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Foods, nutrients and hip fracture risk: A prospective study of middle-aged women

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SUMMARY

Background and aims: Hip fracture affects 1.6 million people globally each year, and increases morbidity and mortality. There is potential for risk reduction through diet modification, but prospective evidence for associations between intake of several foods and nutrients and hip fracture risk is limited. This study aimed to investigate associations between food and nutrient intakes and hip fracture risk in the UK Women's Cohort Study, and to determine the role of body mass index (BMI) as a potential effect modifier.
Methods: Dietary, lifestyle, anthropometric, and socio-economic information of UK women, ages 35–69 years, were collected in a survey at recruitment (1995–1998), and included a validated 217-item food frequency questionnaire. Hip fracture cases were identified by linking participant data at recruitment with their Hospital Episode Statistics (HES) up to March 2019. Cox regression models were used to estimate associations between standard portions of food and nutrient intakes and hip fracture risk over a median follow-up time of 22.3 years.
Results: Among 26,318 women linked to HES data (556,331 person-years), 822 hip fracture cases were identified. After adjustment for confounders, every additional cup of tea or coffee per day was associated with a 4% lower risk of hip fracture (HR (95% CI): 0.96 (0.92, 1.00)). A 25 g/day increment of dietary protein intake was also associated with a 14% lower risk of hip fracture (0.86 (0.73, 1.00)). In subgroup analyses, BMI modified linear associations between dietary intakes of protein, calcium, total dairy, milk, and tea and hip fracture risk ($p_{interaction} = 0.02, 0.002, 0.003, 0.001$, and 0.003, respectively); these foods and nutrients were associated with a reduced risk of hip fracture in underweight but not healthy or overweight participants. In particular, risk of hip fracture in underweight participants (28 cases, 545 participants) was 45% lower for every 25 g/day protein consumed (0.55 (0.38, 0.78)).
Conclusions: This is the first prospective cohort study internationally of multiple food and nutrient intakes in relation to hip fracture risk by BMI using linkage to hospital records. Results suggest that the potential roles of some foods and nutrients in hip fracture prevention, particularly protein, tea and coffee in underweight women, merit confirmation.
Protocol registration: Clinicaltrials.gov NCT05081466.

1. Introduction

Hip fractures are the most common fractures resulting in hospitalisation, particularly among older women [1]. Around 1.6 million cases occur globally each year and rates are increasing [2], particularly in Europe and Asia [3,4]. Mobility and independence decrease after hip fracture incidence whilst risk of comorbidities increases, resulting in a reduced health-related quality of life and increased mortality [1,5,6]. Hip fractures also burden healthcare systems, costing the UK £2–3 billion and the US healthcare system $6 billion per year, respectively [7,8]. There is potential for risk reduction through diet modification [9], but the extent to which dietary intake of specific foods and nutrients impact hip fracture risk remains unclear.

Adequate bone health and muscle function are important in preventing hip fracture [10,11]. The importance of protein, calcium,

Abbreviations: BMI, Body mass index; BMD, Bone mineral density; SES, Socio-economic status; HR, Hazard ratio; 95% CI, 95% confidence interval; SFA, Saturated fat; MUFA, Monounsaturated fat; PUFA, Polyunsaturated fat.

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and vitamin D to bone health and muscle function are becoming increasingly recognised [12–15]; experimental evidence suggests a reduced risk of hip fracture with concurrent supplementation of calcium and vitamin D [16], but the impact of dietary protein, calcium, and vitamin D intakes on hip fracture risk are less clear [9]. Dietary intake of other nutrients including fat, vitamin A, and B-vitamins have also been associated with bone health and hip fracture risk in observational studies [17–19], but prospective evidence is limited for many nutrients in relation to hip fracture risk.

Consumption of foods in which nutrients important to bone health are abundant may also be associated with hip fracture risk. Higher intakes of fruits and vegetables have been inversely associated with hip fracture risk, possibly through reducing oxidative stress and consequently reducing bone loss [20,21]. Protective roles for meat, fish, and dairy products are also plausible due to their protein, calcium, and vitamin D contents, but inconclusive [9,22–24]. Our previous umbrella review of dietary risk factors for hip fracture showed potential associations between hip fracture risk and intake of several foods and nutrients, but with low or very low quality evidence for all exposures [9]. There is a lack of prospective evidence investigating hip fracture risk in relation to intake of many foods and nutrients. Previous studies are limited by small sample sizes, selective loss to follow-up due to identification of hip fracture cases through self-reported measures, or study durations too short for a long-term effect of diet to be observed. Associations between food and nutrient intakes and hip fracture risk require further investigation.

Many foods and nutrients are individually associated with BMI, which is positively associated with hip fracture risk [25]. Associations between foods, nutrients and hip fracture risk may depend on BMI, and may be more pronounced in underweight individuals where bone and muscle health are more likely to be inadequate [26], though this remains unclear. This study aimed to investigate associations between food and nutrient intakes and hip fracture risk in the UK Women's Cohort Study (UKWCS), and to determine if these associations are modified by BMI.

2. Methods

We followed the Strengthening the Reporting of Observational Studies in Epidemiology – Nutritional Epidemiology (STROBE-nut) guidelines for the reporting of cohort studies (Additional file 1: Table S1) [27].

2.1. Study design

The UKWCS is a prospective cohort study of 35,372 middle-aged women (ages 35–69 years at recruitment) recruited via postal questionnaire across the UK between 1995 and 1998. The recruitment process has been detailed elsewhere [28]. Dietary, lifestyle, demographic, and anthropometric data were collected through the questionnaire at recruitment. Participants were then excluded for the following reasons: lived outside of England (n = 3821), had a hip fracture on or before the date of recruitment according to hospital episode statistics (n = 2), had missing age data (n = 341), or had outlier dietary or covariate data (daily energy intake <500 kcal or > 5000 kcal, BMI <10 or >60 kg/m2, or food intakes >3 standard deviations from the mean; n = 941), leaving 30,244 participants potentially eligible for inclusion in this study (Additional file 1: Fig. S1). Ethical approval was obtained at the cohort's inception in 1993 from the National Research Ethics Service Committee for Yorkshire & the Humber – Leeds East (reference 15/YH/0027). This has now become the UK Women's Cohort Study – HES research database with ethical approval 17/YH/0144, in addition to an NHS Digital Data Sharing Agreement DARS-NIC-109867-M8S6B-v1.5.

2.2. Dietary assessment

At recruitment, dietary information of participants was collected via a self-administered 217-item food frequency questionnaire (FFQ) that was based on the Oxford branch of the European Prospective Investigation into Cancer and Nutrition (EPIC) study [29]. The FFQ was validated against four-day weighed food diaries and a repeat FFQ on 283 women, both administered three years after recruitment [28].

