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Original article

Do all vegetarians have a lower cardiovascular risk? A prospective study

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SUMMARY

Background: Vegetarian diets are heterogeneous and their health benefits may vary. This study aimed to compare the cardiovascular risk among vegetarian diets that meet existing health guidelines, those that do not, and diets that include red meat.

Methods: 391,124 participants (55.5% women) from the UK Biobank prospective population-based study were included. Using data from a food frequency questionnaire, participants were categorised into lacto-vegetarian or meat-eaters. Then, both groups were dichotomised into a healthier and less healthy group using an unweighted score based on current UK guidelines. Ischaemic heart disease (IHD) and myocardial infarction (MI) incidence – both separately and as a composite of major adverse cardiovascular events (MACE) – were the outcomes included. Associations between types of diets and health outcomes were investigated using Cox proportional hazard models adjusted for confounder factors.

Results: After a median follow-up of 10.4 years, there were 40,048 MACE. When the analyses were adjusted for prevalent morbidity and lifestyle factors, people who followed healthier vegetarian and meat-eater diets had 18% (95% CI: 0.73 to 0.92) and 5% (95% CI: 0.93 to 0.97) lower risk of MACE than less healthy meat-eaters. Similar patterns were identified for the individual outcomes, with the strongest association observed for MI. The cardiovaculasr risk among less healthy vegetarians and less healthy meat-eaters were not significnatly different.

Conclusions: Vegetarian diets are heterogeneous and the cardiovascular risk varied accordingly. Future studies should consider the overall dietary patterns of vegetarians rather than just based on meat consumption. Guidelines advocating a plant-based diet need to stress the importance of overall diet quality in addition to the reduction of meat.

1. Introduction

Cardiovascular disease (CVD) – especially ischaemic heart disease (IHD) – remains the leading cause of premature mortality across the globe [1]. According to the report from the Global Burden of Disease study (2020) [1], 18.6 million individuals died due to CVD in 2019. In the United Kingdom, around 7.6 million people are living with heart or circulatory diseases, and a quarter of all deaths are attributable to these conditions [2].

Among all modifiable risk factors for CVD, dietary patterns have remained the second top contributor [1]. Although several dietary patterns have gained popularity over the last few decades; vegetarianism remains one of the most popular [3]. The potential health benefits of a vegetarian diet include lower blood pressure, triglycerides, cholesterol, glucose, inflammatory markers [3] and CVD risk [4,5]. However, the motivations for adopting a vegetarian diet are not restricted to its health benefits but also include moral values, eating disorders, social experience, identity, religion, culture, and planetary health [6,7].

Owing to these, vegetarian diets are highly heterogeneous [8–10]. Even if people do not eat meat, they may nonetheless consume large amounts of unhealthy foods [8]. For instance, Gehring et al. demonstrated that vegetarian diets were associated

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with higher consumption of ultra-processed foods [11]. Borude reported that Indian vegetarians had a higher incidence of morbid obesity than many western studies and were more likely to have bariatric surgery [9]. Using data from three ongoing prospective studies, Satija et al. concluded that an unhealthy plant-based diet was associated with a 1.32-times higher risk of coronary heart disease than people following a healthy plant-based diet based on an index in their study [10].

Since vegetarian diets are heterogeneous, their health benefits might not be the same. This study used the UK Biobank prospective cohort study to compare the cardiovascular risk among vegetarian diets that meet existing health guidelines, those that do not, and diets that include red meat.

2. Methods

2.1. General information

UK Biobank recruited over 500,000 participants (5.5% response rate) from the general population between 2006 and 2010 [12]. Participants (aged 37–73 years) attended one of 22 assessment centres across Wales, Scotland, and England [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 Ethics Committee (Ref: 11/NW/0382). The study protocol is available online (http://www.ukbiobank.ac.uk/). This work was conducted under the UK Biobank application number 7155. More information about the UK Biobank protocol can be found online (http://www.ukbiobank.ac.uk).

2.2. Vegetarians and meat-eaters

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 dichotomised into consumed or not consumed.

Using these variables, participants were excluded if they had missing dietary data (n = 9007), self-reported at baseline that their diet often varied (n = 45,019), or if they consumed fish and/or poultry but not red meat (n = 15,459). Vegan participants were also excluded due to the small sample size (n = 57). The remaining 432,870 participants were categorised into Lacto-vegetarian (consumption of cheese and/or milk but not fish, poultry or red meat); or meat-eater (consumption of cheese, milk, fish, poultry and red meat) as described elsewhere [15].

