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Original Article

Mediterranean diet associated with lower frailty risk: A large cohort study of 21,643 women admitted to hospitals

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ABSTRACT

Background: Mediterranean diet is traditionally considered as a healthy dietary pattern, while its association with frailty has not been confirmed. This study investigated associations between Mediterranean diet and risk of frailty among women admitted to hospitals in England from an older-aged women's cohort study.

Methods: A modified Mediterranean diet was evaluated from a validated 217-item food frequency questionnaire. Incident frailty was determined using a hospital frailty risk score based on linkage to Hospital Episode Statistics up to March 2019. Cox proportional hazard models were conducted to estimate hazard ratios (HR) and 95% confidence intervals (CI). Further subgroup analyses stratified by age and body mass index (BMI), and sensitivity analyses were additionally explored.

Results: Over a mean follow-up of 13 years, there were 14,838 (68.6%) cases of frailty out of 21,643 individuals included in this study. Compared with low adherence to Mediterranean diet, moderate adherence was associated with 5% (HR = 0.95, 95%CI: 0.91, 0.99) lower risk of frailty, with high adherence associated with even lower risk (HR = 0.89, 95%CI: 0.85, 0.94). The magnitude of above associations remained consistent in subgroups stratified by age and BMI, except the association between moderate adherence and risk of frailty was attenuated in the ≥60-year (HR = 0.99, 95%CI: 0.93, 1.06) and the BMI > 24.9 kg/m^2 (HR = 0.97, 95%CI: 0.91, 1.03) subgroups.

Conclusions: Adherence to Mediterranean diet was associated with lower risk of frailty. The better the adherence, the greater the magnitude of the protective association. Older and overweight women may potentially benefit from greater adherence to the Mediterranean diet regarding frailty prevention.

1. Introduction

Frailty is a clinical syndrome characterized by cumulative loss of strength, endurance, and physiological capacity, which increases an individual's vulnerability to stressors. It is highly associated with increased risks of adverse outcomes including delirium, falls, fractures, disability, and early mortality [1]. Both frailty itself and related adverse outcomes are common reasons for high incidence of hospitalisations, requiring extra home care and long-term care admission, which puts unpredictable pressure on health-care systems [2–4]. One meta-analysis reported that the prevalence of frailty in older population was 26.9% overall, 29.8% in hospital settings and as high as 51.5% in nursing home settings [5].

The prevalence of frailty varies with many factors, including age, gender, and body mass index (BMI). Frailty is an age-related complex condition and its prevalence increases with age. A Chinese Longitudinal Healthy Longevity Surveys (CLHLS) randomly sampling from 85% of total population reported 64.7%, 81.4%, 88.9% and 95% prevalence rates of

Abbreviations: 95% CI, confidence intervals; BMI, body mass index; FFQ, food frequency questionnaire; hFRS, hospital frailty risk score; HR, hazard ratios; HRT, hormone replacement therapy; ICD, International Classification of Diseases; NCDs, non-communicable chronic diseases; SES, socio-economic status; UKWCS, United Kingdom's Women's Cohort Study.

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frailty and pre-frailty among age groups of 65–79, 80–89, 90–99, and ≥100 years respectively, and women in this study had a higher prevalence of frailty than men in all age groups [6]. In addition, women in UK Biobank study were also reported having increasing prevalence rate of frailty and pre-frailty with age, which were 41%, 42%, 43%, and 47% in age groups of 37–45, 45–55, 55–65, and 65–73 years [7]. A frailty index score was found to be positively correlated with BMI in two large European cohorts [8], and obese older people were reported more likely to be frail than those with a normal BMI [9]. Given the rapidly growing aging and obese population, frailty is increasingly becoming one of the most serious public health challenges worldwide [2].

As a polyetiological syndrome, frailty has multidimensional and complex risk factors including age, social economics and lifestyle aspects; however, it is still unclear how diet, and in particular, the Mediterranean diet, as a popular "protective dietary pattern", is associated with risk of frailty. Although most observational studies suggest that a Mediterranean diet is associated with lower risk of frailty [10], there are other reports showing no significant evidence for an association between Mediterranean Diet score and incident frailty in multivariate adjusted models [11]. Given these inconsistent findings, further research on this topic is needed.

