European Heart Journal (2021) **42**, 1136–1143
doi:10.1093/eurheartj/ehaa939

European Society of Cardiology

CLINICAL RESEARCH
Epidemiology and prevention

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

Fanny Petermann-Rocha [1,2], Solange Parra-Soto [1,2], Stuart Gray [2], Jana Anderson [1], Paul Welsh [2], Jason Gill [2], Naveed Sattar [2], Frederick K. Ho [1†], Carlos Celis-Morales [1,2,3,4†], and Jill P. Pell[1,*,†]

[1]Institute of Health and Wellbeing, University of Glasgow, Glasgow G12 8RZ, UK; [2]British Heart Foundation Glasgow Cardiovascular Research Centre, Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK; [3]Centre of Exercise Physiology Research (CIFE), Universidad Mayor, Santiago, Chile; and [4]Research Group in Education, Physical Activity and Health, University Catolica del Maule, Talca, Chile

Received 13 May 2020; revised 30 June 2020; editorial decision 29 October 2020; accepted 30 October 2020; online publish-ahead-of-print 14 December 2020

See page 1144 for the editorial comment on this article (doi: 10.1093/eurheartj/ehaa1088)

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 diets—including vegetarians, fish eaters, fish and poultry eaters, and meat-eaters—using data from UK Biobank.

Methods and results

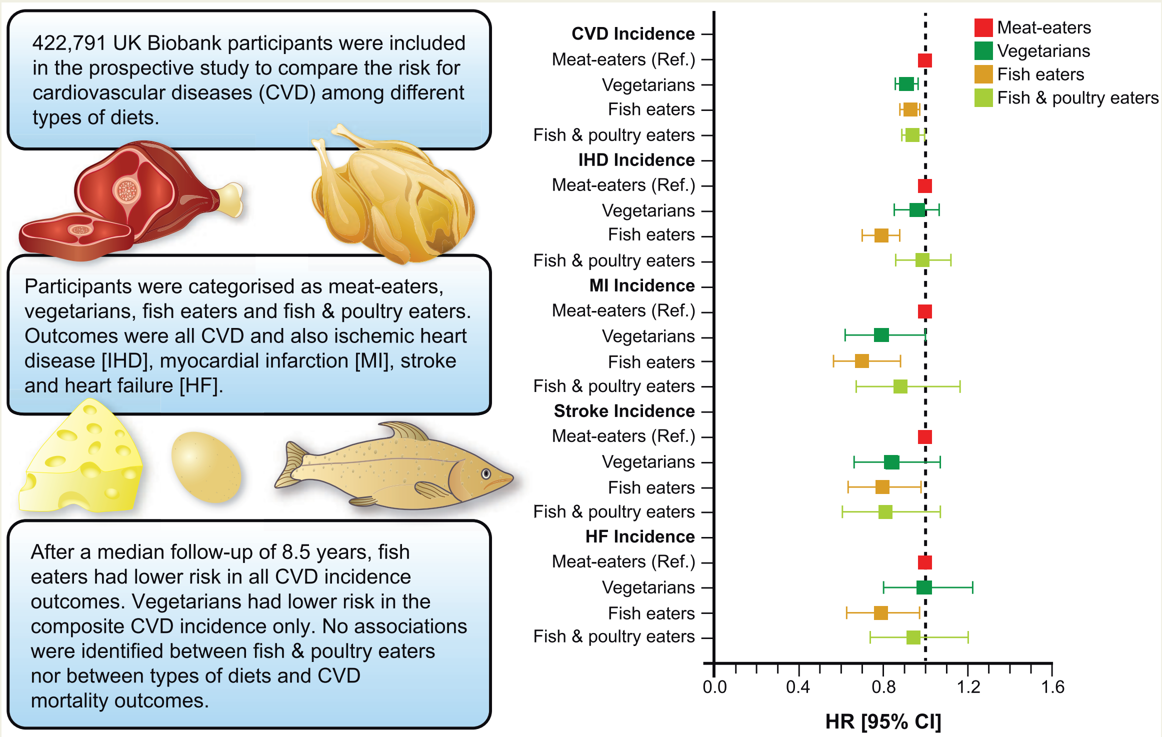
A total of 422 791 participants (55.4% women) were included in this prospective analysis. Using data from a food frequency questionnaire, four types of diets were derived. Associations between types of diets and health outcomes were investigated using Cox proportional hazard models. Meat-eaters comprised 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 (CI): 0.88–0.97]}, IHD [HR: 0.79 (95% CI: 0.70–0.88)], MI [HR: 0.70 (95% CI: 0.56–0.88)], stroke [HR: 0.79 (95% CI: 0.63–0.98)] and HF [HR: 0.78 (95% CI: 0.63–0.97)], after adjusting for confounders. Vegetarians had lower risk of CVD incidence [HR: 0.91 (95% CI: 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.