Then, both meat-eaters and vegetarians were dichotomised into a healthier and less healthy group. To create this classification, we first ran a latent class analysis to identify i) which food elements self-reported at baseline differed most among vegetarians from a list of 10 foods, and ii) the number of groups we had to create to classify the vegetarians included in this study. Compared with different latent class models, a 2-latent class model achieved a better Bayesian Information Criterion and was used to create the groups. We created a 2-latent class model with the following dietary components: fruit & vegetables, spread type, cereal, salt, water, milk, cheese, coffee, tea and bread, scored as meeting (0 points) or not meeting the recommendations (1 point) as described in a perivous publication [16]. As none of these elements had information about sugar intake, for this analysis, we also included the variable “never eat sugar or foods containing sugar” (Additional file 1: Fig. S1 and Table S1). Six of the aforementioned elements presented higher differences between the two classes and were, therefore, selected to be included in the classification to create the two vegetarians' categories: fruit & vegetables, cereal, salt, milk, spread type, and never eat sugar. The score was then derived by assigning 1 point to each of these 6-food items whose values did not meet the current intake recommendations [16]. Then, points from these 6-food elements were summed to create an unweighted score ranging from 0 (meeting all the recommendations of the selected food elements) to 6 (meeting none). Finally, the median score (3 points) was used as a cut-off to create the two categories: healthier ($\leq$3 points) and less healthy (>3 points) vegetarians. For a better comparison, the same classification and food elements were used to create healthier and less healthy meat-eaters categories. Both healthier and less healthy meat-eaters and vegetarians were mutually exclusive categories (Fig. 1).

2.3. Outcomes

The primary outcome of the study included two cardiovascular outcomes (IHD and myocardial infarction [MI]) – separately and as a composite outcome of major adverse cardiovascular events (MACE). The outcomes were ascertained from linked hospitalisation and death records using the relevant International Classification of Diseases 10 revision (ICD10) codes: MACE (ICD10: I20-I25, I60-I64, I50, I70-I74), IHD (ICD10: I20-I25) and MI (ICD10: I21-I23). The 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 (HES) (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. Hospital admissions data were available until September 2021 in England, July 2021 in Scotland and February 2018 in Wales. Therefore, incident event models were censored on these dates or the date of death if this occurred earlier. Mortality data were available until the end of October 2021. Therefore, follow-up was censored at these dates.

2.4. Covariates

Age was calculated from dates of birth and baseline assessment (for the descriptive analysis, this was also categorised into tertiles: <56 years, 56–65 years and >65 years). Sex was self-reported. Deprivation (area-based socioeconomic status) was derived from the postcode of residence, using the Townsend score [17]. Ethnicity was self-reported and categorised into white and others (South Asian, black, Chinese, and mixed ethnic background). Self-reported smoking status was categorised as never, former or current smoker. Frequency of alcohol intake was self-reported at baseline and analysed as five categories: daily/almost daily, 3–4 times a week, once/twice a week, 1–3 times a month, special occasions only, or never. Type and duration of physical activity were self-reported using the International Physical Activity Questionnaire short form [18]. Total time spent in discretionary sedentary behaviours was derived from the sum of self-reported time spent driving, using a computer and watching television through leisure time. Prevalent morbidity was ascertained during a nurse-led interview at baseline. We calculated morbidity count based on 43 long-term conditions (including depression) selected initially for a large epidemiological study in Scotland and subsequently adapted for UK Biobank [19,20]. This was then classified as: no prevalent morbidity or $\geq$1 prevalent morbidity. Trained nurses measured height and body weight during the initial assessment. Body mass index (BMI) was calculated as (weight in kg)/(height in m)^2 and the WHO criteria were applied to categorise participants into underweight <18.5 kg/m^2, normal

