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THE IMPACT OF DIETARY FACTORS ON INDICES OF CHRONIC DISEASE IN OLDER PEOPLE: A SYSTEMATIC REVIEW

C.A. NOWSON[1], C. SERVICE[1], J. APPLETON[1], J.A. GRIEGER[2]

1. Institute for Physical Activity and Nutrition (IPAN), School of Exercise and Nutrition Sciences, Deakin University, Geelong, VIC, Australia; 2. Robinson Research Institute, University of Adelaide, Australia. Corresponding author: Caryl Nowson, Deakin University, Geelong, VIC, Australia, caryl.nowson@deakin.edu.au

Abstract: *Objectives:* There has been little evaluation of the evidence relating dietary factors to functional capacity in older adults. The aims were to i) conduct a systematic review of studies assessing dietary factors in relation to six key functional indicators which impact on quality of life in adults ≥65 yrs: non-fatal cardiovascular events, cognition, mental health, falls and fractures, physical health (muscle mass, strength) and frailty; and ii) assess if there was sufficient evidence to devise food-based dietary recommendations. *Design:* Systematic review. *Participants:* Cross-sectional and prospective cohort studies were included together with intervention studies that evaluated food/drink interventions (excluding supplements). Evidence base statements were determined according to the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) levels of evidence criteria (Grades (A-excellent; B-good; C-satisfactory; D-poor). *Results:* There was good evidence that the Mediterranean type diet (MD) reduced the risk of non-fatal cardiovascular events (Grade B) and reduced cognitive decline (Grade B). There was some evidence indicating that a MD decreases the likelihood of frailty (Grade C), consistent but weaker evidence that ≥3 servings/d of vegetables is associated with reduced cognitive decline (Grade D), a modest increase in protein may be associated with improved cognition (Grade C) and decreased frailty (Grade C), and that protein plus resistance exercise training in frail elderly may enhance physical strength (Grade C). *Conclusion:* It is recommended that older adults adopt the characteristics of a Mediterranean type diet such as including olive oil and eating ≥3 servings/d of vegetables to reduce their risk of chronic disease, impaired cognition and frailty. Consumption of dietary protein above the current dietary requirements would be recommended to reduce risk of frailty and impaired cognition. A modest increase in dietary protein when combined with resistance exercise would be recommended to help maintain muscle mass and strength and to enhance functional capacity.

Key words: Elderly, Mediterranean diet, protein, muscle strength, cardiovascular, cognition.

Introduction

The emphasis of health promotion nutritional messages to the general population focuses on the prevention of obesity with recommendations to moderate overall energy intake, reduce saturated fat, and eat more fruits and vegetables (1). There is little acknowledgement that these nutritional messages may not be appropriate for those over 65 yrs of age and completely inappropriate for older more frail people who live in residential care establishments or live at home in supported living situations. Thus, although the evidence base to develop the Dietary Guidelines around the world was extensive (1-3), the majority of studies assessed were conducted in younger and middle-aged populations.

There is increasing evidence that older people have different dietary requirements compared to younger people, specifically increased dietary protein (4) calcium, and vitamin B6, and vitamin D (5, 6). Although this is recognised in the Australian and US Recommended Daily Intakes (7, 8) it is not reflected within the UK's Reference Nutrient Intakes (RNIs) (9). There has been no assessment of evidence base assessing the impact of food and dietary intake on functional indices that impact on quality of life in those over the age of 65 yrs. As people are living longer, there is concern that they may be living longer with a disability or impaired quality of life. Thus we need to know which dietary factors are likely to maintain function and therefore optimize quality of life as the population ages.

Key functional outcomes that impact on health and daily activities include non-fatal cardiovascular events (10), cognition (impaired cognition) (11), mental health (depressive symptoms), falls and fractures (11), physical health (muscle strength and muscle mass), and frailty (11). In Australia, the most significant non-fatal burden of disease in those aged 65-74 yrs includes musculoskeletal conditions (arthritis and osteoporosis, 91%), neurological conditions including dementia (87%), and type 2 diabetes (65%) (12). Additionally of those over the age of 65 yrs, 38% have hypertension, 30% have cardiovascular disease (CVD) and 23% suffer limited activity due to stroke (13). Frailty is now recognised as an independent geriatric syndrome (14) and studies from the US demonstrate frailty occurs in up to 25% of free-living individuals aged 65 yrs and older; this proportion increases up to about 40% in those aged 80 yrs and above (14). Studies from around the world have also demonstrated frailty is associated with many indices of brain function including poor cognitive function (15), depression (16) and anxiety (17), but it also increases risk of falls, hospitalization, disability, loss of independent living and death (18). Moreover, poor physical function, namely muscle weakness, is associated with age-related muscle loss which in turn is related to osteoporosis, falls and fractures, leading to a

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life of restricted mobility, loss of independence and reduced life expectancy (19). Importantly, dietary factors are likely to impact on functional indices in older people which may impact on their quality of life.

It is timely therefore, to undertake a systematic review to assess the evidence relating dietary factors (consumption of food and nutrients) to functional capacity and some key indicators of chronic health conditions in those over the age of 65 yrs. Secondly, to determine if there is sufficient evidence on which to base dietary recommendations that might be able to address multiple indices of chronic disease that would assist older people to maintain a high quality of life into old age.

Methods

We conducted a systematic search of the literature assessing the impact of nutrition and dietary components consumed as foods on functional outcomes related to chronic disease, including: non-fatal cardiovascular (CV) events; cognition; mental health; falls and fractures; physical health (muscle mass and strength); and frailty. We then applied a GRADE (Grades of Recommendation, Assessment, Development and Evaluation) level of evidence (20).

Search strategy

Potential studies were located through electronic searches (Ebscohost (Medline), Ebscohost (CINAHL), Scopus, and Informit) and manual searches of references in review articles. Search strategies were built around six functional health outcome measures: non-fatal CV events, cognition, mental health, falls and fractures, physical health (muscle mass and strength), and frailty. Specific nutrients were not included in the search criteria, and we used the following as dietary search terms: food OR nutrition OR diet (see Appendix). Limits of full text, English language, academic journals, and we only examined published content. Review articles were checked for any additional and relevant articles, and relevant articles identified by expert opinion (CAN) were also included. The search was performed by the primary reviewer (JAG) in December 2014 for the period January 1994 to December 2015, and then updated in January 2017.

We followed the MOOSE (Meta-Analysis of Observational Studies in Epidemiology) checklist for background, design, analysis, and interpretation (48). Search terms were mapped to appropriate subject headings and searched as key words in title and abstract in each database. Citation searching of relevant systematic reviews and studies identified in the primary searches was also undertaken, including examining papers which had cited primary studies. An initial screen of titles and abstracts was undertaken to identify eligible studies. This resulted in three categories of articles: 1) articles appearing to meet the selection criteria; 2) unsure articles (potentially eligible but further information required); 3) excluded articles. The full text of potentially eligible articles (1 and 2) were retrieved and assessed for eligibility. A second reviewer (CS) cross-checked a random 10% of the "potentially eligible articles (1 and 2 above)" and 10% of the excluded articles (3 above), for each outcome by reading titles and (if necessary) abstracts and full text. In a few cases where reviewers allocated the studies differently, the final decision was made by consensus with input from CAN. One researcher (JAG) extracted the data and consulted with CAN to ensure appropriateness of studies for inclusion and complications in extraction of relevant data were resolved through discussion following allocation utilising PRISMA (49) guidelines. Supplementary Figure 1 describes the PRISMA flow charts for each outcome.

