

A review of nutritional requirements for adults aged ≥ 65 years in the UK

Article

Supplemental Material

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A review of nutritional requirements for adults aged ≥ 65 y in the UK.

Dorrington, Online Supplementary Material.

Supplemental Table 1. Current UK population nutritional recommendations for UK adults aged ≥ 65 y and age-associated physiological function for each nutrient.

Nutrient	Current recommendation	Current maximum recommended intake	Details of recommendation	Physiological function
Carbohydrates ²	50% energy intake	-	Population average intake advised in SACN 2015 <i>Carbohydrates and health</i> report for general population (1)	-
Free sugars ²	<5% energy intake	-	Population average intake advised in SACN 2015 <i>Carbohydrates and health</i> report for general population (1)	Obesity Type 2 diabetes Dental caries
Protein ³	0.75 g·kg ⁻¹ ·day ⁻¹	-	RNI advised by COMA in 1991 for general population (2)	Musculoskeletal health
Fat ³	<33% energy intake	-	Population average intake advised by COMA in 1991 for general population (2)	CVD
SFA ³	<10% energy intake	-	RNI advised in SACN 2019 <i>Saturated fat and health</i> report for general population (3)	CVD
Trans fatty acids ⁴	<2% energy intake	-	Population average intake advised in SACN 2007 <i>Update on trans fatty acids and health</i> report for general population (4)	CVD
PUFA ³	6% energy intake	-	Population average intake advised by COMA in 1991 for general population (2)	CVD
MUFA ³	12% energy intake	-	Population average intake advised by COMA in 1991 for general population (2)	CVD
LC n-3 PUFA ⁵	450 mg·day ⁻¹	-	RNI advised in SACN 2004 <i>Advice on fish consumption: benefits and risks</i> report for general population (5)	CVD
Dietary fibre ²	30 g·day ⁻¹	-	RNI advised in SACN 2015 <i>Carbohydrates and health</i> report for general population (1)	CVD Colorectal cancer Constipation
Calcium ³	700 mg·day ⁻¹	-	RNI advised by COMA in 1991 for adults ≥ 50 y (2)	Musculoskeletal health

Sodium ⁶	1600 mg·day ⁻¹	Graded response	RNI advised by COMA in 1991 for adults ≥50y (2)	CVD
Salt ⁶	-	6 g·day ⁻¹	Maximum intake advised in SACN 2003 <i>Salt and health</i> report for general population (6)	CVD
Potassium ³	3500 mg·day ⁻¹	-	RNI advised by COMA in 1991 for adults ≥50y (2)	CVD Musculoskeletal health
Iron ³	8.7 mg·day ⁻¹	17 mg·day ⁻¹	RNI advised by COMA in 1991 for adults ≥50y (2) Maximum intake suggested as likely safe by COT in 2003 for general population (7)	Anemia prevention
Zinc ³	9.5 mg·day ⁻¹ (men) 7 mg·day ⁻¹ (women)	25 mg·day ⁻¹	RNI advised by COMA in 1991 for adults ≥50y (2) SUL advised by COT in 2003 for general population (7)	Immune function
Vitamin A ³	700 µg·day ⁻¹ (men) 600 µg·day ⁻¹ (women)	1500 µg·day ⁻¹	RNI advised by COMA in 1991 for adults ≥50y (2) Maximum intake suggested as likely safe by COT in 2003 for general population (7)	CVD Bone health
Vitamin C ³	40 mg·day ⁻¹	-	RNI advised by COMA in 1991 for adults ≥50y (2)	CVD
Vitamin D ⁷	10 µg·day ⁻¹	25 µg·day ⁻¹	RNI advised in SACN 2016 <i>Vitamin D and health</i> report for older adults (8) Maximum intake suggested as likely safe by COT in 2003 for general population (7)	Musculoskeletal health
Vitamin E ³	4 mg·day ⁻¹ (men) 3 mg·day ⁻¹ (women)	-	RNI advised by COMA in 1991 for adults ≥50y (2)	CVD
Vitamin K ³	1 µg·kg ⁻¹ ·day ⁻¹	-	Safe intake advised by COMA in 1991 for adults ≥50y (2)	Musculoskeletal health
Folate ³	200 µg·day ⁻¹	1 mg·day ⁻¹	RNI advised by COMA in 1991 for adults ≥50y (2) Maximum intake advised in SACN 2006 <i>Folate and disease prevention</i> report for older adults (9)	Cognitive function Anemia prevention
Vitamin B-12 ³	1.5 µg·day ⁻¹	-	RNI advised by COMA in 1991 for adults ≥50y (2)	Cognitive function
Vitamin B-6 ³	1.4 mg·day ⁻¹ (men) 1.2 mg·day ⁻¹ (women)	10 mg·day ⁻¹	RNI advised by COMA in 1991 for adults ≥50y (2) SUL advised by COT in 2003 for general population (7)	Cognitive function

Alcohol ⁸	≤14 units·week ⁻¹	-	Safe limit advised in Chief Medical Officer's 2016 <i>Low risk drinking guidelines</i> for the general population (10)	CVD Cognitive function
Fluid ⁹	1.2-1.6L·day ⁻¹	-	Recommended intake advised in Public Health England 2016 update of the <i>Eatwell Guide</i> for general population (11)	Dehydration prevention Constipation

¹ All macronutrients included to ensure appropriate balance; other nutrients selected based on proposed physiological roles in older adults; prioritisation of major chronic diseases including cardiovascular disease, type 2 diabetes and osteoporosis, underweight and obesity, cognition, immune function and leading modifiable risk factors for morbidity (2); COMA, Committee on Medical Aspects of Food Policy; COT, Committee on Toxicity; CVD, cardiovascular disease; LC n-3 PUFA, long chain n-3 polyunsaturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; RNI, reference nutrient intake; SACN, Scientific Advisory Committee for Nutrition; SFA, saturated fatty acids.

Supplemental Table 2. Details of studies used to guide setting of nutritional recommendations for carbohydrates, free sugars, dietary fibre, sodium, potassium, iron, zinc, vitamin A, vitamin C, vitamin D, vitamin K and fluid¹

Study details	Study design	Study duration	Study population	Sample size	Exposure	Summary of results
Carbohydrates						
SACN (2015) ⁽¹⁾	Review	-	-	-	-	Recommendation of 50% of energy intake from carbohydrates. Total carbohydrates neither beneficial nor detrimental to health.
Fukagawa <i>et al.</i> (1990), US ⁽¹²⁾	Experimental study	21-28 days	Men and women aged 67-86y	<i>n</i> = 6	High carbohydrate (68% total energy), high fibre (35g/1000kcal) diet	High carbohydrate high fibre diet associated with reduced cholesterol, glucose and insulin concentrations over 2-4 weeks and improved peripheral insulin sensitivity.
Gopinath <i>et al.</i> , (2019), Australia ⁽¹³⁾	Longitudinal cohort	5y	Men and women aged ≥60y	<i>n</i> = 844	Dietary carbohydrate from FFQ at baseline (10y follow-up of main study)	No association between total carbohydrate or dietary glycemic index and glycemic load with 5y incidence of instrumental activities of daily living disability.
García-Gavilán <i>et al.</i> (2018), Spain ⁽¹⁴⁾	Longitudinal cohort	Median 8.9y	Men aged 55-80y and women aged 60-80y at high risk of CVD	<i>n</i> = 870	Tertiles of mean dietary glycemic index and glycemic load from yearly FFQs from baseline to end of follow-up	Highest tertile of dietary glycemic index had 1.80x and dietary glycemic load had 3.20x higher risk of osteoporosis-related fractures compared to lowest tertiles after adjustment for confounders (incl. physical activity, previous fractures and calcium or vitamin D intake). 1.10x increased risk of osteoporotic fractures per 1-point increase in dietary glycemic index.
Feskens <i>et al.</i> (1991), The Netherlands ⁽¹⁵⁾	Longitudinal cohort	4y	Men and women aged 64-87y	<i>n</i> = 175	Dietary carbohydrates from diet history at baseline	Higher % energy intake from carbohydrate associated with increased incidence of glucose tolerance. Pastry consumption positively associated and legumes negatively associated with glucose tolerance incidence.
Sahyoun <i>et al.</i> (2006), US ⁽¹⁶⁾	Longitudinal cohort	14y	Men and women aged 60-98y	<i>n</i> = 535	Wholegrain and refined grain intake from 3-day diet diary at baseline	Higher wholegrain intake associated with lower fasting glucose concentration and BMI, and lower risk of metabolic syndrome, adjusted for confounders (incl. medication and saturated fat intake). Highest quartile of wholegrain intake associated with 52% lower risk of CVD mortality compared to lowest quartile, but not with all-cause mortality, adjusted for confounders. Higher refined grain intake associated with higher fasting glucose concentration and higher risk of metabolic syndrome, adjusted for confounders.

Sjögren <i>et al.</i> (2010), Sweden ⁽¹⁷⁾	Longitudinal cohort	Mean 10.1y	Men aged ≥70y	n = 924	Dietary intake from 7-day diet diary at baseline	Higher adherence to a moderately carbohydrate restricted diet associated with 44% increased risk in CVD mortality. High adherence to carbohydrate restricted diet (mean carbohydrates 40% energy and protein 18% energy) associated with 5x increased risk of CVD mortality.
Garcia <i>et al.</i> (1997), US ⁽¹⁸⁾	Cross-sectional	-	Men and women aged 61-79y and 80-88y	n = 28	-	No difference in glucose tolerance between young and old older adults.
Taylor <i>et al.</i> (2017) ⁽¹⁹⁾	Cross-sectional	-	Men and women aged 65-90y	n = 128	Carbohydrate, sugar, GL and adherence to high GL diet pattern from Diet History Questionnaire II	Higher carbohydrate and sugar intake, glycemic load and higher adherence to high glycemic load diet associated with global amyloid and measures of amyloid burden. Sugar intake but not carbohydrate intake or glycemic load was negatively correlated with neuropsychometric scores.
Free sugars						
SACN (2015) ⁽¹⁾	Review	-	-	-	-	No more than 5% energy intake from free sugars. Higher sugar intake associated with increased risk of dental caries and increased energy intake. Higher sugar-sweetened beverages associated with increased type 2 diabetes risk.
Laclaustra <i>et al.</i> (2018), Spain ⁽²⁰⁾	Longitudinal cohort	3y	Men and women aged ≥60y	n = 1973	Total and added sugars from diet history	2.5x higher odds of frailty, 1.5x higher odds of low physical activity and 1.9x higher odds of unintentional weight loss from ≥36g/day compared to <15g/day added sugar intake, adjusted for confounders. Association between added sugars and frailty stronger for sugars added during food production compared to table sugars. Higher intake of naturally occurring sugars associated with 47% lower risk of frailty.
Charlton <i>et al.</i> (1998), South Africa ⁽²¹⁾	Cross-sectional	-	Men and women aged ≥65y	n = 200	Added sugar intake from FFQ	Lower % energy from added sugars associated with higher % energy from fat and lower dietary fibre and protein in men and women, and thiamine, vitamin E, iron, zinc, copper and magnesium in men only.
Gibson (2001), UK ⁽²²⁾	Cross-sectional	-	Men and women aged ≥65y	n = 806	Non-milk extrinsic sugars from 4-day weighed diet diary	Higher non-milk extrinsic sugar intake associated with higher energy intake. No association between non-milk extrinsic sugar intake and risk of low intake (below the lower reference nutrient intake) of calcium, iron, riboflavin, vitamin C and vitamin D in men and women, and folate in women. Energy intake explained greater proportion of variance of micronutrient intakes than non-milk extrinsic sugars.

Chai <i>et al.</i> (2016), US ⁽²³⁾	Cross-sectional	-	Men and women aged 65-80y	<i>n</i> = 128	Added sugar from FFQ	Higher added sugar intake correlated with higher mean arterial pressure and higher systolic blood pressure.
Moshtaghian <i>et al.</i> (2016), Australia ⁽²⁴⁾	Cross-sectional	-	Men and women aged ≥69y	<i>n</i> = 879	Added sugar from FFQ	Higher % energy from added sugars (>10% vs <5%) associated with higher carbohydrate intake, and lower protein, alcohol, long chain n-3 PUFA, fibre, retinol equivalents, vitamin B-6, B-12, C, D and E, iron, calcium, zinc and iodine, adjusted for confounders (incl. energy intake). Higher % energy from added sugars associated with lower fruit, vegetable and fish intake.
Mansoori <i>et al.</i> (2019), US ⁽²⁵⁾	Cross-sectional	-	Men and women aged 65-80y	<i>n</i> = 128	Added sugar from FFQ	Lower added sugar intake associated with 8.44mmHg reduction in SBP and 3.7mmHg reduction in DBP per 2.3tsp, in females after adjustment for confounders (incl. BMI, physical activity and total calorie intake).
Dietary fibre						
SACN (2015) ⁽¹⁾	Review	-	-	-	-	Recommendation of 30g·day ⁻¹ AOAC fibre. Associated with reduced risk of cardiovascular disease, type 2 diabetes and colorectal cancer in adults.
Gopinath <i>et al.</i> , (2018), Australia ⁽¹³⁾	Longitudinal cohort	5y	Men and women aged ≥60y	<i>n</i> = 844	Dietary fibre from FFQ at baseline (10y follow-up of main study)	61% and 46% lower odds of 5y incident instrumental activities of daily living disability from second and third quartile of dietary fibre intake compared to lowest quartile. 51% lower risk of incident instrumental activities of daily living disability from >19.1g/day compared to ≤19.1g/day fibre intake, adjusted for confounders (incl. walking disability, self-rated poor health and BMI).
Mozaffarian <i>et al.</i> (2003), US ⁽²⁶⁾	Longitudinal cohort	Mean 8.6y	Men and women aged ≥65y	<i>n</i> = 3588	Dietary fibre from FFQ at baseline	21% lower risk of cardiovascular disease from highest quintile (>6.3g·day ⁻¹) of cereal fibre intake compared to lowest quintile (<1.7g·day ⁻¹) adjusted for confounders. Non-significant after adjustment for metabolic and dietary mediators. 14% lower risk of cardiovascular disease for an increase in 2 slices of whole grain bread per day. Fruit, vegetable and total fibre not associated with cardiovascular disease risk.
Fernando <i>et al.</i> (2018), Australia ⁽²⁷⁾	Cross-sectional	-	Men and women aged ≥60y	<i>n</i> = 541	Dietary fibre from FFQ	No association between fibre intake and amyloid-β burden.
Sodium						
Alam, Purdie & Johnson (1999) ⁽²⁸⁾	Meta-analysis	-	Subjects aged ≥60y	11 RCTs	-	Higher dietary sodium chloride intake associated with increased SBP and DBP. Greater effect on SBP than DBP.
SACN (2003) ⁽⁶⁾	Review	-	-	-	-	Recommendation of salt intake of not more than 6g·day ⁻¹ . High salt increases risk of hypertension.