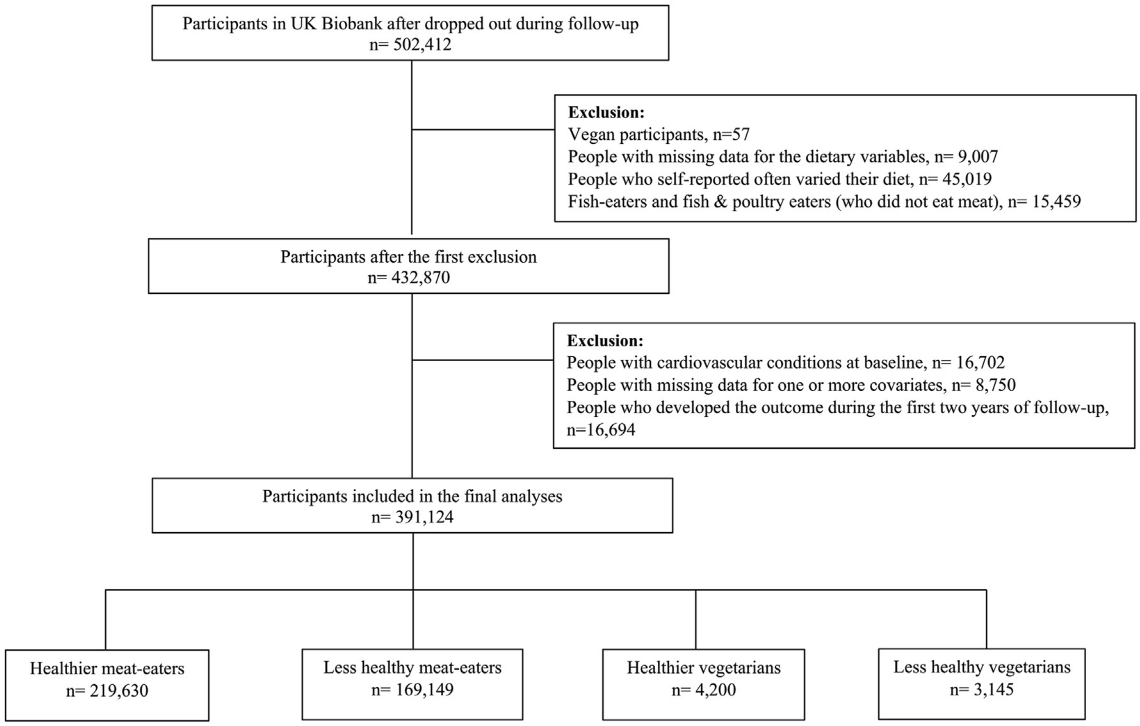

Fig. 1. Diagram - Study population and exclusion criteria.

weight 18.5–24.9 kg/m^2, overweight 25.0–29.9 kg/m^2 and obese ≥30.0 kg/m^2 [21].

2.4.1. *Other variables of interest for participant characterisation*

The following variables were included for a better cohort characterisation: body fat (%), waist circumference, handgrip strength, and TV viewing duration. Body fat was measured using bio-impedance by trained nurses and waist circumference – at the level of the umbilicus – using a Wessex non-stretchable sprung tape measure in cm. Waist circumference was then used to derive central or abdominal obesity, defined as ≥88 cm for women and ≥102 cm for men [21]. Grip strength was measured using a Jamar J00105 hydraulic hand dynamometer. The mean value obtained from the right and left hands was expressed in absolute units (kg) and used in subsequent analyses. TV viewing was self-reported as hours per day. More information about these variables can be found elsewhere [22,23].

Water and fruit and vegetable intake, as well as mineral and minerals and other dietary supplements, were collected through the touch-screen questionnaire at baseline. After the baseline assessment, participants were invited to provide more detailed dietary information by completing the Oxford WebQ [24]; a web-based 24-h recall questionnaire which was developed specifically for use in large population studies and has been validated against an interviewer-administered 24-h recall questionnaire [24]. The Oxford WebQ derives energy intake (total and from specific macronutrients) from the information recorded in McCance and Widdowson's The Composition of Food, 5th edition. However, only ~200,000 participants completed the additional Oxford WebQ. The number of individuals with data available for each variable is shown in the results tables.

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

2.5. *Statistical analyses*

Descriptive characteristics by types of diets (healthier and less healthy meat-eaters and vegetarians) are presented as means with standard deviation (SD) for quantitative variables and as frequencies and percentages for categorical variables (including both covariates and additional descriptive variables).

The cumulative crude hazard rate between types of diets and the cardiovascular outcomes (both MACE and individual outcomes) by follow-up time was estimated using the Nelson-Aalen estimator. Associations between the types of diets and cardiovascular outcomes were also investigated using Cox-proportional hazard models, with the time of follow-up used as the timeline variable. Individuals who self-reported being less healthy meat-eaters were used as the reference group for the main analyses. The results are reported as hazard ratios (HR) and their 95% confidence intervals (95% CI). Participants with MI, IHD, heart failure and/or stroke at baseline were excluded from all analyses (n = 16,702). Analyses were performed using a 2-year landmark analysis, excluding participants who experienced events within the first two years of follow-up (n = 16,694). People with missing data for one or more covariates were also excluded from the analyses (n = 8750). The Cox proportional hazard models were re-run using healthier vegetarians as the referent group in order to directly compare the cardiovascular risk between healthier and less healthy vegetarians.

All analyses were conducted using two incremental models for each outcome: model 1 included sociodemographic covariates (age, sex, deprivation, and ethnicity [white vs others]); model 2 additionally included prevalent morbidity (no vs ≥ 1 morbidity) and lifestyle factors (smoking, total discretionary sedentary time, alcohol intake and type of physical activity). A sensitivity analysis was performed where model 2 was further adjusted for obesity (BMI) at baseline to examine whether, and to what extent, the HRs between types of diets and the cardiovascular outcomes included were attenuated. Moreover, since obesity could be a confounder or mediator, counterfactual-based mediation analyses were also conducted to examine the potential mediating effects of obesity (BMI ≥30 kg/m^2). Natural indirect effect (NIE) and proportion mediation (NIE/total effect) were estimated using bootstrapping with 1000 interactions.

Stata 17 statistical software (StataCorp LP) and R 4.2.2 (package 'poLCA', 'CMAverse', 'haven', and 'survival') were used to perform all analyses. A p-value lower than 0.05 was considered statistically significant.

This study follows the STROBE reporting guidelines for prospective studies [25].

2.6. Patients and public involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for the design or implementation of the study. No patients were asked to advise on the interpretation or writing up of results. There are no plans to disseminate the research results to study participants or the relevant patient community.