Primary foods and nutrients of interest were identified based on potential dietary risk factors for hip fracture identified in previously published studies [9], and included: dietary intake of fruits and vegetables combined, fruit, vegetables, total meat, total fish, total dairy, milk, yoghurt, cheese, tea and coffee combined, tea, coffee, protein, calcium, and vitamin D. Secondary foods and nutrients considered in exploratory analyses included dietary intake of other foods or nutrients with a plausible relation to hip fracture risk but with very limited evidence, and are listed in Additional file 1: Supplementary methods. Each food exposure was calculated by converting responses to each FFQ item to servings per day, multiplying by standard portion sizes to give grams per day (g/day), then summing relevant FFQ items (g/day) that constituted each food exposure. Exposure definitions and their derivations are documented in Additional file 1: Table S2. Standard portion sizes for food exposures were derived by averaging standard portion sizes of all relevant FFQ items (based on the Foods Standards Agency) that constituted an exposure [30]. Nutrient intakes were calculated by multiplying daily intake of each FFQ item (g/day) by each items' specific nutrient contents, and summing the products. Nutrient concentrations for each FFQ item were based on McCance and Widdowson's Food Composition database (5th edition) [31].

2.3. Outcome

First incidence of hip fracture was the primary outcome, and was identified by linking participants' diet and lifestyle characteristics with their Hospital Episode Statistics up to 31st March 2019 (International Classification of Diseases, ICD-9 code 820, ICD-10 codes S72.0–72.2). We also checked for hip fracture cases by searching for hip replacements (ICD-10 code Z96.64), but no cases were identified from this search. The timeframe was person-years until hip fracture incidence, end of study period, or death; whichever came first, with attained age as the timescale [32].

2.4. Statistical analysis

All statistical methods were pre-registered on clinicaltrials.gov (NCT05081466). Dietary, lifestyle, demographic, and anthropometric characteristics of cohort participants at recruitment with and without a hip fracture during the study period were summarised using descriptive statistics. Cox proportional hazard regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (95% CI) for associations between intake of foods and nutrients and hip fracture risk. All exposures were modelled as continuous variables to investigate associations between standard portion sizes of each food and nutrient intake and hip fracture risk. Non-meat-eaters were preferentially sampled into the UKWCS [28]; to account for this and to increase the generalisability of our findings to the UK population, cox models used weights based on the inverse probability of being sampled [33].

We also investigated potential non-linear associations between dietary intake of fruits and vegetables, fruits, vegetables, tea and coffee, tea, coffee, and calcium and hip fracture risk using Cox regression with restricted cubic splines, since previously published studies have suggested potential non-linear relationships between these exposures and hip fracture risk [34–36]. Four knots were placed at the 5th, 35th, 65th, and 95th percentiles of each exposure intake [37]. Reference levels were set to five portions/day for fruits and vegetables combined, and 700 mg/day for dietary calcium, corresponding to UK recommended intakes [38,39]. The reference level was set at three portions/day for fruits and vegetables individually, and zero cups per day for tea and coffee to compare risks in consumers and non-consumers.

Unadjusted and multivariable-adjusted models were applied. Age was controlled for in both models using attained age as the timeframe [32]. Additional potential confounders included in adjusted models for food intake – hip fracture risk associations, and nutrient intake – hip fracture risk associations, were informed by a Directed Acyclic Graph (DAG) for each. Confounders for models with food or nutrient exposures included (all measured at recruitment): ethnicity (white, Asian, black, other), socioeconomic status (SES; professional/managerial, intermediate, routine/manual), marital status (married/living as married, separated/divorced, single/widowed), menopausal status (premenopausal, postmenopausal), number of children (continuous), prevalence of cardiovascular disease (CVD), cancer, or diabetes (yes, no), physical activity in hours per day (continuous), smoking status (current, former, never), alcohol intake (>1/week, ≤ 1/week, never), height (continuous), body weight (continuous), and use of any nutritional supplements (yes, no). All adjusted models were adjusted for energy intake using the all-components method, where all other individual components of energy intake besides the exposure were adjusted for [40]. For models with food exposures, this involved mutual adjustment for other food and beverage groups. Models with primary nutrient exposures (dietary protein, calcium, and vitamin D intakes) were adjusted for dietary carbohydrates (excluding sugar and fibre), fibre, sugar, saturated fat (SFA), monounsaturated fatty acids (MUFA), and polyunsaturated fatty acids (PUFA) intakes, and were mutually adjusted for one-another. Models for secondary nutrients were adjusted for protein, calcium and vitamin D intakes, and were also adjusted for: carbohydrates (excluding sugar and fibre), fibre, SFA, MUFA, PUFA, and sugar intakes except where the exposure of interest was one of these variables, in which case it was omitted from the adjustment set. Confounder variable definitions, DAGs, and informed adjustment sets for each potential association are detailed in Additional file 1: Supplementary methods, Fig. S2, and Tables S3 and S4. The proportional hazards assumption was tested on the basis of Schoenfeld residuals, and was not violated for all terms in adjusted models.

BMI (<18.5, 18.5–24.9, ≥25 kg/m^2) was added to linear adjusted models independently as an interaction term to compare potential associations between standard portion size increments in daily intake of foods and nutrients and hip fracture risk in underweight, healthy weight, and overweight women. We also stratified models with restricted cubic splines by BMI (using the same cut-offs as in linear tests) to test for non-linear associations in each BMI subgroup. Further exploratory analyses included testing for interaction effects with each exposure modelled linearly for: age (≤60, >60), menopausal status (premenopausal, postmenopausal), SES (routine/manual, intermediate, professional/managerial), smoking status (current, former, never), physical activity (<150 min per week, ≥ 150 min per week), and use of nutritional supplements (yes, no). In each case, the potential effect modifier was omitted from the relevant adjustment set.

As a sensitivity analysis, we applied models with and without adjustment for body weight to determine if weight management contributes to any observed associations. Additional sensitivity analyses were as follows: adjusting for BMI rather than height and weight individually; adjusting for energy intake using the energy-partition method to enhance comparison with other studies (see Additional file 1: Supplementary methods for more detail); excluding participants on long-term treatment for illness at baseline who may be generally unhealthier and at a higher risk of hip fracture; excluding participants with short survival times (<5 years) to check for reverse causation; further adjusting for hormone replacement therapy (HRT); and further adjusting for prevalence of fracture at sites other than the hip at recruitment identified in hospital episode statistics. Participants with missing data for a variable required in a given analysis were excluded from that analysis. Statistical analyses were performed in Stata (version 17).

3. Results

3.1. Participants

Of the 30,244 potentially eligible women at recruitment, 26,318 women were included in unadjusted and adjusted analyses after excluding participants with missing covariate data for body weight (n = 596), height (n = 649), ethnicity (n = 811), physical activity (n = 1561), marital status (n = 460), SES (n = 331), or menopausal status (n = 309). The participant flow chart is detailed in Additional file 1: Fig. S1.

