individual food items into food groups for use in the factor analysis and also by mistakenly using frequency of consumption rather than grams of each food as the measure of intake. This meant that the entire process of generating the food group variables, factor analysis and modeling had to be repeated.

Participants and sample size

The Tasmanian Older Adult Cohort (TASOAC) Study was established to investigate relationships between osteoarthritis and lifestyle, genetic, and biochemical factors. At baseline, 1098 participants (50–80 years) were randomly recruited from the electoral roll in Southern Tasmania. Dietary intakes were assessed at baseline in 2002, then after 2.6 and 5 years. The study was approved by the Tasmanian Health and Medical Research Ethics Committee. All participants provided written informed consent.

Dietary intakes

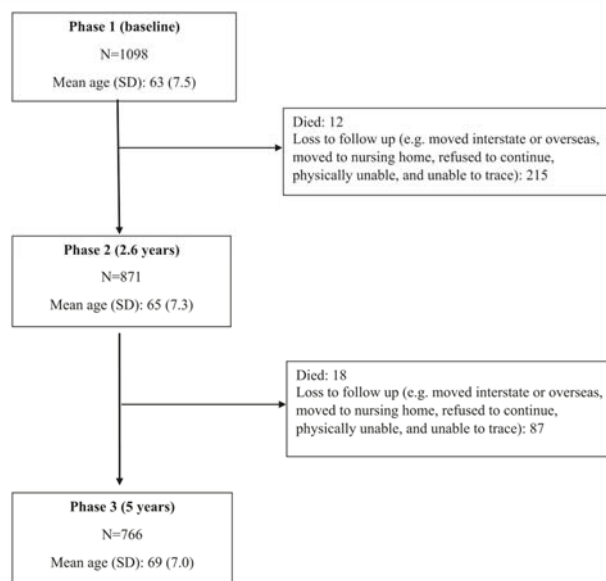
Dietary intakes including beverages were assessed using the Cancer Council of Victoria Food Frequency Questionnaire (CCV-FFQ) [18]. The CCVFFQ includes both a frequency component and portion size of food items, from which food intake is calculated as grams per day. The questionnaire estimates intake over the previous 12 months from 101 food items. The CCV-FFQ has been validated against 7-day weighed food records and the Commonwealth Scientific and Industrial Research Organization FFQ [19].

Sociodemographic and lifestyle factors

Weight was measured using Seca Delta scales (Delta Model 707; Seca, Hamburg, Germany) [20] and height by Leicester stadiometer (Invicta, Leicester, UK) [21]. BMI was calculated (weight (kg)/height (m)²). Date of birth, sex, education level (highest attained), and employment and smoking status were assessed by questionnaire. Education was categorized into primary (no formal qualifications/school or intermediate certificate), secondary (higher school or leaving certificate/trade/apprenticeship), and tertiary (certificate/diploma/ university degree/ higher university degree), and employment status into employed (employed or self-employed either full- or part-time), unemployed (home duties/student/ sole parent pension/ disability pension/unemployed), and retired.

To assess area-level socio-economic status, each participant's residential address was matched to the corresponding Australian Bureau of Statistics (ABS) Census Collection District. ABS software (ABS, Canberra, Australia) was used to determine the Socio-Economic Indexes for Areas (SEIFA) value from the 2001 census for each participant [22]. SEIFA is a collection of four separate indices, each constructed from different variables, which summarizes the characteristics of residents within an area (~250 households), thereby providing a single measure to rank the level of advantage and/or disadvantage at the area level, not of the individual level. For this study, we used the three SEIFA that are equivalized for both advantage and disadvantage: the Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD), the Index of Education and Occupation (IEO), and the Economic Resources (IER) [22, 23]. The IRSAD is an aggregate of variables including, but not limited to, household income, car ownership, the number of one parent families, and educational attainment. Similarly, the IEO includes the proportion of employed individuals within the area, educational attainment, and if employed, the type of occupation held. The IER measures area-based household income, markers of dwelling size, and car ownership. For each of IRSAD, IEO, and IER, quartile cut-points were based on the 2001

Fig. 1 Flow of participants through the study.



Tasmanian population [23]. We used the lowest quartile to indicate the most socially disadvantaged group and dichotomized the cohort using this cut-point.

Smoking status was categorized as currently smoking (smoking ≥ 7 cigarettes/week for at least 3 months), being a former smoker or being a never smoker. Physical activity was measured as steps per day using a pedometer as previously reported [24]. Briefly, participants wore a pedometer (HJ-003 & HJ-102, Omron Healthcare, Kyoto, Japan; or SW-200, Yamax USA, San Antonio, Texas, USA) [21] at least 5 days (≥ 8 h/day) at their waist band or belt which was calibrated using a 100-pace walking test at the clinic. Participants were asked to report the duration of wear, reasons for not wearing the pedometer, and other issues that may have influenced the pedometer data.

Statistical analysis

The 101 food items, measured from the CCV-FFQ as grams per day of intake were collapsed into 33 food groups using previously published groupings for this questionnaire [18] (Supplemental Table S1). The food groups were used to identify dietary patterns using exploratory factor analysis. We used the principal-component factor estimation method with varimax rotation so that factors were uncorrelated [25].

We used the Kaiser–Meyer–Olkin (KMO) test to assess sampling adequacy [26]. The number of factors selected were based on established criteria [27]. First, we selected factors according to the Kaiser rule (considering selection of factors only with an eigenvalue >1). Next, we examined the scree plot of eigenvalues of each factor and identified five potential factors with eigenvalues above the point at which the scree plot slope most markedly changed (Supplemental Fig. S1). We then examined the variance explained by these factors and their interpretability before selecting the final clinically interpretable dietary patterns.

A cut-off point of 0.2 for factor loadings was used to select food groups to be included for the generation of dietary pattern scores [18]. For each pattern, scores were calculated by summing intakes of food groups weighted by their loading on each respective pattern. To assess changes in food intake across the three study time points, we applied the baseline dietary factor loadings to generate scores at each time point. We adjusted the dietary pattern scores by total energy intake (i.e., scores per 1000 kJ) and these energy-adjusted dietary pattern scores were used in further analyses. Associations between energy-adjusted dietary pattern scores and participants' sociodemographic and lifestyle characteristics were investigated using linear mixed-effects models. Separate models were fitted for each

sociodemographic exposure of interest. Each model included fixed effect terms for time (in years) and the exposure, with an interaction term for time and exposure. The interaction term estimates the additional change in dietary pattern score per year associated with a unit increase in exposure. A random intercept was specified for each participant to account for individual differences in baseline dietary patterns, and the correlation between the repeated measures was modeled using an exponential covariance structure. Variables were retained for the multivariable model based on significant baseline association ($p < 0.05$) or interaction term ($p < 0.2$), or clinical importance.

We used sensitivity analyses to assess the influence of missing data. We assumed data were missing at random and used a weighted estimating equation method [28, 29] to estimate the probability of an outcome being observed. We fitted a logistic regression model using the background characteristics age, sex, body mass index, energy intake, employment status and all energy-adjusted dietary pattern scores, for which complete data were available. In subsequent analyses, complete cases were weighted by the inverse of their estimated probabilities of being observed. Stata software version 14 (StataCorp, College Station, Texas, USA) was used for data analysis [30]. Associations were considered statistically significant at a two tailed p value < 0.05 .

Results

Participant flow through the study is shown in Fig. 1. Of 1098 participants who completed the food frequency questionnaire at baseline, 766 remained at 5 years. Baseline characteristics of participants are given in Table 1. Their mean age was 63 years and 51% were women.