3. Results

After excluding people with missing data, those who self-reported often changing their diet, those on vegan diets or diets that included fish or poultry but not red meat, and those with CVD at baseline, 391,124 participants were included in this prospective study (Fig. 1). Among these participants, 4200 (1.1%) and 3145 (0.8%) were categorised as healthier and less healthy vegetarians, respectively, and the remainder were meat-eaters (56.1% and 42.0% classified as healthier and less healthy, respectively). The general characteristics of the study population – overall and by types of diets (healthier and less healthy vegetarians and meat-eater) – are reported in Table 1. Compared with meat-eaters, both types of vegetarians were younger, more deprived, more likely to be women and from another ethnic background (not white). They were less likely to have smoked and drank less. They had a lower BMI, waist circumference and body fat. By contrast, meat-eaters had a higher grip strength and were more likely to have more than one prevalent morbidity (Table 1). Compared with unhealthy vegetarians, and even if some differences were slight, healthy vegetarians were less deprived, more likely to be white and less likely to smoke, be obese or centrally obese. In terms of meat-eaters, healthier meat-eaters were older, more likely to be women and walking for pressure. They were also less likely to be deprived and to be a current smoker. They also spent fewer hours viewing TV and on sitting activities (Table 1).

Dietary intake characteristics by types of diets are shown in Table 2. Both healthier and less healthy meat-eaters had the highest intake of protein and the lowest consumption of fibre and fruit & vegetables. Less healthy meat-eaters also consumed takeaway & restaurant meals more frequently. Compared to less healthy vegetarians, healthier vegetarians ate more home-made meals; they consumed less saturated fat and consumed, on average, more fruit & vegetables and fibre. However, they were also more likely to drink sugary drinks daily. Regarding minerals and other dietary supplements, a higher proportion of healthy meat-eaters and vegetarians consumed these types of supplements compared with their less healthy counterparts (Table 2).

After a median follow-up of 10.4 years (interquartile range 9.6–11.2 years), 40,048 individuals developed a MACE. Of these events, 24,344 were IHD and 7379 MI. The crude hazard cumulative rate between types of diets and MACE and the other cardiovascular outcomes are available in Fig. S2. Less healthy vegetarians had a steeper gradient curve than healthier vegetarians, while least healthy meat-eaters had the sharpest curve compared to both vegetarian groups (Fig. S2).

Associations between the types of diets and cardiovascular outcomes are shown in Fig. 2 and Additional file 1: Table S2. In the minimally adjusted model, healthier vegetarians and meat-eaters had 23% (95% CI: 0.68 to 0.87) and 11% (95% CI: 0.87 to 0.91) lower risk of incident MACE compared to less healthy meat-eaters (Additional file 1: Table S2). When the analyses were further adjusted for prevalent morbidity and lifestyle factors (Fig. 2), these associations were slightly attenuated but remained significant for both groups ($HR_{\text{healthier meat-eaters}}$: 0.95 [95% CI: 0.93 to 0.97] and $HR_{\text{healthier vegetarians}}$: 0.82 [95% CI: 0.73 to 0.92]). Similar patterns were identified for the individual outcomes included, with the strongest association observed for MI among individuals in the same healthier categories (Fig. 2). There were no significant difference in cardiovascular risk between less healthy vegetarians and less healthy meat-eaters.

When BMI was included as a covariable in the sensitivity analysis, the associations were slightly attenuated but remained significant for incident MACE both for healthier meat-eaters (HR: 0.95 [95% CI: 0.93 to 0.97]) and healthier vegetarians (HR: 0.88 [95% CI: 0.78 to 0.99], Additional file 1: Table S2). In the counterfactual mediation analysis, obesity (BMI ≥30 kg/m^2) was found to be a significant partial mediator (Table S2).

Finally, when the models were re-run using healthy vegetarians as the referent category, the increased risk of incident MACE and IHD among less healthy vegetarians was not statistically significant (Table S3) possibly due to smaller sample size.

4. Discussion

The main finding of this study was that, compared to less healthy meat-eaters, the risk of incident from individuals and combined MACE was significantly lower among vegetarians whose diets were more compliant with dietary guidelines. Similar associations, albeit less strong, were observed for healthier meat-eaters. Risk among vegetarians with less healthy diets was not significantly different from meat-eaters. Moreover, obesity was a significant partial mediator [26].

Our findings corroborate the hypothesis that vegetarians are not homogeneous and that a vegetarian diet is not necessarily synonymous with a healthy diet. Along the same line, healthier meat-eaters also had a lower risk than their counterparts. This also suggests the lower quality of diet contribute to the increased cardiovascular risk instead of simply the amount of meat. Participants with less healthy diets also tended to have worse lifestyle behaviours than those who had a healthier diet. In this context, participants with less healthy dietary patterns did not get any additional cardiovascular benefits, irrespective if they were vegetarians or meat-eaters.

Existing evidence of cardiovascular benefits from vegetarian diets has generally come from studies that treated vegetarians as a single group [4,5]. This may have led to public misconception that avoiding red meat consumption will result in a healthy diet, irrespective of what is consumed. Considering that the number of vegetarians is continuing to rise [3] and the public health implications of our findings, future guidance should stress that the absence of meat should not simply define a vegetarian diet.

