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

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Statement of Ethical Conduct

‘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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3/2019	The final talk at Menzies Institute for Medical Research seminar (Oral presentation)
2/2019	Practice talk for the final talk at Musculoskeletal group (Oral presentation)
11/2018	The 8th Biennial Australian and New Zealand Falls Prevention Conference (Oral presentation)
9/2018	Certificate for a volunteer to the Graduate Research Conference
8/2017	The grant pitch in Musculoskeletal group (Oral presentation)
4/2017	The World Congress on Public Health in Melbourne (Oral presentation)
11/2016	The Nutrition Society Annual Meeting in Melbourne (Oral presentation)

9/2016	The Graduate Research Conference (Poster presentation)
8/2016	The Menzies Institute for Medical Research Student Showcase (Poster presentation)
3/2016	Data presentation at Menzies Institute for Medical Research (Oral presentation)
9/2015	The Graduate Research Conference (Poster presentation)
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10/2018	Physiotherapy and Allied Health Professionals Research Tasmania Network: "The latest research on stroke, cardiovascular disease and dementia"
9/2018	Menzies Institute for Medical Research Debate: "Surgery is the best therapy for osteoarthritis"
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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

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 TASOAC (1098 older adults at baseline: mean age 63 years and 51% of women). TASOAC 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. TASOAC 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/cm^2/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 (β= 1.70 (95% CI 0.47, 2.93)), leg strength (β= 8.88 (95% CI 0.98, 16.78)) and leg muscle quality (β= 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" (β= -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.

Chapter 3 has been removed for copyright or proprietary reasons.

It has been published as: Nguyen, H. H., Wu, F., Makin, J. K., Oddy, W. H., Wills, K., Jones, G., Winzenberg, T., 2021. Associations of dietary patterns with bone density and fractures in adults : a systematic review and meta-analysis, Australian journal of general practice, 50(6), 394-401.

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/cm^2)

Dual-energy X-ray absorptiometry (DXA) was used to measure BMD (g/cm^2) 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 dB = $-10\log_{10}$ 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).

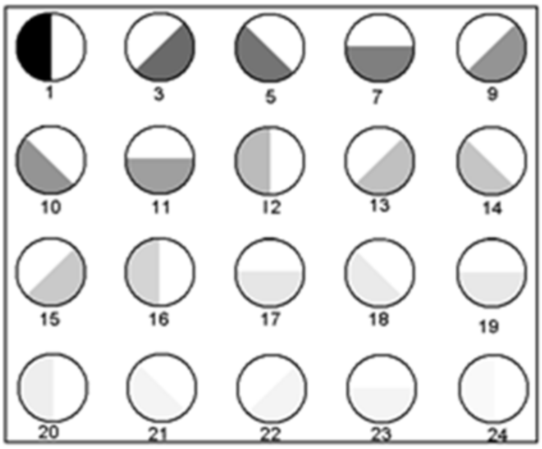

Figure 4-1: Edge contrast sensitivity test

- 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).

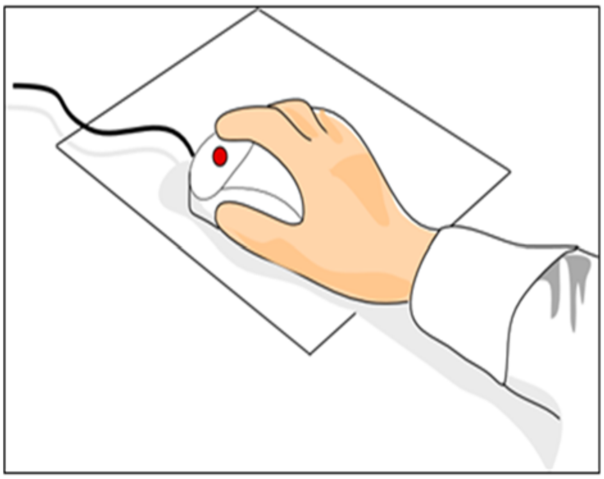

Figure 4-2: Reaction time-hand test

- 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+), fair (1-3), and good (<1).

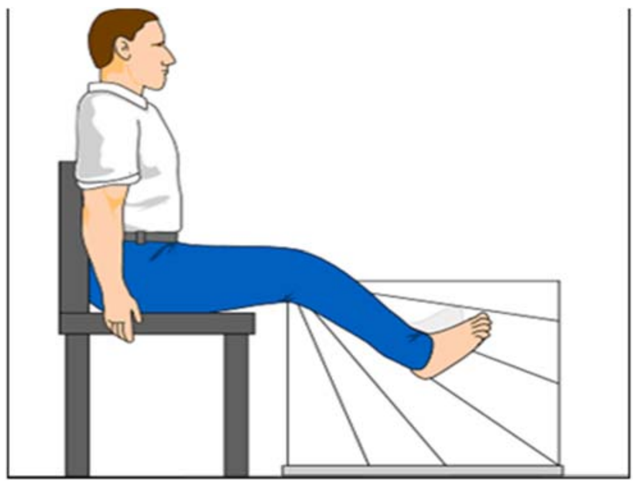

Figure 4-3: A proprioception test

- 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 as 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).