Evidence base statement assessment

Evidence base statements were determined according to the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) levels of evidence criteria, an internationally recognised approach to rate the quality of the evidence and the strength of recommendations (21). Recommendations were graded (A-D) using the National Health and Medical Research Council (NHMRC) FORM methodology (20, 22), which allows for both the quality of the evidence and the strength of recommendations to be determined. Grades (A-excellent; B-good; C-satisfactory; D-poor) were determined according to a criteria matrix where each group of studies were rated according to: level of evidence, consistency of study results, potential clinical impact, generalisability of the studies, and applicability of the studies to the Australian (or other local) healthcare system. As most of the included studies were carried out overseas (and not in Australia), the rating of the applicability to the Australian health care system was considered in the context of typical westernised countries. For example, for a group of studies that included one longitudinal (level III-2 evidence) and two cross-sectional (level IV evidence) studies, that were generally positive, with weak/limited impact between the exposure and outcome, was generalizable (mainly Caucasian: consistent with the Australian population), but lacked applicability to the Australian health care system (e.g. if study was performed by untrained staff), such a group of studies would be given an overall evidence base grade of C.

No evidence base statements were made when there was an insufficient number of eligible studies (<3 studies on a particular exposure and outcome), or where there were several eligible studies but with mostly null studies (Supplementary Material 1). Diet markers in which only one or two eligible studies were identified on a particular outcome (e.g. glycemic load on mental health) were indicated in the PRISMA flow charts (Supplementary Figure 1). Given the large number of observational studies identified compared to the number of RCTs, it was not possible to quantify exposure in all studies due to the nature of observational study designs. However, approximations of dietary intake were derived from the data to provide a suitable context for consumption of certain foods that are associated with various outcomes.

Inclusion and exclusion criteria

Studies included participants with mean age ≥65 yrs and living in the community or in residential aged care facilities. This age group was chosen because there is no universally agreed age cut-off to distinguish between "older" persons and those in middle age, and most studies use either 60 or 65 yrs. Randomized controlled trials (RCT), prospective cohort and cross-sectional studies that assessed: (1) a food/drink intervention compared to a control group, (2) associations between foods and nutrients on the outcome of interest and (3) a priori dietary pattern analyses were included. Case-control studies were not included as the point of this review was to identify associations between the different exposures on the outcome rather than selecting patients that had already suffered a disease/functional outcome. We excluded studies assessing serum/plasma nutrient concentrations, alcohol intake, contaminants in food/water, food insecurity, herbal/amino acid/supplement intake or nutrition interventions that utilised supplements in capsule or tablet form, and studies with mortality or intermediary markers of disease e.g. hypertension as outcomes.

Primary outcomes

1) Non-fatal CV outcomes included CV events such as ischemic heart disease and stroke (but not CV mortality), identified using hospital medical records, annual examinations, telephone calls or population registries.

2) Cognitive function was described using multi-domain questionnaires including the Mini Mental State Questionnaire (MMSE) (23), the Modified Mini-Mental State Examination (3MS, 100 points, expansion of MMSE) (24), the telephone interview for cognitive status (TICS) (25), and the Short-Portable Mental State Questionnaire (SPMSQ), an adaptation of the MMSE (26); Visuo-spatial skills included short form of Block Design (mBD) (27); semantic memory (Controlled Oral Word Association Test, S-Task) (28); episodic memory (East Boston tests of immediate and delayed recall) (29); Rey-Osterrieth Figure Test Complex (30); Rey Auditory Verbal Learning Test (RAVLT) for short-term auditory-verbal memory and rate of learning (31); Kendrick object learning test (KOLT) (32); attention executive function (Trail Making Test Part A and B) (33); Digit Symbol Test (DST) (27), and reaction time (computerized finger-cuing task) (34); Digit Span (backward) and Wechsler Adult Intelligence Scale (35); neurological impairment (Symbol digit modalities tests) (36); Seven-minute Screen (7MS) (37) which includes the Clock Drawing Test (38); Category fluency (39); as well as diagnosis of Alzheimer's disease (AD), Mild Cognitive Impairment (MCI) and Dementia, determined by documented criteria (40, 41).

3) Mental health was reported using the Geriatric Depression Scale (GDS) (42); Center for Epidemiologic Studies Depression Scale (CESD) (43), mental component score of SF-36 (44), and EURO-D (45) for measuring depression symptoms scale scores; and the ICD-10 (46) for clinical diagnosis of depression.

4) Physical health determinants such as total body and leg lean mass, lean mass and skeletal muscle mass, was assessed using dual-energy X-ray absorptiometry; muscle strength utilising leg-extension strength test, quadriceps strength, peak power for knee extensors, and hand grip strength. Falls and fractures were assessed through self-report over various periods of time or checked via medical records.

5) Most studies assessing frailty used the "Fried criteria" which defines frailty as the presence of at least three of five items: unintentional weight loss, self-reported exhaustion, weakness, slow walking speed and low physical activity (18); although some studies used a different number of criteria to define frailty, and one studied used a modified definition which included 1) slowness and weakness, 2) exhaustion, 3) low physical activity, and 4) unintentional weight loss (47).

Dietary methodologies

Methods of assessments of dietary intakes included food frequency questionnaires, 24-hr dietary recall, dietary records or diet history method.

Assessment of study methodological quality

Two investigators (JAG and JA) independently appraised the methodological quality of included prospective and cross-sectional studies using a modified version of the Newcastle-Ottawa Scale (NOS) (50) (Supplementary Material 2). This tool assigns stars to indicate higher quality based on three broad criteria, specific to the study design (i.e. selection of study groups, comparability and outcome assessment). A study can be awarded a maximum of 4 stars for Selection, 2 stars for Comparability, and 3 stars for Outcome, with the best quality paper scoring a 9. We defined studies of high quality as those that scored ≥7 stars on the NOS; studies of medium quality scored 5-6 stars. Study quality for randomised controlled trials (RCTs) was assessed by the primary reviewer (JAG) using Cochrane's Collaboration tool for assessing risk of bias in randomised trials (51) (Supplementary Material 3).

Results

Overall Quality assessment of studies included

The studies where there was sufficient evidence on which to make some dietary recommendation are described within the paper. Risk of bias was assessed in the 13 RCTs (Supplementary Material 3) and there was a mix of low, high and unclear risk of bias. Most longitudinal and cross-sectional were of medium quality (quality scores 5-6) based upon NOS (Supplementary Material 2). The quality criteria failed by most studies were poor general population representation of the exposed cohort: many used self-report questionnaires for exposure or outcome data rather than assessments made by, for example, qualified psychologists or neuropsychologists,

Table 1a
Mediterranean Diet and non-fatal cardiovascular events (Evidence Grade B)

Reference	Level of evidence	Time	Population	Outcome	Diet marker	Effect	Overall effect	Quality score[1]/ bias[2]
(53)	II (RCT)	4.8 yrs	Spain, PREDIMED (n=7447)	CV events	Control group (n=2450) vs. Mediterranean diet + extra virgin olive oil (n=2543)	30% ↓ risk for CV events (0.70; 0.54, 0.92)	+	Low
					Control group (n=2450) vs. Mediterranean diet + nuts (n=2454)	28% ↓ risk for CV events (0.72; 0.54, 0.96)	+	
(54)	III-2	11.3 yrs	British men, British Regional Heart Study (n=3328)	CV events; CHD events	↑ 5 points of Elderly Dietary Index (modified version of MDS)	34% reduced risk in CHD events (NS CV events)	+	6
(56)	III-2	9.0 yrs	US black and Hispanic, Northern Manhattan Study (n=2568)	Incident ischemic stroke and MI	↑ 1SD MDS	NS ischemic stroke (HR 1.00; 95% CI: 0.90,1.10)	NS	7
					0-2 MDS vs. 6-9 MDS	NS with ischemic stroke only (HR 1.03; 95% CI: 0.61, 1.73	NS	
					↑ 1SD on MDS	NS with MI (HR 0.94; 95% CI: 0.84,1.05)	NS	
					0-2 MDS vs. 6-9 MDS	NS with MI (HR 0.65; 95% CI: 0.38, 1.12)	NS	
(55)	III-2	5.7 yrs	Hong Kong adults (n=2735)	Ischemic and hae-morrhagic stroke	Highest (6-9) vs. lowest (0-3) level of MDS	NS	NS	6