* Corresponding author. Tel: +44 0141 330 3239, Email: jill.pell@glasgow.ac.uk
†These authors contributed equally to this work and are joint senior authors.
Listen to the audio abstract of this contribution.

Graphical Abstract



Keywords Cardiovascular diseases • Vegetarians • Meat • Incidence • Mortality

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 ∼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 150 000 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 (<50 000), 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 500 000 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 I00–I99, i.e. all diseases from the circulatory system], IHD (ICD10 I20–I25), myocardial infarction (MI) (ICD10 I21–I23), stroke (I60, I61, I63, or I64), and heart failure (HF) (I50.0, I50.1, I50.9). 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* = 45 028, 8.99%). Therefore, 448 396 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. Area-based 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 touch-screen questionnaire at baseline. In turn, dietary information for macro- and 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 200 000 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 (CI). The proportional hazard assumptions were checked using Schoenfeld residuals. Participants with MI and/or stroke at baseline were also excluded from all analyses (*n* = 15 737, 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: 24 343 for overall CVD incidence (4504 IHD, 1026 MI, 689 strokes and 600 HF) and 538 for overall CVD mortality (258 IHD, 97 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 ≥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 ≥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 422 791 participants (55.4% women) had data available for the types of diets and covariates of this study (Supplementary material online, *Figure S1*). 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, 106 690 (24.3%) developed CVD (24 794 IHD, 6770 MI, 5946 stroke, and 7685 HF) and 6580 (1.5%) died from CVD (2767 IHD, 885 MI, 1088 stroke, and 965 HF).

Table 1. 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)	400 470 (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)	218 307 (54.1)
Deprivation, *n* (%)				
Lower	1965 (26.0)	2893 (29.1)	1381 (28.6)	139 264 (34.8)
Middle	2425 (32.2)	3315 (33.3)	1558 (32.2)	135 436 (33.8)
Higher	3147 (41.8)	3743 (37.6)	1894 (39.2)	125 770 (31.4)
Ethnicity, *n* (%)				
White	6150 (81.6)	9372 (94.2)	4377 (90.6)	382 551 (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 kg/m ^{2})	128 (1.7)	162 (1.6)	76 (1.5)	1867 (0.4)
Normal weight (18.5–24.9 kg/m ^{2})	3730 (49.5)	5262 (52.9)	2423 (50.1)	131 241 (32.8)
Overweight (25.0–29.9 kg/m^2)	2629 (34.9)	3354 (33.7)	1631 (33.8)	172 577 (43.1)
Obese (≥30.0 kg/m^2)	1050 (13.9)	1173 (11.8)	703 (11.6)	94 785 (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)	223 054 (55.7)
Previous	2197 (29.2)	3564 (35.8)	1571 (32.5)	137 220 (34.3)
Current	515 (6.8)	691 (6.9)	367 (7.6)	40 196 (10.0)
Alcohol intake frequency, *n* (%)				
Daily or almost daily	1069 (14.2)	1905 (19.1)	685 (14.2)	82 898 (20.7)
3–4 times a week	1347 (17.9)	2414 (24.3)	862 (17.8)	95 137 (23.8)
Once or twice a week	1514 (20.1)	2299 (23.1)	1112 (23.0)	105 521 (26.4)
1–3 times a month	885 (11.7)	1162 (11.7)	547 (11.3)	44 535 (11.1)
Special occasions only	1059 (14.0)	1143 (11.5)	866 (17.9)	44 214 (11.0)
Never	1663 (22.1)	1028 (10.3)	761 (15.8)	28 165 (7.0)
Health status				
Multimorbidity, *n* (%)				
None	3122 (41.4)	4172 (41.9)	1770 (36.6)	143 910 (35.9)
≥1	4415 (58.6)	5779 (58.1)	3063 (63.4)	256 560 (64.1)

BMI, body mass index; MET, metabolic equivalent; PA, physical activity; SD, standard deviation.