Four dietary patterns were identified which we labeled fruit and vegetable, animal protein, snack and western dietary patterns based on the key food groups of which they were composed (Table 2). The KMO was 0.71, indicating sufficient common variance for factor analysis. The proportion of variance explained by each dietary pattern was 6.67%, 6.26%, 5.10%, and 5.06%, respectively. Food groups with the largest loadings on the fruit and vegetable pattern were vegetables, potatoes and fruits; on the animal protein pattern were poultry, red meats and fish; on the snack pattern were snacks, sweets and nuts; and on the western pattern were meat pies, hamburgers and pizzas. The mean (standard deviation) and range of the baseline energy-adjusted scores (score per 1000 kJ) was 23.4 (9.7) and 2–68 for the fruit and vegetable pattern, 23.4 (8.2) and 4–69 for the animal protein pattern, 18.7 (7.9) and 2–52 for the snack pattern, 7.9 (3.3) and 1–26 for the western dietary pattern. At baseline, there was a positive correlation of energy with

Table 1 Characteristics of participants at baseline.

Characteristics	<i>N</i> = 1098 ^a
Age (years), mean (SD)	63.0 (7.5)
Women, <i>n</i> (%)	562 (51.2)
Body mass index (kg/m ²), mean (SD)	27.9 (4.8)
Education, <i>n</i> (%)	
Primary	398 (36.2)
Secondary	358 (32.6)
Tertiary	341 (31.1)
Employment status, <i>n</i> (%)	
Employed	432 (39.3)
Unemployed	248 (22.6)
Retired	418 (38.1)
Smoking status, <i>n</i> (%)	
Never	542 (49.4)
Former	423 (38.5)
Current	131 (11.9)
Physical activity (steps/day), mean (SD)	8617 (3356)
Energy intake (kJ), mean (SD)	7669 (2835)

^aMissing data: education ($n = 1$); smoking status ($n = 2$); physical activity ($n = 50$).

SD standard deviation, kJ kilojoules.

fruit and vegetable (0.4), animal protein (0.8), snack (0.6), and western pattern (0.7).

In adjusted analyses (Table 3), older age was associated with lower animal protein and western pattern scores at baseline, with the effect of age decreasing over time ($\beta = 0.01$, 95% confidence interval = 0.004, 0.02) unit per 1000 kJ per year for age–time interaction) (See Fig. 2A). Older age was associated with higher snack pattern scores at baseline, also with a reduction in the effect of age over time ($\beta = -0.02$, 95% CI = -0.03 , -0.001) unit per 1000 kJ per year for age–time interaction (Fig. 2B).

Table 3 gives the adjusted models for the associations between participants' characteristics at baseline and change in dietary pattern scores. Being a man was associated with lower fruit and vegetable and snack patterns scores, but higher animal protein and western scores at baseline. The sex difference in animal protein pattern score increased over time ($\beta = 0.27$, 95% CI = 0.06, 0.48) unit per 1000 kJ per year (Fig. 2C), but there were no other sex–time interactions.

There were no associations between education and dietary pattern scores, except that people with primary vs tertiary education had slightly greater decrease in western pattern scores over time ($\beta = -0.10$, 95% CI = -0.20 , -0.004) unit per 1000 kJ per year (Fig. 2D). Being retired vs employed was associated with lower baseline animal protein pattern scores ($\beta = -1.87$, 95% CI = -3.01 , -0.72) unit per 1000 kJ but with no interaction with time. Being a

Longitudinal associations of dietary patterns with sociodemographic and lifestyle factors in older...

Table 2 Factor loadings for the three major dietary patterns identified by exploratory factor analysis^a.

Food groups	Fruit and vegetable	Animal protein	Snack	Western
Green leafy vegetables	0.54		0.21	
Fruits	0.28		0.38	
Cruciferous vegetables	0.73			
Potatoes	0.58			
Dark-yellow vegetables	0.79			
Other vegetables ^b	0.36	0.22		
Other breakfast cereals ^c	0.26		0.45	
Fish		0.53		
Chips		0.22		
Processed meats		0.28		0.28
Red meats		0.65		
Poultry		0.78		
Refined grain		0.40		0.22
Sweets		0.23	0.49	0.36
Condiments		0.30	0.36	
Fruit juice		0.39		
Pizzas				0.55
Hamburgers				0.63
Meat pies				0.71
Nuts			0.45	
Snacks			0.67	
Variance explained (%) ^d	6.67	6.26	5.10	5.06

^aOnly factor loadings ≥ 0.2 are presented (factor loading shows the correlation between food items and these dietary patterns).

^bOther vegetables: celery, mushrooms, capsicum, beetroot and onion.

^cOther breakfast cereals: all bran, branflakes, weet bix, and cornflakes.

^dGives the proportion of variance accounted for each factor.

The bold values are the proportion of variance accounted for each factor.

current smoker was associated with higher animal protein and western pattern scores but lower fruit and vegetable and snack pattern scores at baseline, and being more physically active was associated with higher baseline snack pattern scores ($\beta = 0.24$, 95% CI = 0.11, 0.37) unit per 1000 kJ. There were no significant interactions with time for these variables.

There were similar results for all dietary patterns in the sensitivity analyses accounting for missing data (Supplementary Table S2) and the complete case analysis (Table 3) with very small changes in the parameter estimates and no changes in statistical inference.

Energy-adjusted fruit and vegetable and animal protein pattern scores were not associated with any of the three SEIFA indices in either adjusted or unadjusted analyses (data not shown). Residing in a socially disadvantaged area (vs. advantaged), as determined by the IRSAD, was associated with lower baseline snack pattern scores ($\beta = -1.80$, 95% CI = -3.00, -0.60) unit per 1000 kJ but higher baseline western pattern scores ($\beta = 0.52$, 95% CI = 0.01, 1.04) unit per 1000 kJ, with no time interactions. Similar

small baseline differences were observed using the IER and IEO (data not shown).

Discussions

This longitudinal study identified four dietary patterns and determined their associations with demographic, socio-economic, and lifestyle factors in a population of older adults. Four distinct dietary patterns were identified namely fruit and vegetable, animal protein, snack and western patterns. Men and current smokers had higher scores of animal protein and western patterns but lower scores of fruit and vegetable pattern. Retired people also had lower animal protein scores, and those residing in a socioeconomically disadvantaged area had higher western pattern scores. These data may help to identify suitable groups to target for interventions to improve diet quality in older adults.

Although the exact food groups comprising dietary patterns differ across studies, the fruit and vegetable, animal protein and western dietary patterns derived in our study contained a core of similar food groups to healthy, high protein, and unhealthy patterns described in other studies of older adults [8–12, 14, 15] and particularly in Australian populations [13, 18]. For example, fruits and vegetables were major components of the pattern we termed the fruit and vegetable pattern, and also of healthy patterns in other studies [8–12, 14, 15, 18]. Similarly, the red/processed meats, refined grain, sweets or take away foods of the western dietary pattern in our study are also seen in such patterns in other studies [8–11, 14, 15, 18]. Lastly, high protein diets like the animal protein pattern in our study [8, 12, 14] have poultry, fish, red/processed meats in common. Nonetheless, there were also differences in the content of these patterns in different populations—for instance, the animal protein pattern in our study included refined grains, while in another study whole grains were included in a protein pattern [14]. The similarities mean that there is potential value in comparing predictors of patterns, but the differences will likely contribute to a degree of inconsistency across studies in different populations.