1. Newcastle-Ottawa quality assessment scale: cross-sectional & cohort studies (Supplementary Material 2), 2Cochrane's Collaboration: risk of bias in randomised trials (Supplementary Material 3); CHD, coronary heart disease; CV, cardiovascular; CVD, cardiovascular disease; HR, hazard ratio; MDS, Mediterranean Diet Score; MI myocardial infarction; NS, not significant.

or by checking medical histories or record linkage data, and a few studies did not adjust for appropriate confounders (e.g. age, gender, BMI, energy intake). Published papers including assessment of dietary factors for which there was insufficient evidence on which to base dietary recommendations are described in Supplementary Material 1.

Mediterranean diet

The Mediterranean diet (MD) includes higher consumption of olive oil, fresh fruits and vegetables, protein-rich legumes, fish, whole grains, and with moderate amounts of wine and red meat, with scoring of beneficial and presumed detrimental components defined previously (52). This review identified 25 studies which assessed the association of the MD on functional outcomes.

Non-fatal cardiovascular events

One RCT of 4.7 years, (53) with low risk of bias (Supplementary Material 3) and three longitudinal studies (5.7-11.3 years) of medium and high quality (54-56) assessed a MD on CV events (Table 1a). The RCT (53) reported a clinically important effect with a 28% and 30% reduced risk of CV events following a MD supplemented with mixed nuts (30 g/d) or olive oil (~4 tablespoons/d), respectively, whilst the 11 year longitudinal study revealed a 34% reduced risk for CHD events with a 5 point increase in the Elderly Dietary Index (54). The remaining two longitudinal studies did not find a positive association with the Mediterranean Diet Score (MDS) (55, 56). When rated for quality out of a maximum of 9, the three longitudinal studies scored either 6 or 7 stars. Accordingly, there was evidence (Grade B) that a diet with MD characteristics reduces the risk of non-fatal CV events in older people.

Cognition

Eighteen studies assessed the MD on cognitive function (2 RCT, 13 longitudinal and 3 cross-sectional): 13 studies found positive associations with enhanced cognition and five studies reported no association (Table 1b). One large RCT, with low risk of bias, identified that those in the MD supplemented with either olive oil (~4 tablespoons/d) or mixed nuts (30 g/d) had a higher mean MMSE by 0.62 points and 0.57 points compared to the control group, respectively (57). The range of MMSE score is between 0-30, with >24 typically considered adequate cognition, while a score <12 can indicate severe dementia. However, a more recent RCT using the same intervention with smaller sample size (also with low risk of bias), found the MD did not impact on MMSE but the MD with olive oil group scored better on short-term memory and learning, and attention and executive function, compared with controls (58). Five positive longitudinal studies (range of follow-up 4.1-10.6 yrs) (59-63) and two cross-sectional studies (64, 65), all of medium quality, indicated that a higher MDS was associated with better cognition (i.e. MMSE >24) or reduced cognitive decline. Moving from the lowest to the highest tertile of the MDS (i.e. score from 1 to 7) would be equivalent to consuming on average/d: an extra ¾ cup fruit, ½ cup vegetables, and 5 g fish. In those with normal cognition, an approximate 5-6 point higher MDS was associated with 34%-54% reduced risk of Alzheimer's disease (AD) over 4-5 years (66-68); and in those with moderate cognitive impairment (MCI), a 3 point higher MDS was associated with a 48% reduction in risk for AD over 4.5 years (69). Four longitudinal (range of follow-up 3.5-6 yrs) and one cross-sectional analysis, all medium quality, reported

Table 1b
Mediterranean Diet and cognitive function (Evidence Grade B)

Reference	Level of evidence	Time	Population	Outcome	Diet marker	Effect	Overall effect	Quality score[1]/ bias[2]
(57)	II (RCT)	6.5 yrs	Spain, PREDIMED (n=7447)	1) MMSE 2) Clock Drawing Test 3) Incident events including MCI and dementia	RCT: 1) Mediterranean diet supplemented with extra-virgin olive oil (n=2543) 2) Mediterranean diet supplemented with mixed nuts (n=2454) 3) Control diet: advice to reduce dietary fat (n=2450)	1) Mean (95% CI) MMSE was 0.62 (0.18, 1.05) units ↑ in olive oil group vs. control. 2) Mean (95% CI) MMSE was 0.57 (0.11, 1.03) units ↑ in nut group vs. control.	+	Low
(58)	II	4.1 yrs	Spain, PREDIMED (n=334)	Neuropsychological test battery: 1) MMSE 2) RAVLT 3) Animals Semantic Fluency 4) Digit Span subtest from the Wechsler Adult Intelligence Scale 5) Verbal Paired Associates from the Wechsler Memory Scale 6) Color Trail Test	RCT: 1) Mediterranean diet supplemented with either extra-virgin olive oil (n=127) 2) Mediterranean diet supplemented with mixed nuts (n=112) 3) Control diet: advice to reduce dietary fat (n=95)	1) Mean change in RAVLT learning was significantly better in olive oil vs. control group: mean change: 4.50 (3.24, 5.77) vs. 2.10 (0.64, 3.57, P=0.04). 2) Mean change in Color trail test improved in olive oil vs. control (mean change: -5.77 vs. 4.53, P=0.045). 3) NS for MMSE, verbal fluency, digit span test.	+	Low
(63)	III-2	10.6 yrs	USA, the Cache County Study (n=3831)	3MS	Each quintile increase in MDS ranked score	1) Highest 4 quintiles (quintiles 2–5) of MDS had 3MS scores 0.68, 0.62, 0.83, and 0.94 points higher at the baseline interview vs. lowest (first) quintile of MDS.	+	7
(61)	III-2	7.6 yrs	USA blacks (n=2280) and whites, Chicago Health and Aging Project (n=1510)	1) East Boston tests of immediate and delayed recall 2) MMSE 3) Symbol Digit Modalities Test z scores converted to create "global cognitive functioning"	↑ 1 points MDS	0.0014 ↓ points in global cognitive functioning	+	4
(60)	III-2	5.3 yrs	China, China Health and Nutrition Survey (n=1650)	Immediate and delayed recall	↑ 5 points MDS	5% slower rate of cognitive decline in verbal scores	+	7
				Global cognitive functioning	↑ 2 points MDS	0.13 ↓ points in global cognitive functioning	+	
				Global cognitive functioning	↑ 5 points MDS	0.28 ↓ points in global cognitive functioning	+	
(59)	III-2	5.0 yrs	France, Three-City cohort 2001-2002 (n=1410)	MMSE	↑ 1 points MDS	0.006 ↓ points in MMSE	+	7
(67)	III-2	4.5 yrs	USA, Rush Memory and Aging Project (n=923)	AD	↑ 6 points MDS	↓ 54% risk over 4.5 years	+	6
(69)	III-2	4.5 yrs	USA, WHICAP 1992 + WHICAP 1999 (n=1393)	MCI	↑ 1 points MDS	↓ 8% risk over 4.5 years	+	6
				MCI	↑ 5 points MDS	↓ 28% risk over 4.5 years	+	
				MCI to AD	↑ 5 points MDS	↓ 48% risk over 4.5 years	+	
(62)	III-2	4.1 yrs	USA, Memory and Aging Project (n=826)	Battery of 19 cognitive tests summarized as a global measure of cognition	↑ 1 point MDS	0.002 ↓ points in global cognitive functioning	+	6
(68)	III-2	4.0 yrs	USA, WHICAP 1992 + WHICAP 1999 (n=2258)	AD	↑ 1 points MDS	↓ 9% risk over 4 years	+	6
				AD	↑ 5 points MDS	↓ 40% risk over 4 years	+	
(66)	III-2	4.0 yrs	Dutch (n=1219)	AD	↑ 5 points MDS	↓ 34% risk over 4 years	+	5
(64)	IV	-	Greek, the Velestino Study (n=557)	MMSE <24 (impaired cognition)	↑ 1 points MDS	↓ 12% in men	+	5
		-	Greek	MMSE <24 (impaired cognition)	↑ 1 points MDS	↓ 11% in women	-	
(65)	IV	-	Israel, MABAT ZAHAV (n=1786)	Global cognitive function (intelligent test)	↑ 4 points MDS	↓ 17% improvement	+	5
		-	USA, NHANES (n=2791)	Global cognitive function (Wechsler adult intelligence scale)	↑ 4 points MDS	↓ 2% improvement	+	