						Older adults have a reduced capacity for sodium excretion due to impaired kidney function.
SACN and Committee on Toxicity (2017) ⁽²⁹⁾	Review	-	-	-	-	Low sodium intake reduces systolic and diastolic blood pressure, risk of stroke and risk of coronary heart disease mortality.
Kalogeropoulos <i>et al.</i> (2015), US ⁽³⁰⁾	Longitudinal cohort	10y	Men and women aged 71-80y	<i>n</i> = 2642	Dietary sodium from FFQ at baseline	No association between sodium intake and mortality, CVD risk or heart failure.
Nowak <i>et al.</i> (2018), US ⁽³¹⁾	Longitudinal cohort	Mean 6.9y	Men and women aged 70-79y	<i>n</i> = 1194	Dietary sodium and potassium intake from FFQ	No association between dietary sodium intake and cognitive impairment or brain magnetic resonance imaging indices. 2.0x increased risk of cognitive impairment per every unit increase in dietary sodium to potassium ratio.
Gezmen-Karadag <i>et al.</i> (2012), Turkey ⁽³²⁾	Cross-sectional	-	Men and women aged ≥65y	<i>n</i> = 390	Dietary sodium from 24h recall	Inverse association between daily sodium intake and SBP in hypertensive subjects.
Mazza <i>et al.</i> (2018), Italy ⁽³³⁾	Cross-sectional	-	Women aged ≥65y	<i>n</i> = 108	Sodium intake from 7-day food record and 24h recall	Higher sodium intake associated with increased carotid intima-media thickness, adjusted for confounders (incl. smoking, medications and WC). Higher atherosclerotic plaque prevalence from highest tertile (2005-2330mg·day ⁻¹) compared to lowest tertile (780-900mg·day ⁻¹) of sodium intake.
Mendes <i>et al.</i> (2019), Portugal ⁽³⁴⁾	Cross-sectional	-	Men and women aged 65-94y	<i>n</i> = 735	Sodium and potassium intake from 24h urinary sodium and potassium excretion	2.0x and 2.2x higher risk of low handgrip strength for women and men respectively with highest quartile of sodium to potassium ratio.
Potassium						
SACN and Committee on Toxicity (2017) ⁽²⁹⁾	Review	-	-	-	-	High potassium intake reduces systolic and diastolic blood pressure and risk of stroke. High potassium intake detrimental for those with undiagnosed chronic kidney disease which increases with prevalence with age. Potassium intake restriction only likely necessary if renal function is less than 40% of normal.
Tucker <i>et al.</i> (1999), US ⁽³⁵⁾	Longitudinal cohort Cross-sectional	4y	Men and women aged 69-97y	<i>n</i> = 907	Dietary potassium and fruit and vegetable intake from FFQ at baseline	Potassium intake positively associated with BMD in men and women in cross-sectional analysis. Potassium intake associated with reduced loss of femoral neck and trochanter BMD in men over follow up but not in women, adjusted for confounders (incl. calcium and vitamin D).

						Fruit and vegetable intake positively associated with Ward's area BMD in men but not women, adjusted for confounders. Fruit and vegetables provide half dietary potassium intake.
Zhu <i>et al.</i> (2009), Australia ⁽³⁶⁾	Longitudinal cohort	5y	Women aged ≥70y	n = 266	Urinary potassium excretion at baseline	Higher urinary potassium excretion associated with 6% higher hip and 4% total body BMD at 5y, adjusted for confounders. Positive association between vegetable consumption of ≥4 types per day and urinary potassium excretion. Urinary potassium excretion weakly correlated with dietary potassium intake.
Nowak <i>et al.</i> (2018), US ⁽³¹⁾	Longitudinal cohort	Mean 6.9y	Men and women aged 70-79y	n = 1194	Dietary sodium and potassium intake from FFQ	No association between dietary potassium intake and cognitive impairment or brain magnetic resonance imaging indices. 2.0x increased risk of cognitive impairment per every unit increase in dietary sodium to potassium ratio.
McGill <i>et al.</i> (2008), US ⁽³⁷⁾	Cross-sectional	-	Men and women aged ≥51y	n = 4106	Dietary potassium and dairy intake from 24h recall	Higher mean potassium intake for those meeting dairy recommendations. ≥3 servings per day of dairy (1 serving = 1 cup milk or cottage cheese, 8 ounces yoghurt) more likely to achieve potassium recommendations. Other dietary sources of potassium include fruit and vegetables, wholegrains, nuts, seeds and dried beans.
Gezmen-Karadag <i>et al.</i> (2012), Turkey ⁽³²⁾	Cross-sectional	-	Men and women aged ≥65y	n = 390	Dietary sodium and potassium from 24h recall	Inverse association between sodium to potassium ratio and SBP in hypertensive subjects.
Mendes <i>et al.</i> (2019), Portugal ⁽³⁴⁾	Cross-sectional	-	Men and women aged 65-94y	n = 735	Sodium and potassium intake from 24h urinary sodium and potassium excretion	2.0x and 2.2x higher risk of low handgrip strength for women and men respectively with highest quartile of sodium to potassium ratio.
Iron						
van Dronkelaar <i>et al.</i> (2018) ⁽³⁸⁾	Systematic review	-	Men and women average age ≥65y	1 longitudinal cohort study 1 cross-sectional study	-	Higher iron intake associated with improved gait speed in men.
Doyle <i>et al.</i> , (1999), UK ⁽³⁹⁾	Cross-sectional	-	Men and women aged ≥65y	n = 1268	Dietary intake from 4-day weighed diet diary	Vitamin C, heme and non-heme iron and protein positively associated with iron status. Meal, poultry and fish, and vegetable positively associated with iron status. Calcium and dairy products negatively associated with iron status.
Fleming <i>et al.</i> (2002), US ⁽⁴⁰⁾	Cross-sectional	-	Men and women aged 68-93y	n = 1268	Dietary intake from FFQ	Higher fruit intake of >21 servings per week (serving size not specified) compared to ≤14 servings per week associated with decreased risk of low iron stores.

						Higher red meat intake of 4-7 servings/week compared to ≤ 4 servings per week associated with higher iron stores. Higher intake of wholegrains of >7 servings per week associated with reduced iron stores.
Yavuz <i>et al.</i> (2012), Turkey ⁽⁴¹⁾	Cross-sectional	-	Men and women mean age 72y	$n = 622$	Biochemical iron parameters	Plasma iron and transferrin saturation negatively associated with mini mental state examination score. Lower transferrin saturation in patients with dementia. Association with cognitive function independent of anemia (diagnosed by low hemoglobin, transferrin saturation or ferritin).
Li <i>et al.</i> (2019), US ⁽⁴²⁾	Cross-sectional	-	Men and women aged ≥ 60 y	$n = 2503$	Dietary iron intake from 2 x 24h recalls	Higher dietary and total iron intake associated with better cognitive performance, adjusted for confounders (incl. educational level).
Zinc						
Vishwanathan <i>et al.</i> (2013) ⁽⁴³⁾	Systematic review	-	Men and women aged ≥ 50 y	4 RCTs 4 prospective cohort studies 2 retrospective cohort studies	-	Inconclusive evidence on zinc intake and age-related macular degeneration.
van Dronkelaar <i>et al.</i> (2018) ⁽³⁸⁾	Systematic review	-	Men and women average age ≥ 65 y	2 cross-sectional studies 1 case-control study	-	Higher zinc intake associated with improved gait speed in men and women.
Costarelli <i>et al.</i> (2014), Italy ⁽⁴⁴⁾	RCT	2 x 2 month	Men and women aged ≥ 82 y	$n = 21$	4mg/day zinc in skim milk	Lower incidence of infection in zinc group. Increase in thymulin activity and T cell maturation and differentiation in zinc group.
Couzy <i>et al.</i> (1993), Switzerland ⁽⁴⁵⁾	Experimental study	-	Elderly men aged 70-83y Younger men aged 24-40y	$n = 17$	0.8mg zinc labelled isotope Test meal with varied phytic acid content	Zinc absorption not significantly different between young adults and elderly. Reduced absorption of zinc from high phytic acid meal but not different between young adults and elderly.
Couzy <i>et al.</i> (1998), Switzerland ⁽⁴⁶⁾	Experimental study	-	Elderly men and women aged 71-78y Younger men and women aged 23-43y	$n = 19$	200ml soya milk fortified with 50mg of zinc Three levels of phytic acid	Reduced absorption of zinc from high phytic acid with no difference between young adults and elderly.
Li <i>et al.</i> (2019), US ⁽⁴²⁾	Cross-sectional	-	Men and women aged ≥ 60 y	$n = 2503$	Dietary zinc intake from 2 x 24h recalls	Higher dietary and total zinc intake associated with better cognitive performance, adjusted for confounders (incl. educational level).
Vitamin A						

Borel <i>et al.</i> (1998), France ⁽⁴⁷⁾	Experimental study	24h	Elderly men and women aged 64-72y Younger men and women aged 20-30y	$n = 16$	Test meal containing 23,300 retinol equivalents of retinyl palmitate	No effect of age on intestinal absorption efficiency of vitamin A or on retinol esterification. Potential effect of age on postprandial transport and regulation of plasma concentration.
Feskanich <i>et al.</i> (2002), US ⁽⁴⁸⁾	Longitudinal cohort	18y	Post-menopausal women aged 34-77y	$n = 72337$	Dietary intake from FFQ at baseline and throughout follow-up	48% increased risk of hip fracture from vitamin A intake of $\geq 3000\mu\text{g}/\text{day}$ from food and supplements compared to $< 1250\mu\text{g}/\text{day}$, adjusted for confounders (incl. calcium and vitamin D). No increased risk from vitamin A from food only. 89% increased risk of hip fracture from retinol intake of $2000\mu\text{g}/\text{day}$ compared to $< 500\mu\text{g}/\text{day}$ from food and supplements, adjusted for confounders. Increased risk of hip fracture by 33% per $500\mu\text{g}/\text{day}$ increase in retinol from food, adjusted for confounders.
Min & Min (2014), US ⁽⁴⁹⁾	Longitudinal cohort	Mean 11.4y	Men and women aged $\geq 50\text{y}$	$n = 6069$	Serum vitamin A at baseline	U-shaped relationship between serum vitamin A and all-cause, CVD-related and coronary artery disease-related mortality. Higher risk for deficient concentrations of $< 30\mu\text{g}\cdot\text{dL}^{-1}$ and excessive of $> 80\mu\text{g}\cdot\text{dL}^{-1}$.
De Jonge <i>et al.</i> (2015), The Netherlands ⁽⁵⁰⁾	Longitudinal cohort	Mean 13.9y	Men and women aged $\geq 55\text{y}$	$n = 5288$	Dietary vitamin A from FFQ at baseline	Higher vitamin A intake associated with higher BMD, adjusted for confounders (incl. calcium intake). Not associated when adjusted for BMI. Higher retinol intake associated with lower fracture risk in subjects with BMI $> 25\text{kg}/\text{m}^2$ (incl. when adjusted for baseline BMD) but not BMI $\leq 25\text{kg}/\text{m}^2$.
Balboa-Castillo <i>et al.</i> (2018), Spain ⁽⁵¹⁾	Longitudinal cohort	3.5y	Men and women aged $\geq 60\text{y}$	$n = 1643$	Vitamin A intake from diet history	No association between vitamin A intake and incident frailty.
Vitamin C						
Sahyoun <i>et al.</i> (1996), US ⁽⁵²⁾	Longitudinal cohort	9-12y	Men and women aged $\geq 60\text{y}$	$n = 725$	Plasma vitamin C at baseline Dietary vitamin C from 3-day diet diary at baseline	Highest quintile of plasma vitamin C associated with 46% lower risk of mortality and quintile 2-4 with 36% lower risk compared to lowest quintile, adjusted for confounders (incl. vitamin E and carotenoids intake). Highest total intake of vitamin C from food and supplements ($> 388\text{mg}\cdot\text{day}^{-1}$) associated with 45% lower risk of overall mortality and 62% lower risk of mortality from heart disease compared to lowest intake ($90\text{mg}/\text{day}$), adjusted for confounders. No association between vitamin C intake and mortality when considering only those not taking vitamin C supplements.