Our findings that the healthy fruit and vegetable pattern score was lower and western pattern scores higher in men and current smokers are consistent with other studies [8–11, 13, 15]. Compared to women and non-smokers, men and smokers are at increased risk for heart disease, cancer, lower respiratory disease, stroke and diabetes which contribute to the top six leading causes of death among men in the United States [31]. Consequently, they should be an important target population for nutritional intervention programs. People residing in areas that are socio-economically disadvantaged are also more likely to consume a western dietary pattern and are another target

Table 3 Adjusted linear mixed-effects models for the association between participants' characteristics at baseline and change in dietary pattern scores during follow-up in the TASOAC study.

Variables ^a	Fruit and vegetable β (95% CI) ^b	Animal protein β (95% CI) ^b	Snack β (95% CI) ^b	Western β (95% CI) ^b
Time	0.26 (0.14, 0.37)	-0.36 (-0.51, -0.22)	1.16 (0.29, 2.03)	-0.76 (-1.15, -0.38)
Age (years)	0.02 (-0.05, 0.09)	-0.08 (-0.15, -0.002)	0.09 (0.02, 0.15)	-0.07 (-0.10, -0.05)
Age by time (years)			-0.02 (-0.03, -0.001)	0.01 (0.004, 0.02)
Sex				
Women	Reference	Reference	Reference	Reference
Men	-3.76 (-4.77, -2.74)	1.12 (0.11, 2.12)	-2.89 (-3.72, -2.06)	1.06 (0.73, 1.40)
Sex by time (years)				
Women		Reference		
Men		0.27 (0.06, 0.48)		
Education				
Tertiary				Reference
Secondary				0.30 (-0.15, 0.75)
Primary				0.43 (-0.01, 0.88)
Education by time (years)				
Tertiary				Reference
Secondary				0.001 (-0.10, 0.10)
Primary				-0.10 (-0.20, -0.004)
Employment status				
Employed		Reference		
Unemployed		-1.12 (-2.40, 0.16)		
Retired		-1.87 (-3.01, -0.72)		
Smoking status				
Never	Reference	Reference	Reference	Reference
Former	0.16 (-0.93, 1.25)	1.05 (0.16, 1.95)	-0.22 (-1.09, 0.66)	0.14 (-0.22, 0.49)
Current	-3.78 (-5.39, -2.16)	3.01 (1.52, 4.49)	-3.68 (-5.06, -2.30)	1.47 (0.90, 2.04)
Physical activity (1000 steps/day)		-0.14 (-0.28, 0.001)	0.24 (0.11, 0.37)	

The blank spaces indicated that variables were not included in the model. We selected potential variables in the models depending on the significant baseline ($p < 0.05$), significant interaction ($p < 0.2$) and clinical meaning.

The bold number indicates statistically significant ($p < 0.05$).

CI confidence interval.

^aEach variable was adjusted for other variables in the column.

^bThe energy-adjusted dietary pattern score, that is dietary pattern score per 1000 kJ energy intake.

group for intervention. This result is consistent with a systematic review that higher socioeconomic status or living in urban areas was associated with a healthier dietary pattern [32].

Associations of dietary pattern scores with socio-demographic characteristics and lifestyle factors besides sex and smoking status in older adults are less consistent across studies. For example, age was negatively associated with western pattern scores in our study and also in a French study [10] but other studies reported positive [9] or no association [8, 11, 15]. Snack pattern scores were positively associated with age in our study but not in a Chinese population [12]. Education level was negatively associated with animal protein scores in men in one study [12], but had a positive association in another study [8] and no association in our study and one other [14]. In our study and the only other longitudinal study [15], there were no associations between healthy pattern score and physical activity.

However, positive associations have been reported in cross-sectional studies [8, 9]. These conflicting results could be explained by variations in study design and methods used to identify dietary patterns and calculate diet score. For example, most previous studies were cross-sectional [8, 9, 11, 12] only our study and one other reporting longitudinal data [15]. Although both were longitudinal studies, a latent class analysis was used to identify dietary patterns in the Irish study [15], which may account for the differing results [33]. Different methodological decisions for deriving dietary patterns and generating diet scores reflect the lack of a gold standard approach [34].

Being retired was associated with lower scores of animal protein pattern in our study but no previous studies [8, 12, 14] have investigated associations between dietary patterns and employment status. Although high intakes of animal protein may have detrimental effects, equally the nearly 50% of older American adults who did not meet

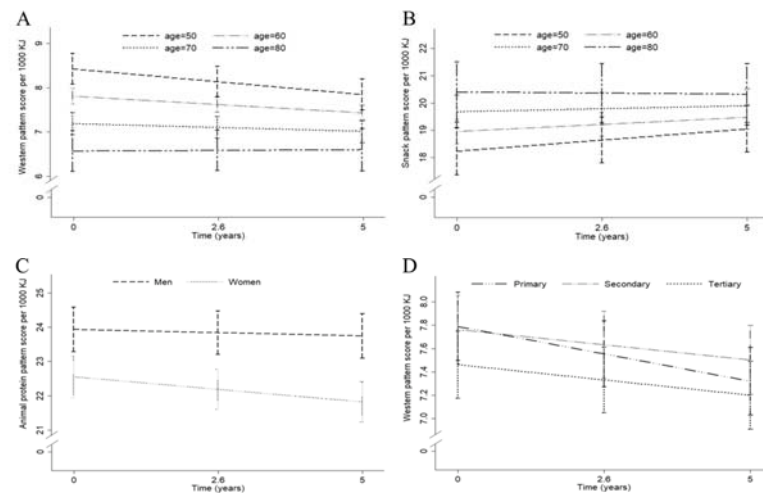


Fig. 2 The energy-adjusted dietary pattern scores. Changes in the energy-adjusted dietary pattern scores by age (a, b), sex (c) and education (d) from adjusted models. The 95% confidence intervals of

all dietary pattern scores at each time point are shown. The range of baseline age of participants was 50–80 and we selected four examples of age values, such as, 50, 60, 70, and 80 to show in this figure.

recommended levels of protein intake had more functional limitations [35]. A lower protein intake also relates to many health problems such as acute and chronic diseases in the elderly [36, 37]. It is therefore likely that advice addressing protein intake will need to be tailored according to whether a person's intake is potentially too high or too low.

Strengths of our study include that it provides novel information about longitudinal changes in dietary pattern scores and their associations with characteristics of older people from a large, population-based sample. Our study also has potential limitations. By their nature, a posteriori-derived dietary patterns vary across studies, limiting the ability to directly compare results of different studies. The fruit and vegetable, animal protein and western dietary patterns we identified were comparable to those in previous studies, suggesting that it is reasonable to compare findings for these dietary patterns. Missing data are another potential limitation, however, missing data of predictors/exposures in our study were very low (<5%) reducing the risk of biased results. We used linear mixed-effects model to utilize all available data to minimize the impact of missing data. More importantly, the results for all dietary patterns in the sensitivity analyses accounting for missing data were very similar to those in the complete case analysis, suggesting the impact of missing data was minimal.

In conclusion, we identified four dietary patterns among Tasmanian older adults, namely fruit and vegetable, animal

protein, snack, and western dietary patterns. The higher scores on healthy and/or lower scores on unhealthy patterns in men, smokers, retirees, and those experiencing social disadvantage suggest these could be target groups for interventions to improve diet quality in older adults.

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Author contributions TW contributed to developing the research proposal and data analysis. GJ, Chief Investigator of TASOAC contributed access to the study, expertise in identifying exposures, confounders and outcomes. KW contributed to the design and implementation of the data analysis. WO provided advice relating to interpretation of the dietary patterns identified in this study and of the study results. FW contributed to the interpretation of findings. SB-O cross-matched and coded the SEIFA data, and contributed to the

interpretation of findings relating to those data. HHN wrote the research proposal and manuscript, analyzed and interpreted the data, and edited the manuscript for publication. All authors contributed to the writing and revision of the manuscript for publication.