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[a]	Vegetarians	Fish eaters	Fish and poultry eaters	Meat-eaters
Total energy intake (kcal/day)	183 318	2117 (725)	2126 (674)	2032 (701)	2170 (657)
CHO intake (% of TE)	183 310	52.1 (8.1)	50.1 (8.1)	50.2 (8.6)	47.0 (8.0)
Sugar intake (% of TE)	183 310	24.1 (7.4)	23.7 (7.0)	25.1 (7.6)	22.4 (6.9)
Fibre intake (g/day)	188 318	20.4 (8.0)	19.3 (7.2)	18.5 (7.6)	16.2 (6.4)
Protein intake (% of TE)	183 310	12.4 (2.3)	13.6 (2.7)	15.1 (3.5)	15.7 (3.6)
Fat intake (% of TE)	183 310	31.8 (7.1)	31.9 (7.0)	30.9 (7.3)	32.1 (6.7)
Polyunsaturated fat intake (% of TE)	183 310	6.2 (2.4)	6.2 (2.3)	6.0 (2.3)	5.9 (2.2)
Saturated fat intake (% of TE)	183 310	12.0 (3.6)	11.8 (3.4)	11.4 (3.5)	12.4 (3.3)
Fruit and vegetables intake (g/day)	422 791	403.9 (234.8)	406.3 (216.3)	418.7 (241.7)	323.6 (187.5)
Water intake (glasses/day)	391 410	3.5 (2.6)	3.4 (2.4)	3.6 (2.6)	2.8 (2.2)
Vegetarian alternatives intake, *n* (%), yes	183 305	2158 (53.8)	2174 (40.2)	470 (22.2)	6788 (4.0)
Crisp intake (amount/day), *n* (%)					
Half small bag	55 180	244 (18.7)	398 (25.3)	131 (27.1)	12 271 (23.7)
One small bag		919 (70.6)	1023 (65.1)	308 (63.6)	34 865 (67.3)
Two or more small bags		140 (10.7)	151 (9.6)	45 (0.3)	4685 (9.0)
Pizza intake (amount/day), *n* (%)					
≤ one medium slice	13 130	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* (%)[b]	59 353				
≤1 glass/can		863 (72.1)	1034 (69.3)	387 (70.8)	40 319 (71.8)
>1 glass/can		334 (27.9)	458 (30.7)	160 (29.2)	15 798 (28.2)
Smoothie drinks intake (amount/day), *n* (%)[b]					
≤1 glass/bottle/250 mL	21 235	504 (88.0)	634 (90.4)	323 (90.7)	17 924 (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	178 168	43 (1.1)	47 (0.9)	30 (1.5)	2929 (1.8)
Restaurant meals		295 (7.6)	445 (8.4)	152 (7.4)	14 755 (8.8)
Bought sandwiches		408 (10.5)	554 (10.5)	165 (8.1)	17 167 (10.3)
Ready meals		888 (22.8)	1353 (25.7)	431 (21.1)	37 429 (22.4)
Home-cooked meals		2258 (58.0)	2874 (54.5)	1265 (61.9)	94 690 (56.7)

The average of five 24-h recall was used for this study (except for water and fruit and vegetable intake).
[a]Data available for the different subcomponents of diet in the dataset.
[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 ≥25 kg/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_{CVD}: 0.81 (95% CI: 0.78–0.85)], IHD [HR_{IHD}: 0.68 (95% CI: 0.61–0.76)], MI [HR_{MI}: 0.63 (95% CI: 0.50–0.79)], stroke [HR_{stroke}: 0.73 (95% CI: 0.59–0.91)] and HF [HR_{HF}: 0.62 (95% CI: 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_{CVD}: 0.93 (95% CI: 0.88–0.97), HR_{IHD}: 0.79 (95% CI: 0.70–0.88), HR_{MI}: 0.70 (95% CI: 0.56–0.88), HR_{stroke}: 0.79 (95% CI: 0.63–0.98), and HR_{HF}: 0.78 (95% CI: 0.63–0.97)]. Vegetarians, in contrast, showed a lower risk of MI in Models 1–3; however, this association was attenuated after adjusting for BMI [$HR_{Model\ 4}$: 0.79 (95% CI: 0.62–1.00)]. For CVD incidence, vegetarians showed an association across the four models studied [$HR_{Model\ 4}$: 0.91 (95% CI: 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,