Our study aimed to investigate associations between Mediterranean diet and risk of frailty in women from a large population-based cohort who were admitted to hospitals in England, and additionally conducted subgroup analyses stratified by age and BMI.

2. Methods and materials

This cohort study was reported following the Strengthening the Reporting of Observational Studies in Epidemiology — Nutritional Epidemiology (STROBE-nut) guidelines [12] (Additional file 1).

2.1. Study population

The UK Women's Cohort Study (UKWCS) was initiated in 1993 to explore potential dietary risk factors for chronic diseases, as detailed elsewhere [13]. Briefly, the UKWCS recruited 35,372 women aged 35–69 years across England, Scotland, and Wales via postal questionnaires, and collected anthropometric, demographic, lifestyle and health-related information at baseline between 1995 and 1998. The UKWCS was linked with electronic medical data from Hospital Episode Statistics of UK National Health Service up to 31 March 2019. In this study, of the 35,372 women at baseline, participants were excluded who did not have Hospital Episode Statistics records (n = 9980), who had incomplete hospital records (n = 206), and who had missing data in covariates (n = 3543), leaving 21,643 subjects eligible for analyses (Additional file 2: Fig. S1).

Informed consent has been obtained from all subjects involved in the study at recruitment of the cohort. Ethical approval was granted from National Research Ethics Service (NRES) Committee for Yorkshire & the Humber — Leeds East (Ref: 15/YH/0027) at the cohort's inception in 1993, and is now covered by Health Research Authority (REC Reference: 17/YH/0144), along with an NHS Digital Data Sharing Agreement (DARS-NIC-109867-M8S6B-v1.5) for the UKWCS-HES database to include matched medical records.

2.2. Assessment of diet

A self-administered 217-food item food frequency questionnaire (FFQ) was used to collect dietary information at baseline, adapted from the FFQ for the European Prospective Investigation into Cancer and Nutrition (EPIC) study [14] and validated elsewhere [15,16] (Additional file 2: Supplementary method). Adherence to a Mediterranean diet was scaled through a modified 10-point Trichopoulou version of the Mediterranean diet [17,18]. Briefly, of ten components traditionally consumed in the Mediterranean diet, six considered beneficial (vegetables, legumes, fruits and nuts, cereals, fish, and fatty acid ratio of monounsaturated plus polyunsaturated fatty acids to saturated fatty acids, namely MUFA + PUFA: SFA), were given a point of 1 if consumed at or above the median. Another three components (meat, poultry, and dairy) considered potentially detrimental were assigned 1 if consumed below the median. Women who consumed 5–25 g/d of alcohol were given an additional score of 1 point. The cut-points in each component are shown in Additional file 2: Table S1. Overall, Mediterranean diet score ranges from the lowest adherence of 0 to the highest adherence of 10, with higher scores meaning better dietary adherence. We further divided Mediterranean diet score into three levels: 0–3 (low adherence), 4–6 (moderate adherence), and 7–10 (high adherence).

2.3. Case definition

A hospital Frailty Risk Score (hFRS) was used to identify incident cases of frailty in this study. It was developed based on International Classification of Diseases (ICD)-10 diagnostic codes that were the most related to five frailty phenotypes (unintentional weight loss, exhaustion, slowness, low activity level, and weakness), and was validated in a UK national cohort of more than one million patients and a local cohort of 569 patients [19]. The hFRS was assessed on UKWCS participants who were admitted to hospitals during follow-up and had complete electronic medical records containing ICD-10 diagnostic codes. The electronic data may contain multiple hospitalisation records for each included participant with the main and secondary diagnostic ICD codes. The ICD codes listed in Additional file 2: Table S2 were assigned a corresponding point, while those not listed were given a 0. A hFRS for each participant was calculated by summing points from all diagnostic codes of each admitted hospital record. Cases of frailty were defined if any hFRS >0. Additionally, a more stringent standard (hFRS ≥2) to define frailty cases was conducted as supplementary analyses.