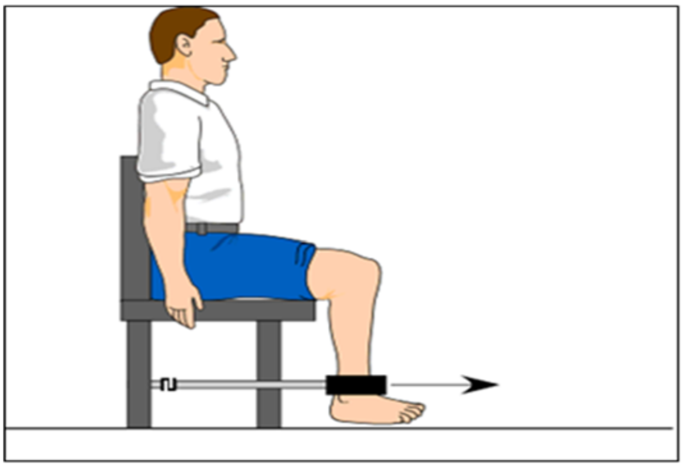

Figure 4-4: Knee extension strength test

- 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.

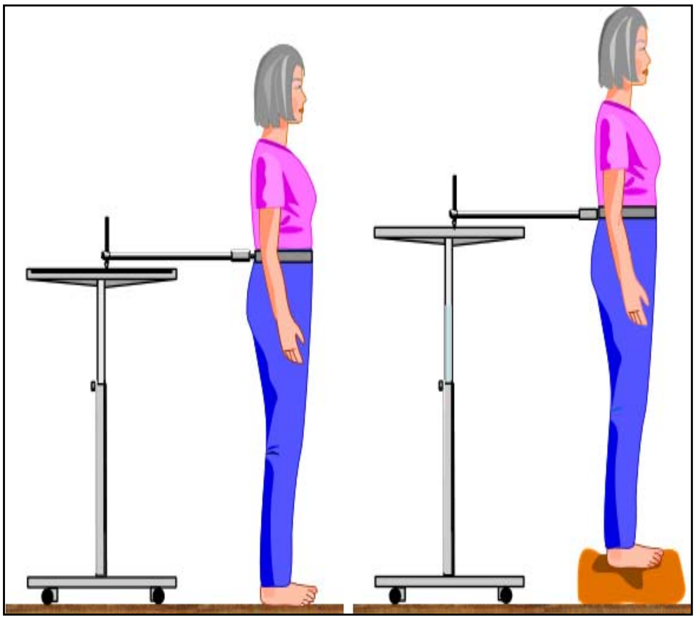

Figure 4-5: A body sway test

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 (≥8h/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.