						Highest total vegetable intake (275g·day ⁻¹) and dark green/orange vegetable intake (63g·day ⁻¹) associated with 51% and 49% reduced risk of mortality, respectively, compared to lowest intake (89g·day ⁻¹ , 0g·day ⁻¹), adjusted for confounders (incl. citrus fruit and fruit juice).
Paleologos <i>et al.</i> (1998), Australia ⁽⁵³⁾	Longitudinal cohort	4y	Men and women aged 69-91y	n = 117	Dietary vitamin C from FFQ at baseline	Higher vitamin C intake associated with lower risk of cognitive impairment. 10% reduced risk of cognitive impairment per 100mg·day ⁻¹ of dietary vitamin C.
Wengreen <i>et al.</i> (2007), US ⁽⁵⁴⁾	Longitudinal cohort	7y	Men and women aged ≥65y	n = 3831	Dietary vitamin C from FFQ at baseline	Higher vitamin C intake from food associated with reduced rate of cognitive decline.
Sahni <i>et al.</i> (2008), US ⁽⁵⁵⁾	Longitudinal cohort	4y	Men and women mean age 75y	n = 884	Dietary intake from FFQ at baseline	Higher vitamin C intake associated with reduced loss of femoral neck and trochanter BMD in men with low vitamin E or calcium intake, not in women. Higher dietary vitamin C intake associated with reduced loss of trochanter and lumbar spine in men but not women, attenuated by potassium intake (marker of fruit and vegetables).
Sahni <i>et al.</i> (2009), US ⁽⁵⁶⁾	Longitudinal cohort	15-17y	Men and women mean age 75y	n = 958	Dietary intake from FFQ at baseline	Highest tertile of total vitamin C intake (313mg·day ⁻¹) associated with 44% lower risk of hip fracture than lowest tertile (94mg·day ⁻¹), and 34% lower risk of non-vertebral fracture (308mg·day ⁻¹ vs 85mg·day ⁻¹). No association between dietary vitamin C and fractures.
Balboa-Castillo <i>et al.</i> (2018), Spain ⁽⁵¹⁾	Longitudinal cohort	3.5y	Men and women aged ≥60y	n = 1643	Vitamin C intake from diet history	No association between vitamin C intake and incident frailty
Prynne <i>et al.</i> (2006), UK ⁽⁵⁷⁾	Cross-sectional	-	Men and women aged 60-83y	n = 146	Dietary vitamin C from 7-day diet diary	Positive association between fruit and vegetable intake and bone mineral status in women.
Vitamin D						
SACN (2016) ⁽⁸⁾	Review	-	-	-	-	Recommendation of 10µg·day ⁻¹ of vitamin D from natural food, fortified foods and dietary supplements. Beneficial for musculoskeletal health including improving muscle function and reducing fracture risk and falls.
Vitamin E						
Dong <i>et al.</i> (2018) ⁽⁵⁸⁾	Meta-analysis	-	-	17 case-control	Serum vitamin E	Lower serum vitamin E concentration associated with increased risk of Alzheimer's disease.
Mezzetti <i>et al.</i> (2001), Italy ⁽⁵⁹⁾	Longitudinal cohort	Mean 47.4 months	Men and women aged ≥80y	n = 102	Plasma vitamin E at baseline	Highest quartile of plasma vitamin E concentration associated with 84% lower risk of cardiovascular events compared to lowest quartile.
Balboa-Castillo <i>et al.</i> (2018), Spain ⁽⁵¹⁾	Longitudinal cohort	3.5y	Men and women aged ≥60y	n = 1643	Vitamin E intake from diet history	No association between vitamin E intake and incident frailty.

Ortega <i>et al.</i> (2002), Spain ⁽⁶⁰⁾	Cross-sectional	-	Men and women aged 65-91y	<i>n</i> = 120	Dietary vitamin E from 5-day weighed diet diary	Dietary vitamin E of less than 50% of reference nutrient intake associated with poor cognitive function. Higher serum α -tocopherol concentration in those with better cognitive function.
Ble <i>et al.</i> (2006), Italy ⁽⁶¹⁾	Cross-sectional	-	Men and women aged ≥ 65 y	<i>n</i> = 827	Plasma vitamin E	Middle and highest tertiles of plasma vitamin E concentration associated with reduced risk of frailty, adjusted for confounders.
Capuron <i>et al.</i> (2009), France ⁽⁶²⁾	Cross-sectional	-	Men and women mean age 79y	<i>n</i> = 69	Plasma vitamin E	Low plasma vitamin E concentration associated with increased inflammatory markers. Higher plasma vitamin E concentration associated with higher physical and mental health scores.
Vitamin K						
Bulló <i>et al.</i> (2011), Spain ⁽⁶³⁾	Longitudinal cohort Cross-sectional	2y	Men and women aged 55-80y	<i>n</i> = 365	Dietary vitamin K from FFQ at baseline	Dietary vitamin K intake correlated with higher BMD cross-sectionally. Loss of BMD lower for those increasing vitamin K intake over follow up.
Misra <i>et al.</i> (2013), US ⁽⁶⁴⁾	Longitudinal cohort	30 months	Men and women mean age 62y	<i>n</i> = 1180	Plasma phylloquinone at baseline	Vitamin K deficiency associated with 56% increased risk of incident radiographic knee osteoarthritis and 139% increased risk of cartilage lesions.
Shea <i>et al.</i> (2015), US ⁽⁶⁵⁾	Longitudinal cohort	3y	Men and women aged 70-79y	<i>n</i> = 791	Plasma phylloquinone at baseline	Low plasma phylloquinone associated with 1.7x increased risk of worsening cartilage and 2.6x increased risk of worsening meniscal damage.
Shea <i>et al.</i> (2016), US ⁽⁶⁶⁾	Longitudinal cohort Cross-sectional	5y	Men and women mean age 74y	<i>n</i> = 1089	Plasma phylloquinone at baseline	Higher plasma phylloquinone concentration associated with higher short physical performance battery scores and faster 20m gait speed in cross-sectional analysis. Higher plasma phylloquinone associated with higher short physical performance battery score and faster gait speed but not walking endurance over follow up.
van Ballegooijen <i>et al.</i> (2018) ⁽⁶⁷⁾	Longitudinal cohort	Mean 11.1y	Men and women aged 55-65y	<i>n</i> = 633	Plasma dephospho-uncarboxylated matrix Gla protein	Higher dephospho-uncarboxylated matrix Gla protein concentration associated with lower handgrip strength and calf circumference, and with lower physical performance in women only.
Presse <i>et al.</i> (2013), Canada ⁽⁶⁸⁾	Cross-sectional	-	Men and women aged 70-85y	<i>n</i> = 320	Serum phylloquinone	Higher serum phylloquinone associated with better verbal episodic memory but not non-verbal episodic memory, executive function or processing speed.
Chouet <i>et al.</i> (2015), France ⁽⁶⁹⁾	Cross-sectional	-	Men and women aged ≥ 65 y	<i>n</i> = 192	Dietary vitamin K from FFQ	Dietary phylloquinone intake positively associated with mini-mental state examination score and inversely associated with frontotemporal behavioural rating scale score.
Fluid recommendations						
Hooper <i>et al.</i> (2014) ⁽⁷⁰⁾	Review	-	-	-	-	Risk of dehydration increases with age due to reduced buffering capacity from decrease in body fluid, decreased kidney function and less effective thirst response.

Scherer <i>et al.</i> (2016) ⁽⁷¹⁾	Review	-	-	-	-	Europe 1.6L·day ⁻¹ for women and 2L·day ⁻¹ for men from beverages. Germany, Austria and Switzerland 1310mL from beverages Canada and US 2.1L·day ⁻¹ for women and 3L·day ⁻¹ for men from beverages. Australia and New Zealand 6.6L·day ⁻¹ for men and 2.1L·day ⁻¹ for women. WHO 1.5L·day ⁻¹ for women and 2L·day ⁻¹ for men.
Volkert <i>et al.</i> (2019) ⁽⁷²⁾	Review	-	-	-	-	1.6L·day ⁻¹ for women and 2.0L·day ⁻¹ for men unless clinical condition requires difference approach.
Bialecka-Dębek & Pletruszka (2019), Poland ⁽⁷³⁾	Cross-sectional	-	Men and women aged 60-93y	<i>n</i> = 60	Water intake from 3-day food records and urine specific gravity	No association between water intake and hydration status and cognitive function measures.
Mendes <i>et al.</i> (2019), Portugal ⁽³⁴⁾	Cross-sectional	-	Men and women aged 65-94y	<i>n</i> = 735	Free water reserve from 24h urine collection	2.1x higher risk of low handgrip strength for women at risk of hypohydration compared to euhydrated women, but no association in men.

¹ AOAC, Association of Official Analytical Chemists; BMD, bone mineral density; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; FFQ, food frequency questionnaire; PUFA, polyunsaturated fatty acids; RNI, reference nutrient intake; SBP, systolic blood pressure.

Supplemental Table 3. Details of studies used to guide setting of nutritional recommendations for protein¹

Study details	Study design	Study duration	Study population	Sample size	Exposure	Summary of results
Protein absorption and utilisation						
Katsanos <i>et al.</i> (2005), US ⁽⁷⁴⁾	Experimental study	-	Elderly men mean age 68y Younger men mean age 31y	<i>n</i> = 19	Bolus 7g essential amino acids	Diminished protein accretion (measured by net uptake of phenylalanine) in response to bolus of essential amino acids in elderly compared to younger adults.
Milan <i>et al.</i> (2015), New Zealand ⁽⁷⁵⁾	Experimental study	-	Elderly men and women aged 60-75y Younger men and women aged 20-25y	<i>n</i> = 30	Mixed meal with high protein load	Delayed increase in postprandial serum concentration of total, branched chain and essential amino acids, and lower at 1 hour post meal in elderly subjects compared to younger subjects. Peak serum concentration of total, branched chain and essential amino acids at 3 hours post meal in elderly subjects compared to 1 hour post meal in younger subjects.
Rafii <i>et al.</i> (2016), Canada ⁽⁷⁶⁾	Experimental study	-	Men aged ≥65y	<i>n</i> = 6	Test protein intake 0.2-2g·kg ⁻¹ ·day ⁻¹	Protein requirements estimated to be 0.94-1.24g·kg ⁻¹ ·day ⁻¹ based on amino acid oxidation method (phenylalanine). Estimation similar to that for younger adults based on kg body weight but higher when adjusted to be calculated per kg fat free mass.
Protein and muscle outcomes						
Coelho-Júnior <i>et al.</i> (2018) ⁽⁷⁷⁾	Meta-analysis	-	-	5 prospective cohort studies 2 cross-sectional studies 1 case-control study	Dietary protein intake	Higher percentage of lean mass in those with high (≥1.0g·kg ⁻¹ ·day ⁻¹) and very high (≥1.2g·kg ⁻¹ ·day ⁻¹) protein intake compared to low (<0.8g·kg ⁻¹ ·day ⁻¹) and middle (0.8-1.0g·kg ⁻¹ ·day ⁻¹) protein intake. Greater knee extensor strength and performance in short physical performance battery test in those with high and very high protein intake compared to low protein intake. No association between protein intake and handgrip strength or chair rise tests.
Ottestad <i>et al.</i> (2017), Norway ⁽⁷⁸⁾	RCT	12 weeks	Men and women aged ≥70y	<i>n</i> = 36	Protein enriched milk (20g protein) or isocaloric carbohydrate drink (0g protein) 400mL at breakfast and evening meal	No increase in muscle mass or changes in body composition from protein enriched milk or control drink. Improved chest press from protein enriched milk and control drink, but no significant difference in changes. Improved stair climb test from protein enriched milk but not control drink, and no significant difference. No change in leg press, repeated chair rise, stair climb test and handgrip strength from protein enriched milk or control drink.
Mitchell <i>et al.</i> (2017), US ⁽⁷⁹⁾	RCT	10 weeks	Men aged ≥70y	<i>n</i> = 29	Protein 0.8g·kg ⁻¹ ·day ⁻¹ or 1.6g·kg ⁻¹ ·day ⁻¹	Increase in whole body lean mass and knee-extension power from 1.6g·kg ⁻¹ ·day ⁻¹ protein but no change in 0.8g·kg ⁻¹ ·day ⁻¹ .