The heterogeneity of vegetarian diets may explain the conflicting results obtained from previous studies. Whilst the study of Seventh-Day Adventists has shown a protective effect of vegetarian diets against CVD [8,27,28], previous UK cohort studies have reported inconsistent findings [29,30]. Appleby et al. did not find any difference regarding mortality for circulatory disease and IHD between vegetarians and regular meat-eaters in the EPIC-Oxford and

Table 1
Sociodemographic characteristics of the study population by types of diets.

	Total	Meat-eaters		Vegetarians	
			Less healthy	Healthier	Less healthy
Socio-demographics					
Total n (%)	391,124 (100)	219,630 (56.1)	164,149 (42.0)	4200 (1.1)	3145 (0.8)
Age (years), mean (SD)	56.2 (8.1)	57.2 (7.9)	55.1 (8.2)	53.5 (7.9)	52.1 (7.8)
Age categories, n (%)					
<56 years	169,843 (43.5)	83,414 (38.0)	81,975 (49.9)	2417 (57.6)	2037 (64.8)
56–65 years	167,914 (42.9)	102,088 (46.5)	63,381 (38.6)	1502 (35.8)	943 (30.0)
>65 years	53,367 (13.6)	34,128 (15.5)	18,793 (11.5)	281 (6.6)	165 (5.2)
Sex (female), n (%)	216,936 (55.5)	130,279 (59.3)	81,721 (49.8)	2854 (68.0)	2082 (66.2)
Deprivation, n (%)					
Lower	136,279 (34.8)	82,016 (37.3)	52,344 (31.9)	1188 (28.3)	731 (23.2)
Middle	132,390 (33.9)	75,969 (34.6)	54,056 (32.9)	1397 (33.3)	968 (30.8)
Higher	122,455 (31.3)	61,645 (28.1)	57,749 (35.2)	1615 (38.4)	1446 (46.0)
Ethnicity, n (%)					
White	372,666 (95.3)	211,916 (96.5)	154,724 (94.3)	3660 (87.1)	2366 (75.2)
Others	18,458 (4.7)	7714 (3.5)	9425 (5.7)	540 (12.9)	779 (24.8)
Lifestyle and health status					
Smoking status, n (%)					
Never	220,771 (56.4)	131,308 (59.8)	84,48 (51.6)	2722 (64.8)	1993 (63.4)
Previous	131,770 (33.7)	74,375 (33.9)	55,261 (33.7)	1262 (30.1)	872 (27.7)
Current	38,583 (9.9)	13,947 (6.3)	24,140 (14.7)	216 (5.1)	280 (8.9)
Alcohol frequency intake, n (%)					
Daily or almost daily	80,599 (20.6)	40,932 (18.6)	38,623 (23.5)	539 (12.8)	505 (16.0)
3-4 times a week	93,061 (23.8)	52,710 (24.0)	39,032 (23.8)	786 (18.7)	533 (17.0)
Once or twice a week	102,956 (26.3)	59,664 (27.2)	41,805 (25.5)	905 (21.6)	582 (18.5)
1-3 times a month	43,652 (11.2)	25,500 (11.6)	17,289 (10.5)	554 (13.2)	309 (9.8)
Special occasions only	42,999 (11.0)	25,361 (11.6)	16,606 (10.1)	598 (14.2)	434 (13.8)
Never	27,857 (7.1)	15,463 (7.0)	10,794 (6.6)	818 (19.5)	782 (24.9)
Weight (kg), mean (SD)	77.6 (15.6)	76.8 (15.3)	79.0 (16.0)	70.9 (14.3)	71.5 (14.9)
Height (m), mean (SD)	1.68 (0.09)	1.68 (0.09)	1.69 (0.09)	1.67 (0.09)	1.66 (0.09)
BMI kg/m^2, mean (SD)	27.3 (4.7)	27.1 (4.6)	27.5 (4.8)	25.3 (4.4)	25.8 (4.8)
BMI Categories, n (%)					
Underweight (<18.5 kg/m^2)	1920 (0.5)	942 (0.4)	852 (0.5)	77 (1.8)	49 (1.6)
Normal weight (18.5–24.9 kg/m^2)	131,508 (33.6)	76,746 (34.9)	51,097 (31.1)	2143 (51.1)	1522 (48.4)
Overweight (25.0–29.9 kg/m^2)	167,850 (42.9)	94,215 (42.9)	71,097 (43.3)	1442 (34.3)	1096 (34.8)
Obese (≥30.0 kg/m^2)	89,846 (23.0)	47,727 (21.7)	41,103 (25.1)	538 (12.8)	478 (15.2)
Body fat (%), mean (SD)*	31.3 (8.5)	31.6 (8.5)	31.1 (8.5)	30.2 (8.6)	30.9 (8.7)
Waist circumference (cm), mean (SD)*	89.7 (13.2)	88.8 (13.0)	91.1 (13.3)	84.0 (12.4)	85.7 (13.0)
Central obesity (yes), n (%)*	125,782 (32.2)	68,006 (31.0)	56,069 (34.2)	912 (21.7)	795 (25.3)
Type of physical activity, n (%)					
Walking for pleasure (not as a means of transport)	280,302 (71.7)	165,027 (75.1)	109,915 (67.0)	3191 (76.0)	2169 (69.0)
Other exercises (e.g.: swimming, cycling, keep fit, bowling)	48,902 (12.5)	26,827 (12.2)	21,177 (12.9)	511 (12.2)	387 (12.3)
Strenuous sports	3196 (0.8)	1525 (0.7)	1605 (1.0)	42 (1.0)	24 (0.8)
Light DIY (e.g.: pruning, watering the lawn)	25,717 (6.6)	12,099 (5.5)	13,168 (8.0)	217 (5.2)	233 (7.4)
Heavy DIY (e.g.: weeding, lawn mowing, carpentry, digging)	9697 (2.4)	4509 (2.1)	5078 (3.1)	56 (1.3)	54 (1.7)
None of the above	22,982 (5.9)	9496 (4.3)	13,036 (7.9)	180 (4.2)	270 (8.6)
Prefer not to answer	328 (0.1)	147 (0.1)	170 (0.1)	3 (0.1)	8 (0.2)
Handgrip strength (kg), mean (SD)*	30.8 (11.0)	30.1 (10.8)	31.8 (11.2)	28.6 (9.9)	27.9 (10.0)
Sitting time (h/day), mean (SD)	5.0 (2.2)	4.9 (2.1)	5.2 (2.3)	4.2 (2.1)	4.4 (2.4)
TV viewing (h/day), mean (SD)*	2.8 (1.5)	2.7 (1.5)	2.9 (1.6)	2.1 (1.4)	2.2 (1.5)
Morbidity count, n (%)					
None	145,376 (37.2)	79,190 (36.1)	63,090 (38.4)	1757 (41.8)	1339 (42.6)
≥1	245,748 (62.8)	140,440 (63.9)	101,059 (61.6)	2443 (58.2)	1806 (57.4)