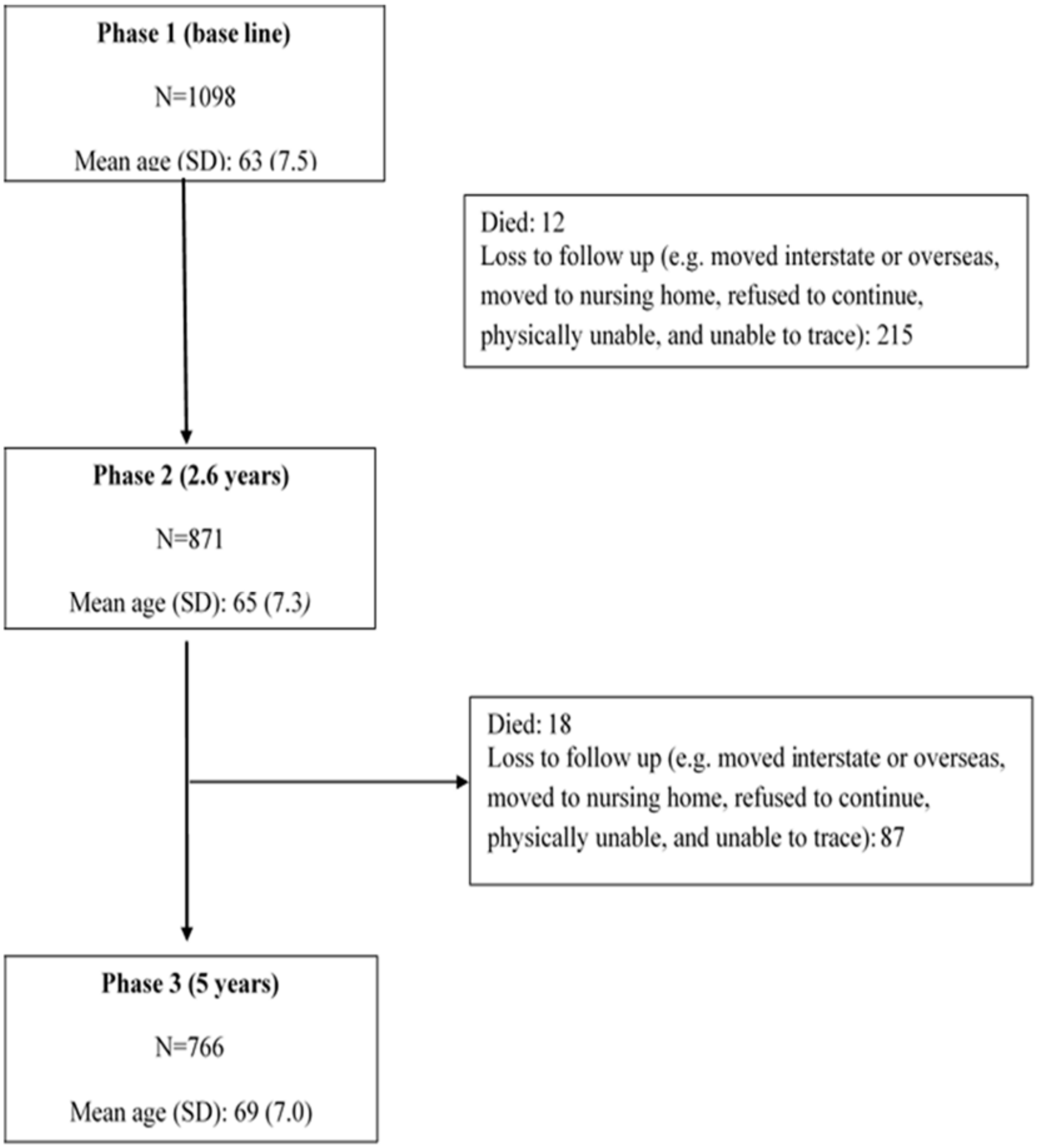

Figure 5-1: Flow of participants through the study

Table 5-1: Characteristics of participants at baseline

Characteristics	***N =1098*** [a]
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]

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*	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

Variables[a]	***Fruit and vegetable*** ***β (95% CI)****	***Animal protein*** ***β (95% CI)****	***Snack*** ***β (95% CI)****	***Western*** ***β (95% CI)****
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

Variables [a]	***Fruit and vegetable*** *β (95% CI)**	***Animal protein*** *β (95% CI)**	***Snack*** *β (95% CI)**	***Western*** *β (95% CI)**
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)**	

[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.

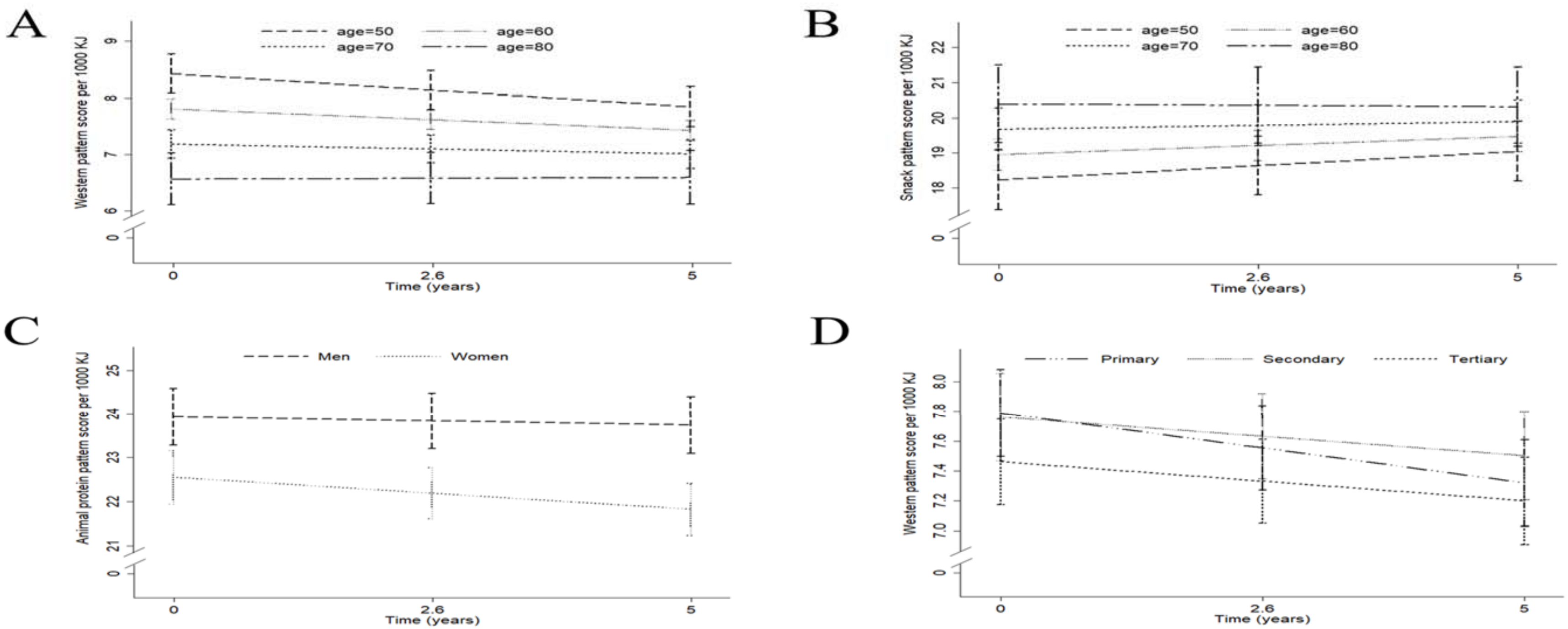

Figure 5-2: Changes in dietary pattern scores over time by age (a, b), sex (c) and education (d) from the adjusted models.