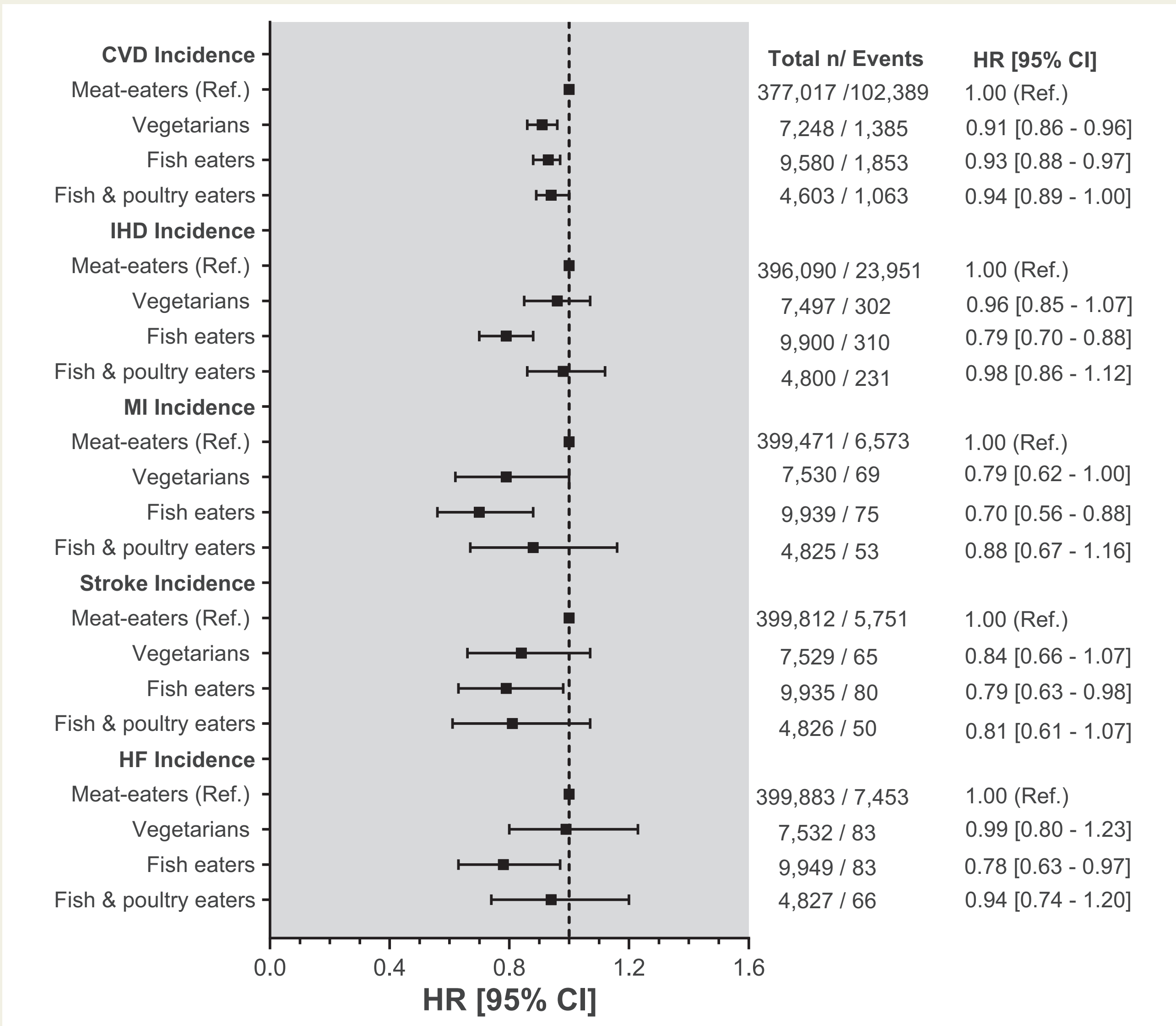


Figure 1 Associations between types of diets and incident cardiovascular diseases. Data presented as adjusted hazard ratio and its 95% confidence interval by types of diets. Meat-eaters were used as the reference group. All analyses were performed using a 2-year landmark analysis, excluding participants who experienced events within the first 2 years of follow-up: 24 343 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 outcomes—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 meta-analysis 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 [HR_{IHD}: 0.96 (95% CI: 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 (∼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 meat-eaters. 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.