Compliance with ethical standards

Conflict of interest There is no conflict of interest of any of the co-authors of this manuscript.

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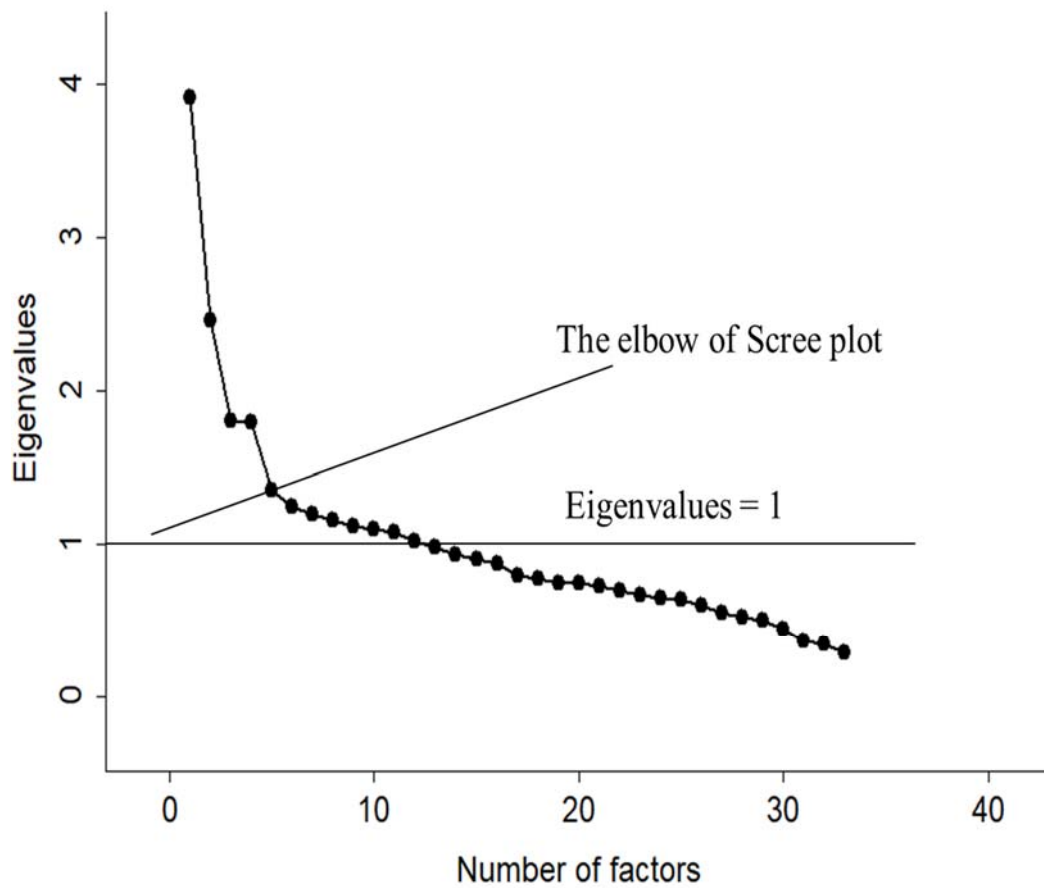
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Appendix 5-3: Scree plot of eigenvalues derived from factor analysis



Appendix 5-4: Adjusted linear mixed-effects models for the association between participants' characteristics at baseline and change in dietary pattern scores (dropping low/high energy intake)

<i>Variables ^a</i>	<i>Fruit and vegetable β (95% CI)*</i>	<i>Animal protein β (95% CI)*</i>	<i>Snack β (95% CI)*</i>	<i>Western β (95% CI)*</i>
Time	0.25 (0.14, 0.36)	-0.35 (-0.50, -0.21)	1.12 (0.24, 1.99)	-0.76 (-1.15, -0.37)
Age (years)	0.02 (-0.05, 0.08)	-0.07 (-0.14, 0.0003)	0.09 (0.02, 0.15)	-0.07 (-0.10, -0.05)
Age by time (years)			-0.01 (-0.03, -0.0002)	0.01 (0.004, 0.02)
Sex				
Women	Reference	Reference	Reference	Reference
Men	-3.57 (-4.58, -2.56)	1.06 (0.07, 2.04)	-2.83 (-3.65, -2.00)	1.06 (0.72, 1.39)
Sex by time (years)				
Women		Reference		
Men		0.28 (0.07, 0.49)		
Education				
Tertiary				Reference
Secondary				0.29 (-0.16, 0.73)
Primary				0.46 (0.02, 0.91)
Education by time (years)				
Tertiary				Reference
Secondary				-0.003 (-0.10, 0.10)

Appendices

Primary					-0.10 (-0.20, -0.002)
Employment status					
Employed		Reference			
Unemployed		-1.29 (-2.55, -0.03)			
Retired		-1.95 (-3.10, -0.81)			
Smoking status					
Never	Reference	Reference	Reference	Reference	
Former	-0.03 (-1.11, 1.05)	1.05 (0.16, 1.93)	-0.28 (-1.15, 0.59)	0.12 (-0.24, 0.47)	
Current	-3.86 (-5.50, -2.23)	3.16 (1.68, 4.64)	-3.83 (-5.22, -2.44)	1.51 (0.94, 2.08)	
Physical activity (1000 steps/day)		-0.16 (-0.31, -0.03)	0.25 (0.12, 0.39)		

Appendix 6-1: Publication paper

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ARTICLE

Nutrition and Health (including climate and ecological aspects)



Associations between dietary patterns and osteoporosis-related outcomes in older adults: a longitudinal study

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Abstracts

Background/Objectives To describe the associations of baseline dietary pattern scores with falls risk, bone mineral density (BMD), and incident fractures measured over 10 years in older adults.

Subjects/Methods Dietary patterns were identified using exploratory factor analysis. Femoral neck (FN), hip, and lumbar spine (LS) BMD were measured using dual-energy X-ray absorptiometry, falls risk z-score using the Physiological Profile Assessment, and incident fractures by self-report. Linear mixed-effects models and log-binomial regression were used to estimate associations between baseline dietary pattern z-scores and outcomes.

Results Of 1098 participants at baseline, 567 were retained over 10 years. Four dietary patterns were derived: fruit and vegetable (FV), animal protein (AP), snack, and Western. FV pattern reduced falls risk at baseline by $\beta = 0.05$ – 0.08 /SD and the annual decreases of FN and hip BMD were less for higher Western or AP pattern scores in all populations and women. The annual increase in LS of the entire population was greater with higher scores of FV, AP, and Western patterns (all $\beta = 0.001$ g/cm²/year/SD, $p < 0.05$). Higher scores of FV and snack were associated with a higher risk of LS BMD increasing over 10 years ($p < 0.05$ for all, except snack pattern in men) and incident fracture was not associated with any dietary pattern in the overall cohort and both men and women separately.

Conclusions An FV dietary pattern may be beneficial for reducing falls risk. The associations of dietary patterns and BMD are modest in magnitude and did not translate into an improved fracture risk. Associations between diet and LS BMD may reflect osteoarthritis rather than osteoporosis.

Introduction

Fractures are a major public health issue in adults 50 years or older [1], with more than 8.9 million osteoporotic fractures occurring annually worldwide [2]. Fractures lead to many severe health consequences, such as increased mortality and reduced quality of life [3]. The annual economic burden due to incident fractures is substantial, estimated to

be about US\$17 billion in 2005 and is predicted to increase by nearly 50% by the year 2025 [4]. Low bone mineral density (BMD) and falls are two major risk factors for fractures in older people [5, 6]. Therefore, preventing low BMD and reducing falls risk are critically important for the prevention of fractures in older adults.