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/cm^2)

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 (m^2) 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.

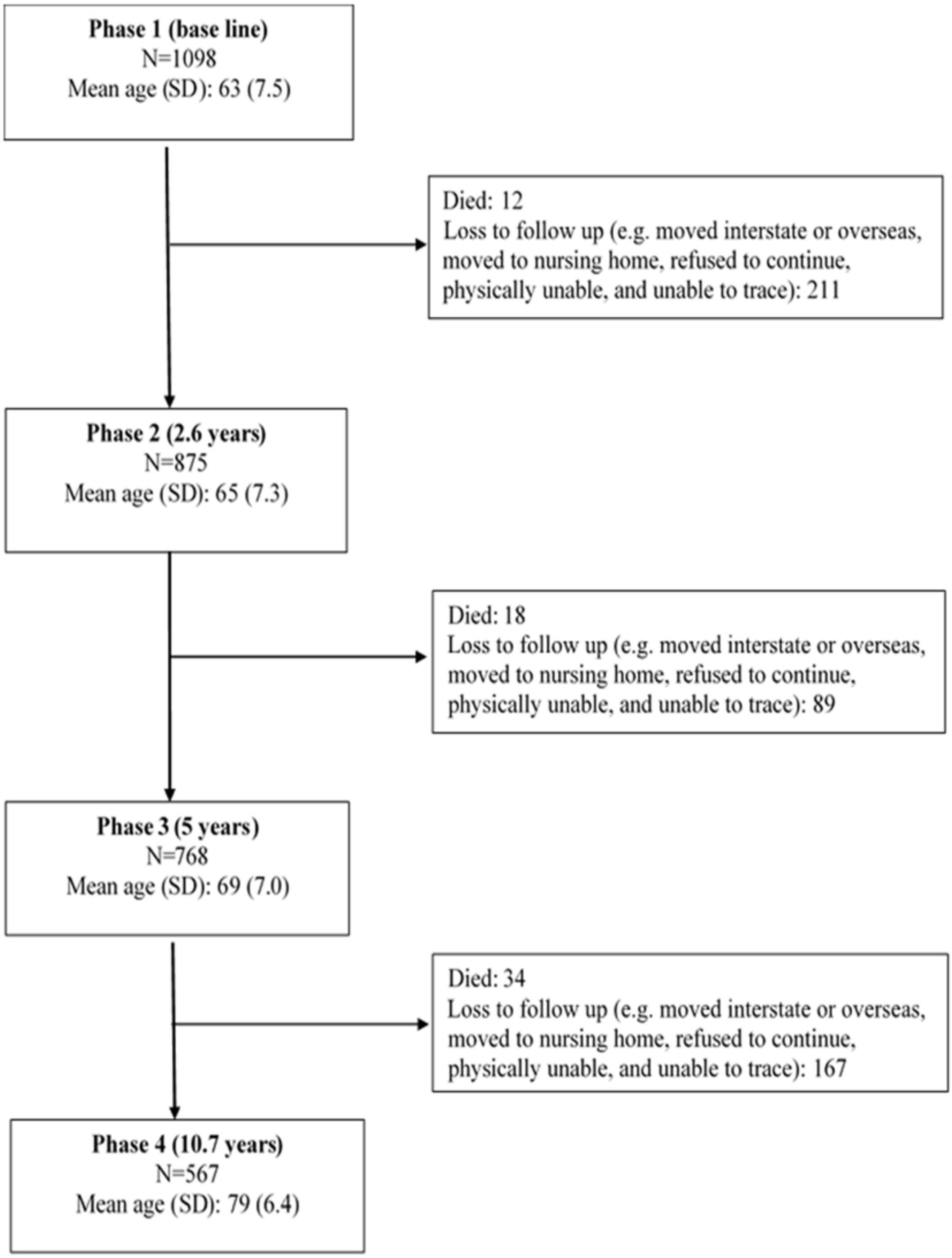

Figure 6-1: Flow of participants through the study

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

Variables	***Total sample***[a] ***(n=1098)***	***Retained a ten 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^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

	Falls risk z-score
	β (95% CI)[a]
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/cm^2 per annum at the FN, and by 0.004 (95% CI -0.004, -0.003) g/cm^2 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/cm^2 annually. The change in LS BMD was 0.001 g/cm^2 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/cm^2)

	Femoral neck BMD ***β (95% CI)***[a]	***Hip BMD*** ***β (95% CI)***[a]	***Lumbar spine BMD*** ***β (95% CI)***[a]
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/cm^2) with and without adjustment for BMI

	Femoral neck BMD		***Hip BMD***		***Lumbar spine BMD***	
	β (p value)[a]	***β (p value)***[b]	***β (p value)***[a]	***β (p value)***[b]	***β (p value)***[a]	***β (p value)***[b]
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*	
	Unadjusted model	***Adjusted model***
	RR (95% CI)	***RR (95% CI)***[a]
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	
	Unadjusted model	***Adjusted model***
	RR (95% CI)	***RR (95% CI)[a]***
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 (β= 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 (β= -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 (β= -0.002 (95% CI -0.002, -0.001) and β= -0.004 (95% CI -0.004, -0.003) g/cm^2 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/cm^2 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.

