# Vegetarians, fish, poultry, and meat-eaters: who has higher risk of cardiovascular disease incidence and mortality? A prospective study from UK Biobank 

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| Aims | To compare the incidence and mortality risk for cardiovascular diseases (CVD) [CVD and also ischaemic heart disease (IHD), myocardial infarction (MI), stroke, and heart failure (HF)] among people with different types of dietsincluding vegetarians, fish eaters, fish and poultry eaters, and meat-eaters-using data from UK Biobank. |
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| Methods and results | A total of 422791 participants ( $55.4 \%$ women) were included in this prospective analysis. Using data from a food frequency questionnaire, four types of diets were derived. Associations between types of diets and health outcomes were investigated using Cox proportional hazard models. Meat-eaters comprised $94.7 \%$ of the cohort and were more likely to be obese than other diet groups. After a median follow-up of 8.5 years, fish eaters, compared with meat-eaters, had lower risks of incident CVD \{hazard ratios (HR): 0.93 [ $95 \%$ confidence intervals (Cl): 0.88$0.97]\}$, IHD [HR: 0.79 ( $95 \% \mathrm{Cl}: 0.70-0.88$ )], MI [HR: 0.70 ( $95 \% \mathrm{Cl}: 0.56-0.88$ )], stroke [HR: 0.79 ( $95 \% \mathrm{Cl}: 0.63-$ $0.98)$ ] and HF [HR: 0.78 ( $95 \% \mathrm{Cl}: 0.63-0.97$ )], after adjusting for confounders. Vegetarians had lower risk of CVD incidence [HR: 0.91 ( $95 \% \mathrm{Cl}: 0.86-0.96$ )] relative to meat-eaters. In contrast, the risk of adverse outcomes was not different in fish and poultry eaters compared with meat-eaters. No associations were identified between types of diets and CVD mortality. |
| Conclusion | Eating fish rather than meat or poultry was associated with a lower risk of a range of adverse cardiovascular outcomes. Vegetarianism was only associated with a lower risk of CVD incidence. |

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## Graphical Abstract



Keywords Candiovascưar diseases - Vegetarians • Meat - Incidence - Mortãlity

## Introduction

Cardiovascular diseases (CVD) remain one of the top 10 causes of death worldwide. ${ }^{1}$ Although there are several behavioural risk factors for CVD, a poor diet accounts for $\sim 10$ million deaths worldwide. ${ }^{2}$ Of these, 3.8 million deaths have been attributable to a diet low in fruit and vegetables, 1.4 million to a diet low in seafood intake, and 150000 to high red and processed meat intake. ${ }^{2}$ With current dietary guidelines encouraging people to limit their intake of red and processed meat ${ }^{2,3}$ and increase their intake of fruit and vegetable as well as fish, ${ }^{4}$ alternative diets, which restrict the intake of either meats or animal products, have become more popular in recent years.

Due to the health benefits of plant-based diets, as well as concerns over animal protein (animal welfare and apprehension over antibiotics use) and the environmental protection, some of the most popular diets are vegetarian and vegan. ${ }^{5}$ Vegetarian diets have been associated with lower CVD ${ }^{6}$ and cancer ${ }^{7}$ risk in comparison to all nonvegetarian diets due to their higher content of fibre, vitamins, and minerals, and lower content of saturated fat. ${ }^{8,9}$ However, the relative merits of vegetarianism compared with other alternative diets have been less well studied.

Previous studies have shown heterogeneous findings when comparing the risk of CVD associated with vegetarian, vegan, and
pescatarian diets to diets containing meat. ${ }^{6,10,11}$ For instance, some have reported a higher risk of CVD among fish eaters compared with meat-eaters, while others have demonstrated that despite vegetarians having a lower risk of ischaemic heart diseases (IHD), they had a higher risk of stroke. ${ }^{6,10,11}$ However, although these studies had a long follow-up, smaller sample sizes ( $<50000$ ), as well as the multifactorial nature of CVD, ${ }^{1}$ may explain some of the discrepancies in previous studies. Therefore, data from larger prospective studies are still needed. Hence, this study aimed to compare the incidence and mortality risk for a range of CVD outcomes among people with different types of diets-vegetarians, fish eaters, fish and poultry eaters, and meat-eaters-using data from UK Biobank.