						Decrease in appendicular lean mass from $0.8\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ protein but no change from $1.6\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$.
Kim <i>et al.</i> (2018), US ⁽⁸⁰⁾	RCT	8 weeks	Men and women aged 51-69y	$n = 19$	Uneven protein distribution (15/20/65% at breakfast, lunch and dinner) or even protein distribution (33% at each meal)	No changes in lean body mass or muscle strength after intervention and no differences between intervention groups in any functional measures. No effect of protein distribution on nitrogen balance, protein synthesis, protein breakdown or muscle protein synthesis.
Kim <i>et al.</i> (2015), US ⁽⁸¹⁾	Experimental study	-	Men and women aged 52-75y	$n = 20$	Protein $0.8\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ or $1.5\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ Uneven or even distribution patterns	$1.5\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ of protein increased net balance and protein synthesis more than $0.7\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$, and increased plasma leucine concentration to a greater degree. No effect of distribution of protein intake on protein balance, but higher plasma leucine response from even compared to uneven protein distribution. Plasma leucine positively correlated with protein synthesis.
Houston <i>et al.</i> (2008), US ⁽⁸²⁾	Longitudinal cohort	3y	Men and women aged 70-79y	$n = 2066$	Dietary protein intake from FFQ at baseline	40% lower loss of lean mass and appendicular lean mass for those in the highest quartile and consuming $1.1\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ compared to lowest protein quartile and consuming $0.7\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$. Total and animal protein intake positively associated with change in lean mass. Adjusted for confounders (incl. physical activity). No association with change in lean mass for vegetable protein.
Isanejad <i>et al.</i> (2015), Finland ⁽⁸³⁾	Longitudinal cohort Cross-sectional	3y	Women aged 65-72y	$n = 554$	Dietary protein intake from 3-day diet diary at baseline	Total and animal protein intake positively associated with lean mass, appendicular lean mass and trunk lean mass in cross-sectional analysis, adjusted for confounders (incl. physical activity). No association between plant protein intake and lean mass. Total and animal protein intake positively associated with change in lean mass and appendicular lean mass over 3y, and plant protein with change in appendicular lean mass, adjusted for confounders.
Farsijani <i>et al.</i> (2016), Canada ⁽⁸⁴⁾	Longitudinal cohort Cross-sectional	2y	Men and women aged 67-84y	$n = 712$	Dietary protein intake and distribution from 3x 24h recalls at baseline	Positive association between protein intake and lean mass and appendicular lean mass in men in but not women in cross-sectional analysis. More even protein distribution associated with greater lean mass and appendicular lean mass in men but not women in cross-sectional analysis. No association between protein intake and changes in lean mass over 2y. More even protein distribution associated with greater lean mass and appendicular lean mass across 2y, independent of total protein intake, but no association with rate of decline in lean mass.

Isanejad <i>et al.</i> (2016), Finland ⁽⁸⁵⁾	Longitudinal cohort Cross-sectional	3y	Women aged 65-72y	$n = 554$	Dietary protein from 3-day diet diary at baseline	Protein intake of $\geq 1.2\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ was associated with better measures of physical performance and muscle strength in cross-sectional analysis and at follow up, adjusted for confounders (incl. physical activity). No difference in effect on muscle strength between animal and plant protein.
McDonald <i>et al.</i> (2016), Denmark ⁽⁸⁶⁾	Longitudinal cohort	6y	Men and women aged $\geq 65\text{y}$ (sub-analysis)	$n = 79$	Leucine intake from diet history at baseline	Linear relationship between leucine intake and lean body mass change. Only those in the highest quartile of leucine intake ($7.12\text{g}\cdot\text{day}^{-1}$) maintained lean body mass, in the presence of adequate protein intake ($1.26\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$).
McLean <i>et al.</i> (2016), US ⁽⁸⁷⁾	Longitudinal cohort	6y	Men and women aged $\geq 60\text{y}$ (age stratified analyses)	$n = 646$	Dietary protein from FFQ at baseline	Reduced loss of grip strength associated with higher ($1.2\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$) total and animal protein intake compared to lower ($0.8\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$) intake. No association between grip strength and plant protein.
Farsijani <i>et al.</i> (2017), Canada ⁽⁸⁸⁾	Longitudinal cohort	3y	Men and women aged 67-84y	$n = 1741$	Dietary protein intake and distribution from 3x 24h recalls at baseline and 2y	More even protein distribution associated with higher muscle strength across follow-up, adjusted for confounders (incl. total protein), but not mobility score. Higher protein intake associated with higher muscle strength in women but not men. No association between protein distribution and rate of decline of muscle strength or mobility score.
Verreijen <i>et al.</i> (2019), US ⁽⁸⁹⁾	Longitudinal cohort	5y	Men and women aged 70-79y	$n = 1561$	Dietary protein intake from FFQ at year 2	No association between protein intake and 5y change in mid-thigh muscle area.
Asp <i>et al.</i> (2012), US ⁽⁹⁰⁾	Cross-sectional	-	Men and women aged 60-88y	$n = 142$	Dietary protein from diet history questionnaire	Positive association between beef intake and mid-arm muscle area independent of total protein or total meat, fish or poultry intake. Total protein intake positively associated with calf circumference, BMI and mini-nutritional assessment score.
Loenneke <i>et al.</i> (2016), US ⁽⁹¹⁾	Cross-sectional	-	Men and women aged 50-85y	$n = 1081$	Meal protein from 24h recall	Consuming protein in quantities above the anabolic threshold more frequently (30g-45g protein per meal) associated with increased muscle strength and leg lean mass. Plateau in anabolic response at higher protein intake in those eating more meals containing 30-45g protein.
Gingrich <i>et al.</i> (2017), Germany ⁽⁹²⁾	Cross-sectional	-	Men and women aged 75-85y	$n = 97$	Dietary protein intake from 7 day food record	More even protein distribution correlated with higher skeletal muscle mass index in men but not women. No other associations between protein intake or distribution and skeletal muscle measurements.
Alexandrov <i>et al.</i> (2018), The Netherlands ⁽⁹³⁾	Cross-sectional	-	Men and women aged 18-91y	$n = 76,633$ ($n = 4875$ aged $>65\text{y}$)	Dietary protein intake from FFQ at baseline	Higher total protein, total animal protein and fish/meat/egg protein intake associated with higher creatinine excretion in men and women aged $>65\text{y}$.

						No associations between dairy and plant protein intake and creatinine excretion after adjustment for confounders (incl. energy intake and physical activity).
ten Haaf <i>et al.</i> (2018), The Netherlands ⁽⁹⁴⁾	Cross-sectional	-	Men and women aged ≥ 65 y	$n = 140$	Dietary protein intake from 2 x 24h recalls	No association between total protein intake and measures of physical function. Greater evenness of protein distribution associated with higher gait speed associated. No association between evenness of protein distribution and other measures of physical function or Quality-Adjusted Life Years. Interaction between physical activity and total protein intake positively associated with Quality-Adjusted Life Years.
Coelho-Júnior <i>et al.</i> (2019), Brazil ⁽⁹⁵⁾	Cross-sectional	-	Men and women aged 60-85y	$n = 90$	Dietary protein from 24h recall	Higher relative protein intake associated with higher usual walking speed and higher body-weight adjusted protein intake associated with higher isometric handgrip strength. Lower animal protein intake and higher plant protein intake associated with higher fast walking speed.
Krok-Schoen <i>et al.</i> (2019), US ⁽⁹⁶⁾	Cross-sectional	-	Men and women aged ≥ 51 y	$n = 11680$ ($n = 7664$ aged ≥ 65 y_	Dietary protein from 24h recall	Higher risk of physical limitations for those not meeting protein recommendations ($0.8\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$). Lower hand grip strength for those not meeting protein recommendations in participants aged >70 y.
Protein and other health outcomes						
Coelho-Júnior <i>et al.</i> (2018) ⁽⁹⁷⁾	Meta-analysis	-	-	3 prospective cohort studies 7 cross-sectional studies	Dietary protein intake	33% lower risk of frailty from high compared to low protein intake in cross-sectional analysis. Higher protein intake associated with lower frailty risk in 2 of 3 longitudinal studies.
Groenendijk <i>et al.</i> (2019), The Netherlands ⁽⁹⁸⁾	Meta-analysis	-	-	1 RCT 12 prospective cohort studies	Dietary protein intake	Inconsistent evidence for effects of protein intake on total body BMC and BMD, and on total hip, femoral neck and lumbar spine BMD. 11% lower risk of hip fractures from high compared to low protein intake.
Mendonça <i>et al.</i> (2019), UK ⁽⁹⁹⁾	Longitudinal cohort	5y	Men and women aged ≥ 85 y	$n = 668$	Dietary protein intake from 2 x 24h recalls at baseline	56% lower risk of transitioning from pre-frail to frail per increase of 1 unit of protein intake, adjusted for confounders (incl. age and number of chronic diseases). 40% reduced risk of incident frailty from pre-frailty from $\geq 0.8\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ and 37% reduced risk from $\geq 1.0\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$. Associations attenuated after adjustment for energy intake.
Mendonça <i>et al.</i> (2019), UK ⁽¹⁰⁰⁾	Longitudinal cohort	5y	Men and women aged ≥ 85 y	$n = 722$	Dietary protein intake from 2 x 24h recalls at baseline	Protein intake $\geq 1.0\text{g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ associated with 2.7x increased likelihood of being in low and 2.1x increased likelihood of being in mild disability trajectory than severe disability trajectory, adjusted for confounders (incl. energy intake and physical activity).

Ortolá <i>et al.</i> (2020), Spain ⁽¹⁰¹⁾	Longitudinal cohort	Median 8.2y	Men and women aged ≥60y	n = 1951	Animal and vegetable protein intake from diet history at baseline	2% increase compared to >2% decrease in vegetable protein intake associated with lower deficit accumulation, adjusted for confounders (incl. change in fat intake). Replacement of 1% of energy from animal, dairy or meat protein with vegetable protein associated with lower deficit accumulation. No association between deficit accumulation and replacement of egg or fish protein with vegetable protein.
Fernando <i>et al.</i> (2018), Australia ⁽²⁷⁾	Cross-sectional	-	Men and women aged ≥60y	n = 541	Dietary protein intake from FFQ	12.6x higher odds of high brain amyloid-β burden from lowest tertile of protein intake compared to highest.
Langsetmo <i>et al.</i> (2018), US ⁽¹⁰²⁾	Cross-sectional	-	Men aged 78-98y	n = 1016	Dietary protein intake from FFQ	Higher dairy protein intake associated with higher distal radius failure load, lower total area, higher total BMD, higher compartmental BMD, thicker cortices and trabeculae, and higher trabecular number. Higher dairy protein intake associated with higher distal tibia failure load, lower total area, higher total BMD, higher compartmental BMD and thicker cortices. Higher dairy protein associated with higher total BMD and thicker cortices in the diaphyseal tibia. No association between plant protein intake and distal radius or tibia failure load. Higher non-dairy animal protein associated with higher distal radius failure load, total BMD, higher cortical BMD, higher cortical area and thicker cortices. No association between non-dairy animal protein and distal tibia failure load.
Nilsson <i>et al.</i> (2018), Sweden ⁽¹⁰³⁾	Cross-sectional	-	Women aged 65-70y	n = 106	Dietary protein intake from 6 day food record	Skeletal muscle mass index lower in those with <0.8g·kg ⁻¹ ·day ⁻¹ compared to ≥1.1g·kg ⁻¹ ·day ⁻¹ protein intake. Higher risk of physical limitation from <0.8g·kg ⁻¹ ·day ⁻¹ or <1.1g·kg ⁻¹ ·day ⁻¹ compared to ≥1.1g·kg ⁻¹ ·day ⁻¹ protein intake, after adjustment for skeletal muscle mass index.
International recommendations						
Bauer <i>et al.</i> (2013) ⁽¹⁰⁴⁾	Review	-	-	-	-	Recommendation of 1.0-1.2g·kg ⁻¹ ·day ⁻¹ of protein in healthy older adults. Higher per-meal anabolic threshold of dietary protein intake in older adults compared to younger adults, requiring 25-30g per meal with 2.5-2.8g leucine. Exercise recommended in combination with high protein diet.

¹ BMD, bone mineral density; FFQ, food frequency questionnaire

Supplemental Table 4. Details of studies used to guide setting of nutritional recommendations for dietary fat and fatty acids¹

Study details	Study design	Study duration	Study population	Sample size	Exposure	Summary of results
Dietary fat and cardiovascular outcomes						
SACN (2004) ⁽⁵⁾	Review	-	-	-	-	Recommendation of 2 portions of fish per week, 1 of which is oily, to meet intake of long chain n-3 PUFA of 450mg/day Average portion size to be 140g. Reduces risk of cardiovascular disease.
SACN (2007) ⁽⁴⁾	Review	-	-	-	-	Recommendation of <2% total energy intake from trans fats. Trans fatty acids adversely affect coronary heart disease risk by increasing LDL-C and decreasing HDL-C.
SACN (2019) ⁽³⁾	Review	-	-	-	-	Recommendation of ≤10% total energy intake from SFA and substitution with unsaturated fats. Higher intake of SFA associated with higher risk of CVD and CHD events. Limited evidence in older age groups so no evidence for changing existing recommendations for this group.
Margolin <i>et al.</i> (1991), US ⁽¹⁰⁵⁾	RCT	2 x 8 weeks	Men and women aged ≥60y with mild hypertension	n = 46	9g/day fish oil 9g/day corn oil	Fish oil and corn oil lowered blood pressure similarly. Rise in SBP towards baseline for corn oil group but not for fish oil group in second 8-week treatment. Lower triacylglycerols from fish oil.
Houston <i>et al.</i> (2011), US ⁽¹⁰⁶⁾	Longitudinal cohort	9y	Men and women aged 70-79y	n = 1941	Dietary fat from FFQ at baseline	No association between dietary total fat, SFA, MUFA and trans fatty acids and cardiovascular disease risk, adjusted for confounders (incl. diet and medication).
Blekkhorst <i>et al.</i> (2015), Australia ⁽¹⁰⁷⁾	Longitudinal cohort	10y	Women aged ≥70y	n = 1369	Dietary saturated fat from FFQ at baseline	Higher SFA intake associated with 77% increased risk of atherosclerotic vascular disease mortality per every 11.26g·day ⁻¹ increase, adjusted for confounders (incl. diet and medication) SFA intake >31.28g·day ⁻¹ associated with 3x increased risk of atherosclerotic vascular disease mortality compared to <17.39g·day ⁻¹ . Higher MUFA associated with 50% reduced risk of atherosclerotic vascular disease mortality per every 8.7g·day ⁻¹ increase, adjusted for confounders.
Marklund <i>et al.</i> (2015), Sweden ⁽¹⁰⁸⁾	Longitudinal cohort	Median 14.5y	Men and women aged ≥60y	n = 4232	Serum cholesterol esters at baseline	Higher serum cholesterol ester EPA and DHA associated with lower incident CVD in women, and higher DHA with lower incident CVD in men and women combined, adjusted for confounders (incl. comorbid conditions). Higher serum cholesterol ester EPA and DHA associated with lower all-cause mortality risk, adjusted for confounders.