Diet is considered an important modifiable risk factor for bone quality and fracture risk [7]. There is evidence that single nutrients or food items (e.g., calcium, vitamin D, phosphorus, magnesium, fruit, and vegetables) could influence bone health [7]. However, the approach of examining a single nutrient or food item is limited because it does not account for the high correlation between individual nutrients and food items and the fact they are consumed together in the diet [8]. Taking a dietary pattern approach may address this issue [9]. There are two ways to derive dietary patterns: the a priori approach using nutrition theory/knowledge and the a posteriori approach using statistical methods [8]. The a priori method uses a predetermined scoring system to measure adherence to a particular pattern, such as the Mediterranean

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Diet Score, the Healthy Diet Index [10], and the Healthy Eating Index [11]. The a posteriori method, by contrast, describes existing dietary patterns in the population using statistical methods (e.g., factor analysis, principal component analysis, cluster analysis, and reduced rank regression) [9]. We chose that approach because we aimed to identify dietary patterns of Tasmanian older adults without holding any prior theory about their patterns.

No previous study has examined dietary patterns using the a posteriori method and falls risk, and there are limited longitudinal studies examining BMD and fracture in the elderly [12]. A systematic review and meta-analysis [12] found that a healthy dietary pattern is beneficial and a Western dietary pattern is detrimental to bone health, but included predominantly cross-sectional studies with only a single longitudinal study being identified for BMD outcome. To fill this gap in the literature, we therefore aimed to describe the association of dietary pattern z-scores with osteoporosis-related outcomes of falls risk z-scores, BMD, and incident fracture in a population-based cohort of Tasmanian older adults. We hypothesised that healthier dietary patterns would be associated with lower falls risk, higher bone density, and reduced risk of fractures.

Materials and methods

Participants

Participants ($N = 1098$, aged ≥ 50 years) were from the Tasmanian Older Adult Cohort (TASOAC) study. The detailed study design is published elsewhere [13]. Briefly, participants aged 50 years and older were randomly recruited using the electoral roll in Southern Tasmania and assessed at baseline and at an average of 2.6, 5, and 10.7 years later. People in whom magnetic resonance imaging was contraindicated and those who were institutionalized were excluded. The study was approved by the Tasmanian Health and Medical Research Ethics Committee. All participants gave written informed consent.

Dietary intake at baseline and the identification of dietary patterns

The Cancer Council Victoria food frequency questionnaire (CCVFFQ) including 101 food items was used to estimate participants' dietary intake by asking about their usual eating habits over the last 12 months [14]. Briefly, this instrument includes four sections ascertaining: (1) the frequency of consumption of 101 specific foods (cereal foods, sweets, and snacks; dairy products, meat and fish; fruit; and vegetables); (2) the frequency of drinking beverages such as beer, wine, and/or spirits; (3) the usual portion size of

potatoes, vegetables, steak, and meat/vegetable casserole; and (4) the type of bread (e.g., whole meal), milk (e.g., reduced fat), spread (e.g., butter) usually consumed. This self-report questionnaire has been validated against the Commonwealth Scientific and Industrial Research Organization FFQ and weighed food records [15]. We converted all dietary intakes of foods and drinks to grams per day for our analysis. Energy intake (KJ) was calculated from this CCVFFQ by Australian food composition tables [16].

We classified the 101 food and drink items into 33 food groups as previously done [14] (Supplementary Table 1). Exploratory factor analysis with a varimax rotation was used to identify dietary patterns [14]. The number of dietary patterns was determined based on the following criteria: the Kaiser rule (Eigenvalues > 1), the elbow of scree plot, variance explained by each pattern, as well as interpretation and meaning of each pattern [17]. Four dietary patterns were identified (Supplementary Table 2): a fruit and vegetable (FV) pattern characterized by high consumption of fruits, potatoes, vegetables, breakfast cereals excluding muesli and porridge; an animal protein (AP) pattern composed of fish, poultry, red and processed meats; a snack pattern of snacks, sweets, nuts and condiments; and a Western pattern of hamburgers, meat pies, pizzas, and sweets. The percentage variance explained by each dietary pattern was 6.67%, 6.26%, 5.10%, and 5.06%, respectively. Scores for each dietary pattern were calculated for each participant as the sum of the intake of each food group weighted by their factor loadings (≥ 0.20) [14]. Dietary pattern scores were standardized to z-scores to enable comparison of associations among dietary patterns.

Falls risk z-score

We calculated fall risk z-scores at baseline, 2.6, 5, and 10.7 years using the short form of the physiological profile assessment (Prince of Wales Medical Research Institute, Sydney, Australia) [18]. This assessment has five domains: edge contrast sensitivity, hand reaction time, proprioception (position sense), knee extension, and sway test and is a valid and reliable tool for falls risk assessment in older adults [18]. The falls risk z-scores using these tests were assessed for each participant at each time point, with a higher score indicating a higher risk of falls [19].

Bone mineral density (BMD) (g/cm²)

We used dual-energy X-ray absorptiometry (Hologic, Waltham, MA, USA) [13] to measure BMD of femoral neck (FN), hip, and lumbar spine (LS) at baseline, 2.6, 5, and 10.7 years. The Hologic densitometer was calibrated automatically using the internal software system and

the longitudinal coefficient of variation for BMD was 0.39% [19].

Fracture

We used a self-administered questionnaire, that has been validated with radiologic reports and medical records in older adults [20] at baseline, 2.6, 5, and 10.7 years to collect fracture data over 10 years as described previously [18]. Participants listed any fractures they had since their previous visit and the site of each fracture. We coded participants who experienced at least one fracture as "1" and those without incident fracture as "0".

Other baseline explanatory factors

Body mass index (BMI) was calculated as weight (kg) measured by Seca Delta scales (Delta Model 707; Seca, Hamburg, Germany) [13] divided by squared height (m²) measured by stadiometer. We used a self-reported questionnaire to obtain information about age (years), sex, education (primary, secondary, and tertiary), smoking status (never smoked, former, or current smoker), medical history (yes/no), and current use of medications (yes/no) affecting bone metabolism. We included six groups of medication for bone density and fracture outcomes, described as hormone replacement therapy, corticosteroid, bisphosphonates/ denosumab, vitamin D, calcium, and others (e.g., anticoagulants, diuretics, anticonvulsants, antidepressants, beta-blockers, and renin-angiotensin). There were three medication groups for falls risk including antihypertensives, psychotropic medications, and opioids. We measured physical activity as steps per day using a validated Omron pedometer (HJ-003 & HJ-102, Omron Healthcare, Kyoto, Japan) and Yamax pedometer (SW-200, Yamax USA, San Antonio, Texas, USA) as previous study reported [21]. There was a strong linear correlation of the estimates of these pedometers ($r=0.88$) although the mean steps of Omron pedometer were 10% higher than Yamax pedometer. Participants were guided to wear a pedometer at least 5 days/week (≥ 8 hours/day) and report the duration of wear and any problem relating to this data collection.

Statistical analysis

We report the baseline characteristics of participants as mean (standard deviation (SD)) or frequency (%) for continuous and categorical variables respectively. Linear mixed-effects models were used to estimate the association of baseline dietary pattern z-scores with falls risk z-score and BMD. Each model included fixed effect terms for time (years since baseline) and dietary pattern score, and an interaction term for dietary pattern score with time.

