TITLE PAGE

Title: Association between Planetary Health Diet and Cardiovascular Disease: A Prospective Study from the UK Biobank

Brief title: Planetary Health Diet and Cardiovascular Disease

Authors: Mercedes Sotos-Prieto[1,2,3,4], PhD; Rosario Ortolá[1,2], MD, PhD, Javier Maroto-Rodriguez[1], PhDc; Adrián Carballo-Casla[2,5], PhD, Stefanos N Kales[4,6], MD; Fernando Rodríguez-Artalejo[1,2,3] MD, PhD

Departments and institutions

[1] Department of Preventive Medicine and Public Health. School of Medicine. Universidad Autónoma de Madrid, Calle del Arzobispo Morcillo, 4. 28029, Madrid, Spain.

[2] CIBERESP (CIBER of Epidemiology and Public Health), Av. Monforte de Lemos, 3-5. 28029, Madrid, Spain.

[3] IMDEA-Food Institute. CEI UAM+CSIC, Ctra. de Canto Blanco 8, E. 28049, Madrid, Spain.

[4] Department of Environmental Health, Harvard T.H. Chan School of Public Health, 665 Huntington Avenue. Boston, Massachusetts 02115, USA.

[5] Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institute & Stockholm University. Tomtebodavägen 18a, 171 65 Solna, Sweden.

[6] Occupational Medicine, Cambridge Health Alliance/Harvard Medical School

Address for correspondence:

Mercedes Sotos Prieto, PhD

Department of Preventive Medicine and Public Health, School of Medicine, Universidad Autónoma de Madrid, Calle del Arzobispo Morcillo 4, 28029 Madrid, Spain. Telephone: (+34) 91 497 54 41. E-mail: mercedes.sotos@uam.es

Word count: 3,059

Number of tables: 2

Number of figures: 1

Number of references: 41

Supplementary file

ABSTRACT

Background: The Planetary Health Diet index (PHDI) prioritizes the well-being of both individuals and the planet but has yielded mixed results on cardiovascular disease (CVD). Our aim was to assess the association between the PHDI and risk of CVD.

Methods: A cohort of 118,469 individuals aged 40-69 years from the UK Biobank, who were free of CVD at 2009-2012 and followed-up to 2021. The PHDI was calculated using at least two 24-h dietary assessments and included 14 food groups, with a possible range from 0 to130 points. CVD incidence was defined as primary myocardial infarction or stroke and obtained from clinical records and death registries.

Results: During a 9.4-year follow-up, 5,257 incident cases of CVD were ascertained. When comparing the highest (89.9-128.5 points) versus the lowest quartile (21.1-71.1 points) of PHDI adherence, the multivariable-adjusted hazard ratio (95% confidence interval) was 0.86 (0.79, 0.94) for CVD, 0.88 (0.80, 0.97) for myocardial infarction, and 0.82 (0.70, 0.97) for stroke. The association was linear until a plateau effect was reached at 80 points of adherence to PHDI. Results remained robust when excluding participants with type 2 diabetes, including only those with three or more diet assessments, or excluding CVD cases in the first three years of follow-up. The food group components of the PHDI more strongly associated with reduced CVD risk were higher consumption of whole grains, whole fruits, fish and lower consumption of added sugars and fruit juices.

Conclusion: In this large cohort of middle-aged and older British adults, adherence to the PHDI was associated with lower risk of CVD. These results provide empirical evidence that this dietary pattern, thought to be environmentally sustainable, benefits cardiovascular health.

Keywords: epidemiology, sustainable diet, planetary health, cardiovascular incidence.

Abbreviations: CVD: cardiovascular disease; PHDI: Planetary Health Diet Index; HR: hazard ratios; ICD: International Classification of Diseases; BMI: Body Mass Index

Lay summary

This study found that adherence to the Planetary Health Diet Index (PHDI) was associated with a reduced risk of cardiovascular disease (CVD) among middle-aged and older adults in the UK.

Key Findings:

- Higher adherence to the PHDI, which emphasizes whole grains, fruits, fish, and reduced intake of added sugars and fruit juices, is linked to a significantly lower risk of CVD, myocardial infarction, and stroke.
- The results were consistent even after accounting for various factors, including excluding participants with type 2 diabetes and focusing on those with more dietary assessments, highlighting the robustness of the association between the PHDI and cardiovascular health.