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**
Study design		
a.	Prospective cohort/RCTs study was used	V
b.	The percentage of withdrawals ≤ 20%	V
c.	Information about completers vs withdrawals	I
d.	Duration of the study reported (date of start and completion)	I
Study population		
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 ≥ 80% or ≥ 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	
Study design	
a.	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. 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.
b.	Adequate if the total withdrawal rate ≤ 20%. Not applicable if study design was not prospective cohort or RCTs.
c.	Adequate if at least 2 out of 5 following information were described for completers and withdrawals: - Age - Sex - BMI - Dietary patterns - Bone mineral status or fracture Not applicable if study design was not prospective cohort or RCTs.
d.	Adequate if the study date of start and completion was described.
Study population	
e.	Adequate if relevant inclusion and exclusion criteria were formulated.
f.	Adequate if the study population was selected before bone mineral density and fracture status were measured. Also adequate if (sub-) groups were selected at a uniform point in the study.
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:

	- 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 ≥ 80% or ≥ 60% and known characteristics of responders and non-responders sufficiently comparable to suggest minimal selection bias
Assessment of dietary patterns (exposures)	
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.
Assessment of bone density (outcome)	
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.

Assessment of fracture (outcome)	
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.
Analysis and data presentation	
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 has been removed for copyright or proprietary reasons.

It is the following published article: Nguyen, H. H., Wu, F., Makin, J. K., Oddy, W. H., Wills, K., Jones, G., Winzenberg, T., 2021. Associations of dietary patterns with bone density and fractures in adults : a systematic review and meta-analysis, Australian journal of general practice, 50(6), 394-401.

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

Dietary Questionnaire

QUESTIONS ABOUT WHAT YOU USUALLY EAT AND DRINK

Please fill in the date you completed this questionnaire:

DAY		MTH	YEAR
		JAN	2004
		FEB	2005
0	0	MAR	2006
1	1	APR	2007
2	2	MAY	2008
3	3	JUN	2009
	4	JUL	2010
	5	AUG	2011
	6	SEP	2012
	7	OCT	2013
	8	NOV	2014
	9	DEC	2015

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.
- Do not use **any** biro or felt tip pen.
- Erase mistakes fully.
- Make no stray marks.

Please MARK LIKE THIS:

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

DO NOT WRITE IN THIS AREA.

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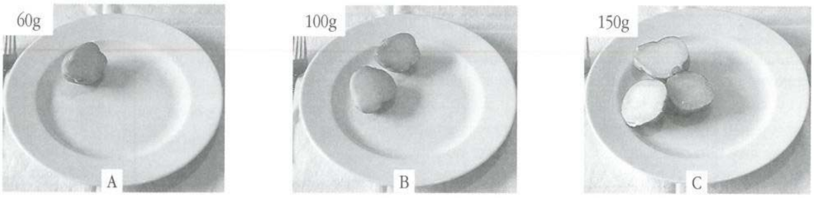
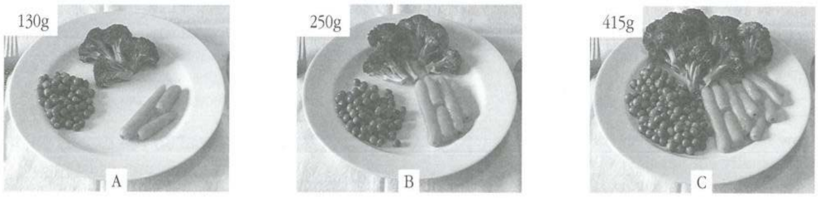
For each food shown on this page, indicate ***how much on average you would usually have eaten at main meals during the past 12 months.*** *When answering each question, think of the* ***amount*** *of that food you usually ate, even though you may rarely have eaten the food on its own.*
If you usually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



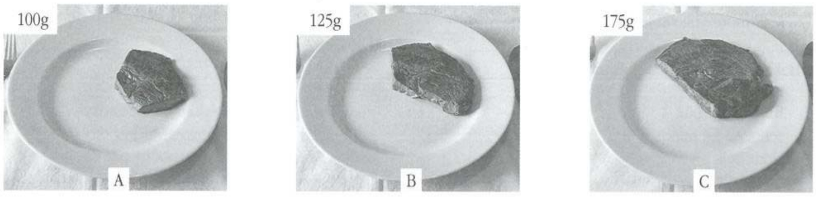
○ Less than A ○ A ○ Between A & B ○ B ○ Between B & C ○ C ○ More than C