## Methods

Between 2006 and 2010, UK Biobank recruited over 500000 participants ( $5.5 \%$ response rate), aged $37-73$ years from the general population. ${ }^{12}$ Participants attended one of the 22 assessment centres across England, Wales, and Scotland ${ }^{13,14}$ where they completed a touch-screen questionnaire, had physical measurements taken, and provided biological samples, as described in detail elsewhere. ${ }^{13,14}$

UK Biobank was approved by the North West Multi-Centre Research Ethical Committee (REF: 11/NW/03820). This study complies with the Declaration of Helsinki.

## Outcomes

The outcomes in the current study were incident (hospitalization or death) and fatal events due to: CVD [International Classification of Diseases 10 revision (ICD10) codes 100-199, i.e. all diseases from the circulatory system], IHD (ICD10 I20-I25), myocardial infarction (MI) (ICD10 121-I23), stroke (160, 161, 163, or 164), and heart failure (HF) (I50.0, $150.1,150.9$ ). Date of death was obtained from death certificates held by the National Health Service (NHS) Information Centre (England and Wales) and the NHS Central Register Scotland (Scotland). Dates and causes of hospital admission were identified via record linkage to Health Episode Statistics (England and Wales) and the Scottish Morbidity Records (SMR01) (Scotland). Details of the linkage procedure can be found at http://content.digital.nhs.uk/services. Death data were available up to June 2020. Follow-up for mortality outcomes was censored on this date or the date of death if that occurred earlier. Hospital admissions were available up to June 2020 in England and March 2017 in Wales and Scotland. Follow-up for incident events was censored on this date or the date of death if this occurred earlier.

## Definitions of types of diets

The touch-screen questionnaire, self-completed at baseline, was used to collect the frequency of consumption of the following items: cheese, milk, fish (oily and non-oily), poultry, and red meat (beef, pork, lamb, and processed red meat) over the previous year. All food items were dichotomized into consumed or not consumed.
Using these variables, participants were categorized into four types of diets: vegetarians (consumption of cheese and/or milk but not fish, poultry, or red meat, i.e. lacto-ovo-vegetarian); fish eaters (consumption of cheese, milk, and fish but not poultry or red meat); fish and poultry eaters (consumption of cheese, milk, fish, and poultry but not red meat); and meat-eaters (consumption of cheese, milk, fish, poultry, and red meat). People with missing data for any of the dietary variables were excluded [ $n=9011(1.8 \%)$ ]. In addition, we excluded vegan participants as the sample size was not sufficient for conducting the analyses ( $n=57,0.01 \%$ ). To take account of people changing their dietary pattern, we excluded people who self-reported at baseline that their diet often varied ( $n=45028$, $8.99 \%$ ). Therefore, 448396 participants had available information for the different types of diets ( $89.2 \%$ ). The groups were mutually exclusive (Supplementary material online, Figure S1).

## Covariates

Age was calculated from dates of birth and baseline assessment. Areabased socioeconomic status (deprivation) was derived from the postcode of residence, using the Townsend score (more details in Supplementary material online). ${ }^{15}$ Self-reported smoking status was categorized as never, former, or current smoker. Total time spent in discretionary sedentary behaviours was derived from the sum of self-reported time spent driving, using a computer and watching television during leisure time. Body mass index (BMI) was calculated from weight/height ${ }^{2}$, and the WHO criteria were applied. ${ }^{16}$ Medical history was also self-reported. Frequency of alcohol intake was self-reported at baseline via touch-screen questionnaire and categorized as daily/almost daily, 3-4 times a week, once/twice a week, 1-3 times a month, special occasions only, and never. Prevalent morbidity was ascertained during a nurse-led interview at baseline. We calculated morbidity count based on 43 long-term conditions developed initially for a large epidemiological study in Scotland and subsequently adapted for UK Biobank ${ }^{17}$ (Table 1).

## Other diet variables

Water and fruit and vegetable intake were collected through the touchscreen questionnaire at baseline. In turn, dietary information for macroand micro-nutrients-as well as other food items (such as fast food intake)—was collected via the Oxford WebQ, a web-based 24-h recall questionnaire (more details in Supplementary material online). ${ }^{18}$ For this study, the average of five 24 -h recalls was used. However, as the average of the 24-h recalls was only available for about 200000 individuals, the number of individuals with data available for each variable is shown in Table 2.