INTRODUCTION

Unhealthy diets and lifestyles are major contributors to the global burden of non-communicable diseases accounting for 11 million deaths and 255 million disability-adjusted life years (DAYLs) worldwide[1]. Furthermore, the current food system, occupying one-third of the world's land surface and responsible for approximately 30% of global greenhouse gas emissions (nearly half of methane emissions, two-thirds of nitrous oxide emissions and 3% of carbon dioxide (CO2) from agriculture sector[2]), not only exacerbates environmental pollution but also may pose serious threats to both planetary and human health[3,4].

In light of these challenges, the EAT-Lancet Commission in 2019[5] recommended adopting an optimally caloric planetary health diet produced in sustainable ways, and consisting mostly of plant-based foods, low amounts of animal source foods, unsaturated fats rather than saturated fats, and limited refined grains, processed foods, and added sugars. Adopting this dietary pattern (under three different approaches: a comparative risk model, Global Burden of Disease model, and Empirical disease risk model) is estimated to prevent 19-24% of premature deaths globally and has potential health benefits, such as reduced cardiovascular disease (CVD) and type 2 diabetes[5,6]. Also, a global shift to this dietary pattern could reduce the impact of diet on global greenhouse gas emissions, land use, and freshwater consumption[5,7,8].

Recognizing its potential impact, several studies have developed indexes to reflect adherence to the planetary health diet recommended by the EAT-Lancet commission.[9–15] Using such dietary indexes, most of the studies have found benefits on mortality[3, 9,15], CVD[9,14], type 2 diabetes[9–11], and cancer[15]; however, a few studies have found null associations with CVD[13,15], cancer[13] or total mortality[9]. Discrepancies might be due to the lack of a standardized scoring system leading to a complex interpretation of results and a difficult comparison between

studies. Of note, two studies have been conducted in UK cohorts. The first one involved 46,069 participants in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Oxford cohort, where the authors found a beneficial association for ischaemic heart disease but not for stroke[9]. Of note is that the EAT-Lancet diet index was built using binary items and the scale ranged from 0 to 14 points, which leads to a somewhat narrow score range that may limit the power to detect the associations. The second study included more than 400,000 participants in the UK biobank, in whom no association of this diet index with CVD was found[15]. Nevertheless, baseline diet was assessed only once and with only 29 questions, so the authors acknowledged that some relevant information to build the diet index could have been missed; the final binary score ranged from 0 to 11 points.

We aimed to overcome these discrepancies and some potential methodological shortfalls by using the Planetary Health Diet Index (PHDI) described by Bui et al.[16], which uses a continuous scale from 0 to 130 points, and used at least two (up to five) 24-hour dietary assessments in a large prospective cohort of British adults, to assess the association between the PHDI and risk of CVD.

METHODS

Study design and population

The UK Biobank is a prospective population-based study conducted in the United Kingdom (specifically, England, Wales, and Scotland) comprising approximately 500,000 individuals aged 40-69 years at the time of enrollment. Detailed study procedures have been previously documented[17,18]. In summary, participant recruitment took place from 2006 to 2010 at twenty-two assessment centers. During their initial visit, participants submitted biological samples, completed a touch-screen questionnaire, participated in a computer-assisted interview, and underwent a physical examination. Subsequently, some participants completed up to five online follow-up 24-hour dietary assessments between 2009 and 2012 (cycle 1: February 2011 to April 2011; cycle 2: June 2011 to September 2011; cycle 3: October 2011 to December 2011; cycle 4: April 2012 to June 2012). For this analysis we included only participants with at least two dietary assessments and plausible energy intake (n= 126,821). We excluded those with missing data on components of the PHDI (n=57), sociodemographics (n=928), lifestyle variables (n=675), chronic diseases (diabetes, CVD, cancer and hypertension) (n=1,438), and cholesterol-lowering medication (n=4). Additionally, to reduce the risk of reverse causation (i.e., health status influencing dietary habits, rather than the opposite) we excluded those participants with prevalent CVD (n=5,246), leaving a final sample of 118,469 persons **(Supplemental Figure 1**).

Ethical approval for this study was granted by the Northwest Multi-Centre Research Ethics Committee (REC reference 11/NW/0382) in 2011 and subsequently renewed in 2016 (16/NW/0274) and 2021 (21/NW/0157). Written informed consent was obtained from all study participants.