3.1.1. Descriptive data

Characteristics of the 26,318 cohort participants at recruitment with and without a hip fracture during the study period are summarised in Table 1. Over a median follow-up time of 22.3 years (556,331 person-years), we observed 822 hip fracture cases – an overall rate of 3.1%. On average, women with a hip fracture were older at recruitment (mean (SD): 62.1 (8.0) years for cases vs 51.8 (9.1) years for non-cases), more likely to be post-menopausal, less likely to have degree-level education, and less likely to be married. BMI and height at recruitment were similar in cases and non-cases. Prevalence of CVD, cancer, or diabetes at recruitment was higher in cases (126 (15.0%) than in non-cases (2262 (9.0%)). Dietary characteristics including energy intake and protein, calcium, and vitamin D intakes were similar in cases and non-cases, as was use of any nutritional supplements. Other food and nutrient intakes of the included participants at recruitment are summarised by hip fracture incidence in Additional file 1: Table S. Across BMI subgroups, hip fracture rates were higher in underweight women (28 cases/545 participants) than in healthy weight (514 cases/16,659 participants) or overweight women (280 cases/9114 participants). Characteristics of the cohort at recruitment were similar when including or restricting to the 3923 women with missing covariate data (Additional file 1: Table S6).

3.1.2. Main results

Amongst primary foods and nutrients investigated, a 25 g/day increment in dietary protein intake was associated with a reduced risk of hip fracture in the adjusted model (0.86 (0.73, 1.00); Fig. 1). One extra cup per day of tea or coffee was also inversely associated with hip fracture risk in the adjusted model (0.96 (0.92, 0.996)). There was no clear evidence of an association between hip fracture risk and dietary calcium (per 300 mg/day), vitamin D (per μg/day), or any other food intakes in adjusted models.

Restricted cubic spline models showed no evidence of non-linear associations between dietary intake of calcium, fruits and vegetables combined, fruits, vegetables, tea and coffee combined, tea, and coffee and hip fracture risk (Additional file 1: Figs. S4–S6).

Table 1
Characteristics of UK Women's Cohort Study participants at recruitment by hip fracture incidence.

Characteristics, n (%) or M (SD)	Total	Cases	Non-cases
Participants (%)	26,318	822 (3.1)	25,496 (96.9)
Socio-demographics			
Age, years (SD)	52.1 (9.2)	62.1 (8.0)	51.8 (9.1)
Degree-level education (%)	6502 (26.8)	155 (22.2)	6347 (27.0)
Socio-economic status			
Professional or managerial (%)	19,057 (72.4)	565 (68.7)	18,492 (72.5)
Intermediate (%)	2440 (9.3)	111 (13.5)	2329 (9.1)
Routine or manual (%)	4821 (18.3)	146 (17.8)	4675 (18.3)
Married (%)	20,268 (77.0)	586 (71.3)	19,682 (77.2)
White ethnicity (%)	25,992 (98.8)	815 (99.1)	25,177 (98.7)
Lifestyle			
Exercise, hours/day (SD)	0.2 (0.5)	0.2 (0.4)	0.2 (0.5)
Smoking status			
Current (%)	3513 (13.3)	112 (13.6)	3401 (13.3)
Former (%)	7947 (30.2)	255 (31.0)	7692 (30.2)
Never (%)	14,858 (56.5)	455 (55.4)	14,403 (56.5)
Alcohol consumption			
>1 serving/week (%)	13,918 (52.9)	389 (47.3)	13,529 (53.1)
≤1 serving/week (%)	9290 (35.3)	280 (34.1)	9010 (35.3)
Never (%)	3110 (11.8)	153 (18.6)	2957 (11.6)
Nutritional supplementation (%)	14,009 (53.2)	425 (51.7)	13,584 (53.3)
Anthropometrics			
BMI, kg/m^2 (SD)	24.4 (4.2)	24.2 (4.3)	24.4 (4.2)
<18.5 (%)	545 (2.1)	28 (3.4)	517 (2.0)
18.5–24.9 (%)	16,659 (63.3)	514 (62.5)	16,145 (63.3)
≥25 (%)	9114 (34.6)	280 (34.1)	8834 (34.6)
Height, m (SD)	1.6 (0.1)	1.6 (0.1)	1.6 (0.1)
Diet and nutritional intake			
Dietary pattern			
Regular meat-eater (%)	12,221 (46.4)	394 (47.9)	11,827 (46.4)
Occasional meat-eater (%)	6902 (26.2)	247 (30.0)	6655 (26.1)
Pescatarian (%)	3377 (12.8)	80 (9.7)	3297 (12.9)
Vegetarian (%)	3818 (14.5)	101 (12.3)	3717 (14.6)
Energy, kcal/day (SD)	2300 (654.8)	2346 (696.6)	2298 (653.4)
Fruits and vegetables, g/day (SD)	648.7 (299.8)	679.5 (313.0)	647.7 (299.4)
Fruit, g/day (SD)	377.4 (227.3)	395.1 (231.9)	376.9 (227.1)
Vegetables, g/day (SD)	271.3 (139.0)	284.4 (146.3)	270.9 (138.7)
Total meat, g/day (SD)	86.5 (81.2)	87.5 (77.4)	86.4 (81.3)
Total fish, g/day (SD)	33.7 (29.6)	36.1 (30.6)	33.6 (29.6)
Total dairy, g/day (SD)	412.8 (213.6)	432.7 (218.5)	412.1 (213.5)
Milk, ml/day (SD)	304.1 (190.0)	317.5 (198.0)	303.6 (189.7)
Yogurt, g/day (SD)	59.6 (68.2)	61.0 (67.5)	59.5 (68.2)
Cheese, g/day (SD)	27.4 (27.6)	26.7 (34.8)	27.5 (27.4)
Tea and coffee, cups/day (SD)	5.0 (2.2)	4.8 (2.2)	5.0 (2.2)
Tea, cups/day (SD)	3.0 (2.0)	3.0 (2.0)	3.0 (2.0)
Coffee, cups/day (SD)	2.0 (1.8)	1.8 (1.7)	2.0 (1.8)
Protein, g/day (SD)	88.1 (26.3)	89.7 (27.2)	88.1 (26.2)
Calcium, mg/day (SD)	1135 (365.4)	1160 (377.1)	1134 (365.0)
Vitamin D, μg/day (SD)	3.1 (1.7)	3.4 (1.8)	3.1 (1.7)
Other			
Menopausal status			
Postmenopausal (%)	14,611 (55.5)	734 (89.3)	13,877 (54.4)
Premenopausal (%)	11,707 (44.5)	88 (10.7)	11,619 (45.6)
≥1 children (%)	20,723 (78.7)	667 (81.1)	20,056 (78.7)
Prevalence of CVD, cancer, or diabetes (%)	2388 (9.1)	126 (15.3)	2262 (8.9)