Further details of these measurements can be found in the UK Biobank online protocol (http://www.ukbiobank.ac.uk).

## Statistical analyses

Associations between types of diets and cardiovascular events (CVD, HF, IHD, MI, and stroke) were investigated using Cox proportional hazard models with the time of follow-up used as the timeline variable. Individuals who self-reported being meat-eaters were used as the reference group. The results are reported as hazard ratios (HR) and their $95 \%$ confidence intervals (Cl). The proportional hazard assumptions were checked using Schoenfeld residuals. Participants with MI and/or stroke at baseline were also excluded from all analyses ( $n=15737,3.6 \%$ ). For CVD incidence (outcome with the highest numbers of events), the Kaplan-Meier survival estimate was also calculated.

All Cox proportional analyses were performed using a 2 -year landmark analysis, excluding participants who experienced events within the first 2 years of follow-up: 24343 for overall CVD incidence ( 4504 IHD, $1026 \mathrm{MI}, 689$ strokes and 600 HF ) and 538 for overall CVD mortality ( $258 \mathrm{IHD}, 97 \mathrm{MI}, 82$ strokes and 47 HF ).

We ran four incremental models for each outcome: 'model 1' included sociodemographic covariates (age, sex, deprivation, and ethnicity); 'model 2' additionally included multimorbidity (based on 43 diseases and coded as ordinal $1,2,3,4$, and $\geq 5$ ); 'model 3 ' additionally included lifestyle factors (smoking, total discretionary sedentary time, alcohol intake, and total physical activity); and 'model 4' additionally included BMI at baseline.

In addition, to investigate whether the associations between the different types of diets and cardiovascular outcomes differed by subgroups, the models were re-run stratified by sex, age category ( $<60$ and $\geq 60$ years), BMI (normal/overweight and obese), and deprivation (below and above median).

Finally, we created a propensity score based in all the relevant covariates included in the study to investigate the associations between types of diets and the outcome using a matched propensity score design (see Supplementary material online, pages 14-16).

STATA 16 statistical software (StataCorp LP) was used to perform all analyses.

## Results

A total of 422791 participants ( $55.4 \%$ women) had data available for the types of diets and covariates of this study (Supplementary material online, Figure S 1 ). Excluding the 2 -year landmark period, the median follow-up period was 8.5 (interquartile range: 7.0-9.5) years for CVD incidence and 9.3 (interquartile range: 8.6-10.0) years for CVD mortality. Over the follow-up period, 106690 (24.3\%) developed CVD ( 24794 IHD, $6770 \mathrm{MI}, 5946$ stroke, and 7685 HF ) and 6580 (1.5\%) died from CVD ( 2767 IHD, $885 \mathrm{MI}, 1088$ stroke, and 965 HF ).

Table I. Sociodemographic characteristics of the study population by types of diets.