2.4. Statistical analysis

Baseline socio-demographic and lifestyle characteristics for UKWCS participants were summarized by three levels of adherence to Mediterranean diet. Hazard ratios (HR) and 95% confidence intervals (95% CI) were estimated for associations between adherence to Mediterranean diet and risk of frailty by modelling Cox proportional hazards regression with the low adherence as the reference. Participants were followed from recruitment till first diagnosis of an event associated with frailty, date of death, or the censor date (31 March 2019) whichever came first. The minimal adjustment was taken to be adjusting for age at baseline as a continuous variable, since frailty usually depends strongly on age. Other potential confounders identified in the literature previously were additionally adjusted in the fully-adjusted model, including: ethnicity, marital status, socio-economic status (SES), physical activity, smoking status, alcohol consumption, BMI, daily energy intake, and menopausal status (details in Additional file 2: Supplementary method).

To explore baseline age and BMI as potential effect modifiers, subgroup analyses were conducted by fitting the fully-adjusted models in separate age groups (<60, ≥60 years), and BMI groups (normal-weight with BMI < 24.9, and overweight with BMI ≥ 24.9 kg/m^2). Baseline age (continuous, years) and BMI (continuous, kg/m^2) were also separately added to the fully-adjusted models as interaction terms with levels of adherence to Mediterranean diet where they were modelled linearly. Further subgroup analyses stratified by more subdivided age groups (<45, 45–49, 50–59, and ≥60 years, where these cut-offs were defined to ensure a similar number of individuals in each stratum) were conducted to explore specific associations between one-point increase of Mediterranean diet score and risk of frailty in different age groups.

Further sensitivity analysis was performed to check for possibility of reverse causation by excluding participants who had less than 3-year survival time. Additional sensitivity analyses were conducted by fitting the fully-adjusted models under the following conditions: 1. To exclude participants having any two or more kinds of chronic diseases (coronary heart disease, angina, stroke, hypertension, hyperlipidaemia, diabetes,

Table 1
Baseline demographic characteristics of participants in a UK women's cohort admitted to hospitals.

		Low adherence (N = 5172, 23.9%)	Moderate adherence (N = 11,670, 53.9%)	High adherence (N = 4801, 22.2%)	All participants (N = 21,643)
Age at baseline (years)	Mean (standard deviation)	53.9 (9.4)	52.8 (9.3)	51.1 (9.0)	52.7 (9.3)
Follow-up time (years)	Mean (standard deviation)	12.3 (6.3)	12.8 (6.3)	13.3 (6.4)	12.8 (6.3)
Ethnicity (N, %)	White	5147 (99.5%)	11,526 (98.8%)	4724 (98.4%)	21,397 (98.9%)
	Asian	12 (0.2%)	65 (0.6%)	31 (0.6%)	108 (0.5%)
	Black	1 (0.02%)	19 (0.2%)	4 (0.1%)	24 (0.1%)
	other	12 (0.2%)	60 (0.5%)	42 (0.9%)	114 (0.6%)
Educational level (N, %)	No qualifications	1059 (22.9%)	1895 (17.8%)	516 (11.5%)	3470 (17.5%)
	O-level or equivalent	1681 (36.4%)	3425 (32.1%)	1283 (28.5%)	6389 (32.3%)
	A-level or equivalent	998 (21.6%)	2603 (24.4%)	1184 (26.3%)	4785 (24.2%)
	University degree	879 (19.1%)	2737 (25.7%)	1518 (33.7%)	5134 (26.0%)
Marital status (N, %)	Married or living as married	3989 (77.1%)	8907 (76.3%)	3661 (76.2%)	16,557 (76.5%)
	Separated or divorced	451 (8.7%)	1238 (10.6%)	600 (12.5%)	2289 (10.6%)
	Single or widowed	732 (14.2%)	1525 (13.1%)	540 (11.3%)	2797 (12.9%)
Socio-economic status (SES) (N, %)	Routine and manual	608 (11.8%)	1105 (9.5%)	321 (6.7%)	2034 (9.4%)
	Intermediate	1706 (33.0%)	3279 (28.1%)	1120 (23.3%)	6105 (28.2%)
	Professional and managerial	2858 (55.2%)	7286 (62.4%)	3360 (70.0%)	13,504 (62.4%)
Physical activity (N, %)	Low level	733 (14.2%)	1233 (10.6%)	336 (7.0%)	2302 (10.6%)
	Moderate level	2812 (54.4%)	5838 (50.0%)	2185 (45.5%)	10,835 (50.1%)
	High level	1627 (31.5%)	4599 (39.4%)	2280 (47.5%)	8506 (39.3%)
Body mass index (BMI) (kg/m^2)	Mean (standard deviation)	25.4 (4.6)	24.6 (4.3)	23.6 (3.7)	24.6 (4.3)
Alcohol (g/d)	Mean (standard deviation)	7.4 (11.3)	8.8 (10.6)	9.8 (8.8)	8.7 (10.4)
Smoking status (N, %)	Never smoked	2992 (57.8%)	6758 (57.9%)	2619 (54.5%)	12,369 (57.1%)
	Ex-smoker	1457 (28.2%)	3674 (31.5%)	1723 (35.9%)	6854 (31.7%)
	Current smoker	723 (14.0%)	1238 (10.6%)	459 (9.6%)	2420 (11.2%)
Menopausal status	Premenopausal	2038 (39.4%)	5162 (44.2%)	2512 (52.3%)	9712 (44.9%)
	Postmenopausal	3134 (60.6%)	6508 (55.8%)	2289 (47.7%)	11,931 (55.1%)