Assessment of Planetary Health Diet

Food consumption at baseline (from 2009 to 2012) was gathered using the Oxford WebQ, a web-based 24-hour dietary assessment tool[19]. To capture the participants' typical dietary habits, we only included the 126,821 individuals with a minimum of two (up to a maximum of five) dietary assessments, and the mean values were used in the analyses. Among the included participants, 44,779 had undertaken two dietary assessments, 39,744 three, 28,518 four, and 5,428 five assessments. Comprehensive information concerning the estimation of food group consumption, as well as nutrient and total energy intake, has been documented elsewhere[20,21]. We calculated the PHDI following the procedure published by Bui et al.[16], with the primary objective of measuring compliance with the dietary guidelines in the EAT-Lancet report[5] except for the unsaturated fatty acid component, due to lack of information. Briefly, 14 food groups were created. The minimum score assigned to each food group, which is 0, is determined by the level of consumption associated with the most unfavorable health impact, often set at 0 g/day for healthful food groups. Conversely, the maximum score assigned to each food group, which is 10 (with exceptions for non-soy legumes with a maximum score of 5, and soy foods with a maximum score of 5), is based on the level of consumption associated with the most favorable health impact, usually set at 0 g/day for unhealthful food groups. Intermediate scores were assigned proportionally to consumption levels between the minimum and maximum (**Supplemental Table 1**). The possible range of the PHDI is 0 to 130 points, and a higher score indicates higher adherence to the Planetary Health Diet.

Assessment of cardiovascular disease

Incident CVD was defined as a primary myocardial infarction (MI) or stroke event, according to the International Classification of Diseases (ICD) 10th edition. CVD was defined as ischemic

heart disease (I20), MI (I21-I23, I24.1, or I25.2), and stroke (I60, I61, I63, or I64). Ischemic stroke (I63) and haemorrhagic stroke (I61) were analyzed jointly or separately, as appropiate. Incidence of CVD was defined as the first CVD-related hospital admission or death identified by linkage to the Hospital Episode Statistics (HES) and national death index, respectively[17]. Hospital admission data was available up until September 2021 for England, until July 2021 for Scotland, and until February 2018 for Wales. Information on vital status and date of death based on central registers were obtained for England and Scotland up to the 30th of September 2021, and up to the 31st of October 2021 for Wales. Length of follow-up was estimated as time from the last dietary assessment (2009-2012) to the date of the first CVD-related hospitalization, death, or end of follow-up, whichever came first.

Assessment of potential confounders

At baseline, participants reported demographic information, including sex, age, ethnicity, educational attainment, socioeconomic status (determined by the Townsend deprivation index[22]), and data on smoking habits (never, former, or current), alcohol consumption, physical activity, and the use of medications and vitamin supplements. The presence of pre-existing medical conditions, as classified using ICD10 coding, and the use of cholesterol-lowering medications were also self-reported. Baseline body mass index (BMI) was calculated as measured weight (kg) divided by the square of measured height (m).

Statistical analysis

Multivariable Cox proportional-hazard models, using age as the underlying timescale, were used to compute hazard ratios (HR) and their corresponding 95% confidence intervals (CI) for

the association between the PHDI and incident CVD. The PHDI was categorized into quartiles and analyzed per 20-point increment, with the lowest quartile (representing the lowest adherence) serving as the reference. We fitted three progressively adjusted models: Model 1, adjusted for sociodemographic variables (sex, ethnicity, educational level, deprivation index) and region of assessment center; Model 2, further adjusted for lifestyle variables at baseline (smoking status, total energy intake, alcohol intake, and physical activity); and Model 3 further adjusted for intermediate conditions (type 2 diabetes, BMI, cancer, and hypertension), cholesterol-lowering medications, number of medications, and vitamin supplement use at baseline. *P*-trends were calculated by entering the PHDI in quartiles as a continuous variable in the models. We conducted separate analyses for each food group within the PHDI (per 2-point increment). Additionally, we assessed deviation from linearity by modeling the PHDI as a restricted cubic spline in a Cox regression model adjusted as Model 3.

We implemented a series of sensitivity analyses. First, we repeated the main analyses excluding participants with type 2 diabetes and cancer at recruitment, given its association with CVD; second, we replicated the main analysis within the participants having at least three dietary assessments; and third, we excluded the participants with incident CVD during the initial three years of follow-up. Additionally, to investigate potential effect modification, we conducted stratified analysis and tested interaction terms between the PHDI and sex, age (<65, ≥65 years), deprivation index (at or below the median, above the median), physical activity (tertiles), smoking status (never, former, and current), BMI (<25, 25-29.9, ≥30 kg/m^2), hypertension and diabetes. We also evaluated the Fine Gray model for competing mortality risks. Finally, in secondary analysis we assessed the association between a similar previously derived healthful plant-based diet and risk of CVD[23].