|  | Vegetarians | Fish eaters | Fish and poultry eaters | Meat-eaters |
| :---: | :---: | :---: | :---: | :---: |
| Socio-demographics |  |  |  |  |
| Total, $n$ (\%) | 7537 (1.8) | 9951 (2.4) | 4883 (1.1) | 400470 (94.7) |
| Age (years), mean (SD) | 53.1 (7.9) | 54.0 (8.0) | 56.3 (8.1) | 56.5 (8.1) |
| Sex (female), $n(\%)$ | 5042 (66.9) | 7197 (72.3) | 3721 (77.0) | 218307 (54.1) |
| Deprivation, $n(\%)$ |  |  |  |  |
| Lower | 1965 (26.0) | 2893 (29.1) | 1381 (28.6) | 139264 (34.8) |
| Middle | 2425 (32.2) | 3315 (33.3) | 1558 (32.2) | 135436 (33.8) |
| Higher | 3147 (41.8) | 3743 (37.6) | 1894 (39.2) | 125770 (31.4) |
| Ethnicity, $n$ (\%) |  |  |  |  |
| White | 6150 (81.6) | 9372 (94.2) | 4377 (90.6) | 382551 (95.5) |
| Mixed | 118 (1.6) | 158 (1.6) | 103 (2.1) | 5360 (1.3) |
| South Asian | 1231 (16.3) | 285 (2.9) | 213 (4.4) | 5550 (1.4) |
| Black | 29 (0.4) | 126 (1.2) | 135 (2.8) | 5784 (1.5) |
| Chinese | 9 (0.1) | 10 (0.1) | 5 (0.1) | 1225 (0.3) |
| Obesity-related markers |  |  |  |  |
| BMI, mean (SD) | 25.6 (4.6) | 25.2 (4.2) | 25.5 (4.5) | 27.4 (4.7) |
| BMI categories, $n(\%)$ |  |  |  |  |
| Underweight ( $<18.5 \mathrm{~kg} / \mathrm{m}^{2}$ ) | 128 (1.7) | 162 (1.6) | 76 (1.5) | 1867 (0.4) |
| Normal weight ( $18.5-24.9 \mathrm{~kg} / \mathrm{m}^{2}$ ) | 3730 (49.5) | 5262 (52.9) | 2423 (50.1) | 131241 (32.8) |
| Overweight ( $25.0-29.9 \mathrm{~kg} / \mathrm{m}^{2}$ ) | 2629 (34.9) | 3354 (33.7) | 1631 (33.8) | 172577 (43.1) |
| Obese ( $\geq 30.0 \mathrm{~kg} / \mathrm{m}^{2}$ ) | 1050 (13.9) | 1173 (11.8) | 703 (11.6) | 94785 (23.7) |
| Fitness and lifestyle |  |  |  |  |
| Total PA (MET-min/week), mean (SD) | 2811.1 (2930.2) | 2884.2 (2900.6) | 3196.9 (3152.4) | 2818.7 (3019.9) |
| Sedentary behaviour (h/day), mean (SD) | 4.3 (2.2) | 4.3 (2.1) | 4.5 (2.3) | 5.0 (2.2) |
| Smoking status, $n$ (\%) |  |  |  |  |
| Never | 4825 (64.0) | 5696 (57.3) | 2895 (59.9) | 223054 (55.7) |
| Previous | 2197 (29.2) | 3564 (35.8) | 1571 (32.5) | 137220 (34.3) |
| Current | 515 (6.8) | 691 (6.9) | 367 (7.6) | 40196 (10.0) |
| Alcohol intake frequency, $n$ (\%) |  |  |  |  |
| Daily or almost daily | 1069 (14.2) | 1905 (19.1) | 685 (14.2) | 82898 (20.7) |
| 3-4 times a week | 1347 (17.9) | 2414 (24.3) | 862 (17.8) | 95137 (23.8) |
| Once or twice a week | 1514 (20.1) | 2299 (23.1) | 1112 (23.0) | 105521 (26.4) |
| 1-3 times a month | 885 (11.7) | 1162 (11.7) | 547 (11.3) | 44535 (11.1) |
| Special occasions only | 1059 (14.0) | 1143 (11.5) | 866 (17.9) | 44214 (11.0) |
| Never | 1663 (22.1) | 1028 (10.3) | 761 (15.8) | 28165 (7.0) |
| Health status |  |  |  |  |
| Multimorbidity, $n$ (\%) |  |  |  |  |
| None | 3122 (41.4) | 4172 (41.9) | 1770 (36.6) | 143910 (35.9) |
| $\geq 1$ | 4415 (58.6) | 5779 (58.1) | 3063 (63.4) | 256560 (64.1) |

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## Sociodemographic and diet characteristics

The characteristics of the population by type of diet are presented in Table 1. The large majority of the participants were meat-eaters ( $94.7 \%$ ) while fish and poultry eaters only constituted $1.1 \%$. In comparison to meat-eaters, vegetarian, fish, and fish and poultry eaters were younger, more likely to be women, south Asian, and to have a lower BMI. Meat-eaters, in turn, were more likely to have more than one multimorbidity, and to be current smokers (Table 1). Similar
characteristics by event occurrence are shown in Supplementary material online, Table S1.