The interaction term estimates the additional change in the outcome per year associated with a one SD increase in dietary pattern score at baseline. A random intercept was specified for each participant to account for individual differences in baseline dietary patterns, and the correlation between the repeated measurements over time was modeled using an exponential residual variance-covariance structure. When this model would not converge we specified an independent variance-covariance structure with cluster-robust standard errors that allow for correlation among the repeated observations on an individual.

Log-binomial regression models were used to estimate association of baseline dietary pattern z-scores with the risk of fracture and category of change in LS BMD over 10 years. Participants were coded as "0" if their LS BMD did not change or decreased over 10 years and "1" if their LS BMD increased. This categorization was performed because LS BMD increased over time, suggesting an effect of lumbar spinal degenerative disease in older adults [22]. Lumbar degenerative disease defined using radiology is a normal ageing spine feature and has many features of the peripheral joint radiographic osteoarthritis [23]. Participants with increasing LS BMD over 10 years are more likely to have degenerative spine conditions and so this variable was used as a proxy for LS degenerative status.

All models were adjusted for the baseline age, sex, and BMI to account for potential confounding of the association between dietary pattern z-scores and outcomes (falls risk, BMD, and fracture). We additionally assessed potential confounding by energy intake, physical activity, medication, and medical history but as there was no evidence of confounding by these variables, they were not included in the adjusted models. We also present these outcomes stratified by gender.

Missing baseline data for the linear mixed models were imputed using the method of chained equations, assuming data were missing at random [24]. The imputation model included four phases of BMD (FN, hip, and LS) and falls risk z-score; baseline education, physical activity, smoking status, and all variables from the analytical models. Fifty imputed datasets were created and the estimates from the multiple imputed datasets were combined into an overall estimate using Rubin's rules [25]. Missing data in the log-binomial models for fracture were accounted for using inverse probability weighting as previously described [26]. The following baseline variables were used to calculate predicted probability of being observed for each participant: age, sex, physical activity, smoking status, and medication; and a binary variable indicating if any fracture had been observed during the 10-year study period.

As a positive relationship between Western dietary pattern and obesity/overweight [27] may contribute to an increase in LS BMD, we also specifically examined the

association between BMI-adjusted Western pattern scores and LS BMD. We adjusted the dietary pattern scores by BMI and these BMI-adjusted Western dietary pattern scores were used in an additional analysis with LS BMD. The association of dietary pattern z-scores with falls risk z-scores, BMD and fracture were also estimated using unweighted data of complete cases as sensitivity analyses. All analyses were conducted using the Stata software version 14 (StataCorp, College Station, Texas, USA) [28]. A two-tailed p value < 0.05 was considered statistically significant.

Results

Of 1098 participants at baseline, 567 (52%) were retained at 10.7 years (Supplementary Fig. 1). Participant characteristics at baseline are presented in Table 1. Mean age was 63.0 years (SD = 7.5), and 51% were women. People lost to follow up over 10 years had higher falls risk and lower physical activity at baseline (Table 1 and Supplementary Table 3).

On average, falls risk z-score was estimated to increase annually for the entire population as well as for men and women separately (all $p < 0.001$) (Table 2). There was a negative (beneficial) association between the FV dietary pattern z-score and falls risk z-score at baseline for the overall cohort $\beta = -0.05$ (95% confidence interval (CI) $-0.09, -0.01$) and in women -0.08 ($-0.16, -0.01$), but not men -0.02 ($-0.07, 0.03$). In women, a higher score of the Western dietary pattern was associated with higher falls

risk at baseline although it was not statistically significant, and this association became less over time ($p = 0.017$).

FN BMD reduced annually, and this change was less for higher scores of Western dietary patterns in women $\beta = 0.001$ (95% CI 0.0001, 0.002), but not men -0.0002 ($-0.001, 0.0003$) (Supplementary Table 4). The annual decrease of FN BMD was lower with higher scores of AP and Western patterns in the total sample (Fig. 1A, C). The annual decrease of hip BMD was lower with higher scores of AP and Western dietary patterns in the whole sample (Fig. 1B, D) and in men and women separately ($p < 0.05$ for all, except for AP and Western patterns in men) (Supplementary Table 4).

LS BMD increased by 0.004 g/cm²/year in men, but it decreased by 0.001 g/cm²/year in women (Supplementary Table 4). The annual changes in LS BMD in both genders were reduced for higher scores of FV pattern (men $\beta = -0.00003$ (95% CI $-0.001, 0.001$) and women 0.001 (0.0002, 0.002)) (Supplementary Table 4). The annual increase in LS of the entire population was greater with higher scores of FV, AP and Western patterns (Fig. 1E–G). The association between BMI-adjusted Western pattern score LS BMD was similar to that with the unadjusted score, with little difference in the estimated coefficient and no change in statistical inference (data not shown). Baseline scores of FV and snack patterns were associated with a higher risk of LS BMD increasing over 10 years for the whole population and, except for snack pattern in men, for both men and women separately ($p < 0.05$ for all) (Table 3).

Table 1 Baseline characteristics of completers and participants retained over 10 years in the Tasmanian Older Adult Cohort (TASOAC) Study.

Variables	Total sample ^a ($n = 1098$)	Retained over 10 years ^a ($n = 567$)
Age (year)	63 (7.5)	61 (6.6)
Women, N (%)	562 (51.2)	284 (50.1)
Body mass index (kg/m ²)	27.9 (4.8)	27.6 (4.4)
Physical activity (steps/day) ^b	8617 (3356)	9171 (3261)
Energy intake (KJ)	7669 (2835)	7764 (2677)
Fruit and vegetable pattern raw score ^c	170.5 (75.8)	168.9 (70.0)
Animal protein pattern raw score ^c	184.4 (114.3)	186.8 (113.0)
Snack pattern raw score ^c	140.7 (72.8)	139.2 (68.7)
Western pattern raw score ^c	62.3 (41.4)	64.7 (39.9)
Femoral neck BMD (g/cm ³) ^b	0.766 (0.125)	0.776 (0.118)
Hip BMD (g/cm ³) ^b	0.966 (0.156)	0.979 (0.144)
Lumbar spine BMD (g/cm ³) ^b	1.012 (0.174)	1.015 (0.163)
Falls risk z-score ^b	0.185 (0.853)	0.029 (0.758)

BMD bone mineral density, KJ kilojoules.

^aValues are mean (standard deviation) unless otherwise specified.

^bMissing data: physical activity ($n = 50$), femoral neck BMD ($n = 5$), hip BMD ($n = 5$), lumbar spine BMD ($n = 6$), falls risk z-score ($n = 8$).

^cThe range of raw scores for each dietary pattern was 18–585 for the fruit and vegetable pattern, 15–1250 for the animal protein pattern, 7–476 for the snack pattern, and 4–381 for the western pattern.

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Table 2 Linear mixed-effects model for the association between baseline dietary pattern z-scores and falls risk z-scores.