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



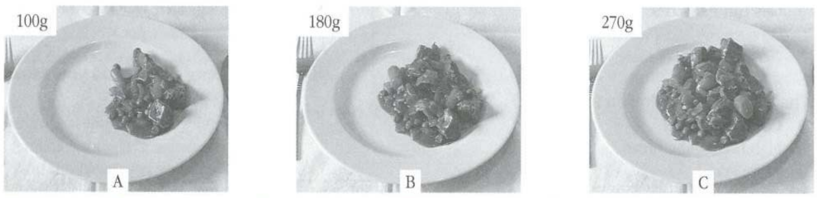
○ Less than A ○ A ○ Between A & B ○ B ○ Between B & C ○ C ○ More than C

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

		NEVER	less than once per month	1 to 3 times per month	1 time per week	2 times per week	3 to 4 times per week	5 to 6 times per week	1 time per day	2 times per day	3 or more times per day
CEREAL FOODS, SWEETS & SNACKS											
All Bran™	A1										
Sultana Bran™, FibrePlus™, Branflakes™	A2										
Weet Bix™, Vita Brits™, Weeties™	A3										
Cornflakes, Nutrigrain™, Special K™	A4										
Porridge	A5										
Muesli	A6										
Rice	A7										
Pasta or noodles (include lasagne)	A8										
Crackers, crispbreads, dry biscuits	A9										
Sweet biscuits	A10										
Cakes, sweet pies, tarts and other sweet pastries	A11										
Meat pies, pasties, quiche and other savoury pastries	A12										
Pizza	A13										
Hamburger with a bun	A14										
Chocolate	A15										
Flavoured milk drink (cocoa, Milo™, etc.)	A16										
Nuts	A17										
Peanut butter or peanut paste	A18										
Corn chips, potato crisps, Twisties™, etc.	A19										
Jam, marmalade, honey or syrups	A20										
Vegemite™, Marmite™ or Promite™	A21										
DAIRY PRODUCTS, MEAT & FISH											
Cheese	B1										
Ice-cream	B2										
Yoghurt	B3										
Beef	B4										
Veal	B5										
Chicken	B6										
Lamb	B7										
Pork	B8										
Bacon	B9										
Ham	B10										
Corned beef, luncheon meats or salami	B11										
Sausages or frankfurters	B12										
Fish, steamed, grilled or baked	B13										
Fish, fried (include take-away)	B14										
Fish, tinned (salmon, tuna, sardines, etc.)	B15										
FRUIT											
Tinned or frozen fruit (any kind)	C1										
Fruit juice	C2										
Oranges or other citrus fruit	C3										
Apples	C4										
Pears	C5										
Bananas	C6										
Watermelon, rockmelon (cantaloupe), honeydew, etc.	C7										
Pineapple	C8										
Strawberries	C9										
Apricots	C10										
Peaches or nectarines	C11										
Mango or paw paw	C12										
Avocado	C13										

3

Times You Have Eaten
CONTINUED

VEGETABLES (INCLUDING FRESH, FROZEN AND TINNED)		NEVER	less than once per month	1 to 3 times per month	1 time per week	2 times per week	3 to 4 times per week	5 to 6 times per week	1 time per day	2 times per day	3 or more times per day
Potatoes, roasted or fried (include hot chips)	D1	○	○	○	○	○	○	○	○	○	○
Potatoes cooked without fat	D2	○	○	○	○	○	○	○	○	○	○
Tomato sauce, tomato paste or dried tomatoes	D3	○	○	○	○	○	○	○	○	○	○
Fresh or tinned tomatoes	D4	○	○	○	○	○	○	○	○	○	○
Peppers (capsicum)	D5	○	○	○	○	○	○	○	○	○	○
Lettuce, endive, or other salad greens	D6	○	○	○	○	○	○	○	○	○	○
Cucumber	D7	○	○	○	○	○	○	○	○	○	○
Celery	D8	○	○	○	○	○	○	○	○	○	○
Beetroot	D9	○	○	○	○	○	○	○	○	○	○
Carrots	D10	○	○	○	○	○	○	○	○	○	○
Cabbage or Brussels sprouts	D11	○	○	○	○	○	○	○	○	○	○
Cauliflower	D12	○	○	○	○	○	○	○	○	○	○
Broccoli	D13	○	○	○	○	○	○	○	○	○	○
Silverbeet or spinach	D14	○	○	○	○	○	○	○	○	○	○
Peas	D15	○	○	○	○	○	○	○	○	○	○
Green beans	D16	○	○	○	○	○	○	○	○	○	○
Bean sprouts or alfalfa sprouts	D17	○	○	○	○	○	○	○	○	○	○
Baked beans	D18	○	○	○	○	○	○	○	○	○	○
Soy beans, soy bean curd or tofu	D19	○	○	○	○	○	○	○	○	○	○
Other beans (include chick peas, lentils, etc.)	D20	○	○	○	○	○	○	○	○	○	○
Pumpkin	D21	○	○	○	○	○	○	○	○	○	○
Onion or leeks	D22	○	○	○	○	○	○	○	○	○	○
Garlic (not garlic tablets)	D23	○	○	○	○	○	○	○	○	○	○
Mushrooms	D24	○	○	○	○	○	○	○	○	○	○
Zucchini	D25	○	○	○	○	○	○	○	○	○	○