Table 1b (continued)

Reference	Level of evidence	Time	Population	Outcome	Diet marker	Effect	Overall effect	Quality score[1]/ bias[2]
(70)	III-2	5.6 yrs	USA, Women's Health Study (n=6174)	1) TICS 2) Immediate recall of the East Boston Memory Test 3) Delayed recall of the East Boston Memory test 4) Delayed recall of the TICS 10-word list 5) Category fluency 6) Digit span-backward A global cognitive score was computed as the mean of Z-scores of all 6 cognitive tests	MDS (0-9 points)	NS	NS	5
(73)	III-2	5.0 yrs	Sweden, Prospective Investigation of the Vasculature in Uppsala Seniors cohort (n=194)	7MS	MDS	NS	NS	5
(74)	III-2	3.5 yrs	USA, Women's Antioxidant Cardiovascular Study (n=2504)	1) TICS 2) Immediate recall of the East Boston Memory Test 3) Delayed recall of the East Boston Memory test 4) Delayed recall of the TICS 10-word list. 5) Category fluency. A global cognitive function score was derived by averaging standardized z-scores from all individual tests	MDS	NS	NS	5
(72)	IV	-	USA, Health ABC (n=2225)	3MS	MDS	NS	NS	4

1. Newcastle-Ottawa quality assessment scale: cross-sectional & cohort studies (Supplementary Material 2); 2. Cochrane's Collaboration: risk of bias in randomised trials (Supplementary Material 3); 3. MS, modified mini-mental state examination; 7MS, modified mini mental state score; AD Alzheimer's disease; MCI mild cognitive impairment; MMSE, mini mental state examination; NS, not significant; RAVLT, rey auditory verbal learning test; RCT, randomised control trial; TICS, telephone interview for cognitive status.

Table 1c
Mediterranean Diet and frailty (Evidence Grade C)

Reference	Level of evidence	Time	Population	Outcome	Diet marker	Effect	Overall effect	Quality score[1]
(76)	III-2	6.0 yrs	Italy, InCHIANTI study (n=690)	Frailty: ≥2 of: poor muscle strength; feeling of exhaustion; low walking speed; low physical activity	↑ 4 points MDS	↓ 70% odds for developing frailty	+	5
				Low physical activity	↑ 4 points MDS	↓ 38% odds for low physical activity	+	
				Low walking speed	↑ 4 points MDS	↓ 52% odds for low walking speed	+	
(75)	III-2	3.5 yrs	Spain, EPIC-cohort study (n=1872)	Frailty: ≥3 of: poor muscle strength; feeling of exhaustion; low walking speed; low physical activity; weight loss	↑ 3 points MDS	↓ 41% odds for developing frailty	+	5
					↑ 5 points MDS	↓ 52% odds for developing frailty	+	
(77)	IV	-	Germany (n=192)	Frailty (all 5 criteria)	↑ 6 points MDS	↓ risk of frailty reduced by 20%	+	4
				Weight loss (single criteria)	↑ 3 points MDS	↓ risk of weight loss by 35%	+	
				Low walking speed (single criteria)	↑ 6 points MDS	↓ risk of low walking speed by 71%	+	
				Low physical activity (single criteria)	↑ 6 points MDS	↓ risk of low physical activity loss by 87%	+	

1. Newcastle-Ottawa quality assessment scale: cross-sectional & cohort studies (Supplementary Material 2); MDS, Mediterranean diet score

no association between MD score and cognition (70-74). The RCTs (n=2) assessing the MD with cognition had a low risk of bias. Therefore, there is evidence (Grade B) that a diet with MD characteristics is associated with reduced cognitive decline.

Frailty

Two longitudinal studies (75, 76) and one cross-sectional study (77), assessed the MD and frailty (Table 1c). The 6yr longitudinal study indicated that greater adherence to the MD (i.e. an increase in 4 points on the MDS) was associated with a 70% reduced odds for developing frailty (>=2 of 4 criteria, of which a criterium for weight loss was not included), and a 38% and 52% reduced odds for low physical activity and low walking speed, respectively (76). Over 3.5 years, an increase of 3 points on the MDS was associated with a 41% reduced odds for becoming frail (≥2 of 5 criteria) (75). In a cross-sectional study, a 6 point higher MDS was associated with a 20% reduced risk of frailty (all 5 frailty criteria) (77). All studies were rated 4 or 5 stars. Therefore, there is evidence (Grade C) that following a diet with Mediterranean dietary characteristics may be associated with decreased likelihood of frailty.

Vegetables

Cognition

Two positive longitudinal studies over 3-6 yrs (78, 79), and five cross-sectional studies (two with positive results, two with null results, one with mixed results) assessed vegetable intake and cognition (80-84) (Table 2). A median intake of 2.8 servings/d vegetables was associated with 35% slower rate of cognitive decline per year compared to a median intake of 0.9 servings/d (79). Over 3 years, those consuming vegetables each day or almost every day were 34% less likely to experience cognitive decline (78). Cross-sectional data showed consumption of ~2 servings/d was associated with better cognitive scores compared to ~ ½ serving/d (81), while Korean women (but not men) with normal cognition had a higher vegetable intake vs. those with poor cognition (~3 servings/d vs. ~2.7 servings/d) (80). Overall, the quality of the 7 studies was poor, with an average quality star rating score of 3.1 (range 2-6 stars), and although the two longitudinal studies rated 4 and 6, and were both positive, the cross-sectional studies rated only 2 or 3. However, they were all generally positive studies. Therefore, there is consistent but weak evidence that ≥3 servings/d of vegetables was associated with reduced cognitive decline (Grade D). A Grade D recommendation suggests the body of evidence is weak and recommendation must be applied with caution.