						Higher serum cholesterol ester linoleic acid associated with reduced risk of all-cause mortality but not incident CVD. Higher serum cholesterol ester α -linolenic acid associated with reduced risk of incident CVD in women but not in men or all-cause mortality.
Lemaitre <i>et al.</i> (2003), US ⁽¹⁰⁹⁾	Nested case-control	7y	Men and women aged ≥ 65 y	$n = 358$	Plasma phospholipids at baseline or at follow-up	Lower phospholipid concentration of EPA, DHA and α -linolenic acid and higher linoleic acid associated with increased risk of fatal ischemic heart disease, adjusted for confounders (incl. SBP and fasting plasma glucose). No association between phospholipid concentrations and non-fatal myocardial infarction.
Clarke <i>et al.</i> (2009), UK ⁽¹¹⁰⁾	Nested case-control	8y	Men mean age 79y	$n = 355$	Plasma phospholipids at baseline	Phospholipid concentrations of SFA positively correlated with apolipoprotein B, total cholesterol, LDL-C, C-reactive protein and fibrinogen, and PUFA inversely associated with C-reactive protein. Higher phospholipid concentrations of SFA and lower PUFA associated with increased risk of coronary heart disease mortality, adjusted for confounders (incl. SBP), but not when adjusted for lipids and inflammatory markers. No association between phospholipid concentrations of MUFA intake and coronary heart disease mortality.
Julibert <i>et al.</i> (2019), Spain ⁽¹¹¹⁾	Cross-sectional	-	Men and women aged 55-80y	$n = 477$	Dietary fat and fatty acid intake from FFQ	Higher total fat and MUFA intake in those with metabolic syndrome compared to no metabolic syndrome. Increased likelihood of exceeding the Institute of Medicine acceptable macronutrient distribution range for total fat and MUFA in those with metabolic syndrome compared to no metabolic syndrome. Lower PUFA, SFA, trans fatty acids, linoleic acid and α -linolenic acid intake associated with lower risk of hypertension, and higher PUFA and vegetable fat intake associated with higher risk of abdominal obesity, adjusted for confounders (incl. BMI, total energy intake and physical activity).
Alagheband <i>et al.</i> (2017), Finland ⁽¹¹²⁾	Cross-sectional	-	Women aged ≥ 65 y	$n =$	Dietary fat and fatty acids from 3-day food diary	No associations between fat and fatty acid intake and lipoprotein subclasses after adjustment for multiple testing.
Mazza <i>et al.</i> (2018), Italy ⁽³³⁾	Cross-sectional	-	Women aged ≥ 65 y	$n = 108$	Sodium intake from 7-day food record and 24h recall	Higher PUFA intake associated with reduced carotid intima-media thickness, adjusted for confounders (incl. smoking, medications and waist circumference). Lower atherosclerotic plaque prevalence from highest tertile (8.9-11.1g \cdot day ⁻¹) compared to lowest tertile (5.5-6.6g \cdot day ⁻¹) of PUFA intake.
Dietary fat and other health outcomes						
Meyer <i>et al.</i> (2001), US ⁽¹¹³⁾	Longitudinal cohort	11y	Women aged 55-69y	$n = 35988$	Dietary fat from FFQ at baseline	No association between animal fat and incident type 2 diabetes after adjustment for confounders (incl. fibre).

						Higher vegetable fat intake associated with lower risk of incident type 2 diabetes, independent of animal fat and total fat intake. Higher PUFA intake associated with lower risk of incident type 2 diabetes, independent of total fat, MUFA, trans fatty acids and n-3 PUFA intake. Substitution of SFA with PUFA or animal fat with vegetable fat associated with reduced risk of diabetes.
Solfrizzi <i>et al.</i> (2006), Italy ⁽¹¹⁴⁾	Longitudinal cohort	Mean 8.5y	Men and women aged 65-84y	<i>n</i> = 95	Dietary fatty acids from FFQ at baseline	Higher MUFA and PUFA intake associated with better cognitive performance.
Naqvi <i>et al.</i> (2011), US ⁽¹¹⁵⁾	Longitudinal cohort	3y	Men and women aged ≥60y	<i>n</i> = 482	Dietary fatty acids from FFQ at baseline and once throughout follow up	Higher MUFA intake associated with reduced risk of cognitive decline, adjusted for confounders (incl. other fatty acids). No association between SFA intake and cognitive decline when adjusted for MUFA.
Jayanama <i>et al.</i> (2020), US ⁽¹¹⁶⁾	Longitudinal cohort	12.5y	Men and women aged 50-85y	<i>n</i> = 4062	Dietary fat and fatty acids from 24h recall	Higher % SFA and % fatty acid intake associated with higher frailty index scores. Higher SFA and % SFA intake associated with higher risk of mortality. Higher PUFA, linoleic acid, n-3 fatty acids and DPA and % PUFA intake associated with lower risk of mortality.
Martínez-Ramírez <i>et al.</i> (2007), Spain ⁽¹¹⁷⁾	Case-control	-	Men and women aged ≥65y	<i>n</i> = 334	Dietary fatty acids from FFQ	Higher intake of PUFA (≥15g·day ⁻¹) and n-6 PUFA (≥18g·day ⁻¹), but not n-3 PUFA, associated with increased risk of osteoporotic fracture, adjusted for confounders (incl. calcium and physical activity). Higher MUFA:PUFA ratio (≥3.4) associated with reduced risk of fracture.
Muka <i>et al.</i> (2017), Australia ⁽¹¹⁸⁾	Cross-sectional	-	Women aged ≥70y	<i>n</i> = 891	Dietary fat from FFQ at baseline	No association between PUFA intake and body fat mass or body fat distribution.
Dietary fat sources and health outcomes						
de Oliveira <i>et al.</i> (2017), Brazil ⁽¹¹⁹⁾	RCT	90 days	Men and women aged 60-95y with BMI ≥27kg/m ²	<i>n</i> = 76	30ml/day flaxseed oil, olive oil or sunflower oil	Decrease in apolipoprotein B to apolipoprotein A ratio from sunflower and olive oil consumption compared to baseline. Improvement in flow-mediated vasodilation in sunflower oil group from baseline, and improvement in carotid intima-media thickness in all groups.
Polychronopoulos <i>et al.</i> (2010), Greece ⁽¹²⁰⁾	Cross-sectional	-	Men and women aged ≥65y	<i>n</i> = 1486	Dietary fat from FFQ	Higher meat fat intake associated with 21% increased risk of having one additional CVD risk factor, per 5% energy adjusted increase in intake, adjusted for confounders (incl. Med diet score).
Laguzzi <i>et al.</i> (2016), Sweden ⁽¹²¹⁾	Cross-sectional	-	Men and women mean age 60y	<i>n</i> = 4232	Dietary fat from questionnaire	Higher fish intake associated with higher serum cholesterol ester EPA and DHA. Higher intake of vegetable oils and margarines associated with higher serum cholesterol ester total PUFA and linoleic acid and lower serum SFA.

Liu <i>et al.</i> (2019), Australia ⁽¹²²⁾	Cross-sectional	-	Men and women aged 53-100y		Dietary fat and fatty acid intake based on visual estimation of consumption	0.05-0.15mmol/L higher HDL-C per every 10g higher intake of total fat and SFA from dairy or meat foods. Higher total fat and SFA intake from dairy foods but not meat associated with lower TC;HDL-C. No association between fat from dairy, meat or discretionary foods and TC or LDL-C.
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¹ BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular disease; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FFQ, food frequency questionnaire; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; SBP, systolic blood pressure; SFA, saturated fatty acids; TC, total cholesterol.

Supplemental Table 5. Details of studies used to guide setting of nutritional recommendations for calcium¹

Study details	Study design	Study duration	Study population	Sample size	Exposure	Summary of results
Calcium and health outcomes						
Bolland <i>et al.</i> (2015) ⁽¹²³⁾	Systematic review	-	-	58 longitudinal cohort studies	-	Only two randomized controlled trials of dietary calcium identified relating to fracture outcomes. 74% of cohort studies reported no association between dietary calcium intake and fracture outcome. No evidence to suggest 1200mg·day ⁻¹ has additional benefits compared to lower intake. Reduced risk of total and vertebral fracture from calcium supplementation, but not hip or forearm fracture, in randomized controlled trials. No association when considering trials at lowest risk of bias.
van Dronkelaar <i>et al.</i> (2018) ⁽³⁸⁾	Systematic review	-	Men and women average age ≥65y	4 cross-sectional studies 1 case-control study	-	Higher calcium intake associated with increased muscle mass. Inconclusive evidence for association between calcium intake and sarcopenia prevalence.
Dawson-Hughes <i>et al.</i> (1990), US ⁽¹²⁴⁾	RCT	2y	Post-menopausal women aged 40-70y	<i>n</i> = 301	500mg calcium carbonate, calcium citrate malate or placebo Dietary calcium from FFQ repeated throughout intervention	No effect of calcium supplementation on BMD in those who had undergone menopause ≤5y prior to study enrolment. Reduced loss of bone density at spine, femoral neck and radius from calcium citrate malate supplementation compared to placebo in those who had undergone menopause >5y prior to study enrolment. Benefit only if dietary calcium intake <400mg·day ⁻¹ , not if 400-650mg·day ⁻¹ .
Nieves <i>et al.</i> (2008), US ⁽¹²⁵⁾	Longitudinal cohort	3y	Women aged ≥50y	<i>n</i> = 36209	Dietary calcium from questionnaire at baseline	25% reduced risk of osteoporosis from calcium intake of >800mg·day ⁻¹ compared to 500mg·day ⁻¹ , adjusted for confounders. No association between calcium intake and risk of osteoporosis related clinical fractures.
Warensjö <i>et al.</i> (2011), Sweden ⁽¹²⁶⁾	Longitudinal cohort	Median 19.2y	Women aged ≥50y	<i>n</i> = 61433	Dietary calcium from FFQ repeated throughout follow up	Calcium intake <751mg·day ⁻¹ associated with 18% increased risk of fracture, 29% increased risk of hip fracture and 47% increased risk of osteoporosis vs 822-996mg·day ⁻¹ , adjusted for confounders (incl. vitamin D and physical activity). Calcium intake >751mg·day ⁻¹ was sufficient to maintain musculoskeletal health.