gallstones, polyps in the large intestine, or any cancer) at baseline; 2. To exclude participants on long-term treatment for illness at baseline; 3. To exclude participants having ≥1 year hormone replacement therapy (HRT) at baseline. All statistical analyses were conducted using Stata/MP, version 17.0 (Stata Corp LP).

3. Results

Baseline characteristics of the UKWCS participants admitted to hospitals are summarised in Table 1 by three levels of adherence to Mediterranean diet. Most of the middle-aged women (mean age = 52.7, standard deviation (SD) = 9.3 years) were White (98.9%), and married or living as married (76.5%) at baseline. High adherence to Mediterranean diet was associated with higher levels of education (A-level and university degree 60% vs. 40.7% in low adherence and 50.1% in moderate adherence), high level of SES (professional and managerial 70.0% vs. 55.2% in low adherence and 62.4% in moderate adherence), and high level of physical activity (47.5% vs. 31.5% in low adherence and 39.4% in moderate adherence). Participants with low adherence to Mediterranean diet had a higher mean BMI of 25.4 kg/m^2 at baseline, compared to those with moderate adherence (24.6 kg/m^2) and high adherence (23.6 kg/m^2).

During 277,122 person-years observation, there were 14,838 cases of frailty identified via hFRS (>0) over a mean follow-up time of 12.8 years. Compared with low adherence to Mediterranean diet, both moderate

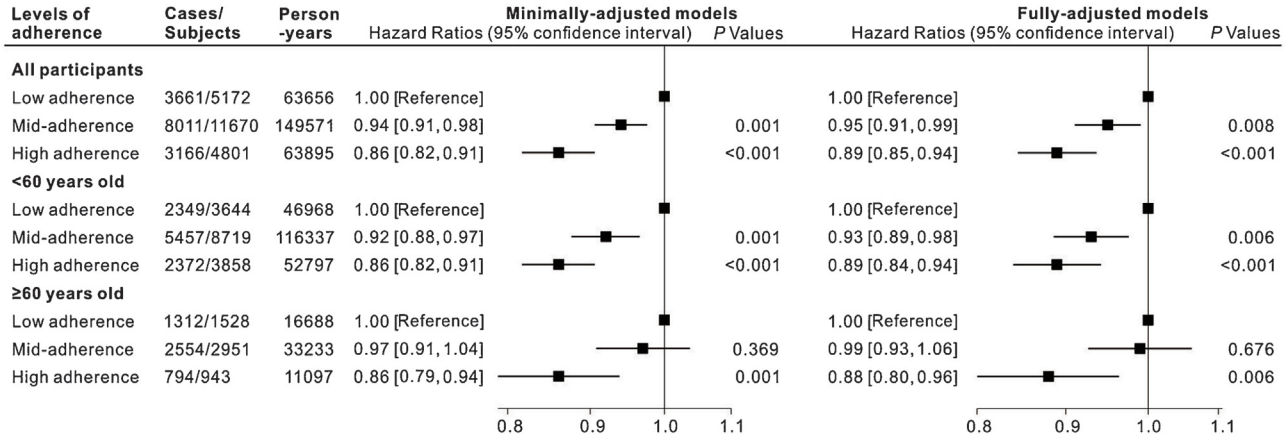

Fig. 1. Associations of Mediterranean diet with frailty risk within a UK women's cohort admitted to hospitals.
Age was adjusted in the minimally-adjusted model; additionally, ethnicity, marital status, socioeconomic status, physical activity, body mass index, smoking status, alcohol consumption, total energy intake, and menopausal status were adjusted in the fully-adjusted model in the figure.