Protein

Cognition

Seven studies assessed dietary protein intake and cognitive function (Table 3a). Three RCTs in frail elderly (2 positive), three longitudinal (1 positive) and one cross-sectional study (negative) were identified. One RCT of 24 weeks found that 2 x15 g/d protein supplementation (a dairy based 250 mL protein-supplemented beverage), taking average daily protein intake to 78 g/d, resulted in an improvement in reaction time information processing speed compared to placebo, but no change in other cognitive domains (85), and no change in MMSE, with mean protein intakes in the intervention group of 1.0 g/kg/d (86). However, in a similar RCT that utilised the same protein intervention (2x15 g/d in a dairy based 250 mL protein-supplemented beverage) combined with resistance training (2 sessions/wk), found an improvement in information processing speed; however further benefits of including exercise with a protein supplement were not found for other cognitive measures, and total daily protein intake was not reported (87). The positive 6 yr longitudinal study reported for every 1 SD increase in protein (median intake at 6 yrs, 72 g/d) improved logical memory test by 0.20 points and improved episodic memory by 0.19 points (88).

There was a low risk of bias in the 3 RCTs assessing protein supplementation on cognitive function, however for the three longitudinal (88-90) and one cross-sectional study (82) the average study quality rating was 2.5 stars (range 2-4). The different cognitive domains tested, with varying levels of baseline cognition function complicates the interpretation of data although there is some evidence (Grade C) that modestly higher intake of protein (above the Recommended Nutrient Intake, RNI) (9) may be associated with improved cognitive function.

Frailty

One longitudinal and three cross-sectional studies assessed protein intake and frailty, all were positive (Table 3b). Protein consumption of ≥1.4 g/kg/d was associated with 35% reduced likelihood of frailty over 3 yrs (91) and ≥85 g/d protein (approximately ≥1.64 g/kg body weight/d) was associated with a 35% reduced risk for frailty (47). A 1g/kg protein intake was associated with 59% likelihood of frailty (92), and those with lower protein intakes (i.e. <66 g/d in men and <55 g/d women) were 2-fold more likely to be frail (93). Assessment of study quality indicated three studies scored 5 and one study scored 2, with an average quality star rating of 4.3. Accordingly, there is consistent evidence (Grade C) that protein intakes higher than the RNI may assist in reducing risk for frailty.

Muscle strength, muscle mass: indicators of physical function

We separated out studies assessing the impact of protein intake alone from those assessing increased dietary protein in combination with resistance exercise. Resistance exercise at least twice a week helps maintain muscle strength and muscle mass, reducing falls and fractures (19). There was insufficient evidence to link dietary protein intake with falls and fracture (Supplementary Table 8a). There was insufficient evidence that increased dietary protein alone increases muscle mass and strength (Supplementary Table 8b).

Table 2
Vegetable consumption and cognition (Evidence Grade D)

Reference	Level of evidence	Time	Population	Outcome	Diet marker	Effect	Overall effect	Quality score[1]
(79)	III-2	3 and 6 yrs	USA, Chicago Health and Aging Project (n=3718)	1) MMSE 2) East Boston Tests of immediate and delayed recall 3) Symbol digit modalities test (converted to z scores as "global measure of cognitive function")	Quintiles of vegetables: 0–1.1 servings/d; 1.2–1.7 servings/d; 1.8–2.4 servings/d; 2.5–3.3 3.4–8.2 servings/d	35% reduction in annual rate of cognitive decline over the 6 yrs.	+	4
(78)	III-2	3 yrs	Chinese illiterate, Chinese Longitudinal Health Longevity Study (n=6911)	MMSE <18 at follow-up (cognitive decline) (i.e. ↓7 points)	Always/nearly every day included vegetables vs. no consumption	↓ 34% reduced likelihood to experience cognitive decline	+	6
(81)	IV	-	Norway, Hordaland Health Study (n=2031)	KOLT	Vegetables (≥167 g/d vs. ≤44 g/d)	↑ 8.5% better score	+	2
				TMT-A	Vegetables (≥167 g/d vs. ≤44 g/d)	19% quicker score	+	
				mDST	Vegetables (≥167 g/d vs. ≤44 g/d)	↑ 21% better score	+	
				m-BD	Vegetables (≥167 g/d vs. ≤44 g/d)	↑ 4% better score	+	
				m-MMSE	Vegetables (≥167 g/d vs. ≤44 g/d)	↑ 3% better score	+	
				S-task	Vegetables (≥167 g/d vs. ≤44 g/d)	↑ 18% better score	+	
(80)	IV	-	Korea (n=449)	MMSE-Korean version: Normal ≤24 vs. inadequate 19-<24 vs. poor ≤19 cognition	Vegetables (g/d)	Women (but not men) with normal cognition had higher vegetable intake (228.5 ± 99.7 g/d) vs. poor (199.6 ± 107.8 g/d)	+	3
(83)	IV	-	USA, State-wide Survey of Alabama's Elderly (n=1056)	Mental Status Questionnaire (<9/10=cognitive impairment)	Vegetables (1-2x/wk, most days, or every day vs. <1x/wk, never)	NS	NS	3
(82)	IV	-	Spain (n=260)	MMSE	Vegetable intake	NS	NS	2
				PMSQ: intellectually intact (0-2 errors); slight intellectual deterioration (3-4 errors); moderate intellectual deterioration (5-7 errors)	Vegetable intake	Men and women with poorer PMSQ (PMSQ >0) had lower vegetable intakes (233 ± 121 g/d in men and 206 ± 97g/d in women vs. 238 ± 98 g/d in men and 278 ± 139 g/d in women) than those with PMSQ=0	+	
(84)	IV	-	Taiwan, 2005 National Health Interview Survey (n=2119)	MMSE (≤23 indicates cognitive impairment)	Fruit and vegetable intake (low: ≤2x/wk fruits and ≤5x/wk vegetables; medium; and high: 1x/d fruit and 1x/d vegetables)	NS	NS	2

1. Newcastle-Ottawa quality assessment scale: cross-sectional & cohort studies (Supplementary Material 2); KOLT, Kendrick object learning test; M-BD, short form of block design; MDST, modified digit symbol test; m-MMSE, modified mini mental state examination; MMSE, mini mental state examination; NS, not significant; PMSQ, short-portable mental state questionnaire; TMT-A, trail making test part A.

Seven RCTs addressed the impact on muscle mass and strength of the combined approach of resistance exercise and increased dietary protein Three studies found a greater effect in those randomised to higher protein combined with resistance training and four found no additional benefit when compared to exercise alone (Table 4). The trials were of a relatively short duration (3 to 18 months) with a mix of higher protein foods or drink supplements combined with resistance exercise at least 2-3 times/wk. None assessed the impact on falls. One study in older adults from Chile showed 12 months consumption of a protein enriched snack (15 g/d protein from supplement) is beneficial in combination with resistance exercise (3/wk) to increase hand grip strength (94). In a RCT over 6 months, resistance-type exercise training improved leg muscle strength in both groups (i.e. with and without a 250 ml protein supplement drink (total protein intake 1.3 g/kg/d)) and the protein group also achieved a greater increase in skeletal muscle mass (95). Another RCT which assessed resistance training plus 2x80 g/d lean red meat (1.3 g/kg/body weight) over 4 months demonstrated greater gains in total body lean mass, and an 18% increase in muscle strength compared to exercise alone (96). The latter two positive RCTs had low risk of bias, whilst the risk of bias in the study by Bunout et al. (94) was unclear/low.