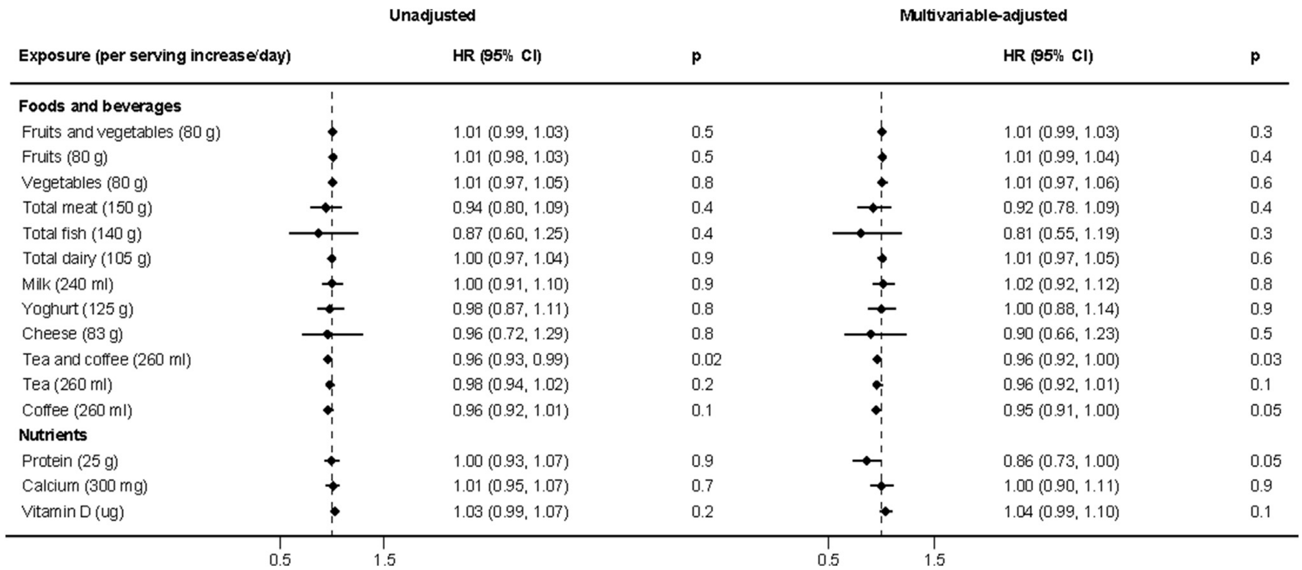
Nutritional intakes are from diet sources only and do not include supplementary sources. M (SD): mean (standard deviation); BMI: body mass index; CVD: cardiovascular disease.

Among secondary foods and nutrients, after adjusting for confounders, a 10 g/day increment in fat intake was associated with an higher risk of hip fracture (1.04 (1.00, 1.08)). There was no clear evidence of associations of other secondary foods or nutrients with hip fracture risk.

3.2. Subgroup analyses

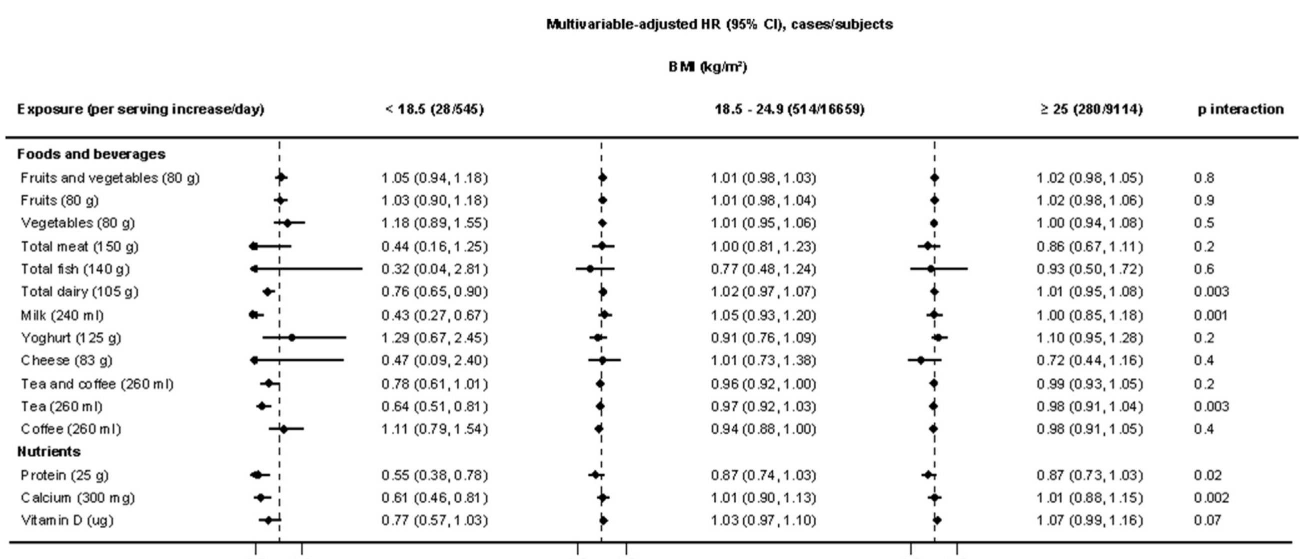
BMI modified linear associations between increments in dietary protein (25 g/day) and calcium (300 mg/day) intakes and hip fracture risk ($p_{interaction} = 0.02$ and $p_{interaction} = 0.002$, respectively; Fig. 2). A 25 g/day increment in protein intake was associated with a reduced risk of hip fracture in underweight women, but less so in healthy or overweight women. A 300 mg/day increment in dietary calcium intake was associated with a reduced risk of hip fracture in underweight women only. Whilst there was no evidence of an overall association between vitamin D intake and hip fracture risk, there was some evidence for a more potential protective association in underweight women ($p_{interaction} = 0.07$).

BMI also modified linear associations between hip fracture risk and dietary intake of total dairy, milk, and tea ($p_{interaction} = 0.003$, $p_{interaction} = 0.001$, and $p_{interaction} = 0.003$, respectively). Increments of 105 g/day of total dairy, 240 ml/day of milk, and 260 ml/day of tea were associated with reduced risks of hip fracture in underweight