BMI: body mass index; n: number; SD: standard deviation; DIY: do it yourself.
*These data were used for participant characterisation only and were not used in the main analyses.

Oxford Vegetarian cohorts [29]. Similar results were reported by Key et al. regarding circulatory disease mortality [30]. A systematic review and meta-analysis of 183,321 participants from eight studies suggested a modest cardiovascular benefit associated with vegetarian diets but concluded that the evidence was less clear or unproven outside the Adventist population [28]. After conducting a meta-analysis of 197,737 participants from seven prospective studies, Glenn et al. concluded that the quality of the existing evidence was very low due to the heterogeneous nature of vegetarian diets [31]. This corroborates the relevance of investigating individuals' lifestyles, which benefits might go beyond the single label of eating or not eating meat. That is the case of healthier vegetarians in our study, who were less likely to be current smokers and obese and reported eating – on average – more fibre and fruit & vegetables than less healthy vegetarians.

Lacto-ovo-vegetarian, vegan, and pesco-vegetarian are the classic sub-categories applied to vegetarians [8]. This classification system provides additional information, over and above the exclusion of meat and poultry, on the consumption of fish and other animal products such as milk and eggs. Nonetheless, it still does not provide information on overall diet quality. For example, other food preferences – like ultra-processed foods – might obviate the protective benefit of not eating meat, as demonstrated by Gehring et al. [11] and Segovia-Siapco & Sabaté [32]. Segovia-Siapco & Sabaté showed that vegetarians and vegans from the EPIC-Oxford cohort had a higher intake of sweetened beverages than fish- and meat-