Four RCTs which combined protein drinks (ranging from 15-40 g/d extra protein) with resistance exercise vs. exercise alone reported no significantly greater improvements in

Table 3a
Protein consumption and cognition (Evidence Grade C)

Reference	Level of evidence	Time	Population	Outcome	Diet marker	Effect	Overall effect	Quality score[1]/bias[2]
(85)	II (RCT)	24 wks	Frail elderly, Netherlands (n=65)	Battery of neuropsychological tests (episodic memory, attention and working memory, information processing speed, and executive functioning).	1) Protein group (2x250 mL protein supplemented beverage containing 15 g protein each (total 30 g protein). Total protein intake 78 g/d (n=34) 2) Placebo group (2x250 mL drink without protein). Total protein intake 74 g/d (n=31)	1) Reaction time improved more in the protein group (68 ms) than in the placebo group (18 ms, P=0.03). 2) NS for other cognitive domain scores.	+	Low
(86)	II	24 wks	Frail elderly, Netherlands (n=62)	MMSE	Same intervention as above: 1) Protein group (2x250 mL protein supplemented beverage containing 15 g protein each (total 30 g protein). Total protein intake 1 g/kg/d (n=31) 2) Placebo group (2x250 mL drink without protein). Total protein intake 74 g/d (n=31)	NS	NS	Low
(87)	II	24 wks	Frail elderly, Netherlands (n=127)	Battery of neuropsychological tests	1) Resistance-type exercise program of two sessions per week plus protein (2x250 mL protein supplemented beverage containing 15 g protein; total 30 g/d protein in supplement) (n=31) 2) Resistance-type exercise program of two sessions per week plus a placebo drink (2x250 mL without protein) (n=31) 3) No exercise program plus protein (2x250 mL protein supplemented beverage containing 15 g protein; total 30 g/d protein in supplement) (n=34) 4) No exercise program plus a placebo drink (2x250 mL without protein) (n=31)	1) Protein drink + exercise improved information processing speed vs protein drink + non-exercise group (change in domain score 0.08 ± 0.51 vs. -0.23 ± 0.19, P=0.04). 2) Protein drink + non-exercise group improved on Verbal Fluency (2.4 ± 4.1 vs. -0.6 ± 4.1) vs. protein drink + exercise group. 3) Neither exercise with protein supplementation nor exercise without protein supplementation showed a significant benefit vs. non-exercise.	+	Low
(88)	III-2	6.0 yrs	New Mexico (n=137)	Logical Memory and Visual Reproduction test	For every 1SD increase in protein	Logical memory test improved by 0.20 points	+	2
				Rey-Osterrieth Complex Figure test	For every 1SD increase in protein	Rey-Osterrieth Complex Figure test improved by 0.19 points	+	
(89)	III-2	8.5 yrs	Italy (n=559)	MMSE	For each daily dietary intake at baseline (per g/d SD increment in protein (SD 26.5g)	NS	NS	4
(90)	III-2	8.5 mo	Portugal (n=187)	MMSE	Protein intake	NS	NS	2
(82)	IV	-	Spain (n=260)	MMSE (<28 vs. ≥28)	Protein intake (81 g/d men; 72 g/d women vs. 82 g/d men; 74 g/d women)	NS	NS	2
				PMSQ: intellectually intact (0-2 errors); slight intellectual deterioration (3-4 errors); moderate intellectual deterioration (5-7 errors)	Protein intake (81 g/d men; 70 g/d women vs. 82 g/d men; 75 g/d women)	NS	NS	

1. Newcastle-Ottawa quality assessment scale: cross-sectional & cohort studies (Supplementary Material 2), 2Cochrane's Collaboration: risk of bias in randomised trials (Supplementary Material 3); MMSE, mini mental state examination; NS not significant; PMSQ short-portable mental state questionnaire; SD, standard deviation.

physical or muscle function to exercise alone (97-100). The risk of bias was low in two studies (97, 99), despite one of these studies having poor compliance to the supplement (97); risk of bias was unclear/high (100) and unclear/low (98) in the others.

Overall, there is some evidence that higher protein intakes (e.g. higher than current guidelines) (Grade C), combined with resistance training enhances physical health (muscle mass and strength) in the short term, based on 3 RCT with low risk of bias. No long term longitudinal studies assessing the combination of resistance exercise with higher protein on falls and other indices of function were identified.

Discussion

This systematic review identified three specific dietary components/dietary patterns where there was sufficient evidence to support dietary recommendations related to indices of function in those aged >65 yrs. There was good evidence that the Mediterranean type diet reduced the risk of non-fatal cardiovascular events (Grade B) and reduced cognitive decline (Grade B). There was some evidence indicating that a Mediterranean type diet may decrease the likelihood of frailty (Grade C), that a modest increase in protein may be associated

Table 3b
Protein consumption and frailty (Evidence Grade C)

Reference	Level of evidence	Time	Population	Outcome	Diet marker	Effect	Overall effect	Quality score[1]
(91)	III-2	3.0 yrs	US, Women's Health Initiative (n=24,417)	Frailty: 4 criteria: 1) muscle weakness or slowness (Rand-36 PFS, range 0–100) 2) poor endurance or exhaustion 3) low physical activity (questionnaire) 4) Unintentional weight loss (>5% body weight) Points were summed and each participant was assigned a frailty score between 0-5; ≥3 points=frailty; 1-2=intermediate	20% ↑ in protein (i.e. ≥1.44 g/kg/d)	↓ 35% risk of frailty	+	5
					20% ↑ in protein as g/kg/d (mean Q1: 1.2 g/kg/d; Q5: 1.44 g/kg/d). Mean protein intake Q1-Q5: 1.0-1.2 g/kg/d	↓ 22% risk of intermediate frailty and ↓ 35% risk of frailty	+	
(92)	IV	-	France, French Three-City cohort (n=1345)	Frailty: 3 of 5 criteria: 1) weight loss 2) exhaustion 3) muscle weakness 4) slowness 5) physical activity	Protein intake set at ≥1 g/kg body weight	↓ 59% risk of frailty	+	5
(47)	IV	-	Japanese women (n=2108)	Frailty: ≥3 of: 1) slowness and weakness (two points) 2) exhaustion 3) low physical activity 4) unintentional weight loss Total frailty score was the sum of all available scores (0-5), with total score ≥3 defined as frail	Total protein intake of increasing quintiles (≤62.9 g/d vs. 63.0-69.8 g/d vs. 69.8-76.1 g/d vs. 76.1-84.3 g/d vs. ≥84.3 g/d, equivalent to ~≤1.22 g/kg/d in Q1 up to ≥1.64 g/kg/d in Q5)	Up to ~35% ↓ likelihood for frailty with increasing quintiles of total protein intake	+	2
					Animal protein intake of ≥54.8 g/d (highest) vs. ≤31.8 g/d (lowest) quintile of intake	↓ 27% risk for frailty	+	
					Plant protein of ≥33.9 g/d (highest) vs. ≤27.1g/d (lowest) quintile of intake inversely	↓ 34% risk for frailty	+	
(93)	IV	-	Italian elderly, In-CHIANTI (n=802)	Frailty: ≥2 of: 1) low muscle strength (grip strength) 2) feeling of exhaustion (self-reported) 3) low walking speed (time to walk 15 feet) 4) reduced physical activity (questionnaire)	Low protein intake (<66 g/d: women, <55 g/d)	2-fold more likely to be frail	+	5

1. Newcastle-Ottawa quality assessment scale: cross-sectional & cohort studies (Supplementary Material 2); PFS, physical functioning scale

with improved cognition (Grade C), decreased frailty (Grade C), and that protein plus resistance exercise training in frail elderly may enhance physical strength (Grade C). There was some evidence, albeit poor quality, indicating ≥3 servings/d of vegetables was associated with reduced cognitive decline (Grade D).