Dietary intake characteristics by types of diets are shown in Table 2. In general, meat-eaters had a higher protein and total fat and lower carbohydrates and sugar intake, compared with the other diets. Meat-eaters showed the lowest consumption of fibre, polyunsaturated fat (PUFA), water, and fruit and vegetables. As expected, vegetarians were more likely to eat and buy vegetarian alternatives in comparison to meat-eaters ( $53.7 \%$ vs. $3.9 \%$ ). However, vegetarians reported consuming more crisps, slices of pizza, and smoothie drinks

Table 2 Dietary characteristics of the study population by types of diets

| Dietary intakes, mean (SD) | Data available in ${ }^{\text {a }}$ | Vegetarians | Fish eaters | Fish and poultry eaters | Meat-eaters |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Total energy intake (kcal/day) | 183318 | 2117 (725) | 2126 (674) | 2032 (701) | 2170 (657) |
| CHO intake (\% of TE) | 183310 | 52.1 (8.1) | 50.1 (8.1) | 50.2 (8.6) | 47.0 (8.0) |
| Sugar intake (\% of TE) | 183310 | 24.1 (7.4) | 23.7 (7.0) | 25.1 (7.6) | 22.4 (6.9) |
| Fibre intake (g/day) | 188318 | 20.4 (8.0) | 19.3 (7.2) | 18.5 (7.6) | 16.2 (6.4) |
| Protein intake (\% of TE) | 183310 | 12.4 (2.3) | 13.6 (2.7) | 15.1 (3.5) | 15.7 (3.6) |
| Fat intake (\% of TE) | 183310 | 31.8 (7.1) | 31.9 (7.0) | 30.9 (7.3) | 32.1 (6.7) |
| Polyunsaturated fat intake (\% of TE) | 183310 | 6.2 (2.4) | 6.2 (2.3) | 6.0 (2.3) | 5.9 (2.2) |
| Saturated fat intake (\% of TE) | 183310 | 12.0 (3.6) | 11.8 (3.4) | 11.4 (3.5) | 12.4 (3.3) |
| Fruit and vegetables intake (g/day) | 422791 | 403.9 (234.8) | 406.3 (216.3) | 418.7 (241.7) | 323.6 (187.5) |
| Water intake (glasses/day) | 391410 | 3.5 (2.6) | 3.4 (2.4) | 3.6 (2.6) | 2.8 (2.2) |
| Vegetarian alternatives intake, $n$ (\%), yes | 183305 | 2158 (53.8) | 2174 (40.2) | 470 (22.2) | 6788 (4.0) |
| Crisp intake (amount/day), $n(\%)$ |  |  |  |  |  |
| Half small bag | 55180 | 244 (18.7) | 398 (25.3) | 131 (27.1) | 12271 (23.7) |
| One small bag |  | 919 (70.6) | 1023 (65.1) | 308 (63.6) | 34865 (67.3) |
| Two or more small bags |  | 140 (10.7) | 151 (9.6) | 45 (0.3) | 4685 (9.0) |
| Pizza intake (amount/day), $n$ (\%) |  |  |  |  |  |
| $\leq$ one medium slice | 13130 | 145 (31.3) | 167 (33.7) | 48 (33.1) | 4642 (38.6) |
| Two to three medium slices |  | 220 (47.5) | 218 (44.0) | 67 (46.2) | 5184 (43.1) |
| Four or more medium slices |  | 98 (21.2) | 111 (22.3) | 30 (20.7) | 2200 (18.3) |
| Sugary drinks intake (amount/day), $n$ (\%) ${ }^{\text {b }}$ | 59353 |  |  |  |  |
| $\leq 1$ glass/can |  | 863 (72.1) | 1034 (69.3) | 387 (70.8) | 40319 (71.8) |
| >1 glass/can |  | 334 (27.9) | 458 (30.7) | 160 (29.2) | 15798 (28.2) |
| Smoothie drinks intake (amount/day), $n(\%)^{\text {b }}$ |  |  |  |  |  |
| $\leq 1$ glass/bottle/ 250 mL | 21235 | 504 (88.0) | 634 (90.4) | 323 (90.7) | 17924 (91.4) |
| $>1$ glass/bottle/ 250 mL |  | 69 (12.0) | 67 (9.6) | 33 (9.3) | 1681 (8.6) |
| Type of meals eaten, $n(\%)$ |  |  |  |  |  |
| Takeaway meals | 178168 | 43 (1.1) | 47 (0.9) | 30 (1.5) | 2929 (1.8) |
| Restaurant meals |  | 295 (7.6) | 445 (8.4) | 152 (7.4) | 14755 (8.8) |
| Bought sandwiches |  | 408 (10.5) | 554 (10.5) | 165 (8.1) | 17167 (10.3) |
| Ready meals |  | 888 (22.8) | 1353 (25.7) | 431 (21.1) | 37429 (22.4) |
| Home-cooked meals |  | 2258 (58.0) | 2874 (54.5) | 1265 (61.9) | 94690 (56.7) |