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

	Data available in*	Total	Meat-eaters		Vegetarians	
			Healthier	Less healthy	Healthier	Less healthy
Total energy intake (kcal/day)	169,900	2169 (659)	2152 (639)	2198 (682)	2134 (716)	2098 (740)
CHO intake (% of TE)	169,892	47.1 (8.0)	48.1 (7.8)	45.3 (8.1)	52.9 (7.7)	50.8 (8.4)
Sugar intake (% of TE)	169,892	22.5 (6.9)	23.4 (6.8)	21.1 (6.8)	25.0 (7.2)	22.8 (7.4)
Fibre intake (g/day)	169,900	16.3 (6.5)	17.2 (6.5)	14.7 (6.0)	21.3 (8.0)	19.2 (7.8)
Protein intake (% of TE)	169,892	15.6 (3.6)	15.9 (3.5)	15.3 (3.7)	12.6 (2.2)	12.1 (2.4)
Fat intake (% of TE)	169,892	32.1 (6.7)	31.2 (6.5)	33.4 (6.7)	31.0 (6.9)	33.0 (7.2)
Polyunsaturated fat intake (% of TE)	169,892	5.9 (2.2)	5.8 (2.2)	6.0 (2.3)	6.2 (2.4)	6.4 (2.5)
Saturated fat intake (% of TE)	169,892	12.4 (3.3)	11.9 (3.2)	13.1 (3.4)	11.5 (3.4)	12.6 (3.8)
Fruit and Vegetables intake (g/day)	391,124	325.2 (188.3)	383.9 (187.2)	243.2 (153.6)	453.3 (220.3)	335.6 (229.9)
Water intake (glasses/day)	361,680	2.8 (2.2)	3.0 (2.2)	2.6 (2.1)	3.5 (2.6)	3.4 (2.6)
Vegetarian alternatives intake (yes), n (%)	169,889	8707 (5.1)	4400 (4.4)	2188 (3.3)	1305 (54.9)	814 (52.6)
Crisp intake (amount/day), n (%)	51,464					
≤Half small bag		12,122 (23.6)	7390 (27.4)	4495 (19.4)	138 (19.9)	99 (17.0)
One small bag		34,670 (67.4)	17,598 (65.2)	16,169 (69.7)	501 (72.2)	402 (69.1)
Two or more small bags		4672 (9.0)	2012 (7.4)	2524 (10.9)	55 (7.9)	81 (13.9)
Pizza intake (amount/day), n (%)	12,137					
≤ one medium slice		4633 (38.2)	2664 (40.1)	1828 (36.2)	88 (32.8)	53 (28.3)
Two to three medium slices		5258 (43.3)	2844 (42.9)	2198 (43.6)	126 (47.0)	90 (48.2)
Four or more medium slices		2246 (18.5)	1129 (17.0)	1019 (20.2)	54 (20.2)	44 (23.5)
Sugary drinks intake (amount/day), n (%)[¥]	55,377					
≤1 glass/can		39,817 (71.9)	22,085 (73.0)	16,888 (70.4)	478 (70.8)	366 (73.6)
>1 glass/can		15,560 (28.1)	8146 (27.0)	7086 (29.6)	197 (29.2)	131 (26.4)
Smoothie drinks intake (amount/day), n (%)[¥]	19,461					
≤1 glass/bottle/250 ml		17,776 (91.3)	10,637 (91.4)	6652 (91.5)	313 (88.4)	174 (87.0)
>1 glass/bottle/250 ml		1685 (8.7)	998 (8.6)	620 (8.5)	41 (11.6)	26 (13.0)
Type of meals eaten, n (%)	165,141					
Takeaway meal		2875 (1.7)	1232 (1.3)	1602 (2.5)	22 (0.9)	19 (1.3)
Restaurant meals		14,554 (8.8)	7824 (8.1)	6443 (10.0)	165 (7.2)	122 (8.1)
Bought sandwiches		17,092 (10.4)	9106 (9.4)	7583 (11.7)	231 (10.0)	172 (11.5)
Ready meals		37,167 (22.5)	21,826 (22.6)	14,467 (22.4)	530 (23.0)	344 (22.9)
Home-cooked meals		93,453 (56.6)	56,728 (58.6)	34,521 (53.4)	1361 (58.9)	843 (56.2)
Mineral and other dietary supplements, n (%)	391,123					
Fish oil (including cod liver oil)		123,002 (31.4)	79,170 (36.1)	43,029 (26.2)	501 (11.9)	302 (9.6)
Glucosamine		27,980 (7.2)	16,872 (7.7)	10,237 (6.2)	591 (14.1)	280 (8.9)
Calcium		8691 (2.2)	5028 (2.3)	3171 (1.9)	268 (6.4)	224 (7.1)
Zinc		3185 (0.8)	1750 (0.8)	1286 (0.8)	103 (2.4)	46 (1.5)
Iron		3924 (1.0)	1846 (0.8)	1749 (1.1)	172 (4.1)	157 (5.0)
Selenium		1020 (0.3)	590 (0.3)	388 (0.2)	29 (0.7)	13 (0.4)
None of the above		222,684 (56.9)	114,066 (51.9)	103,982 (63.4)	2522 (60.1)	2114 (67.2)
Prefer not to answer		637 (0.2)	307 (0.1)	307 (0.2)	14 (0.3)	9 (0.3)

The average of five 24-h recall was used for this study (except for water and fruit and vegetable intake).
*Data available for the different subcomponents of diet in the dataset. These data were used for better sample characterisation and were not used in the main analyses.
¥ 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.