Table 2
Subgroup analysis by body mass index on associations between Mediterranean diet and frailty risk.

Body mass index (BMI)	Cases/subjects	Person-years	Hazard ratio (95% Confidence Interval)	P*
Normal-weight (BMI ≤ 24.9 kg/m^2, N = 13,648)				
Low adherence	1919/2837	35,959	1.00 (Reference)	
Moderate adherence	4810/7314	96,027	0.93 (0.89, 0.99)	0.012
High adherence	2270/3497	46,871	0.90 (0.85, 0.96)	0.002
Overweight (BMI > 24.9 kg/m^2, N = 7995)				
Low adherence	1742/2335	27,697	1.00 (Reference)	
Moderate adherence	3201/4356	53,544	0.97 (0.91, 1.03)	0.294
High adherence	896/1304	17,023	0.83 (0.76, 0.90)	<0.001

* Adjusted for age, ethnicity, marital status, socioeconomic status, physical activity, body mass index, smoking status, alcohol consumption, total energy intake, and menopausal status.

Table 3
Sensitivity analysis by excluding specific subjects on associations between Mediterranean diet and frailty risk.

	Cases/subjects	Person-years	Hazard ratio (95% Confidence Interval)	P*
Fully-adjusted model				
Low adherence	3661/5172	63,656	1.00 (Reference)	
Moderate adherence	8011/11,670	149,571	0.95 (0.91, 0.99)	0.008
High adherence	3166/4801	63,895	0.89 (0.85, 0.94)	<0.001
Excluding subjects with <3 years of follow-up (N = 1812)				
Low adherence	3267/4677	62,808	1.00 (Reference)	
Moderate adherence	7251/10,706	147,863	0.95 (0.91, 0.99)	0.022
High adherence	2910/4448	63,242	0.90 (0.85, 0.94)	<0.001
Excluding subjects with over any two kinds of chronic diseases (N = 1829)				
Low adherence	3252/4697	58,680	1.00 (Reference)	
Moderate adherence	7154/10,669	139,550	0.93 (0.89, 0.97)	0.001
High adherence	2882/4448	59,949	0.88 (0.84, 0.93)	<0.001
Excluding subjects on long-term treatment for illness (N = 6899)				
Low adherence	2191/3346	43,521	1.00 (Reference)	
Moderate adherence	5100/7916	106,927	0.95 (0.91, 1.00)	0.050
High adherence	2153/3482	47,710	0.91 (0.85, 0.97)	0.003
Excluding subjects with ≥1 year hormone replacement therapy (HRT) (N = 4764)				
Low adherence	2705/3938	49,004	1.00 (Reference)	
Moderate adherence	6076/9111	117,479	0.95 (0.91, 1.00)	0.050
High adherence	2464/3830	51,399	0.89 (0.84, 0.95)	<0.001

* Adjusted for age, ethnicity, marital status, socioeconomic status, physical activity, body mass index, smoking status, alcohol consumption, total energy intake, and menopausal status.

adherence (HR = 0.95 (95% CI 0.91, 0.99)) and high adherence (0.89 (0.85, 0.94)) had lower risk of frailty in the fully adjusted models (Fig. 1). Subgroup analysis by age showed that the above associations remain in women <60 years old; however, among women ≥60 years, magnitude of the association between to Mediterranean diet and risk of frailty was attenuated in moderate adherence (0.99 (0.93, 1.06)) but not in high adherence (0.88 (0.80, 0.96)) groups (Fig. 1). There was some evidence of effect modification by age with moderate adherence to Mediterranean diet (*P*-interaction = 0.031).

For subgroup analyses by BMI in Table 2, a lower risk of frailty associated with high adherence to Mediterranean diet was observed in both the normal-weight (0.90 (0.85, 0.96)) and the overweight (0.83 (0.76, 0.90)) subgroups. However, there was potential effect modification by BMI on frailty risk, where moderate adherence was associated with lower risk of frailty in the normal-weight women only (0.93 (0.89, 0.99) *P*-interaction = 0.004). Results from sensitivity analyses were robust when excluding participants with <3 years survival time, or with any two or more chronic diseases, or on long-time treatment for illness, or with ≥1 year HRT history, whereas estimates remain broadly unchanged (Table 3).