The average of five 24-h recall was used for this study (except for water and fruit and vegetable intake).
${ }^{\text {a }}$ Data available for the different subcomponents of diet in the dataset.
${ }^{\mathrm{b}}$ Sugary drinks were derived from fizzy and squash drinks. Smoothie drinks were derived from fruit and dairy smoothie drinks. CHO, total carbohydrates; TE, total energy.
than meat-eaters. Fish eaters were more likely to drink more than one glass/can of sugary drinks compared with the other groups and had the highest prevalence of ready meal consumption but also reported the lowest prevalence of takeaways. Fish and poultry eaters were more likely to eat home-cooked meals, followed by vegetarians (Table 2). Diet characteristics by the different types of diets and BMI ( $<25$ and $\geq 25 \mathrm{~kg} / \mathrm{m}^{2}$ ) and by event occurrence (develop or no develop the event) are shown in Supplementary material online, Tables S2 and S3, respectively.

## Associations between types of diets and cardiovascular disease incidence and mortality

The associations of types of diets with incident CVD are shown in Figure 1 and Supplementary material online, Table S4. In the minimally adjusted model (Model 1), fish eaters had lower incident risk for

CVD [HR ${ }_{\text {CVD }}: 0.81$ (95\% Cl: 0.78-0.85)], IHD [HR ${ }_{\text {IHD: }} 0.68$ ( $95 \% \mathrm{Cl}$ : $0.61-0.76)]$, MI [HR ${ }_{\text {MI: }} 0.63$ ( $95 \% \mathrm{Cl}: 0.50-0.79$ )], stroke [ $\mathrm{HR}_{\text {stroke }}$ : 0.73 ( $95 \% \mathrm{Cl}: 0.59-0.91$ )] and HF [HR HF: 0.62 ( $95 \% \mathrm{Cl}: 0.50-0.76$ )] compared with meat-eaters. After adjusting for multimorbidity, lifestyle, and BMI (Models 2-4), the associations were attenuated but remained significant [HR $\mathrm{CVD}: 0.93$ ( $95 \% \mathrm{Cl}: 0.88-0.97$ ), $\mathrm{HR}_{\mathrm{IHD}}: 0.79$ ( $95 \% \mathrm{Cl}: 0.70-0.88$ ), $\mathrm{HR}_{\text {MI: }}: 0.70$ ( $95 \% \mathrm{Cl}: 0.56-0.88$ ), $\mathrm{HR}_{\text {stroke: }}: 0.79$ ( $95 \% \mathrm{Cl}: 0.63-0.98$ ), and $\mathrm{HR}_{\text {HF: }} 0.78$ ( $95 \% \mathrm{Cl}: 0.63-0.97$ )]. Vegetarians, in contrast, showed a lower risk of Ml in Models 1-3; however, this association was attenuated after adjusting for BMI [HR ${ }_{\text {Model 4: }} 0.79$ ( $95 \% \mathrm{Cl}: 0.62-1.00$ )]. For CVD incidence, vegetarians showed an association across the four models studied $\left[H R_{\text {Model }}\right.$ 4: 0.91 ( $95 \% \mathrm{Cl}: 0.86-0.96$ )] (Figure 1). Although fish and poultry eaters were associated with CVD incidence, this association fully attenuated after the adjustments. No other associations were observed. The adjusted Kaplan-Meir survival estimated also showed that,


Figure I Associations between types of diets and incident cardiovascular diseases. Data presented as adjusted hazard ratio and its $95 \%$ confidence interval by types of diets. Meat-eaters were used as the reference group. All analyses were performed using a 2-year landmark analysis, excluding participants who experienced events within the first 2 years of follow-up: 24343 for overall cardiovascular disease incidence ( 4504 ischaemic heart disease, 1026 myocardial infarction, 689 strokes, and 600 heart failure). Analyses were adjusted by age, sex, deprivation, ethnicity, comorbidities, smoking, alcohol intake, total sedentary time, physical activity, and body mass index.
compared with meat-eaters, the other types of diets had a higher probability of survival in terms of CVD incidence (Supplementary material online, Figure S2).