Acknowledgements

We are grateful to UK Biobank participants. This research has been conducted using the UK Biobank resource under application number 7155.

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/).

Funding

UK Biobank was established by the Wellcome Trust medical charity, Medical Research Council, Department of Health, Scottish Government, and the Northwest Regional Development Agency. It has also had funding from the Welsh Assembly Government and the British Heart Foundation. All authors had final responsibility for submission for publication. F.P.-R. and S.P.-S. receive financial support from the Chilean Government for doing their PhD (ANID-Becas Chile).

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.

References

1. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney M-T, Corrà U, Cosyns B, Deaton C, Graham I, Hall MS, Hobbs FDR, Løchen M-L, Löllgen H, Marques-Vidal P, Perk J, Prescott E, Redon J, Richter DJ, Sattar N, Smulders Y, Tiberi M, van der Worp HB, van Dis I, Verschuren WMM, Binno S; Group ESD. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2016;**37**:2315–2381.
2. GD Collaborators. Health effects of dietary risks in 195 countries, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2019;**393**:1958–1972.
3. Willett W, Rockström J, Loken B, Springmann M, Lang T, Vermeulen S, Garnett T, Tilman D, DeClerck F, Wood A, Jonell M, Clark M, Gordon LJ, Fanzo J, Hawkes C, Zurayk R, Rivera JA, De Vries W, Majele Sibanda L, Afshin A, Chaudhary A, Herrero M, Agustina R, Branca F, Lartey A, Fan S, Crona B, Fox E, Bignet V, Troell M, Lindahl T, Singh S, Cornell SE, Srinath Reddy K, Narain S, Nishtar S, Murray CJL. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. *Lancet* 2019;**393**:447–492.
4. Johnston BC, Zeraatkar D, Han MA, Vernooij RWM, Valli C, El Dib R, Marshall C, Stover PJ, Fairweather-Taitt S, Wójcik G, Bhatia F, de Souza R, Brotons C, Meerpohl JJ, Patel CJ, Djulbegovic B, Alonso-Coello P, Bala MM, Guyatt GH. Unprocessed red meat and processed meat consumption: dietary guideline recommendations from the Nutritional Recommendations (NutriRECS) consortium. *Ann Intern Med* 2019;**171**:756–764.
5. Rosenfeld DL, Burrow AL. Vegetarian on purpose: understanding the motivations of plant-based dieters. *Appetite* 2017;**116**:456–463.
6. Tong TYN, Appleby PN, Bradbury KE, Perez-Cornago A, Travis RC, Clarke R, Key TJ. Risks of ischaemic heart disease and stroke in meat eaters, fish eaters, and vegetarians over 18 years of follow-up: results from the prospective EPIC-Oxford study. *BMJ* 2019;**366**:l4897.
7. Tantamango-Bartley Y, Jaceldo-Siegl K, Fan J, Fraser G. Vegetarian diets and the incidence of cancer in a low-risk population. *Cancer Epidemiol Biomarkers Prev* 2013;**22**:286–294.
8. Craig WJ. Health effects of vegan diets. *Am J Clin Nutr* 2009;**89**:1627s–1633s.
9. Kahleova H, Levin S, Barnard N. Cardio-metabolic benefits of plant-based diets. *Nutrients* 2017;**9**:848.
10. Appleby PN, Crowe FL, Bradbury KE, Travis RC, Key TJ. Mortality in vegetarians and comparable nonvegetarians in the United Kingdom. *Am J Clin Nutr* 2016;**103**:218–230.
11. Key TJ, Appleby PN, Spencer EA, Travis RC, Roddam AW, Allen NE. Mortality in British vegetarians: results from the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford). *Am J Clin Nutr* 2009;**89**:1613s–1619s.
12. Collins R. What makes UK Biobank special? *Lancet* 2012;**379**:1173–1174.