When taking hFRS ≥2 as the stringent standard of frailty determination, there were 5815 (26.9%) cases of frailty. The associations between risk of frailty and adherence to Mediterranean diet remained (Additional file 2: Fig. S2). Results from the stratified analyses remain similar in the age subgroups (Additional file 2: Fig. S2), but changed a bit in BMI subgroups (Additional file 2: Table S3). Results were robust to the further removal of participants with any characteristic above-mentioned (Additional file 2: Table S4).

When taking the Mediterranean diet score as a continuous variable, one-point increase of adherence to this dietary pattern was associated with 2% (0.98 (0.97, 0.99)) lower risk of frailty (Additional file 2: Table S5). Further subgroup analyses stratified by more subdivided age groups showed similar associations between one-point increase of Mediterranean diet score and risk of frailty in age groups of <45, 45–49, 50–59, and ≥60 years (Additional file 2: Table S5).

4. Discussion

In this prospective women's cohort adherence to Mediterranean diet was found to be associated with lower risk of frailty in those admitted to hospital, with a dose-response showing greater adherence associated with lower risk. Although different measurement tools were used, our results are consistent with the main evidence of a meta-analysis and systematic review which showed a 38% reduction in frailty risk by medium adherence to Mediterranean diet, and a 56% reduction by high adherence using FRAIL scale or Modified Cardiovascular Health Study frailty criteria (mCHS) [10]. Similar associations can also be observed in other areas and male populations. Among 15,249 men and women in US, Mediterranean diet score was inversely correlated with the frailty index [20]. A Greek longitudinal study recently reported that each unit of Mediterranean diet score was associated with a 5% or 10% decrease in the risk of incident frailty

when the Frailty Index and the Tilburg Frailty Indicator used respectively [21]. Those findings together imply a protective association between adherence to Mediterranean diet and risk of frailty, irrespective of measurement tools used, or populations investigated.

Stratified analyses showed there was some evidence of effect modification by age and BMI, where differences in associations were observed between separate age groups and BMI groups. A similar effect modification by age was also reported in the Framingham Offspring Study, where lower risk of frailty in relation to per unit higher Mediterranean diet was stronger in participants aged <60 years compared to those aged ≥60 years [22]. In our study, there was no evidence that moderate adherence to the Mediterranean diet was associated with risk of frailty in the ≥60-year, which was similarly observed in the prospective Seniors-ENRICA-1 cohort (≥60 years) [23], the Italian InCHIANTI cohort (≥65 years) [24], and the French Three-City cohort (≥75 years) [25], whereas high adherence was associated with up to 74% lower risk of frailty in those studies. The inverse association between adherence to Mediterranean diet and risk of frailty potentially changes during aging, which may be more obvious in relatively younger groups such as those less than 60 years of age. Suggesting that older people should adopt the Mediterranean-type diet closely if considering risk of frailty. In addition, our results showed higher magnitude of associations among individuals with being normal-weight compared to being overweight, implying that weight management is potentially an important consideration in controlling risk of frailty related to Mediterranean diet. However, since evidence on effect modification of BMI in associations between Mediterranean diet and frailty risk is limited, further related research is needed.

The rationale for the association between Mediterranean diet and frailty risk remain unclear. One potential mechanism may be the benefits of Mediterranean diet in affecting various chronic health outcomes. Previous evidence has shown that higher adherence to Mediterranean diet was associated with lower risk of several non-communicable chronic diseases (NCDs) including cardiovascular diseases, cancer, cognitive decline, fragility fractures, etc. [26]. Some frailty assessment tools such as frailty index [27] and hFRS [19] measure the cumulative state of chronic diseases which are the basis of frailty. A lower incidence of numerous age-associated NCDs may help to explain the benefit of a Mediterranean diet regarding frailty. The Mediterranean diet is considered to be a healthy, plant-based diet. Plant-based diets are found to be protective against frailty risk [28]. Besides, high consumption of fruits and vegetables, the main sources of antioxidants [29], has been associated with lower risk of frailty [30,31]. In addition, some previous epidemiological studies reported a protective association of a Mediterranean-type diet rather than one food group alone with risk of frailty [32], indicating the potential interactive or additive action between "healthy foods" that may prevent the pathogenesis of frailty.