	Unadjusted		Multivariable-adjusted	
Exposure (per serving increase/day)	HR (95% CI)	p	HR (95% CI)	p
Foods and beverages				
Fruits and vegetables (80 g)	1.01 (0.99, 1.03)	0.5	1.01 (0.99, 1.03)	0.3
Fruits (80 g)	1.01 (0.98, 1.03)	0.5	1.01 (0.99, 1.04)	0.4
Vegetables (80 g)	1.01 (0.97, 1.05)	0.8	1.01 (0.97, 1.06)	0.6
Total meat (150 g)	0.94 (0.80, 1.09)	0.4	0.92 (0.78. 1.09)	0.4
Total fish (140 g)	0.87 (0.60, 1.25)	0.4	0.81 (0.55, 1.19)	0.3
Total dairy (105 g)	1.00 (0.97, 1.04)	0.9	1.01 (0.97, 1.05)	0.6
Milk (240 ml)	1.00 (0.91, 1.10)	0.9	1.02 (0.92, 1.12)	0.8
Yoghurt (125 g)	0.98 (0.87, 1.11)	0.8	1.00 (0.88, 1.14)	0.9
Cheese (83 g)	0.96 (0.72, 1.29)	0.8	0.90 (0.66, 1.23)	0.5
Tea and coffee (260 ml)	0.96 (0.93, 0.99)	0.02	0.96 (0.92, 1.00)	0.03
Tea (260 ml)	0.98 (0.94, 1.02)	0.2	0.96 (0.92, 1.01)	0.1
Coffee (260 ml)	0.96 (0.92, 1.01)	0.1	0.95 (0.91, 1.00)	0.05
Nutrients				
Protein (25 g)	1.00 (0.93, 1.07)	0.9	0.86 (0.73, 1.00)	0.05
Calcium (300 mg)	1.01 (0.95, 1.07)	0.7	1.00 (0.90, 1.11)	0.9
Vitamin D (ug)	1.03 (0.99, 1.07)	0.2	1.04 (0.99, 1.10)	0.1

Fig. 1. Associations between dietary intake of foods, nutrients and risk of hip fracture in UK Women's Cohort Study participants. Unadjusted and adjusted models were based on 26,318 women with 822 hip fracture cases (556,331 person-years), and both controlled for age. All adjusted models were also adjusted for (all at recruitment): ethnicity (white, Asian, black, other), socio-economic status (SES; professional/managerial, intermediate, routine/manual), marital status (married/living as married, separated/divorced, single/widowed), menopausal status (premenopausal, postmenopausal), number of children (continuous), prevalence of cardiovascular disease, cancer, or diabetes (yes, no), physical activity in hours per day (continuous), smoking status (current, former, never), alcohol intake (>1/week, ≤ 1/week, never), height (continuous), weight (continuous), and use of any nutritional supplements (yes, no). Models with food exposures were mutually adjusted for other major foods and beverages. Models for protein, calcium, and vitamin D intakes were adjusted for carbohydrates (excluding sugar and fibre), fibre, sugar, saturated fat, monounsaturated fatty acids (MUFA), and polyunsaturated fatty acids (PUFA) intakes, and were mutually adjusted for one-another. HR (95% CI): hazard ratio (95% confidence interval).



	Multivariable-adjusted HR (95% CI), cases/subjects			
	BMI (kg/m²)			
Exposure (per serving increase/day)	< 18.5 (28/545)	18.5 - 24.9 (514/16659)	≥ 25 (280/9114)	p interaction
Foods and beverages				
Fruits and vegetables (80 g)	1.05 (0.94, 1.18)	1.01 (0.98, 1.03)	1.02 (0.98, 1.05)	0.8
Fruits (80 g)	1.03 (0.90, 1.18)	1.01 (0.98, 1.04)	1.02 (0.98, 1.06)	0.9
Vegetables (80 g)	1.18 (0.89, 1.55)	1.01 (0.95, 1.06)	1.00 (0.94, 1.08)	0.5
Total meat (150 g)	0.44 (0.16, 1.25)	1.00 (0.81, 1.23)	0.86 (0.67, 1.11)	0.2
Total fish (140 g)	0.32 (0.04, 2.81)	0.77 (0.48, 1.24)	0.93 (0.50, 1.72)	0.6
Total dairy (105 g)	0.76 (0.65, 0.90)	1.02 (0.97, 1.07)	1.01 (0.95, 1.08)	0.003
Milk (240 ml)	0.43 (0.27, 0.67)	1.05 (0.93, 1.20)	1.00 (0.85, 1.18)	0.001
Yoghurt (125 g)	1.29 (0.67, 2.45)	0.91 (0.76, 1.09)	1.10 (0.95, 1.28)	0.2
Cheese (83 g)	0.47 (0.09, 2.40)	1.01 (0.73, 1.38)	0.72 (0.44, 1.16)	0.4
Tea and coffee (260 ml)	0.78 (0.61, 1.01)	0.96 (0.92, 1.00)	0.99 (0.93, 1.05)	0.2
Tea (260 ml)	0.64 (0.51, 0.81)	0.97 (0.92, 1.03)	0.98 (0.91, 1.04)	0.003
Coffee (260 ml)	1.11 (0.79, 1.54)	0.94 (0.88, 1.00)	0.98 (0.91, 1.05)	0.4
Nutrients				
Protein (25 g)	0.55 (0.38, 0.78)	0.87 (0.74, 1.03)	0.87 (0.73, 1.03)	0.02
Calcium (300 mg)	0.61 (0.46, 0.81)	1.01 (0.90, 1.13)	1.01 (0.88, 1.15)	0.002
Vitamin D (ug)	0.77 (0.57, 1.03)	1.03 (0.97, 1.10)	1.07 (0.99, 1.16)	0.07

Fig. 2. Associations between dietary intake of foods, nutrients and risk of hip fracture in UK Women's Cohort Study participants by body mass index (BMI). All models were adjusted for (all at recruitment): ethnicity (white, Asian, black, other), socio-economic status (SES; professional/managerial, intermediate, routine/manual), marital status (married/living as married, separated/divorced, single/widowed), menopausal status (premenopausal, postmenopausal), number of children (continuous), prevalence of cardiovascular disease, cancer, or diabetes (yes, no), physical activity in hours per day (continuous), smoking status (current, former, never), alcohol intake (>1/week, ≤ 1/week, never), and use of any nutritional supplements (yes, no). Models with food exposures were mutually adjusted for other major foods and beverages. Models for protein, calcium, and vitamin D intakes were adjusted for carbohydrates (excluding sugar and fibre), fibre, sugar, saturated fat, monounsaturated fatty acids (MUFA), and polyunsaturated fatty acids (PUFA) intakes, and were mutually adjusted for one-another. HR (95% CI): hazard ratio (95% confidence interval).

women only. In analyses of secondary foods and nutrients, BMI modified linear associations between dietary intake of vitamin B2, vitamin B12, and zinc hip fracture risk ($p_{interaction}$ = 0.02, $p_{interaction}$ = 0.03, and $p_{interaction}$ = 0.02, respectively; Table S8). There was no clear evidence of a non-linear association between any food or nutrient intake and hip fracture risk in any BMI category (Additional file 1: Figs. S7–S9). Results of other subgroup analyses by age, menopausal status, SES, smoking status, physical activity, and use of nutritional supplements are presented and described in Additional file 1: Tables S9–14 and Supplementary results.

3.3. Sensitivity analyses

All adjusted estimates remained broadly unchanged across most sensitivity analyses, though excluding participants on long-term treatment for illness changed the association of total fish intake with hip fracture risk from 0.81 (0.55, 1.19) to 1.16 (0.74, 1.82) (Additional file 1: Table S15).