16. Over the last 12 months, how often did you drink beer, wine and/or spirits?

Times That You Drank		NEVER	less than once a month	1-3 days per month	1 day per week	2 days per week	3 days per week	4 days per week	5 days per week	6 days per week	every day
Beer (low alcohol)	1	○	○	○	○	○	○	○	○	○	○
Beer (full strength)	2	○	○	○	○	○	○	○	○	○	○
Red wine	3	○	○	○	○	○	○	○	○	○	○
White wine (include sparkling wines)	4	○	○	○	○	○	○	○	○	○	○
Fortified wines, port, sherry, etc.	5	○	○	○	○	○	○	○	○	○	○
Spirits, liqueurs, etc.	6	○	○	○	○	○	○	○	○	○	○

When answering the next two questions, please convert the amounts you drank into glasses using the examples given below. For spirits, liqueurs, and mixed drinks containing spirits, please count each nip (30 ml) as one glass.

1 can or stubby of beer = 2 glasses
1 large bottle beer (750 ml) = 4 glasses
1 bottle wine (750 ml) = 6 glasses
1 bottle of port or sherry (750 ml) = 12 glasses

17. Over the last 12 months, on days when you were drinking, how many glasses of beer, wine and/or spirits altogether did you *usually* drink?

	1	2	3	4	5	6	7	8	9	10 or more
TOTAL NUMBER OF GLASSES PER DAY	○	○	○	○	○	○	○	○	○	○

18. Over the last 12 months, what was the *maximum* number of glasses of beer, wine and/or spirits that you drank in 24 hours?

	1-2	3-4	5-6	7-8	9-10	11-12	13-14	15-16	17-18	19 or more
MAXIMUM NUMBER OF GLASSES PER 24 HOURS	○	○	○	○	○	○	○	○	○	○

Thank You for completing this questionnaire

DO NOT WRITE IN THIS AREA.

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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

Hoa H. Nguyen[1,2] · Feitong Wu[1] · Wendy H. Oddy[1] · Karen Wills[1] · Sharon L. Brennan-Olsen[3,4,5,6] · Graeme Jones[1] · Tania Winzenberg[1]

Received: 28 January 2020 / Revised: 1 October 2020 / Accepted: 28 October 2020

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, socio-economic, 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

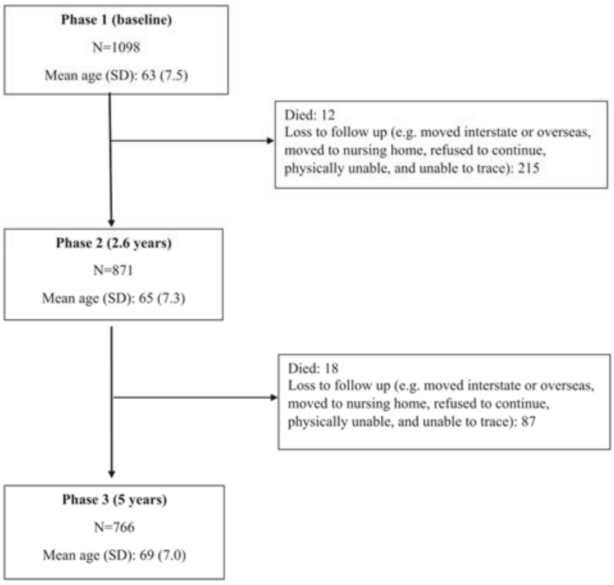
Dietary intakes including beverages were assessed using the Cancer Council of Victoria Food Frequency Questionnaire (CCV-FFQ) [18]. The CCVFFQ includes both a frequency component and portion size of food items, from which food intake is calculated as grams per day. The questionnaire estimates intake 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 analyzes. 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	$N = 1098$[a]
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.

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

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**

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

[b]Other vegetables: celery, mushrooms, capsicum, beetroot and onion.

[c]Other breakfast cereals: all bran, branflakes, weet bix, and cornflakes.

[d]Gives 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 signficant 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 1000KJ, 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, socioeconomic, 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 socioeconomically 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.

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

[b]The 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 heathier 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

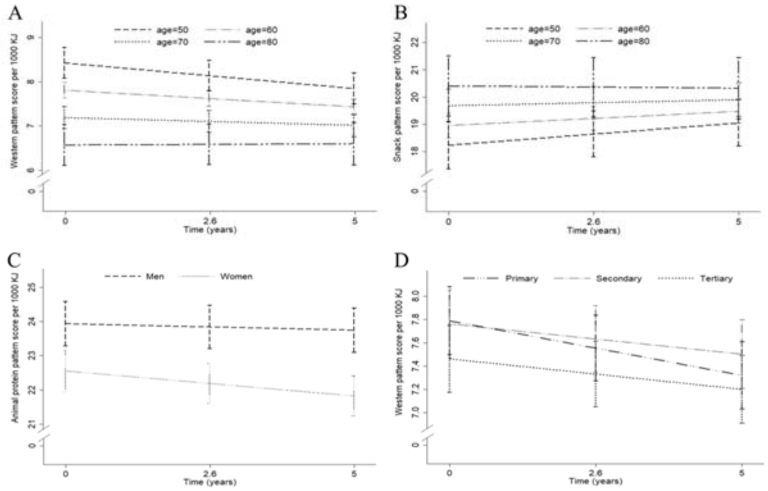


Fig. 2 The energy-adjusted dietary pattern scores. Changes in the energy-adjusted dietary pattern scores by age (**a**, **b**), sex (**c**) and education (**d**) from adjusted models. The 95% confidence intervals of all dietary pattern scores at each time point are shown. The range of baseline age of 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, expertize 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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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)