The MD has been the dietary pattern most extensively studied and the only dietary pattern utilised in RCTs in those over the age of 65 yrs. The MD typically contains greater amounts of fibre, potassium and monounsaturated fats with lower amounts of saturated fat, compared to the usual western type diet which, in younger and middled aged people, has been shown to be protective for CVD mortality (101, 102) and reduce blood pressure (103). The evidence relating the protective effect of a Mediterranean type diet on CVD mortality are supported by a recent meta-analysis of prospective and RCTs in adults ranging from 20-70 yrs, where those in the highest quantile of a MD had 34% lower incidence of CVD compared to those least adherent (104). Accordingly, there is sufficient evidence to recommend that older adults utilise olive oil daily and include as part of their diet, nuts, fruits and vegetable, fish and lean meat, to assist in reducing the risk of stroke and myocardial infarction.

There was evidence from a RCT that the MD (specifically 4 tablespoons daily of olive oil or mixed nuts) improved cognition and that a Mediterranean dietary pattern was associated with reducing the rate of cognitive decline and reducing risk of AD; these results could be generalized for older people, particularly those without initial cognitive impairment. Two recent meta-analyses of nine case-control, longitudinal and cross-sectional studies, showed greater adherence on the MDS (i.e. score of 6-9) was associated with a 40% lower risk of cognitive impairment (reviewed in (105)); whilst a subsequent meta-analysis utilising five prospective cohort studies, with a wide age range, reported that the MDS is associated with a lower risk of cognitive impairment or AD (105).

Table 4
Protein combined with exercise and muscle mass, strength and physical health (Evidence Grade C)

Reference	Level of evidence	Time	Population	Outcome	Diet marker	Effect	Overall effect	Risk of bias[1]
(94)	II (RCT)	18 mo RCT (1 yr follow-up)	Chile (n=101)	1) Upper and lower limb strength 2) Walking capacity 3) HGS	1) Protein supplement + resistance exercise (n=31) 2) Protein supplement and no resistance exercise (n=28) 3) No protein supplement + resistance exercise (2 times/wk) (n=16) 3) No protein supplement and no resistance exercise (n=26) Total protein 15 g/d from supplement	1) Resistance training increased upper and lower limb strength and walking capacity irrespective of the protein supplemented. 2) Protein supplement + resistance training increased right HGS compared to all other groups	+	Unclear/low
(95)	II	6 mo	Netherlands, frail (n=62)	Muscle strength	1) Resistance training 2x/wk + 15 g milk protein in 250 ml drink (30 g/d protein from supplement) (n= 31) 2) Resistance training 2x/wk + placebo drink (n=31)	Protein intake 77 g/d, 1.0 g/kg/d; with extra 30 g/d protein, increased to 1.3 g/kg/d. 1) Leg-press and leg-extension strength improved in both groups (no effect of protein vs. placebo supplement) 2) Short physical performance battery improved in both groups (no effect of protein vs. placebo supplement) 3) Lean body mass increased in the protein group, and did not change in the placebo group.	+	Low
(96)	II	4 mo	Australian females in a retirement village (n=100)	1) Muscle balance and function (i.e. 4-square step test, timed-up-and-go test, and 30 second sit-to-stand test) 2) Muscle strength 3) Lean mass	1) Resistance training 2x/wk + 2x80 g/d servings of cooked lean red meat (n=53) 2) Resistance training 2x/wk + control (provided with and advised to consume 1 serving (75 g cooked) rice and/or pasta/d) (n= 47)	Protein intake 1.3g/kg/d in meat group vs. 1.1g/kg/d in carbohydrate group 1) The higher protein group had an average 18% greater increase in leg-extension muscle strength and greater gains in lean mass (0.45 kg); vs. control group with carbohydrate	+	Low
(99)	II	6 mo	Canada, community dwelling elderly (n=75)	Muscle performance	RCT, double blind 1) Resistance training 3x/wk, plus daily 2x20 g/d milk protein supplement in powder form (n=39) 2) Resistance training 3x/wk, plus iso-caloric control powder (n=36)	Baseline protein intake approx. 71 g/d, 1.0 g/kg/d in both, changed to 1.2 g/kg/d in treatment and 0.9 g/kg/d in placebo groups. Physical performance, muscle strength and lean mass increased in both groups, but was NS between groups	NS	Low
				Physical function		NS between groups for physical function tests, except 400m walk (data not reported in paper)	NS	
(98)	II	9 mo	Frail elderly, France (n=62)	1) Leg extension 2) Gait velocity (6 m) 3) Stair walking 4) Chair rise	1) Nutritional supplement twice daily (200 ml each supplying 843 kJ (200 kcal), with 15 g protein (30% of energy), plus memory activities (n=22) 2) Nutritional supplement plus exercise 3x/wk; 3) Placebo plus exercise 3x/wk (n=20) 4) Placebo plus memory activities (n=20)	Quadriceps muscle power increased in the supplement group but was NS compared to the other groups	NS	Unclear/high
(100)	II	6 mo	Netherlands, elderly (n=53)	Muscle strength	1) Resistance training 3x/wk plus daily 15 g milk protein (80% of casein and 20% of whey) supplement in 250ml drink (n=27) 2) Resistance training 3x/wk plus placebo drink (n=26)	Baseline protein intake in women 1.2 g/kg/d, in men 1.1 g/kg/d increased to approx. 1.4 g/kg/d and 1.3 g/kg/d during intervention. NS between groups in muscle strength tests	NS	Unclear/high
(97)	II	3 mo	Iceland elderly (n=161)	Muscle strength	1) Resistance training 3x/wk plus post-exercise 20 g milk protein in 250 ml drink (n=83) 2) Resistance training 3x/wk plus post-exercise placebo drink (n=78)	Protein intake 79 g/d, 1.0 g/kg/d increased to 1.0 g/kg/d. All groups increased lean body mass, strength and physical function but this was NS between groups No increase in dietary protein with intervention	NS	Unclear/high

1. Cochrane's Collaboration: risk of bias in randomised trials (Supplementary Material 3); HGS, hand grip strength; NS, not significant

Although we did not find studies to support the evidence that a higher intake of fruits and vegetables reduces non-fatal CV events, we found some evidence from two longitudinal studies and two cross-sectional studies that consumption of >3 servings/d or at >200 g/d of vegetables was associated with a lower risk of AD and reduced cognitive decline. Our review did not include populations with impaired cognition on entry so we are not able to make dietary recommendations for those who already have some degree of impaired cognition. Likewise, we did not find sufficient evidence from the five studies to recommend a MD to improve mental health, as four of the studies, including one RCT, produced non-significant results. Although 16 studies assessed the association of consumption of fish and cognition, there was little evidence of any benefit on cognition or reduced risk of dementia. While these results do not support a previous meta-analysis showing protective effects for the MD and mental health (106) or fish and cognition (107), it is possible that the large age range, the use of case-control studies, the analysis of multiple vs. single studies, and differences in populations assessed, may account for differences in results. Furthermore, it is also possible that such a change in diet may be more beneficial for those <65 yrs of age.

There was also some cross-sectional evidence that the MD was associated with reduced risk of frailty (76, 77). However, it is difficult to ascertain if those who have a good appetite and are eating a variety of foods (characteristics of MD) are less frail as a result of what they are eating or if their varied dietary pattern is indicative of their better health status. Currently there are no food based interventions that have been effective in reducing risk of frailty, but it is likely that successful interventions require interventions on a number of levels including diet. To date effective interventions to reduce frailty have utilised a multi-facetted approach which included nutritional supplements, home delivered meals, and exercise, which has demonstrated a reduction in the incidence of frailty at 12 months (108).

We found some evidence from one longitudinal (91) and three cross-sectional (47, 92, 93) studies that higher protein intakes may assist in reducing risk for frailty. As there is no indication that a higher protein intake alone (without exercise) improves strength and increases muscle mass, it is likely that a combination of regular resistance exercises combined with a modest increase in dietary protein above the RNI is required to maintain muscle strength and function and reduce frailty.