Falls risk z-score	Total population β (95% CI) ^a	Men β (95% CI) ^b	Women β (95% CI) ^c
Time (per year)	0.04 (0.04, 0.05)	0.05 (0.04, 0.06)	0.04 (0.03, 0.05)
Fruit and vegetable pattern			
Fruit and vegetable pattern z-scores (per SD) at baseline	-0.05 (-0.09, -0.01)	-0.02 (-0.07, 0.03)	-0.08 (-0.16, -0.01)
Fruit and vegetable pattern z-scores (SD) by time (per year)	-0.0003 (-0.01, 0.01)	-0.004 (-0.01, 0.005)	0.004 (-0.01, 0.02)
Animal protein pattern			
Animal protein pattern z-scores (per SD) at baseline	0.01 (-0.03, 0.05)	0.04 (-0.01, 0.09)	-0.02 (-0.08, 0.03)
Animal protein pattern z-scores by time (per year)	-0.003 (-0.01, 0.004)	-0.01 (-0.02, 0.001)	-0.001 (-0.02, 0.01)
Snack pattern			
Snack pattern z-scores (per SD) at baseline	-0.03 (-0.07, 0.01)	-0.002 (-0.05, 0.05)	-0.06 (-0.14, 0.01)
Snack pattern z-scores by time (per year)	-0.01 (-0.01, 0.002)	-0.01 (-0.02, 0.003)	-0.01 (-0.02, 0.01)
Western pattern			
Western pattern z-scores (per SD) at baseline	0.03 (-0.01, 0.07)	0.05 (-0.002, 0.10)	0.01 (-0.05, 0.08)
Western pattern z-scores by time (per year)	-0.004 (-0.01, 0.002)	-0.003 (-0.01, 0.01)	-0.01 (-0.03, -0.003)

Bold denotes statistical significance, $p < 0.05$.

β beta coefficient, SD standard deviation, CI confidence interval.

^aAdjusted for age, sex, and body mass index at baseline.

^{b,c}Adjusted for age and body mass index at baseline.

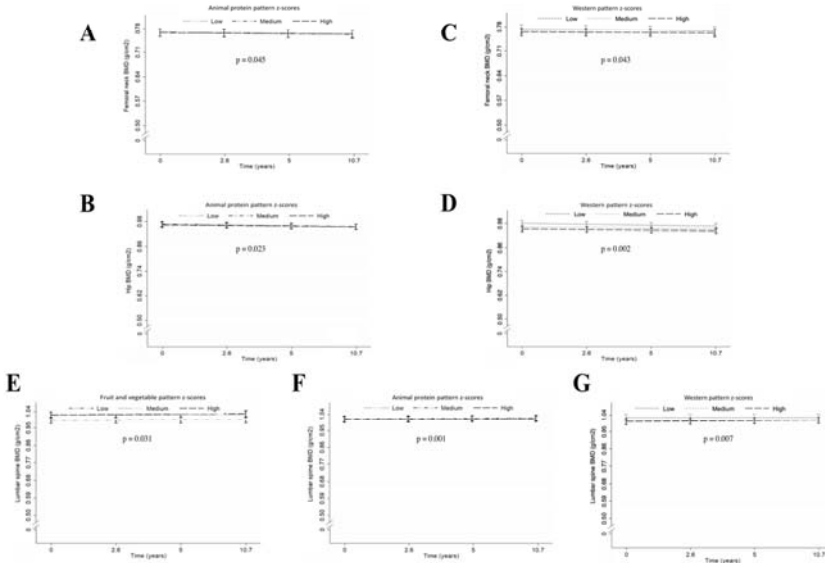


Fig. 1 Associations of dietary pattern z-scores and bone mineral density by time of the total population: femoral neck and hip (A–D) and lumbar spine (E–G). Dietary pattern z-scores were divided into

three tertiles (low, medium and high) and the p values shown are for the comparison of high vs low tertile (reference).

Table 3 Log binomial regression model for the association between baseline dietary pattern z-scores and category of change in lumbar spine bone mineral density (LS BMD) over 10 years.

LS BMD ^a	Unadjusted model	Adjusted models	
	Total population	Men	Women
	RR (95% CI)	RR (95% CI) ^b	RR (95% CI) ^c
Fruit and vegetable pattern z-scores	1.16 (1.14, 1.18)	1.06 (1.03, 1.09)	1.07 (1.04, 1.11)
Animal protein pattern z-scores	1.06 (1.05, 1.07)	1.01 (0.94, 1.09)	1.14 (1.11, 1.17)
Snack pattern z-scores	1.13 (1.06, 1.21)	1.05 (1.00, 1.11)	1.17 (1.03, 1.32)
Western pattern z-scores	1.08 (1.07, 1.10)	1.00 (0.93, 1.06)	1.14 (0.97, 1.33)

RR relative risk, CI confidence interval, BMD bone mineral density.

^aThe LS BMD is coded as a binary variable representing category of change in LS BMD over 10 years: each person was coded as "0" if their LS BMD did not change/decreased LS (reference) or "1" if their LS BMD increased.

^bAdjusted for age, sex, and body mass index at baseline.

^cAdjusted for age and body mass index at baseline.

Table 4 Log binomial regression model for the association between baseline dietary pattern z-scores and incident fracture.

Incident fracture	Unadjusted model	Adjusted models	
	Total population	Men	Women
	RR (95% CI)	RR (95% CI) ^b	RR (95% CI) ^c
Fruit and vegetable pattern z-scores	0.91 (0.77, 1.07)	0.92 (0.78, 1.08)	1.05 (0.85, 1.29)
Animal protein pattern z-scores	1.00 (0.86, 1.15)	1.13 (0.99, 1.28)	1.01 (0.84, 1.22)
Snack pattern z-scores	0.90 (0.76, 1.06)	0.91 (0.76, 1.08)	0.99 (0.80, 1.23)
Western pattern z-scores	0.95 (0.81, 1.11)	1.09 (0.94, 1.27)	1.07 (0.88, 1.31)

RR relative risk, CI confidence interval.

^aAdjusted for age, sex and body mass index at baseline.

^{b,c}Adjusted for age and body mass index at baseline.

There were 259 (45.7%) people having fractures during the follow-up phase. However, there was no evidence for any associations between risk of fracture and baseline scores of any of the dietary patterns for the total population or men and women separately (Table 4).

All results for the associations of dietary patterns with falls risk, BMD and fracture were similar for complete case analyses (data not shown) with only small variations in estimated coefficients and no changes in statistical inference.

Discussions

This longitudinal study identified several osteoporosis-related outcomes that could be influenced by dietary patterns, including for the first time, falls risk. A FV dietary pattern could be beneficial for falls risk and intake of an AP or Western pattern could be beneficial for reducing losses in

FN and hip BMD for the total population and women, but not for men. Higher intake of FV, AP and Western patterns could add to gains in LS BMD over time in the entire population, however, the clinical interpretation of this is unclear as LS BMD mostly increases with degenerative change in older people. There were no associations of any dietary pattern z-scores with incident fractures for all populations and either men and women separately, so these modest effects on falls and BMD did not appear to translate into an improved fracture risk.

A novel finding of our study is that a higher intake of foods comprising a FV (healthy) dietary pattern could be helpful for a 5% and 8% reduction of falls risk in the overall cohort and older women, respectively. The potential importance of a healthy dietary pattern in reducing falls has been largely ignored in elderly people, with no previous studies reporting associations of dietary patterns using the a posteriori method with falls risk. However, our data is consistent with studies that have examined the associations

of dietary patterns with major falls risk factors [29, 30]. In these other studies, higher scores of a healthy patterns were associated with lower risk of frailty [29] and cognitive impairment [30].

Our study is the first longitudinal study examining the association of an AP pattern using the a posteriori method with BMD in older people, finding a positive association between an AP pattern and FN BMD. In contrast, cross-sectional studies [31, 32] have found no associations of dietary protein patterns and FN BMD. Similarly, there was a positive association between AP pattern and LS BMD in our study but a negative relationship of these variables in another study [32]. The inconsistent results could be explained by the study design mentioned above but also the different food components of the patterns. While our study shared similar major food items such as red/processed meat, poultry, and fish with the other studies [31, 32], dairy products were included in the patterns of these two studies [31, 32] but not in ours. As there are a limited number of studies examining the role of dietary protein patterns on bone health, there is a need for more longitudinal or intervention studies investigating this issue in elderly people to clarify our results.