In terms of mortality, fish eaters, compared with meat-eaters, had $30 \%$ and $41 \%$ lower risk of mortality from CVD and IHD, respectively (Supplementary material online, Table S5, Model 1). However, when the analyses were further adjusted, these associations fully attenuated. No other associations between the different types of diets and CVD mortality outcomes were observed (Supplementary material online, Figure S3 and Table 5).

When we investigated whether the association between the different types of diets and cardiovascular outcomes differed by
subgroups, significant interactions were identified for CVD incidence between sex and vegetarians ( $P$-interaction $=0.041$ ) and fish and poultry eaters $(P$-interaction $=0.048)$; age and vegetarians ( $P$-interaction $<0.001$ ); BMI and vegetarians ( $P$-interaction $=0.004$ ), and fish eaters ( $P$-interaction $=0.004$ ). There was also an interaction between age and fish eaters for IHD; age and vegetarians for MI; and among fish eaters, sex and age for stroke (Supplementary material online, Table S6). In terms of mortality, a significant interaction was observed only between sex and CVD mortality for fish eaters and fish and poultry eaters (Supplementary material online, Table S7).

Finally, when the cox proportional analyses were restricted to participants who were matched by the propensity score, similar trends
of associations were observed between types of diets and CVD incidence (Supplementary material online, Table S8). After matching, there was no imbalance in all included covariates (Supplementary material online, Figures S4-S6).

## Discussion

In the current study, we have demonstrated that, compared with meat-eaters, fish eaters had a lower risk of several cardiovascular out-comes-incident CVD, IHD, MI, stroke, and HF-independent of confounders. People who ate poultry, as well as fish, did not have a lower risk, and vegetarians showed only lower risk of CVD incidence. However, previous studies have shown an inverse association between CVD and white meat-eaters (poultry and fish). ${ }^{19,20}$

Overall, the beneficial associations we demonstrated between types of diets and cardiovascular outcomes were strongest in men and individuals who were not obese. A systematic review and metaanalysis showed that Seventh Day Adventists (also vegetarians) had $40 \%$ lower risk of IHD in both sexes, but the associations on mortality and cerebrovascular disease were significant in men only. ${ }^{21}$ On the other hand, in our study, the associations were different according to the outcome studied for deprivation and age. In terms of age, taking into account that the risk of CVD incidence increases with age-and that older adults are more vulnerable to malnutrition-it was expected that older adults with a higher intake of fish could have a lower incidence risk. In addition, more deprived individuals who had a higher intake of fish had a lower risk of CVD incidence, although no interaction was observed. We previously demonstrated that the association between an unhealthy lifestyle and CVD mortality became stronger with increasing levels of deprivation. ${ }^{22}$ Therefore, individuals in our study who were more deprived but adopted a healthier lifestyle, such as fish intake, could have a greater protective effect.

In the UK, the associations between different types of diets and CVD have shown mixed results. For instance, Key et al. ${ }^{11}$ did not find any differences between vegetarians and meat-eaters for circulatory mortality, neither did Appleby et al. ${ }^{10}$ using participants from both the EPIC-Oxford study and the Oxford Vegetarian Study. More recently, Tong et al. ${ }^{6}$ demonstrated that despite vegetarians having a $22 \%$ lower risk of IHD compared with meat-eaters, they had 43\% higher risk of haemorrhagic stroke and $20 \%$ higher risk of total stroke. In this line, other studies have shown that vegetarians from the Adventist Health Study had a lower risk of IHD and CVD compared with nonvegetarians. ${ }^{23}$ However, studies carried out outside the Adventist community did not show the same findings. ${ }^{21}$ In our study, we identified that vegetarians had a lower risk of incident CVD, but no association was identified for IHD as in previous studies. These heterogeneous results could be due to smaller numbers of incident IHD events among vegetarians in our study ( $n=302$ ); therefore, this analysis was probably underpowered $\left[\mathrm{HR}_{\mathrm{IHD}}: 0.96\right.$ ( $95 \% \mathrm{Cl}$ : 0.85-1.07)].