4. Discussion

4.1. Principal findings

In this prospective cohort of middle-aged UK women, there was suggestive evidence of inverse associations between intake of dietary protein, tea and coffee, and hip fracture risk, though confidence intervals were wide for protein, and a large number of exposures were considered. There was no clear evidence of overall associations between hip fracture risk and dietary intake of calcium, vitamin D, or animal foods, including meat, fish, eggs, and dairy products. Subgroup analyses showed suggestive evidence of effect modification by BMI for dietary protein, calcium, total dairy, milk, and tea intakes, where inverse associations were stronger in underweight women.

4.2. Comparison with other studies

There is limited prospective evidence of associations between consumption of many foods and nutrients and hip fracture risk [9]. This study provides further information on relationships of 37 foods, beverages, or nutrients with hip fracture risk.

The inverse association between dietary protein intake and hip fracture risk observed here is largely consistent with previous evidence [12,41–43]. A meta-analysis of observational studies reported a lower risk of hip fracture with higher protein intakes in adults [41]. A more recent study of US adults showed an inverse association in men but not women, though an inverse association was observed when restricted to women <65 years old at recruitment, which resembles the age range of the women in the UKWCS at recruitment [43]. We found that the association for protein was more pronounced in underweight women. Similarly, a recent case-control study in Chinese adults showed an inverse association for protein intake with hip fracture risk that was more evident in those with a lower BMI [42].

We found a small reduction in hip fracture risk for each additional cup of tea or coffee consumed daily, where the association for tea was stronger in underweight participants. Similarly, a meta-analysis of Western studies found that individuals consuming 1–4 cups per day of tea were at a lower risk for hip fracture than non-consumers [44]. In contrast, two meta-analyses found no clear association between coffee consumption and hip fracture risk [44,45]. The majority of studies included in those meta-analyses had insufficient power to detect small associations, and had follow-up durations that may have been too short for a long-term effect of regular tea and coffee consumption to be observed. In the more recently published Singapore-Chinese Health study, an higher risk of hip fracture was observed in men and women with intakes of coffee exceeding four cups per day compared to those that drank coffee less than once per week [34]. An elevated risk of hip fracture at high coffee intakes was not observed here, possibly due to the lower mean coffee consumption in the UK Women's Cohort (2 cups per day).

In line with our previous umbrella review [9], we found no clear evidence of overall associations between hip fracture risk and dietary intake of calcium, vitamin D, or several animal foods. A systematic review also showed no association between dietary intake of calcium, milk, or total dairy and risk of hip fracture [46]. In contrast to our results, meat consumption has been associated with a reduced risk of hip fracture in an American cohort [24]. However, that study identified hip fracture cases through a self-administered questionnaire, which is more prone to selective drop-out than objective record linkage used here, or this could reflect differences in type of meat consumed between the cohorts.

4.3. Possible explanations and implications

The potential linear dose-response relationship between protein intake and hip fracture risk could be explained by the positive effects of protein on bone and muscle properties that decline with age. Protein has been positively associated with BMD directly [47], and stimulates insulin-like growth factor-1 (IGF-1) production which increases formation of osteoblasts, is positively associated with BMD, and is negatively associated with risk of fractures [43,48,49]. Higher protein intakes also contribute to adequate muscle mass, which may reduce risk of fall-related hip fractures, which account for 90% of all hip fractures [11,50,51]. The association between protein intake and hip fracture risk was stronger in underweight women. Given that BMD and muscle mass may decrease with BMI [26,52], protein may be particularly important in contributing to adequate bone and muscle health, mitigating the increased risk of hip fracture observed with particularly low BMD or muscle mass [10,11]. However, statistical power here was limited in underweight participants, and information on BMD and muscle mass was not available. Further research is needed to confirm if the association depends on body weight and body composition, in particular BMD.

Tea and coffee are high in biologically active compounds such as polyphenols and phytoestrogens, particularly catechins, which may enhance osteoblast activity and suppress osteoclastic activity by reducing oxidative stress, resulting in higher BMD and lower risk of hip fracture [44]. A stronger association was observed for tea consumption in underweight women; tea could help to mitigate the low BMD-induced increase in hip fracture risk that may be more prominent at a lower BMI [26]. Further research is needed to clarify associations between tea and coffee consumption and hip fracture risk, and should determine if associations depend on the type of tea or coffee consumed and the amount of milk or sugar added, since polyphenol and nutrient contents vary [53].

We observed inverse associations between hip fracture risk and dietary intake of calcium, vitamin D, milk, and total dairy in underweight women only. Calcium is the dominant mineral in bone and vitamin D aids its absorption [54]. Total calcium intake and serum vitamin D levels may be independently associated with higher BMD [13,55], and therefore could reduce risk of hip fracture when BMD levels are very low, as may be the case in underweight women [26,56]. The abundance of protein, calcium, and vitamin D in dairy products could also explain the inverse association of total dairy and milk intakes with hip fracture risk in underweight women. However, effects of dietary calcium and vitamin D on BMD are less clear, and when determining their associations with hip fracture risk, we could not account for non-dietary sources, including supplements and sunlight exposure, which may modify associations. We also had insufficient power to precisely estimate these associations in the underweight group. Further research is needed to confirm the role of dietary calcium, vitamin D, and foods such as dairy products in which these nutrients are abundant on hip fracture risk with non-dietary sources accounted for, particularly in underweight women who may have lower BMD.

4.4. Strengths and limitations

The large sample size facilitated good statistical power to precisely estimate associations between several foods, nutrients, and hip fracture risk. The large number of foods and nutrients considered increased the risk of a type-one error, but we pre-specified hypothesis-testing primary exposures and hypothesis-generating secondary exposures to reduce this risk. We identified hip fracture cases by linking participants' dietary and lifestyle data with their hospital records, which reduced reporting error and selective drop-out over a long follow-up duration.

We were unable to differentiate between fragility and traumatic hip fractures due to a lack of data on the cause of hip fractures. Whilst we excluded participants with a previous hip fracture at recruitment based on hospital records, this was likely an incomplete exclusion, since the questionnaire did not ask about history of fractures, and hospital data of records before 1997 was not available. Of other limitations, BMI was calculated based on self-reported height and weight, implying potential measurement error. Additionally, the low number of underweight women in this study limited statistical power to precisely estimate associations between foods, nutrients, and hip fracture risk in that group. We adjusted for all potential confounders, but residual confounding remains possible. For example, we could not adjust for calcium or vitamin D supplementation, which could mask true relationships between hip fracture risk and dietary calcium and vitamin D in particular. Whilst we adjusted for alcohol consumption, we were unable to differentiate between moderate and heavy drinkers, who may be at different risks of hip fracture [9]. A validated FFQ was used to measure food and nutrient intake at recruitment only, meaning any changes in food and nutrient intake over time were not captured, potentially resulting in attenuated estimates. Our results may not apply to men or other ethnic groups, and UKWCS participants may be healthier on average than the UK population due to a healthy participant bias, reducing generalisability.