						No additional benefits for higher calcium intake of $>1137\text{mg}\cdot\text{day}^{-1}$ on overall fractures or osteoporosis but 19% increased risk of hip fracture vs $822\text{-}996\text{mg}\cdot\text{day}^{-1}$. Modification of the association between calcium intake and fractures by vitamin D.
Samieri <i>et al.</i> (2013), France ⁽¹²⁷⁾	Longitudinal cohort	8y	Men and women aged 68-95y	$n = 1482$	Dairy intake from FFQ and 24h recall at baseline	Dietary pattern rich in protein, cheese and milk associated with lower risk of wrist or any fracture.
Sahni <i>et al.</i> (2017), US ⁽¹²⁸⁾	Longitudinal cohort Cross-sectional	4y	Men and women aged 69-96y	$n = 628$ $n = 862$	Dairy intake from FFQ at baseline	Higher intake of milk, yoghurt and cheese associated with higher lumbar spine BMD in vitamin D supplement users only in cross-sectional analysis. Higher intake of milk, yoghurt and cheese associated with lower trochanter BMD loss in vitamin D supplement users only, adjusted for confounders (incl. calcium supplement use).
Feskanich <i>et al.</i> (2018), US ⁽¹²⁹⁾	Longitudinal cohort	32y	Post-menopausal women and men aged $\geq 50\text{y}$	$n = 123906$	Dairy intake from FFQ at baseline and throughout follow up	Each additional serving of dairy foods (1 serving = 240mL/1 cup milk, 1 cup yoghurt, 28g/1 ounce hard cheese and cream cheese, ½ cup cottage cheese or ricotta cheese) associated with 6% lower risk of hip fracture. Each additional serving of milk associated with 8% lower risk of hip fracture in men and women, adjusted for confounders (incl. yoghurt and cheese intake). 23% lower risk of hip fracture for those consuming milk 2x per day and 17% lower risk for those consuming milk 1x per day compared to 1x per week. No association between cheese or yoghurt intake and risk of hip fracture. Association between dairy food intake and hip fracture similar for current dairy intake and cumulative average but attenuated when assessing baseline intake as exposure.
Aslam <i>et al.</i> (2019), Australia ⁽¹³⁰⁾	Longitudinal cohort	10y	Women aged $\geq 50\text{y}$	$n = 833$	Dairy intake from questionnaire at baseline, 6y and 10y follow-up	1.6x increased risk of osteoporotic fracture for those consuming none compared to $<250\text{mL}\cdot\text{day}^{-1}$ milk. No association between risk of osteoporotic fracture and milk consumption $250\text{-}500\text{mL}\cdot\text{day}^{-1}$ or $>500\text{mL}\cdot\text{day}^{-1}$ compared to $<250\text{mL}\cdot\text{day}^{-1}$. No association between risk of osteoporotic fracture and total dairy consumption $400\text{-}799\text{g}\cdot\text{day}^{-1}$ or $\geq 800\text{g}\cdot\text{day}^{-1}$ compared to $200\text{-}399\text{g}\cdot\text{day}^{-1}$ total dairy.
Radavelli-Bagatini <i>et al.</i> (2014), Australia ⁽¹³¹⁾	Cross-sectional	-	Women 80-92y	$n = 564$	Dairy intake from FFQ	Dairy intake of ≥ 2.2 servings per day (1 serving = 250g milk, 200g yoghurt, 40g hard, firm, soft and low-fat cheese, 120g cottage or ricotta cheese) associated with higher appendicular total and cortical bone mass and higher total and trabecular volumetric BMD than 1.5 servings per day, adjusted for confounders (incl. calcium and vitamin D supplementation and medication).

Wlodarek <i>et al.</i> (2014), Poland (132)	Cross-sectional	-	Women aged ≥ 55 y	$n = 625$	Calcium intake from dairy from FFQ	Lower calcium intake from dairy in those with osteoporosis diagnosed by femoral neck T-score and those with history of previous fracture compared to those without ($360\text{mg}\cdot\text{day}^{-1}$ vs $431\text{mg}\cdot\text{day}^{-1}$ T score; $390\text{mg}\cdot\text{day}^{-1}$ vs $438\text{mg}\cdot\text{day}^{-1}$ fractures).
Hallkvist <i>et al.</i> (2018), Sweden (133)	Cross-sectional	-	Men and women aged ≥ 70 y	$n = 2040$	Dairy intake from FFQ	Higher dairy product intake associated with higher trabecular and cortical CSA and radius BMD. No association with other bone properties.
International recommendations						
Institute of Medicine (2011) (134)	Other	-	-	-	-	US dietary recommendation of $1000\text{mg}\cdot\text{day}^{-1}$ for men and $1200\text{mg}\cdot\text{day}^{-1}$ for women aged 51-70y, and $1200\text{mg}\cdot\text{day}^{-1}$ for men and women aged >70 y. Set based on studies of supplementation and limited by high levels of intake (not dose-response) and based no decreased calcium absorption with age. Precautionary recommendation based on $200\text{mg}\cdot\text{day}^{-1}$ above that for younger adults for age >70 y.
World Health Organisation (2003) (135)	Other	-	-	-	-	World Health Organisation dietary recommendation of $800\text{-}1200\text{mg}\cdot\text{day}^{-1}$ in the presence of adequate vitamin D. Set based on intervention studies with calcium supplementation. Essential for high vitamin D intake or vitamin D supplementation.
National Health and Medical Research Council (2006) (136)	Other	-	-	-	-	Australia and New Zealand dietary recommendation $1000\text{mg}\cdot\text{day}^{-1}$ for men and $1300\text{mg}\cdot\text{day}^{-1}$ for women aged 51-70y, and $1300\text{mg}\cdot\text{day}^{-1}$ for men aged >70 y. Set based on calcium balance studies, with adjustment for increased daily losses and reduced absorption post-menopause. Precautionary addition of $300\text{mg}\cdot\text{day}^{-1}$ for age >70 y.
Calcium supplementation						
Devine <i>et al.</i> (1997), Australia (137)	RCT	4y	Post-menopausal women aged 54-74y	$n = 84$	$1000\text{mg}/\text{day}$ calcium supplement or placebo	Reduced loss of bone density at mid-tibial, ultradistal tibial, ankle and lumbar spine from calcium supplementation.
Peacock <i>et al.</i> (2000), US (138)	RCT	4y	Men and women aged ≥ 60 y	$n = 438$	$750\text{mg}/\text{day}$ calcium, $15\mu\text{g}/\text{day}$ vitamin D or placebo	Reduction in loss of BMD in the hip, femoral neck, trochanter and Ward's triangle from calcium supplementation compared to placebo. Greater increase in spinal BMD from calcium supplementation compared to placebo. Preservation of cortical thickness in femoral shaft from calcium supplementation.
Grados <i>et al.</i> (2003), France (139)	RCT	1y	Women aged ≥ 65 y with vitamin D deficiency	$n = 192$	$500\text{mg}/\text{day}$ calcium and $400\text{IU}/\text{day}$	Increase in bone mineral density at lumbar spine, femoral neck and trochanter from calcium and vitamin D supplementation.

					vitamin D3 or placebo	
Prince <i>et al.</i> (2006), Australia ⁽¹⁴⁰⁾	RCT	5y	Women aged ≥ 50 y	$n = 1460$	1200mg/day calcium carbonate or placebo	Reduction in all-site clinical fractures, appendicular fractures and upper limb fractures in calcium supplementation group when considering patients who took >80% of tablets.
Zhu <i>et al.</i> (2008), Australia ⁽¹⁴¹⁾	RCT	5y	Women aged 70-80y	$n = 120$	1200mg/day calcium carbonate with or without 1000IU/day vitamin D or double placebo	Better maintenance of hip BMD over 1y in both calcium supplement groups compared to placebo. Better maintenance of hip BMD over 3y and 5y in calcium with vitamin D supplement group compared to placebo, with no bone loss over 5y. Lower fractional calcium absorption in supplement group at 2y compared to baseline but no change in placebo group.
Karkkainen, <i>et al.</i> (2010), Finland ⁽¹⁴²⁾	RCT	2y	Women aged 66-71y	$n = 593$	1000mg/day calcium carbonate and 800IU/day vitamin D or nothing	Greater increase in total BMD and lower bone loss in femoral neck, Ward's triangle and total proximal femur in intervention group.
Saloyaara <i>et al.</i> (2010), Finland ⁽¹⁴³⁾	RCT	3y	Women aged ≥ 65 y	$n = 3432$	1000mg/day calcium and 800IU/day vitamin D3 or placebo	No difference in risk of fracture at any site.
Prentice <i>et al.</i> (2013), US ⁽¹⁴⁴⁾	RCT	7y	Women aged 50-79y	$n = 36282$	1000mg/day calcium and 400IU/day vitamin D3 or placebo	Calcium and vitamin D supplementation for 5 or more years associated with 48% lower risk of hip fracture compared to placebo.

¹ BMD, bone mineral density; FFQ, food frequency questionnaire.

Supplemental Table 6. Details of studies used to guide setting of nutritional recommendations for vitamin B-12, folate and vitamin B-6¹

Study details	Study design	Study duration	Study population	Sample size	Exposure	Summary of results
Folate and health outcomes						
Petridou <i>et al.</i> (2016) ⁽¹⁴⁵⁾	Meta-analysis	-	Men and women aged ≥ 55 y (most ≥ 65 y)	9 cross-sectional 1 case-control 1 longitudinal cohort	Serum folate	Low serum folate concentrations associated with 23% higher risk of depression.
SACN (2006) ⁽⁹⁾	Review	-	-	-	-	Recommendation not to exceed tolerable upper limit of 1mg/day to avoid masking vitamin B-12 deficiency.
Kado <i>et al.</i> (2005), US ⁽¹⁴⁶⁾	Longitudinal cohort	7y	Men and women aged 70-79y	$n = 370$	Plasma folate at baseline	Low plasma folate associated with 1.6x increased risk of cognitive decline over follow up, adjusted for confounders (incl. vitamin B-6, B-12 and Hcy).
Tucker <i>et al.</i> (2005), US ⁽¹⁴⁷⁾	Longitudinal cohort	3y	Men aged 54-81y	$n = 321$	Dietary folate from FFQ at baseline Plasma folate	Positive association between plasma folate and dietary intake of folate and spatial copying, and between dietary intake of folate and verbal fluency, adjusted for confounders. Positive association between plasma folate and dietary intake of folate and spatial copying, independent of vitamin B-6, B-12 and Hcy concentrations.
McLean <i>et al.</i> (2006), US ⁽¹⁴⁸⁾	Longitudinal cohort	4y	Men and women mean age 75y	$n = 1002$	Plasma folate at baseline	No association between plasma folate and mean annual bone loss or hip fracture risk.
Morris <i>et al.</i> (2012), US ⁽¹⁴⁹⁾	Longitudinal cohort	8y	Men and women mean age 75y	$n = 549$	Plasma folate at baseline	No association between plasma folate and change in cognitive function.
Gougeon <i>et al.</i> (2016), Canada ⁽¹⁵¹⁾	Longitudinal cohort	4y	Men and women aged 67-84y	$n = 1368$	Dietary folate from 3x 24h recalls at baseline	No association between depression and dietary folate,
Hughes <i>et al.</i> (2017), The Netherlands ⁽¹⁵²⁾	Longitudinal cohort	4y	Men and women aged ≥ 60 y	$n = 155$	Dietary folate from 4-day diet diary and FFQ at baseline	No association between folate intake or red blood cell folate and cognitive decline.
Balboa-Castillo <i>et al.</i> (2018), Spain ⁽⁵¹⁾	Longitudinal cohort	3.5y	Men and women aged ≥ 60 y	$n = 1643$	Folate intake from diet history	2.3x higher risk of incident frailty for highest compared to lowest tertile of folate intake.
Robins Wahlin <i>et al.</i> (2001), Sweden ⁽¹⁵²⁾	Cross-sectional	-	Men and women aged 75-96y	$n = 230$	Serum folate	Higher serum folate concentration associated with improved cognitive performance.

de Lau <i>et al.</i> (2007), The Netherlands ⁽¹⁵³⁾	Cross-sectional	-	Men and women aged 60-90y	<i>n</i> = 1033	Plasma folate	Higher plasma folate concentration associated with higher global cognitive function, faster psychomotor speed and reduced white matter lesions, adjusted for confounders (incl. plasma Hcy). No association between plasma folate concentration and hippocampal or amygdala volume.
Aparicio Vizuete <i>et al.</i> (2010), Spain ⁽¹⁵⁴⁾	Cross-sectional	-	Institutionalized men and women aged $\geq 65y$	<i>n</i> = 178	Dietary folate from 7-day weighed diet diary	Higher folate intake associated with fewer errors in the Short Portable Mental Status Questionnaire.
McNeill <i>et al.</i> (2011), UK ⁽¹⁵⁵⁾	Cross-sectional	-	Men and women aged 70y	<i>n</i> = 882	Dietary folate from FFQ	No association between folate intake and cognitive test scores.
Mendonça <i>et al.</i> (2017), UK ⁽¹⁵⁶⁾	Cross-sectional	-	Men and women aged $\geq 85y$	<i>n</i> = 793	Dietary folate from 2x 24h recalls	Total folate intake positively associated with red blood cell folate up to $500\mu g \cdot day^{-1}$. High total folate intake ($>264\mu g \cdot day^{-1}$) and folate from cereals, cereal products and vegetables associated with reduced risk of low red blood cell folate concentration ($<600nmol \cdot L^{-1}$).
Moore <i>et al.</i> (2019), Ireland ⁽¹⁵⁷⁾	Cross-sectional	-	Men and women aged $\geq 60y$	<i>n</i> = 5186	Red blood cell folate and intake of B-vitamin fortified foods from FFQ	1.8x increased risk of depression for lowest compared to highest quintile of folate status. 46% lower risk of depression associated with high fortified food intake (>1 portion per day, portion size not specified).
Vitamin B-12 and health outcomes						
Petridou <i>et al.</i> (2016) ⁽¹⁴⁴⁾	Meta-analysis	-	Men and women aged $\geq 55y$ (most $\geq 65y$)	7 cross-sectional 1 case-control 1 longitudinal cohort	Serum vitamin B-12	Low serum vitamin B-12 concentrations associated with 20% higher risk of depression. In women only (gender-specific analysis of 3 studies), low serum vitamin B-12 associated with 33% increased risk of depression.
Kado <i>et al.</i> (2005), US ⁽¹⁴⁶⁾	Longitudinal cohort	7y	Men and women aged 70-79y	<i>n</i> = 370	Plasma vitamin B-12 at baseline	No association between plasma vitamin B-12 and risk of cognitive decline.
Tucker <i>et al.</i> (2005), US ⁽¹⁴⁷⁾	Longitudinal cohort	3y	Men aged 54-81y	<i>n</i> = 321	Dietary vitamin B-12 from FFQ at baseline Plasma vitamin B-12	Positive association between plasma vitamin B-12 and dietary intake of vitamin B-12 and spatial copying, adjusted for confounders, but no association when adjusted for folate, vitamin B-6 or Hcy.
McLean <i>et al.</i> (2006), US ⁽¹⁴⁸⁾	Longitudinal cohort	4y	Men and women mean age 75y	<i>n</i> = 1002	Plasma vitamin B-12	No association between plasma vitamin B-12 and mean annual bone loss or hip fracture risk, adjusted for confounders.