A recent meta-analysis [12] and our longitudinal study provide conflicting evidence for the associations of other dietary patterns with BMD and fracture in older people. For example, we found a positive association between a Western dietary pattern and FN, hip, and LS BMD in the total population. However, in a recent review [12], a meat/Western pattern was positively associated with low BMD risk at the whole body, with no associations of BMD at the femur and LS in the subgroup analyses. Unlike in that review, in our study, there was no association between FV (healthy) dietary pattern and risk of fracture. These inconsistent results could be explained by factors such as differences in study design, methods used to collect dietary data and calculate dietary pattern scores. A key difference is that for BMD outcome in the systematic review [12], 9 out of 10 studies were cross-sectional as compared to our longitudinal cohort study. Given that cross-sectional data provide little support for causation, further longitudinal data or in the case of healthy dietary patterns, even clinical trial data are required to clarify the role of dietary patterns in bone health.

In our cohort, LS BMD increased over 10 years, suggesting a role for degenerative change of the LS that may lead to misinterpretation of BMD in older adults [33]. For all populations, higher scores of the FV, AP, and Western dietary pattern were all associated with increases in LS BMD suggesting these findings may be osteoarthritis rather than osteoporosis as we would expect BMD to decrease over time in those without osteoarthritis. Therefore, the clinical interpretation of our findings is difficult—increasing

LS BMD may be beneficial if some of the increase is due to slowing of age-related bone loss, but detrimental if due to accelerated degenerative change. This, and the modest magnitude of the BMD associations in this study, may explain why the BMD effects seen did not translate to reductions in fracture. There is a lack of studies investigating the potential role of nutrition in slowing down the procession of degenerative change in LS BMD, therefore, this issue could be resolved using lateral scans (which were not available in this study).

In our study, we provide new findings regarding dietary pattern scores and falls risk, BMD and incident fractures in a large population-based cohort study of older adults. The study does have limitations. Using the a posteriori method makes it likely that the food items comprising dietary patterns will vary across different studies [34]. However, the FV, AP, and Western dietary patterns derived in our study contained a core of similar food groups to healthy, high protein and unhealthy patterns described in other studies of older adults [35–41] and particularly in Australian populations [14, 42]. Therefore, there is still value in comparing results across patterns, but the differences will likely contribute to a degree of inconsistency across studies in different populations. We had missing data as in all longitudinal studies. However, multiple imputation and inverse probability weighting methods were used to take missing data into account and the results were largely similar to those using complete-case analysis, suggesting a minor impact of missing data on our findings. LS BMD increased over time and its association with dietary pattern scores could be under-estimate that may relate to osteoarthritis. Some statistically significant results could be due to multiple comparisons rather than real effects, so confirmation of these findings in further longitudinal studies is important.

In conclusion, a FV dietary pattern may be beneficial for reducing falls risk. The associations of dietary patterns and BMD are modest in magnitude and did not translate into an improved fracture risk. Associations between diet and LS BMD may reflect osteoarthritis rather than osteoporosis.

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Author contributions Chief Investigator of TASOAC Study: GJ. Study design: GJ and TW. Manuscript writing, data analysis and data interpretation: HHN. Expertise in statistics: KW. Providing advice relating to dietary patterns: WO and TW. Revising manuscript content: All authors. Responsibility for the final manuscript for publication: GJ.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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References

Appendix 6-2: Linear mixed-effects model for the association between baseline dietary pattern z-scores and bone mineral density (BMD) (g/cm²) - Complete case analysis

	Femoral neck BMD			Hip BMD			Lumbar spine BMD		
	β^a	β^b	LR (p) ^c	β^a	β^b	LR (p) ^c	β^a	β^b	LR (p) ^c
Fruit and vegetable (FV) pattern									
Time	-0.002	-0.002	0.000	-0.004	-0.004	0.000	0.001	0.001	0.000
FV pattern z-scores (per SD) at baseline	0.002	0.002		0.005	0.006		0.009	0.010	
FV pattern z-scores (SD) by time (per year)	0.0001	0.0001		-0.0001	-0.0001		0.001	0.001	
Animal protein (AP) pattern									
Time	-0.002	-0.002	0.000	-0.004	-0.004	0.000	0.001	0.001	0.000
AP pattern z-scores (per SD) at baseline	-0.001	0.001		-0.004	0.001		-0.001	0.002	
AP pattern z-scores by time (per year)	0.001	0.001		0.001	0.001		0.001	0.001	
Snack pattern									
Time	-0.002	-0.002	0.000	-0.004	-0.004	0.000	0.001	0.001	0.000
Snack pattern z-scores (per SD) at baseline	0.004	0.003		0.007	0.005		0.011	0.010	
Snack pattern z-scores by time (per year)	0.0003	0.0002		0.0001	0.0001		0.0003	0.0003	
Western pattern									
Time	-0.002	-0.002	0.000	-0.004	-0.004	0.000	0.001	0.001	0.000
Western pattern z-scores (per SD) at baseline	-0.001	-0.001		-0.007	-0.007		-0.008	-0.008	
Western pattern z-scores by time (per year)	0.001	0.001		0.001	0.001		0.001	0.001	

β , beta coefficient; SD, standard deviation; Bold denotes statistical significance, p<0.05.

^a Adjusted for age, sex and body mass index; ^b Adjusted for age and sex; ^c LR: likelihood ratio test.

Appendix 6-3: Baseline characteristics of people who were lost to follow up over ten years in the TASOAC study

<i>Variables</i>	<i>Lost to follow up^a (n=531)</i>
Age (year)	64 (8.0)
Women, N (%)	278 (52.4)
Body mass index (kg/m ²)	28.2 (5.1)
Physical activity (steps/day)	7995 (3355)
Energy intake (KJ)	7569 (2993)
Fruit and vegetable pattern raw score	172.2 (81.6)
Animal protein pattern raw score	181.8 (115.7)
Snack pattern raw score	142.4 (77.0)
Western pattern raw score	59.8 (42.8)
Femoral neck BMD (g/cm ²)	0.756 (0.131)
Hip BMD (g/cm ²)	0.953 (0.168)
Lumbar spine BMD (g/cm ²)	1.007 (0.184)
Falls risk z-score	0.352 (0.917)

^a Values are mean (standard deviation) unless otherwise specified.
KJ: Kilojoules; BMD: Bone mineral density.

References

Appendix 6-4: Linear mixed effects model for the association between western pattern BMI-adjusted scores and bone mineral density (g/cm²).

<i>Western pattern BMI-adjusted scores</i>	<i>Femoral neck BMD</i> <i>β (95% CI)^a</i>	<i>Hip BMD</i> <i>β (95% CI)^a</i>	<i>Lumbar spine BMD</i> <i>β (95% CI)^a</i>
Time (per year)	-0.002 (-0.002, -0.001)	-0.004 (-0.004, -0.003)	0.001 (0.001, 0.002)
Western pattern BMI-adjusted scores (per SD) at baseline	-0.057 (-0.258, 0.143)	-0.190 (-0.434, 0.053)	-0.231 (-0.520, 0.057)
Western pattern BMI-adjusted scores by time (per year)	0.015 (0.002, 0.028)	0.026 (0.012, 0.040)	0.017 (0.004, 0.031)

β, beta coefficient; SD, standard deviation; CI, confidence interval.

Bold denotes statistical significance, p<0.05.

^a Adjusted for age and sex at baseline.

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