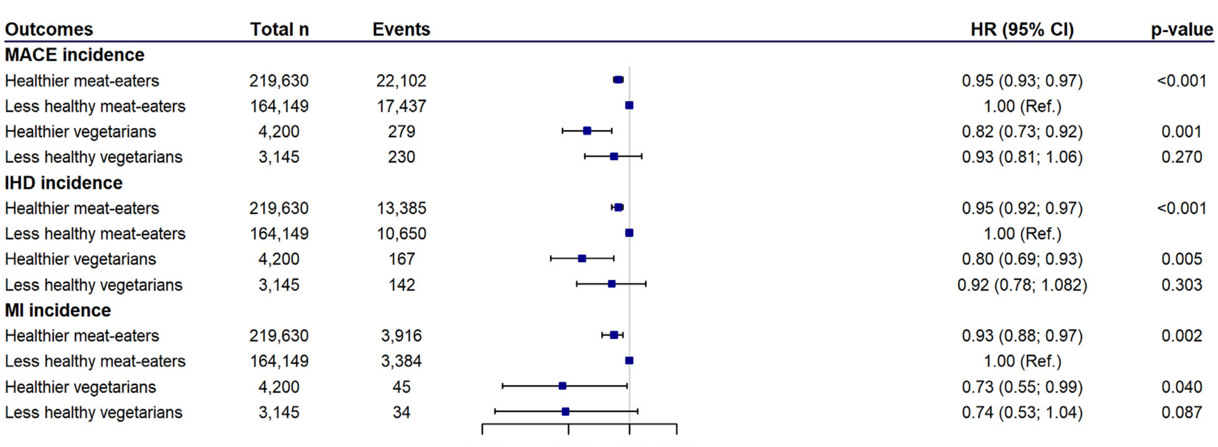

Fig. 2. Associations between the types of diets and incident cardiovascular outcomes.
Data presented as adjusted hazard ratio (HR) and its 95% confidence interval (95% CI) types of diets. Less healthy meat-eaters were used as the reference group. All analyses were performed using a 2-year landmark analysis, excluding participants who experienced events within the first two years of follow-up. Analyses were adjusted by age, sex, deprivation, ethnicity (white vs others), morbidity count, smoking, alcohol intake, total sedentary time and type of physical activity.

eaters [32]. From an analysis of over 4,833,042 person-years of follow-up across three cohort studies, Satija et al. demonstrated that individuals who followed a plant-based diet, but selected less healthy plant foods (such as refined grains, fruit juice, French fries, sugar-sweetened beverages, sweets and desserts), had a 32% (95% CI: 1.20 to 1.46) higher risk of coronary heart disease compared to the most healthful decile of a plant-based diet index [10]. Conversely, vegetarians who adhered to healthier patterns, by consuming whole grains, nuts, legumes, and fruit & vegetables, had a 25% lower risk of coronary heart disease [10].

Clearly, vegetarians are heterogeneous in terms of their diet, and their health risk and should be classified accordingly. Research and guidelines need to better characterise or define what they mean by a vegetarian diet, taking account of overall dietary patterns, rather than simply dichotomising people on the basis of meat consumption.

4.1. Strengths and limitations

UK Biobank is a large, prospective, general population cohort with data available on diet and an extensive range of sociodemographics and lifestyle. Thus, the analyses were able to be adjusted for multiple confounders, including an extensive list of prevalent long-term morbidities. However, our study is not exempt from limitations. Firstly, 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. Secondly, we defined healthier and less healthy vegetarians and meat-eaters by a two-step approach using the food frequency questionnaire. Dichotomising individuals based on dietary guideline adherence simplified the measurement of cumulative dietary risk factors, but this approach reduced statistical power and could not capture any non-linear associations [33]. Thirdly, the Oxford WebQ (24-h recall) was not completed by the whole study population; therefore, dietary intake characteristics across types of diets may not be representative of the full UK Biobank cohort. Moreover, we did not create our types of diet categories from the 24-h recall since the number of participants who had repeated dietary data for this measurement was less than 20% of the original cohort; therefore, insufficient data. Fourthly, while 98.1% of the stud population was classified as a meat-eater, only 1.9% was classified as vegetarian. This is similar to the prevalence of vegetarian diets (~2%) reported by the National Diet and Nutrition Survey 2008–2012 [34]. However, due to the fewer participants in the vegetarian categories, a non-significant result could be due to lower statistical power. Fifthly, we did not conduct analyses by ethnicity due to the small number of participants in the non-white category for vegetarians (1319 participants). Sixthly, despite including a long list of confounding factors in the analyses, unmeasured or residual confounding is possible in any observation study. Moreover, residual confounding might be possible because the morbidities were assumed to have equal weight in the prevalent morbidity variable. Seventhly, UK Biobank is not representative of the UK population in terms of other aspects of lifestyle; therefore, summary statistics should not be generalised to the general population [35]. Finally, it is not possible to infer causation from association due to the observational nature of our study. In addition, reverse causality may occur in observational studies. We tried to avoid such potential reverse causation using a 2-year landmark analysis.

5. Conclusion

Vegetarian diets are heterogeneous and the associated cardiovascular risk varied accordingly. We provided evidence that healthier vegetarians, as well as healthier meat-eaters, had a lower risk of MACE than less healthy meat-eaters; however, the cardiovascular risk of less healthy vegetarians were not significantly different from that of less healthy meat-eaters. Future studies should consider the overall dietary patterns of vegetarians rather than just based on meat consumption. Similarly, guidelines advocating a plant-based diet need to stress the importance of overall diet quality in addition to the reduction of meat.

Authorship contribution

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

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Conflict of Interest

None to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2023.01.010.

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