Fish eaters had a lower risk of incident CVD (for all outcomes included). Other studies have also shown an inverse relationship between fish and HF, ${ }^{19}$ cerebrovascular diseases, ${ }^{24}$ coronary heart disease, ${ }^{25}$ and IHD. ${ }^{6}$ Perhaps this association is not surprising considering that fish is an essential source of PUFA (mainly $n-3$ ),
vitamin $D$, and selenium, nutrients that are cardioprotective. $n-3$ PUFA has been demonstrated to be cardioprotective, and oily fish is one of its rich sources. ${ }^{26}$ In our study, we did not find a significant difference in the overall PUFA intake of vegetarians and fish eaters, but we did not have data on specific categories of PUFA intake ( $n-3, n-6$, or $n-9$ ). Despite this lack of information, it is likely that fish eaters had a higher intake of cardioprotective nutrients and, therefore, could explain the lower risk association between fish eaters and CVD outcomes in our study. However, in contrast to our results, Appleby et al. ${ }^{10}$ identified that fish eaters had $26 \%$ and $45 \%$ higher risk of circulatory and other circulatory diseases than meat-eaters after adjusting by BMI. The disparity between Appleby and our results could be explained by the general characteristic of the UK Biobank population, who-as reported by Fry et al.-have healthier lifestyles than the general UK population. ${ }^{27}$

## Strength and limitations

UK Biobank is a large, prospective, general population cohort with data available on diet and a wide range of potential confounders and health outcomes. As a result, the analyses could be adjusted for multiple confounders and stratified by different subgroups. Among the limitations, our study used a single measure of diet at baseline, and diet may change over time. However, we attempted to mitigate this limitation by excluding those who reported changes in their diet. In addition, the association found was of modest absolute risk difference as shown in the adjusted survival curve. Owing to insufficient statistical power, we were unable to study vegan diets. On the other hand, while $94.7 \%$ of the population was classified as meat-eater, only $1.8 \%$ was classified as vegetarian. Although the National Diet and Nutrition Survey 2008-2012 reported a similar prevalence ( $\sim 2 \%$ ), ${ }^{28}$ UK Biobank is not representative of the UK population in terms of lifestyle; therefore, the summary statistics should not be generalizable to the general population. ${ }^{27}$ In addition, the Vegan Society has reported a higher prevalence of vegans and vegetarians in the last years. ${ }^{29}$ Finally, the Oxford WebQ was not available for the whole population included in this study; therefore, dietary intake characteristics across types of diets may not represent the full UK Biobank cohort.

## Conclusion

Compared with meat-eaters, fish eaters had a lower risk of a range of adverse cardiovascular outcomes, supporting its promotion as a healthy diet that should be encouraged. Vegetarianism was only associated with a lower risk of incident CVD. However, as a group, vegetarians consumed more unhealthy foods, such as crisps, than meateaters. Therefore, vegetarians should not be considered a homogeneous group, and avoidance of meat will not be sufficient to reduce health risk if the overall diet is not healthy.

## Supplementary material

Supplementary material is available at European Heart Journal online.

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## Author contributions

F.P.-R. contributed to the conception and design of the study. C.C.M., F.K.H., and J.P.P. advised on all statistical aspects. F.P.-R. performed the literature search, the analyses, and interpreted the data with support from C.C.-M., F.K.H., and J.P.P. All authors critically reviewed this and previous drafts. All authors approved the final draft for submission. F.K.H., C.C.-M., and J.P.P. contributed equally to this work and are joint senior authors. F.P.-R., C.C.-M., F.K.H., and J.P.P. are the guarantor.

## Data availability

The data of this study can be requested from the UK Biobank (https://www.ukbiobank.ac.uk/).

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Conflict of interest: N.S. has consulted for Amgen, Inc., Sanofi, and Astra Zeneca. J.P.P. has received funding from the Medical Research Council and Chief Scientist Office and has sat on the Medical Research Council Strategy Board and UK Biobank Scientific Advisory Board. None of these disclosures are directly related to the study, nor its conception, analyses, or interpretation.

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[^1]:    BMI, body mass index; MET, metabolic equivalent; PA, physical activity; SD, standard deviation.