13. Palmer LJ. UK Biobank: bank on it. *Lancet* 2007;**369**:1980–1982.
14. Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, Downey P, Elliott P, Green J, Landray M, Liu B, Matthews P, Ong G, Pell J, Silman A, Young A, Sprosen T, Peakman T, Collins R. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med* 2015;**12**:e1001779.
15. Townsend PP, Beattie A. Health and deprivation. Inequality and the North. *Health Policy (New York*) 1988;**10**.
16. WHO. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. In: *World Health Organization Technical Report Series*, i–xii; 2000. p1–253.
17. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;**380**:37–43.
18. Galante J, Adamska L, Young A, Young H, Littlejohns TJ, Gallacher J, Allen N. The acceptability of repeat Internet-based hybrid diet assessment of previous 24-h dietary intake: administration of the Oxford WebQ in UK Biobank. *Br J Nutr* 2016;**115**:681–686.
19. Li YH, Zhou CH, Pei HJ, Zhou XL, Li LH, Wu YJ, Hui RT. Fish consumption and incidence of heart failure: a meta-analysis of prospective cohort studies. *Chin Med J (Engl)* 2013;**126**:942–948.
20. Etemadi A, Sinha R, Ward MH, Graubard BI, Inoue-Choi M, Dawsey SM, Abnet CC. Mortality from different causes associated with meat, heme iron, nitrates, and nitrites in the NIH-AARP Diet and Health Study: population based cohort study. *BMJ* 2017;**357**:j1957–j1957.
21. Kwok CS, Umar S, Myint PK, Mamas MA, Loke YK. Vegetarian diet, Seventh Day Adventists and risk of cardiovascular mortality: a systematic review and meta-analysis. *Int J Cardiol* 2014;**176**:680–686.
22. Foster HME, Celis-Morales CA, Nicholl BI, Petermann-Rocha F, Pell JP, Gill JMR, O'Donnell CA, Mair FS. The effect of socioeconomic deprivation on the association between an extended measurement of unhealthy lifestyle factors and health outcomes: a prospective analysis of the UK Biobank cohort. *Lancet Public Health* 2018;**3**:e576–e585.
23. Orlich MJ, Singh PN, Sabaté J, Jaceldo-Siegl K, Fan J, Knutsen S, Beeson WL, Fraser GE. Vegetarian dietary patterns and mortality in Adventist Health Study 2. *JAMA Intern Med* 2013;**173**:1230–1238.
24. Chowdhury R, Stevens S, Gorman D, Pan A, Warnakula S, Chowdhury S, Ward H, Johnson L, Crowe F, Hu FB, Franco OH. Association between fish consumption, long chain omega 3 fatty acids, and risk of cerebrovascular disease: systematic review and meta-analysis. *BMJ* 2012;**345**:e6698–e6698.
25. Streppel MT, Ocké MC, Boshuizen HC, Kok FJ, Kromhout D. Long-term fish consumption and n-3 fatty acid intake in relation to (sudden) coronary heart disease death: the Zutphen study. *Eur Heart J* 2008;**29**:2024–2030.
26. Hall WL. The future for long chain n-3 PUFA in the prevention of coronary heart disease: do we need to target non-fish-eaters? *Proc Nutr Soc* 2017;**76**:408–418.
27. Fry A, Littlejohns TJ, Sudlow C, Doherty N, Adamska L, Sprosen T, Collins R, Allen NE. Comparison of sociodemographic and health-related characteristics of UK Biobank participants with those of the general population. *Am J Epidemiol* 2017;**186**:1026–1034.
28. Public, Health, England. National Diet and Nutrition Survey: Results from Years 1,2,3,4 (Combined) of the Rolling Programme *(2008/2009–2011/2012)*. https://www.gov.uk/government/statistics/national-diet-and-nutrition-survey-results-from-years-1-to-4-combined-of-the-rolling-programme-for-2008-and-2009-to-2011-and-2012.
29. The, Vegan, Society. *Statistics.* https://www.vegansociety.com/news/media/statistics.