Morris <i>et al.</i> (2012), US ⁽¹⁴⁹⁾	Longitudinal cohort	8y	Men and women mean age 75y	<i>n</i> = 549	Plasma vitamin B-12 at baseline	Low plasma vitamin B-12 (<257pmol·L ⁻¹) associated with greater decline in cognitive function over follow up, adjusted for confounders (incl. plasma folate). Greater impact of low plasma vitamin B-12 on cognitive function in those with high folate status. Greater decline in cognitive function for those on folic acid supplements with low plasma vitamin B-12 but not high plasma vitamin B-12.
Gougeon <i>et al.</i> (2016), Canada ⁽¹⁵⁰⁾	Longitudinal cohort	4y	Men and women aged 67-84y	<i>n</i> = 1368	Dietary vitamin B-12 from 3x 24h recalls at baseline	58% reduced risk of depression for men in highest tertile of dietary vitamin B-12 intake ($\geq 4.79\mu\text{g}\cdot\text{day}^{-1}$) compared to lowest tertile ($\leq 3.16\mu\text{g}\cdot\text{day}^{-1}$), adjusted for confounders. No association between dietary vitamin B-12 intake and depression in women.
Hughes <i>et al.</i> (2017), The Netherlands ⁽¹⁵¹⁾	Longitudinal cohort	4y	Men and women aged ≥ 60 y	<i>n</i> = 155	Dietary vitamin B-12 from 4-day diet diary and FFQ at baseline	No association between vitamin B-12 intake or serum vitamin B-12 and cognitive decline.
Vidoni <i>et al.</i> (2017), US ⁽¹⁵⁸⁾	Longitudinal cohort	Mean 5.4y	Men and women aged ≥ 50 y	<i>n</i> = 774	Serum vitamin B-12 at baseline and throughout follow up	No association between serum vitamin B-12 concentrations and decline in gait speed.
Balboa-Castillo <i>et al.</i> (2018), Spain ⁽⁵¹⁾	Longitudinal cohort	3.5y	Men and women aged ≥ 60 y	<i>n</i> = 1643	Vitamin B-12 intake from diet history	No association between vitamin B-12 intake and incident frailty.
Jelicic <i>et al.</i> (2001), The Netherlands ⁽¹⁵⁹⁾	Cross-sectional	-	Men and women aged 55-85y	<i>n</i> = 698	Blood vitamin B-12	Low vitamin B-12 status associated with slower mental processing speed, independent of folate status.
Hin <i>et al.</i> (2006), UK ⁽¹⁶⁰⁾	Cross-sectional	-	Men and women aged ≥ 75 y	<i>n</i> = 1000	Serum vitamin B-12 HoloTC, tHcy and MMA	Low serum vitamin B-12 concentration (<133pmol·L ⁻¹) or holotranscobalamin associated with a 2-3x higher risk of cognitive impairment, adjusted for confounders. High total Hcy or methylmalonic acid concentrations associated with a 4x higher risk of cognitive impairment.
McNeill <i>et al.</i> (2011), UK ⁽¹⁵⁵⁾	Cross-sectional	-	Men and women aged 70y	<i>n</i> = 882	Dietary vitamin B-12 from FFQ	Higher vitamin B-12 intake associated with better processing speed, adjusted for confounders. Less than 1% of the variance in cognitive test scores was explained by vitamin B-12 intake.
van Wijngaarden <i>et al.</i> (2016), The Netherlands ⁽¹⁶¹⁾	Cross-sectional	-	Men and women aged ≥ 65 y	<i>n</i> = 603	Dietary vitamin B-12 intake from FFQ	Dietary vitamin B-12 intake correlated with serum total B-12, serum holo transcobalamin and serum methylmalonic acid but not with plasma total Hcy. Doubling vitamin B-12 intake associated with 9% higher serum total B-12, 15% higher serum holo transcobalamin, 9% higher serum methylmalonic acid and 2% lower plasma total Hcy.

Mendonça <i>et al.</i> (2017), UK ⁽¹⁵⁶⁾	Cross-sectional	-	Men and women aged ≥ 85 y	$n = 793$	Dietary vitamin B-12 from 2x 24h recalls	Total vitamin B-12 intake weakly associated with plasma vitamin B-12 concentration. High total vitamin B-12 intake ($>2.88\mu\text{g}\cdot\text{day}^{-1}$) associated with 50% reduced risk of low plasma vitamin B-12 compared to low intake ($<1.87\mu\text{g}\cdot\text{day}^{-1}$). High vitamin B-12 intake from meat and meat products associated with reduced risk of low plasma vitamin B-12.
Moore <i>et al.</i> (2019), Ireland ⁽¹⁵⁷⁾	Cross-sectional	-	Men and women aged ≥ 60 y	$n = 5186$	Serum vitamin B-12 and intake of B-vitamin fortified foods from FFQ	No association between serum total B-12 and depression. 46% lower risk of depression associated with high fortified food intake (>1 portion per day, portion size not specified).
Vitamin B-6 and health outcomes						
Kado <i>et al.</i> (2005), US ⁽¹⁴⁶⁾	Longitudinal cohort	7y	Men and women aged 70-79y	$n = 370$	Plasma vitamin B-6 at baseline	No association between plasma vitamin B-6 and risk of cognitive decline after adjustment for confounders (incl. vitamin B-12, B-6 and folate).
Tucker <i>et al.</i> (2005), US ⁽¹⁴⁷⁾	Longitudinal cohort	3y	Men aged 54-81y	$n = 321$	Dietary vitamin B-6 from FFQ at baseline Plasma vitamin B-6 at baseline	Positive association between plasma vitamin B-6 and dietary intake of vitamin B-6 and spatial copying, adjusted for confounders, but not when adjusted for folate, vitamin B-12 or Hcy.
McLean <i>et al.</i> (2006), US ⁽¹⁴⁸⁾	Longitudinal cohort	4y	Men and women mean age 75y	$n = 1002$	Plasma vitamin B-6 at baseline	Plasma vitamin B-6 deficiency associated with greater mean annual bone loss compared to normal plasma concentrations. No association between plasma vitamin B-6 and hip fracture risk, adjusted for confounders.
Gugeon <i>et al.</i> (2016), Canada ⁽¹⁵⁰⁾	Longitudinal cohort	4y	Men and women aged 67-84y	$n = 1368$	Dietary vitamin B-6 from 3x 24h recalls at baseline	43% reduced risk of developing depression for women in highest tertile of dietary vitamin B-6 ($\geq 1.71\text{mg}\cdot\text{day}^{-1}$) compared to lowest tertile ($\leq 1.33\text{mg}\cdot\text{day}^{-1}$), adjusted for confounders. No association between dietary vitamin B-6 intake and depression in men.
Hughes <i>et al.</i> (2017), The Netherlands ⁽¹⁵¹⁾	Longitudinal cohort	4y	Men and women aged ≥ 60 y	$n = 155$	Dietary vitamin B-6 from 4-day diet diary and FFQ at baseline	Lower vitamin B-6 intake ($0.9\text{-}1.4\text{mg}\cdot\text{day}^{-1}$) and low pyridoxal-5-phosphate concentration associated with 3.5-4x higher risk of cognitive decline, adjusted for confounders.
Struijk <i>et al.</i> (2017), Spain ⁽¹⁶²⁾	Longitudinal cohort	4y	Men and women aged ≥ 60 y	$n = 1630$	Dietary vitamin B-6 from FFQ at baseline	Higher vitamin B-6 intake associated with reduced risk of mobility limitation with 19% reduced risk of impaired mobility per $0.5\text{mg}\cdot\text{day}^{-1}$ increase, adjusted for confounders, although not independent of vitamin B-12 and folate intake.
Balboa-Castillo <i>et al.</i> (2018), Spain ⁽⁵¹⁾	Longitudinal cohort	3.5y	Men and women aged ≥ 60 y	$n = 1643$	Vitamin B-6 intake from diet history	2.8x higher risk of incident frailty for highest compared to lowest tertile of vitamin B-6 intake.

McNeill <i>et al.</i> (2011), UK ⁽¹⁵⁵⁾	Cross-sectional	-	Men and women aged 70y	<i>n</i> = 882	Dietary vitamin B-6 from FFQ	No association between vitamin B-6 from foods and cognitive test scores.
Moore <i>et al.</i> (2019), Ireland ⁽¹⁵⁷⁾	Cross-sectional	-	Men and women aged ≥60y	<i>n</i> = 5186	Plasma vitamin B-6 and intake of B-vitamin fortified foods from FFQ	1.5x increased risk of depression for lowest compared to highest quintile of vitamin B-6 status. 46% lower risk of depression associated with high fortified food intake (>1 portion per day, portion size not specified).
Homocysteine, B vitamins and health outcomes						
Tucker <i>et al.</i> (2005), US ⁽¹⁴⁷⁾	Longitudinal cohort	3y	Men aged 54-81y	<i>n</i> = 321	Plasma homocysteine at baseline	Negative association between plasma Hcy and spatial copying and recall memory, adjusted for confounders.
Kado <i>et al.</i> (2005), US ⁽¹⁴⁶⁾	Longitudinal cohort	7y	Men and women aged 70-79y	<i>n</i> = 370	Plasma homocysteine at baseline	No association between plasma Hcy and risk of cognitive decline after adjustment for confounders (incl. vitamin B-12, B-6 and folate).
Hughes <i>et al.</i> (2017), The Netherlands ⁽¹⁵¹⁾	Longitudinal cohort	4y	Men and women aged ≥60y	<i>n</i> = 155	Plasma homocysteine from 4-day diet diary and FFQ at baseline	No association between high Hcy and cognitive decline.
de Lau <i>et al.</i> (2007) ⁽¹⁵³⁾	Cross-sectional	-	Men and women aged 60-90y	<i>n</i> = 1033	Plasma homocysteine	Lower plasma Hcy associated with higher global cognitive function and faster psychomotor speed, adjusted for confounders (incl. plasma folate).
Bonetti <i>et al.</i> (2015) ⁽¹⁶³⁾	Cross-sectional	-	Men and women aged ≥65y			High homocysteine associated with increased risk of dementia independent of folate and vitamin B-12 deficiency. High homocysteine associated with cognitive impairment.
International recommendations						
Institute of Medicine (1998) ⁽¹⁶⁴⁾	-	-	-	-	-	US recommended dietary allowance of 2.4µg·day ⁻¹ vitamin B-12, 1.7mg·day ⁻¹ for men and 1.5mg·day ⁻¹ for women vitamin B-6 and 400µg·day ⁻¹ folate for age 51-70y and >70y. Recommendation that vitamin B-12 fortified foods (eg. cereals) or supplements used to meet much of requirement due to bioavailability not being altered in those with atrophic gastritis compared to vitamin B-12 from animal foods. Vitamin B-12 set based on hematological status. Folate set based on metabolic, observational and epidemiological studies. Vitamin B-6 based on few studies.
World Health Organisation (2003) ⁽¹³⁵⁾	-	-	-	-	-	World Health Organisation dietary recommendation of 2.5µg·day ⁻¹ vitamin B-12 and 400µg·day ⁻¹ folate. Recommendation for vitamin B-12 from supplements or foods fortified with vitamin B-12.

National Health and Medical Research Council (2006) ⁽¹³⁶⁾	-	-	-	-	-	<p>Australia and New Zealand dietary recommendation of 2.4µg·day⁻¹ vitamin B-12 and 400µg·day⁻¹ folate for age >70y.</p> <p>Recommendation for older adults to have higher intake of vitamin B-12 rich foods, vitamin B-12 fortified foods and supplements due to limited absorption.</p> <p>Vitamin B-12 based on old experimental studies.</p> <p>Folate based on observational, metabolic and epidemiological studies.</p> <p>Vitamin B-6 based on few studies.</p>
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¹ FFQ, food frequency questionnaire; Hcy, homocysteine.