5. Conclusion

In this prospective cohort of middle-aged UK women, findings suggest that a higher protein intake and consumption of tea and coffee may each independently reduce risk of hip fracture in a linear dose-response manner, though confidence intervals were wide for protein, and a large number of exposures were considered. There was no clear evidence of overall associations between hip fracture risk and dietary intake of calcium, vitamin D, or animal products, but there was some evidence of stronger inverse associations in underweight women for these foods and nutrients. The potential roles of some foods and nutrients in hip fracture prevention, particularly protein, tea and coffee in underweight women, merit confirmation in further cohort studies and randomised controlled trials to enable the formulation of dietary recommendations for reducing hip fracture risk.

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Author contribution

JEC and DCG conceived and supervised the work. JW analysed the data and wrote the initial draft. All authors provided input on the study design, data analysis, and interpretation of results; revised the paper critically for important intellectual content; and approved the final version.

Conflict of interest

JEC is Director of Dietary Assessment Ltd, a University of Leeds spin out company supporting measurement of food and nutrient intake using myfood24. The authors declare no other conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2022.11.008.

References

[1] Dhanwal DK, Dennison EM, Harvey NC, Cooper C. Epidemiology of hip fracture: worldwide geographic variation. Indian J Orthop 2011;45(1):15–22.
[2] Murphy EA, Ehrhardt B, Gregson CL, von Arx OA, Hartley A, Whitehouse MR, et al. Machine learning outperforms clinical experts in classification of hip fractures. Sci Rep 2022;12(1):2058.
[3] Rosengren BE, Karlsson MK. The annual number of hip fractures in Sweden will double from year 2002 to 2050: projections based on local and nationwide data. Acta Orthop 2014;85(3):234–7.
[4] Cheung CL, Ang SB, Chadha M, Chow ES, Chung YS, Hew FL, et al. An updated hip fracture projection in Asia: the Asian Federation of Osteoporosis Societies study. Osteoporos Sarcopenia 2018;4(1):16–21.
[5] Alexiou KI, Roushias A, Varitimidis SE, Malizos KN. Quality of life and psychological consequences in elderly patients after a hip fracture: a review. Clin Interv Aging 2018;13:143–50.
[6] Peraza-Delgado A, Sánchez-Gómez MB, Gómez-Salgado J, Romero-Martín M, Novo-Muñoz M, Duarte-Clíments G. Non-pharmacological interventions towards preventing the triad osteoporosis-falls risk-hip fracture, in population older than 65. Scoping review. J Clin Med 2020;9(8).
[7] Manetti S, Turchetti G, Fusco F. Determining the cost-effectiveness requirements of an exoskeleton preventing second hip fractures using value of information. BMC Health Serv Res 2020;20(1):955.
[8] Adeyemi A, Delhougne G. Incidence and economic burden of intertrochanteric fracture: a medicare claims database analysis. JB JS Open Access 2019;4(1): e0045.
[9] Webster J, Rycroft CE, Greenwood DC, Cade JE. Dietary risk factors for hip fracture in adults: an umbrella review of meta-analyses of prospective cohort studies. PLoS One 2021;16(11):e0259144.
[10] Bouxsein ML, Eastell R, Lui LY, Wu LA, de Papp AE, Grauer A, et al. Change in bone density and reduction in fracture risk: a meta-regression of published trials. J Bone Miner Res 2019;34(4):632–42.
[11] Lang T, Cauley JA, Tylavsky F, Bauer D, Cummings S, Harris TB. Computed tomographic measurements of thigh muscle cross-sectional area and attenuation coefficient predict hip fracture: the health, aging, and body composition study. J Bone Miner Res 2010;25(3):513–9.
[12] Groenendijk I, den Boeft L, van Loon LJC, de Groot LCPGM. High versus low dietary protein intake and bone health in older adults: a systematic review and meta-analysis. Comput Struct Biotechnol J 2019;17:1101–12.
[13] Vannucci L, Fossi C, Quattrini S, Guasti L, Pampaloni B, Gronchi G, et al. Calcium intake in bone health: a focus on calcium-rich mineral waters. Nutrients 2018;10(12).
[14] Khazai N, Judd SE, Tangpricha V. Calcium and vitamin D: skeletal and extraskeletal health. Curr Rheumatol Rep 2008;10(2):110–7.
[15] Gunton JE, Girgis CM. Vitamin D and muscle. BoneKEy Rep 2018;8:163–7.
[16] Yao P, Bennett D, Mafham M, Lin X, Chen Z, Armitage J, et al. Vitamin D and calcium for the prevention of fracture: a systematic review and meta-analysis. JAMA Netw Open 2019;2(12):e1917789.
[17] Mozaffari H, Djafarian K, Mofrad MD, Shab-Bidar S. Dietary fat, saturated fatty acid, and monounsaturated fatty acid intakes and risk of bone fracture: a systematic review and meta-analysis of observational studies. Osteoporos Int 2018;29(9):1949–61.
[18] Knapik JJ, Hoedebecke SS. Vitamin A and bone fractures: systematic review and meta-analysis. J Spec Oper Med 2021;21(2):100–7.
[19] Dai Z, Wang R, Ang LW, Yuan JM, Koh WP. Dietary B vitamin intake and risk of hip fracture: the Singapore Chinese Health Study. Osteoporos Int 2013;24(7): 2049–59.