Although frailty is not necessarily an inevitable consequence of aging, it was highly influenced by risk factors of aging [33]. This geriatric disease is an age-related complex syndrome that increases individuals' vulnerability to stress events [1]. A Mediterranean diet was reported associated with prolonged life expectancy and lower risk of all-cause mortality among 74,607 old people from nine European countries [18]. It is potentially due to the long-term effect of beneficial aspects of a Mediterranean diet in middle-aged adults that contributes to healthy aging [34]. Frailty could benefit from healthy aging regarding low incidences of negative outcomes.

Frailty was reported associated with an over two-fold increased risk of all-cause mortality in patients over 7-year follow-ups [35] and related to a 54% higher risk of 30-day mortality in the ICU setting [36]. Identification of frailty in hospitals could remind clinicians of applying increased monitoring care, and providing individualized resources and intensive treatment for prevention of adverse outcomes. In our study, the observed lower risk of frailty in women admitted to hospitals with high adherence to a Mediterranean diet compared to those with low adherence, indicates a necessity of investigating patients' previous dietary behaviours as an important aspect of predicting cases of frailty. In addition, clinicians could suggest a Mediterranean-like diet to patients regarding its beneficial effects on reducing frailty and health aging in a clinical trial across five European countries [37]. However, we also recognize that the magnitude of the associations was modest, and more factors regarding cost effectiveness should be considered further.

This study has some limitations. First, the prevalent cases of frailty could not be excluded at baseline since hospital records or measurement of physical mobility at recruitment were not available for analysis. However, in our sensitivity analyses results were robust to exclusion of participants with a survival time <3 years, with two or more chronic diseases, or with long-term treatment for illness. Second, in the primary analysis cases of frailty in this study were not differentiated on the basis of severity. Cases of mild frailty (possible pre-frailty) were therefore included, potentially attenuating associations. Nevertheless, additional analyses using a stringent standard as the cut-point (≥2 score) were conducted as supplementary results and yielded broadly similar results. This study is also weakened by participants being only women, and those admitted to hospitals in England rather than other parts of the UK, which limits generalizability of our findings; therefore, further research is required in other populations.

Strengths of this study comprise the high quality of diet assessment via a validated comprehensive FFQ, a long follow-up prospective cohort study design with a large sample size, and efficient frailty measurement based on linkage data with national hospital diagnostic records. Currently, there are few measurement tools for assessment of frailty in hospital settings, our study provided some evidence for the possibility of using hFRS to assess in-hospital frailty. In contrast to other studies, our study additionally explored effect modifications of age and BMI on associations between Mediterranean diet and frailty risk, which makes the findings more precise and targeted.

Overall, our study suggested a protective association between adherence to Mediterranean diet and risk of frailty, particularly in those of younger age and normal weight. These findings will provide useful insights for developing future intervention programs to encourage healthy population aging.

Authors' contributions

H.Z.: Conceptualization, Formal analysis, Funding acquisition, Methodology, Software, Visualization, Roles/Writing – original draft. *W.L.*: Conceptualization, Methodology, Supervision, Writing – review & editing. *Y.W.*: Conceptualization, Methodology, Supervision, Writing – review & editing. *Y.D.*: Formal analysis, Software, Visualization. *D.C.G.*: Data curation, Investigation, Validation, Writing – review & editing. *L.J. H.*: Methodology, Supervision, Validation, Writing – review & editing. *J. E.C.*: Data curation, Funding acquisition, Investigation, Project administration, Resources, Supervision, Writing – review & editing. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Ethical approval was granted from National Research Ethics Service (NRES) Committee for Yorkshire & the Humber – Leeds East (Ref: 15/YH/0027) at the cohort's inception in 1993, and is now covered by Health Research Authority (REC Reference: 17/YH/0144), along with an NHS Digital Data Sharing Agreement (DARS-NIC-109867-M8S6B-v1.5) for the UKWCS-HES database to include matched medical records. Informed consent has been obtained from all subjects involved in the study at recruitment of the cohort.

Availability of data and materials

The data access policy for the UK Women's Cohort Study is available via the study website (The UK Women's Cohort Study (UKWCS): University of Leeds).

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Competing interests

All authors declare that they have no competing interests.

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Appendix A. Supplementary data

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