Current recommendations for older people call for progressive resistance training to be performed on at least two non-consecutive days of the week (109). Three of the seven RCTs which assessed the impact on muscle mass and strength, with the combined approach of resistance exercise and increased dietary protein, demonstrated improvement in muscle mass and/or strength with protein intake up to 70% higher than RNI. Although the remaining four studies did find increases in muscle mass and strength, the increases were not significantly greater than the control/exercise only groups. The reason for these results is not clear, although the sample sizes were relatively small (with the exception of one negative study (97)), as well as unclear/high level of bias. Nevertheless, the evidence from the positive studies concurs with the recommendations from an expert group who have recommended a daily protein intake of at least 1.2 g/kg/body weight for older adults undertaking resistance exercise (110) and a recent review of protein requirements for older people (111).

There are some limitations to this review: most of the evidence linking these dietary factors with functional health indices has been derived from observational studies, where it is difficult to fully control for confounding. This is particularly the case for cross-sectional studies in older people where current dietary intake is related to current health status, and those who have impaired function may experience reduced appetite or be unable to access and cook a wide range of foods. Moreover, the quality ratings in some of these studies was low, likely impacting study outcomes and results. In comparison, risk of bias was low in studies related to the MD and non-fatal CV events and cognition, as well as protein and cognition. In contrast, there was a mix of low, unclear and potentially high risk of bias in the RCTs assessing protein supplementation in relation to muscle strength and mass, along with issues with dietary compliance. Although the RCTs that have assessed the impact of increased protein alone on function found no benefit, there is some indication from some RCTs that a modest increase in dietary protein combined with resistance exercise can improve muscle mass and strength.

There are relatively large number of studies assessing the MD (25 studies, including 4 RCTs) which met the criteria for inclusion, compared to an insufficient number of studies conducted in the older age group, on other dietary components such as fruit or vegetable intake and mental health. Therefore, there was insufficient evidence on which to make food based recommendations related to those exposures and outcomes. There was also a number of cases where multiple studies which failed to find any significant effects, such as dairy and physical health, and omega 3 fatty acids and cognition (Supplementary Material 1). More high quality RCT and cohort studies assessing these factors in the older population are required to assist in devising dietary recommendations for this group.

The dietary recommendations from this review reflect the evidence base that exists for studies examining the impact of dietary factors on the health of older people. As such the evidence supports the appropriateness of the recommending aspects of the Mediterranean dietary pattern, particularly the use of olive oil and nuts, inclusion of daily serving of vegetables, and a modest increase in dietary protein in combination with resistance exercise to optimise health and function in older people.

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Conflict of Interest: Meat & Livestock Australia funded this review but had no input into the review or the manuscript. Dr. Nowson reports grants from Nestle Health Sciences, grants and consultancy fees from Meat and Livestock Australia, and Dairy Health Nutrition Consortium outside the submitted work and she is a member of AWASH and WASH (Australian Division of World Action on Salt and Health) but does not receive any financial support from these organisations.

Ethical standard: Ethical approval was not required as all the information collated is in the public domain.

Appendix

Ebscohost: Medline
1) (Elderly OR «older adults» OR aged) AND (cardiovascular events OR stroke or myocardial infarction OR heart disease OR cerebral) AND (food OR nutrition OR diet)
2) (Elderly OR «older adults» OR aged) AND (cogni* OR learning memory OR Alzheimer's disease) AND (food OR nutrition OR diet)
3) (Elderly OR «older adults» OR aged) AND (anxiety OR depression OR mental health OR SF-36) AND (food OR nutrition OR diet)
4) (Elderly OR «older adults» OR aged) AND (fracture* OR falls OR mobility OR physical function OR strength) AND (food OR nutrition OR diet)
5) (Elderly OR «older adults» OR aged) AND frail* AND (physical activity or weight loss or exhaustion or weakness or walking speed) AND (food OR nutrition OR diet)
Limiters - Date of Publication: 19940101-20161231; Age Related: Aged: 65+ years; Language: English
Search modes - Boolean/Phrase

Ebscohost: CINAHL
1) (Elderly OR «older adults» OR aged) AND (cardiovascular events OR stroke or myocardial infarction OR heart disease OR cerebral) AND (food OR nutrition OR diet)
2) (Elderly OR «older adults» OR aged) AND (cogni* OR learning memory OR Alzheimer's disease) AND (food OR nutrition OR diet)
3) (Elderly OR «older adults» OR aged) AND (anxiety OR depression OR mental health OR SF-36) AND (food OR nutrition OR diet)
4) (Elderly OR «older adults» OR aged) AND (fracture* OR falls OR mobility OR physical function OR strength) AND (food OR nutrition OR diet)
5) (Elderly OR «older adults» OR aged) AND frail* AND (physical activity or weight loss or exhaustion or weakness or walking speed) AND (food OR nutrition OR diet)
Limiters - Date of Publication: 19940101-20161231; Age Related: Aged: 65+ years; Language: English
Search modes - Boolean/Phrase

SCOPUS
1) TITLE-ABS-KEY((Elderly OR «older adults» OR aged) AND (cardiovascular events OR stroke or myocardial infarction OR heart disease OR cerebral) AND (food OR nutrition OR diet)) AND DOCTYPE(ar OR re) AND PUBYEAR > 1994 AND (LIMIT-TO(LANGUAGE,»English»)) AND (LIMIT-TO(SRCTYPE,»j»))
2) TITLE-ABS-KEY((Elderly OR «older adults» OR aged) AND (cogni* OR learning memory OR Alzheimer's disease) AND (food OR nutrition OR diet)) AND DOCTYPE(ar OR re) AND PUBYEAR > 1994 AND (LIMIT-TO(LANGUAGE,»English»)) AND (LIMIT-TO(SRCTYPE,»j»))
3) TITLE-ABS-KEY((Elderly OR «older adults» OR aged) AND (anxiety OR depression OR mental health OR SF-36) AND (food OR nutrition OR diet)) AND DOCTYPE(ar OR re) AND PUBYEAR > 1994 AND (LIMIT-TO(LANGUAGE,»English»)) AND (LIMIT-TO(SRCTYPE,»j»))
4) TITLE-ABS-KEY((Elderly OR «older adults» OR aged) AND (fracture* OR falls OR mobility OR physical function OR strength) AND (food OR nutrition OR diet)) AND DOCTYPE(ar OR re) AND PUBYEAR > 1994 AND (LIMIT-TO(LANGUAGE,»English»)) AND (LIMIT-TO(SRCTYPE,»j»))
5) TITLE-ABS-KEY((Elderly OR «older adults» OR aged) AND frail* AND (physical activity or weight loss or exhaustion or weakness or walking speed) AND DOCTYPE(ar OR re) AND PUBYEAR > 1994 AND (LIMIT-TO(LANGUAGE,»English»)) AND (LIMIT-TO(SRCTYPE,»j»))

INFORMIT
1. Elderly AND (cogni* OR learning memory OR Alzheimer's disease) AND (food OR nutrition OR diet)
2. Elderly AND (anxiety OR depression OR mental health OR SF-36) AND (food OR nutrition OR diet)
3. Elderly AND falls OR mobility AND (food OR nutrition OR diet)
4. Elderly AND (cardiovascular events OR stroke or myocardial infarction OR heart disease OR cerebral) AND (food OR nutrition OR diet)
5. Elderly AND frail* AND (physical activity or weight loss or exhaustion or weakness or walking speed) AND (food OR nutrition OR diet)
Type: Journal; Year range: 1994-2015

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