[20] Brondani JE, Comim FV, Flores LM, Martini LA, Premaor MO. Fruit and vegetable intake and bones: a systematic review and meta-analysis. PLoS One 2019;14(5):e0217223.
[21] Luo SY, Li Y, Luo H, Yin XH, Lin DR, Zhao K, et al. Increased intake of vegetables, but not fruits, may be associated with reduced risk of hip fracture: a meta-analysis. Sci Rep 2016;6:8.
[22] Hidayat K, Du X, Shi BM, Qin LQ. Systematic review and meta-analysis of the association between dairy consumption and the risk of hip fracture: critical interpretation of the currently available evidence. Osteoporos Int 2020;31(8):1411–25.
[23] Sadeghi O, Djafarian K, Ghorabi S, Khodadost M, Nasiri M, Shab-Bidar S. Dietary intake of fish, n-3 polyunsaturated fatty acids and risk of hip fracture: a systematic review and meta-analysis on observational studies. Crit Rev Food Sci Nutr 2019;59(8):1320–33.
[24] Lousuebsakul-Matthews V, Thorpe DL, Knutsen R, Beeson WL, Fraser GE, Knutsen SF. Legumes and meat analogues consumption are associated with hip fracture risk independently of meat intake among Caucasian men and women: the Adventist Health Study-2. Publ Health Nutr 2014;17(10):2333–43.
[25] Armstrong ME, Cairns BJ, Banks E, Green J, Reeves GK, Beral V. Different effects of age, adiposity and physical activity on the risk of ankle, wrist and hip fractures in postmenopausal women. Bone 2012;50(6):1394–400.
[26] Hariri AF, Almatrafi MN, Zamka AB, Babaker AS, Fallatah TM, Althouwaibi OH, et al. Relationship between body mass index and T-scores of bone mineral density in the hip and spine regions among older adults with diabetes: a retrospective review. J Obes 2019;2019:9827403.
[27] Lachat C, Hawwash D, Ocké MC, Berg C, Forsum E, Hörnell A, et al. Strengthening the reporting of observational studies in epidemiology-nutritional Epidemiology (STROBE-nut): an extension of the STROBE statement. PLoS Med 2016;13(6):e1002036.
[28] Cade JE, Burley VJ, Alwan NA, Hutchinson J, Hancock N, Morris MA, et al. Cohort profile: the UK women's cohort study (UKWCS). Int J Epidemiol 2017;46(2):e11.
[29] Riboli E, Kaaks R. The EPIC project: rationale and study design. European prospective investigation into cancer and nutrition. Int J Epidemiol 1997;26(Suppl 1):S6–14.
[30] Foods Standards Agency. Food portion sizes. London: The Stationery Office; 2002.
[31] Public Health England. McCance and Widdowson's composition of foods integrated dataset. 2019.
[32] Korn EL, Graubard BI, Midthune D. Time-to-event analysis of longitudinal follow-up of a survey: choice of the time-scale. Am J Epidemiol 1997;145(1):72–80.
[33] Rada-Fernandez de Jauregui D, Evans CEL, Jones P, Greenwood DC, Hancock N, Cade JE. Common dietary patterns and risk of cancers of the colon and rectum: analysis from the United Kingdom Women's Cohort Study (UKWCS). Int J Cancer 2018;143(4):773–81.
[34] Dai Z, Jin A, Soh AZ, Ang LW, Yuan JM, Koh WP. Coffee and tea drinking in relation to risk of hip fracture in the Singapore Chinese Health Study. Bone 2018;112:51–7.
[35] Byberg L, Bellavia A, Orsini N, Wolk A, Michaëlsson K. Fruit and vegetable intake and risk of hip fracture: a cohort study of Swedish men and women. J Bone Miner Res 2015;30(6):976–84.
[36] Warensjö E, Byberg L, Melhus H, Gedeborg R, Mallmin H, Wolk A, et al. Dietary calcium intake and risk of fracture and osteoporosis: prospective longitudinal cohort study. BMJ 2011;342:d1473.
[37] Harrell Jr FE, Lee KL, Pollock BG. Regression models in clinical studies: determining relationships between predictors and response. J Natl Cancer Inst 1988;80(15):1198–202.
[38] The NHS. Eatwell guide. 2019. Available from: https://www.nhs.uk/live-well/eat-well/food-guidelines-and-food-labels/the-eatwell-guide/.
[39] Vitamins NHS. And minerals: calcium. 2020 [Available from: https://www.nhs.uk/conditions/vitamins-and-minerals/calcium/.
[40] Tomova GD, Arnold KF, Gilthorpe MS, Tennant PWG. Adjustment for energy intake in nutritional research: a causal inference perspective. Am J Clin Nutr 2022;115(1):189–98.
[41] Wu AM, Sun XL, Lv QB, Zhou Y, Xia DD, Xu HZ, et al. The Relationship between Dietary Protein Consumption and Risk of Fracture: a subgroup and dose-response meta-analysis of prospective cohort studies. Sci Rep 2015;5:8.
[42] Liu ZM, Huang Q, Li SY, Liu YP, Wu Y, Zhang SJ, et al. A 1:1 matched case-control study on dietary protein intakes and hip fracture risk in Chinese elderly men and women. Osteoporos Int 2021;32(11):2205–16.
[43] Fung TT, Meyer HE, Willett WC, Feskanich D. Protein intake and risk of hip fractures in postmenopausal women and men age 50 and older. Osteoporos Int J Established Result Cooperation Between Eur Found Osteoporosis Nat Osteoporosis Found USA 2017;28(4):1401–11.
[44] Sheng J, Qu X, Zhang X, Zhai Z, Li H, Liu X, et al. Coffee, tea, and the risk of hip fracture: a meta-analysis. Osteoporos Int 2014;25(1):141–50.
[45] Li S, Dai Z, Wu Q. Effect of coffee intake on hip fracture: a meta-analysis of prospective cohort studies. Nutr J 2015;14:38.
[46] Bolland MJ, Leung W, Tai V, Bastin S, Gamble GD, Grey A, et al. Calcium intake and risk of fracture: systematic review. BMJ 2015;351:h4580.
[47] Shams-White MM, Chung M, Du M, Fu Z, Insogna KL, Karlsen MC, et al. Dietary protein and bone health: a systematic review and meta-analysis from the National Osteoporosis Foundation. Am J Clin Nutr 2017;105(6):1528–43.
[48] Bonjour JP. The dietary protein, IGF-I, skeletal health axis. Horm Mol Biol Clin Invest 2016;28(1):39–53.
[49] Yuan S, Wan Z-H, Cheng S-L, Michaëlsson K, Larsson SC. Insulin-like growth factor-1, bone mineral density, and fracture: a mendelian randomization study. J Clin Endocrinol Metab 2021;106(4):e1552–8.
[50] Tagawa R, Watanabe D, Ito K, Ueda K, Nakayama K, Sanbongi C, et al. Dose-response relationship between protein intake and muscle mass increase: a systematic review and meta-analysis of randomized controlled trials. Nutr Rev 2020;79(1):66–75.
[51] Hayes WC, Myers ER, Morris JN, Gerhart TN, Yett HS, Lipsitz LA. Impact near the hip dominates fracture risk in elderly nursing home residents who fall. Calcif Tissue Int 1993;52(3):192–8.
[52] Song J, Zhang R, Lv L, Liang J, Wang W, Liu R, et al. The relationship between body mass index and bone mineral density: a mendelian randomization study. Calcif Tissue Int 2020;107(5):440–5.
[53] Liczbiński P, Bukowska B. Tea and coffee polyphenols and their biological properties based on the latest in vitro investigations. Ind Crop Prod 2022;175:114265.
[54] Feskanich D, Willett WC, Colditz GA. Calcium, vitamin D, milk consumption, and hip fractures: a prospective study among postmenopausal women. Am J Clin Nutr 2003;77(2):504–11.
[55] Sadat-Ali M, Al Elq AH, Al-Turki HA, Al-Mulhim FA, Al-Ali AK. Influence of vitamin D levels on bone mineral density and osteoporosis. Ann Saudi Med 2011;31(6):602–8.
[56] Mendes MM, Hart KH, Lanham-New SA, Botelho PB. Association between 25-hydroxyvitamin D, parathyroid hormone, vitamin D and calcium intake, and bone density in healthy adult women: a cross-sectional analysis from the D-SOL study. Nutrients 2019;11(6):1267.