Supplemental Table 7. Details of studies used to guide setting of nutritional recommendations for alcohol¹

Study details	Study design	Study duration	Study population	Sample size	Exposure	Summary of results
Alcohol and cognitive function						
Ruitenberg <i>et al.</i> (2002), The Netherlands ⁽¹⁶⁵⁾	Longitudinal cohort	6y	Men and women aged ≥ 55 y	$n = 5395$	Alcohol intake from FFQ at baseline	Moderate drinking of 1-3 drinks·day ⁻¹ (portion size not specified) associated with 42% reduced risk of any dementia and 71% reduced risk of vascular dementia.
Espeland <i>et al.</i> (2005), US ⁽¹⁶⁶⁾	Longitudinal cohort	6y	Women aged ≥ 65 y	$n = 4461$	Alcohol intake from FFQ at baseline	≥ 1 drink·day ⁻¹ (portion size not specified) associated with higher cognitive function and 47% reduced risk of decline in cognitive function compared to non-drinkers, adjusted for confounders. <1 drink·day ⁻¹ associated with 31% reduced risk of cognitive decline compared to non-drinkers. No association between alcohol intake and incident mild cognitive impairment or dementia when adjusted for confounders.
Stampfer <i>et al.</i> (2005), US ⁽¹⁶⁷⁾	Longitudinal cohort	20y	Women aged ≥ 70 y	$n = 11102$	Alcohol intake from FFQ at baseline and 4-yearly throughout follow up	Moderate alcohol intake (<15g·day ⁻¹) associated with higher cognitive score compared to non-drinkers, adjusted for confounders (incl. education level). Moderate alcohol intake associated with 20% lower risk of cognitive impairment and 15% lower risk of cognitive decline, adjusted for confounders. No association between high alcohol intake (15-30g·day ⁻¹) and risk of cognitive impairment or decline.
Espeland <i>et al.</i> (2006), US ⁽¹⁶⁸⁾	Longitudinal cohort	2-4y	Women aged ≥ 65 y	$n = 2299$	Alcohol intake from FFQ at baseline	Moderate drinking of up to 3 drinks·day ⁻¹ (portion size not specified) associated with higher global cognitive function than non-drinkers. Drinking ≥ 1 drink·day ⁻¹ associated with higher scores on verbal knowledge and phonemic fluency than non-drinking.
McGuire <i>et al.</i> (2007), US ⁽¹⁶⁹⁾	Longitudinal cohort	5y	Men and women aged ≥ 70 y	$n = 2716$	Alcohol intake assessed at baseline and first follow-up	Alcohol intake of ≤ 1 drink·day ⁻¹ (portion size not specified) associated with 33% reduced risk of low cognitive functioning compared to abstainers and women consuming >1 drink/day, adjusted for confounders (incl. education).
Hogekamp <i>et al.</i> (2014), Sweden ⁽¹⁷⁰⁾	Longitudinal cohort Cross-sectional	7y	Men mean age 70y	$n = 652$ $n = 986$	Alcohol intake from questionnaire at baseline	Higher alcohol intake associated with better cognitive performance in cross-sectional analysis and at 7y follow-up, adjusted for confounders (incl. education level). No association between alcohol intake and age-related cognitive decline over follow up.
García-Esquinas <i>et al.</i> (2018), Spain ⁽¹⁷¹⁾	Longitudinal cohort	2.8-7.4y	Men and women aged ≥ 60 y	$n = 5299$	Alcohol intake from diet history at baseline	No association between alcohol intake and depression.

Vasiliadis <i>et al.</i> (2019), Canada ⁽¹⁷²⁾	Longitudinal cohort	3y	Men and women aged ≥ 65 y	$n = 1610$	Alcohol intake from interview at baseline	No association between alcohol intake and cognitive decline.
Corley <i>et al.</i> (2011), UK ⁽¹⁷³⁾	Cross-sectional	-	Men and women aged 70y	$n = 917$	Alcohol intake from FFQ	Moderate alcohol intake of >2 units \cdot day ⁻¹ associated with higher cognitive function compared to intake of ≤ 2 units \cdot day ⁻¹ and non-drinkers, but mostly attenuated after adjustment for childhood IQ and adult social class.
Davis <i>et al.</i> (2014), Iceland ⁽¹⁷⁴⁾	Cross-sectional	-	Men and women mean age 75y	$n = 3363$	Alcohol intake from questionnaire	Light-to-moderate alcohol intake of 1-7 drinks \cdot week ⁻¹ (1 drink = 14g alcohol) associated with higher cognitive function compared to light-drinkers and abstainers.
Downer <i>et al.</i> (2015), US ⁽¹⁷⁵⁾	Cross-sectional	-	Men and women aged ≥ 60 y	$n = 664$	Alcohol intake from questionnaire	Moderate alcohol consumption (7-14 drinks \cdot week ⁻¹ , 1 drink = 12 ounce beer, 4 ounce wine, cocktail containing 1-1.5 ounces liquor) associated with larger hippocampal volume compared to abstainers, adjusted for confounders (incl. education), but not for other brain regions. Light alcohol consumption (1-6 drinks/week) associated with better episodic memory than abstainers.
Alcohol and cardiovascular outcomes						
Mukamal <i>et al.</i> (2004), US ⁽¹⁷⁶⁾	Cross-sectional	-	Men and women aged ≥ 65 y	$n = 5865$	Alcohol intake from questionnaire	Higher alcohol intake associated with a reduction in inflammatory markers, adjusted for confounders.
Bryson <i>et al.</i> (2006), US ⁽¹⁷⁷⁾	Longitudinal cohort	7-10y	Men and women aged ≥ 65 y	$n = 5595$	Alcohol intake from questionnaire at baseline and repeated throughout follow-up	Alcohol intake of 1-6 drinks \cdot week ⁻¹ (portion size not specified) and 7-13 drinks \cdot week ⁻¹ associated with 16% and 31% lower risk of congestive heart failure, respectively, compared to abstention, adjusted for confounders (incl. incident myocardial infarction). Former drinking associated with higher risk of congestive heart failure compared to abstainers, but no increased risk for those abstaining during follow-up.
Mukamal <i>et al.</i> (2006), US ⁽¹⁷⁸⁾	Longitudinal cohort	9.2y	Men and women aged ≥ 65 y	$n = 4410$	Alcohol intake from questionnaire at baseline and annually throughout follow-up	Alcohol intake of >14 drinks \cdot week ⁻¹ (1 drink = 15g alcohol) associated with lower risk of myocardial infarction and coronary death compared to abstainers, adjusted for confounders.
Mukamal <i>et al.</i> (2007), US ⁽¹⁷⁹⁾	Longitudinal cohort	9.1y	Men and women aged ≥ 65 y	$n = 5609$	Alcohol intake from questionnaire at baseline and annually throughout follow-up	No association between current alcohol intake and atrial fibrillation or mortality from atrial fibrillation. Former drinking associated with increased risk of atrial fibrillation, but not when considering those who abstained during follow-up.
Muscari <i>et al.</i> (2015), Italy ⁽¹⁸⁰⁾	Longitudinal cohort	6y	Men and women aged ≥ 65 y	$n = 4299$	Alcohol intake from questionnaire at baseline and repeated throughout follow-up	Light-to-moderate alcohol intake (1-2 units \cdot day ⁻¹) associated with lower risk of mortality compared to abstention, adjusted for confounders. Positive association between light-to-moderate alcohol consumption and mortality partially explained by better perceived health status and physical activity.

Costa <i>et al.</i> (2018), Italy ⁽¹⁸¹⁾	Case-control		Men and women aged ≥ 55 y	$n = 6328$	Alcohol intake from interview	Heavy alcohol intake ($>45\text{g}\cdot\text{day}^{-1}$) associated with 1.4x increased risk of total intra-cerebral hemorrhage and 1.7x increased risk of deep intra-cerebral hemorrhage. No association between heavy alcohol intake and lobar intra-cerebral hemorrhage.
Jaubert <i>et al.</i> (2014), US ⁽¹⁸²⁾	Cross-sectional	-	Men and women mean age 70y	$n = 553$	Alcohol intake from FFQ	Moderate-to-heavy drinking of $>1\text{ drink}\cdot\text{day}^{-1}$ (1 drink = 120mL/4 ounces wine, 360mL/12 ounces beer, 45mL/1.5 ounces liquor) associated with higher daytime and 24-hour diastolic blood pressure compared to infrequent consumption ($<1\text{ drink}\cdot\text{month}^{-1}$), but not systolic blood pressure. Lower daytime blood pressure variability associated with very light (1 $\text{drink}\cdot\text{month}^{-1}$ to 1 $\text{drink}\cdot\text{day}^{-1}$) compared to infrequent consumption ($<1\text{ drink}\cdot\text{month}^{-1}$).
Gonçalves <i>et al.</i> (2015), US ⁽¹⁸³⁾	Cross-sectional	-	Men and women mean age 76y	$n = 4466$	Alcohol intake from questionnaire	Alcohol intake associated changes in cardiac structure and function. Positive association between alcohol intake and left ventricle diastolic and systolic diameter, left ventricle mass in men and lower left ventricle ejection fraction in women.
Alcohol and mortality						
Knott <i>et al.</i> (2015), UK ⁽¹⁸⁴⁾	Longitudinal cohort	6.5-9.7y	Men and women aged ≥ 65 y	$n = 10009$	Alcohol intake from questionnaire	Any alcohol intake associated with lower risk of mortality compared to non-drinkers, with greatest reduction at 1-2 occasions per month and 15-20 units $\cdot\text{month}^{-1}$, adjusted for confounders. Alcohol intake of 3.1-4.5 units on the heaviest day of the week associated with lowest risk of mortality when compared to non-drinkers or never drinkers, adjusted for confounders. Former drinking associated with increased risk of mortality compared to never drinking. No association between alcohol intake and mortality when compared to never drinkers in men, but protective association present in women.
Ortolá <i>et al.</i> (2018), Spain ⁽¹⁸⁵⁾	Longitudinal cohort	7.8y	Men and women aged ≥ 60 y	$n = 3045$	Alcohol intake from diet history at baseline	1.5x increased risk of mortality for ex-drinkers compared to never-drinkers. 1.9x increased risk of mortality for heavy and binge drinkers compared to never-drinkers when considering life-time alcohol intake. No association between alcohol intake and risk of mortality for occasional, light or moderate drinkers compared to never-drinkers when considering current or life-time alcohol intake.
Alcohol and morbidity						
Daskalopoulou <i>et al.</i> (2017) ⁽¹⁸⁶⁾	Meta-analysis	-	-	21 prospective cohort studies	Alcohol intake at baseline	1.3x increased risk of healthy ageing for drinkers compared to non-drinkers. 1.1x increased risk of healthy ageing for light drinking ($<1\text{ drink}\cdot\text{day}^{-1}$, 1 drink = 12g alcohol) and 1.3x increased risk for heavy drinking ($>2\text{-}4\text{ drinks}\cdot\text{day}^{-1}$) compared to non-drinkers.

Mukamal <i>et al.</i> (2004), US ⁽¹⁸⁷⁾	Longitudinal cohort	4y	Men and women aged ≥ 65 y	$n = 5473$	Alcohol intake from questionnaire at baseline	No association between alcohol intake and risk of falls except alcohol intake of ≥ 14 drinks \cdot week $^{-1}$ (portion size not specified) associated with 25% increased risk, adjusted for confounders.
Mukamal <i>et al.</i> (2007), US ⁽¹⁸⁸⁾	Longitudinal cohort	12y	Men and women aged ≥ 65 y	$n = 5865$	Alcohol intake from FFQ at baseline	No association between alcohol intake and risk of hip fractures.
Maraldi <i>et al.</i> (2009), US ⁽¹⁸⁹⁾	Longitudinal cohort	6.5y	Men and women aged 70-79y	$n = 3061$	Alcohol intake from questionnaire at baseline	No association between alcohol intake and risk of mobility limitations and mobility disability after adjustment for confounders.
Ortolá <i>et al.</i> (2017), Spain ⁽¹⁹⁰⁾	Longitudinal cohort	3.3y	Men and women aged ≥ 60 y	$n = 2170$	Alcohol intake from FFQ at baseline	Moderate alcohol intake (<40 g \cdot day $^{-1}$ men and <24 g \cdot day $^{-1}$ women) associated with reduced risk of falls compared to non-drinking.
Buja <i>et al.</i> (2011), Italy ⁽¹⁹¹⁾	Longitudinal cohort	4y	Men and women aged 65-84y	$n = 3404$	Alcohol intake from questionnaire at baseline	No negative effects observed on renal function from moderate alcohol intake.
Shah <i>et al.</i> (2018), US ⁽¹⁹²⁾	Longitudinal cohort	12y	Men and women aged ≥ 65 y	$n = 9499$	Alcohol intake from self-report at baseline	Consuming 1-7 drinks \cdot week $^{-1}$ (portion size not specified) compared with non-drinking associated with 22% lower risk of incident frailty in males and 19% lower risk of incident frailty in females. Consuming 1-7 drinks \cdot week $^{-1}$ compared with non-drinking associated with 37-44% lower risk of incident frailty in those with stable alcohol consumption over past 12y.
Ortolá <i>et al.</i> (2019), Spain ⁽¹⁹³⁾	Longitudinal cohort	8.2y	Men and women aged ≥ 60 y	$n = 571$	Alcohol intake from diet history at baseline and throughout follow up	Reduction in average alcohol intake across 5y by -2.29 g \cdot day $^{-1}$ and 21.7% of participants quit drinking. Greater reduction in alcohol intake for those in highest tertile of change in deficit accumulation index compared to lowest. 2.0x and 2.8x increased likelihood of cessation of drinking for those in intermediate and highest tertile of change in deficit accumulation index compared to lowest. Self-rated health, onset of diabetes, stroke and increased prevalence of hospitalisation associated with increased likelihood of alcohol cessation.
Ganry <i>et al.</i> (2000), France ⁽¹⁹⁴⁾	Cross-sectional	-	Women aged ≥ 75 y	$n = 7598$	Alcohol intake from FFQ	Moderate alcohol consumption of 11-29g \cdot day $^{-1}$ associated with higher trochanteric bone mineral density compared to non-drinkers. Alcohol intake >30 g \cdot day $^{-1}$ associated with lower total bone mineral density.

¹ FFQ, food frequency questionnaire.