Variables [a]	***Fruit and vegetable*** ***β (95% CI)****	***Animal protein*** ***β (95% CI)****	***Snack*** ***β (95% CI)****	***Western*** ***β (95% CI)****
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)

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

European Journal of Clinical Nutrition
https://doi.org/10.1038/s41430-020-00806-0

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/cm^2/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/cm^2)

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 (m^2) 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, antidepressant, 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/cm^2/year in men, but it decreased by 0.001 g/cm^2/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^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)

BMD bone mineral density, *KJ* kilojoules.

[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 18–585 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.

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.

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

[b,c]Adjusted for age and body mass index at baseline.

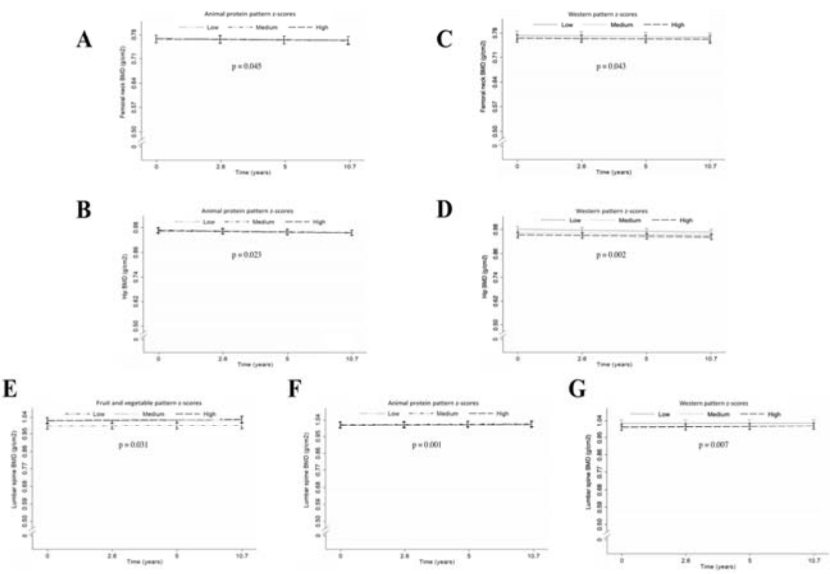

Fig. 1 Associations of dietary pattern z-scores and bone mineral density by time of the total population: femoral neck and hip (**A–D**) and lumbar spine (**E–G**). Dietary pattern z-scores were divided into three tertiles (low, medium and high) and the *p* values shown are for the comparison of high 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*	Unadjusted model Total population	Adjusted models	*Men*	*Women*
	RR (95% CI)	RR (95% CI)[a]	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)	1.31 (1.25, 1.37)
Animal protein pattern z-scores	1.06 (1.05, 1.07)	1.01 (0.94, 1.09)	1.00 (0.92, 1.09)	1.14 (1.11, 1.17)
Snack pattern z-scores	1.13 (1.06, 1.21)	1.05 (1.00. 1.11)	1.03 (0.97, 1.10)	1.17 (1.03, 1.32)
Western pattern z-scores	1.08 (1.07, 1.10)	1.00 (0.93, 1.06)	0.97 (0.89, 1.04)	1.14 (0.97, 1.33)

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

*The 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.

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

[b,c]Adjusted 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 Total population	Adjusted models	*Men*	*Women*
	RR (95% CI)	RR (95% CI)[a]	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)	0.82 (0.63, 1.07)	1.05 (0.85, 1.29)
Animal protein pattern z-scores	1.00 (0.86, 1.15)	1.13 (0.99, 1.28)	1.19 (0.98, 1.45)	1.01 (0.84, 1.22)
Snack pattern z-scores	0.90 (0.76, 1.06)	0.91 (0.76, 1.08)	0.82 (0.63, 1.08)	0.99 (0.80, 1.23)
Western pattern z-scores	0.95 (0.81, 1.11)	1.09 (0.94, 1.27)	1.02 (0.80, 1.30)	1.07 (0.88, 1.31)

RR relative risk, *CI* confidence interval.

[a]Adjusted 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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Compliance with ethical standards

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

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

Variables	***Lost to follow up[a] (n=531)***
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.

Appendix 6-4: Linear mixed effects model for the association between western pattern BMI-adjusted scores and bone mineral density (g/cm^2).

Western pattern BMI-adjusted scores	***Femoral neck BMD*** ***β (95% CI)***[a]	***Hip BMD*** ***β (95% CI)***[a]	***Lumbar spine BMD*** ***β (95% CI)***[a]
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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