Proportional hazards assumption was assessed plotting the survival probability of CVD over follow-up for the PHDI quartiles (which were rather parallel) and using the Schoenfeld residuals method, which nevertheless resulted in a p value <0.05. However, it is expected that the HR will vary somewhat over the follow-up, so the overall HR should be interpreted as a weighted average of the HRs over the follow-up period.

Analyses were conducted using Stata version 17 (Stata-Corp LLC, College Station, Texas). All *p*-values were two-sided, and statistical significance was set at $p < 0.05$

RESULTS

Baseline characteristics of the participants according to quartiles of the PHDI are shown in **Table 1**. Compared to those in the lowest quartile of PHDI, those in the highest quartile (highest adherence) were more likely to be females and non-smokers, and to have higher educational level, lower energy intake, higher physical activity, and normal weight; also, they took vitamins more often, took cholesterol-lowering medications less often and had fewer morbidities. Compared to the analytic sample, the excluded participants were older and more likely former smokers, and more often suffered from obesity, hypertension, diabetes, and took cholesterol-lowering medications (**Supplemental Table 2)**.

After a median follow up of 9.4 years, 5,257 incident cases of CVD were ascertained When comparing the highest versus the lowest quartile of PHDI, the multivariable adjusted HRs (95% CI) were 0.86 (0.79, 0.94) for total CVD, 0.88 (0.80, 0.97) for myocardial infarction, and 0.82 (0.70, 0.97) for stroke (**Table 2**). By subtypes of stroke, participants in the highest versus the lowest quartile of PHDI had lower risk of ischemic stroke (0.77 [0.64, 0.93]) but not for haemorrhagic stroke (0.97 [0.67, 1.39]). Of note was the low number of haemorrhagic stroke cases (Supplemental Table 3). The graphic relationship between the exposure and the outcome confirmed a linear-relationship until a a plateau effect was reached after 80 points of adherence to the PHDI (p values for nonlinearity were: 0.04 for CVD, 0.07 for MI, and 0.08 for stroke)(**Supplemental Figure 2**). An inverse association was also found between the PHDI score (per 20-point increase) and total CVD, myocardial infarction, and stroke (**Table 2**).

The inverse association between PHDI and CVD was consistent in sensitivity analyses when we excluded the participants with type 2 diabetes or cancer (**Supplemental Table 4**), when we included only participants with three or more dietary assessments (**Supplemental Table 5**),

and when we excluded cases of CVD during the three first years of follow-up (**Supplemental Table 6**). In subgroup analyses, the PHDI was somewhat more strongly associated with total CVD, myocardial infarction, and stroke in men than women and in participants with a BMI > 25 kg/m2 or in the highest tertile of physical activitybut there was no evidence of an statistical interaction except for physical activity and CVD (**Supplemental Table 7**). The associations were robust and in the expected direction in all strata. A significant interaction was found for physical activity, smoking, and hypertension for total CVD, so the association was stronger in those with higher physical activity, current smokers, and those without hypertension. (**Supplemental Table 7**). Finally, the results remained also robust after using a competing risk analysis considering death as a competing event (**Supplemental Table 8**).

The associations between each food group (per 2-point increment) of the PHDI and CVD risk are shown in **Figure 1**. While all associations were in the expected direction, the food components most associated with reduced CVD risk were whole grains, whole fruit, fish and avoiding added sugar and fruit juices.

Finally, in the association between a healthful plant-based diet and the risk of CVD which was significant for total CVD: HR and (95%CI) for highest versus lowest quartile of the diet: 0.91 (0.84, 1.00), and for MI: 0.91 (0.82, 1.00) but not for stroke (**Supplemental Table9**).

DISCUSSION

In this large prospective cohort of middle age and older British adults, we found a strong inverse association between higher adherence to the PHDI and the risk of CVD, including myocardial infarction and stroke. Comparing with participants in the lowest quartile of PHDI adherence, those in the highest quartile had a relative 14% lower risk of total CVD, 12% lower risk of myocardial infarction, and 18% lower risk of stroke. These results remained robust in several sensitivity analyses.

Previous studies have also found benefits of the planetary health diets on various health outcomes including mortality [9,12,24], CVD[9,14,25,26], cancer[13,15] and diabetes[9–11,27–29]. In line with our study, the EPIC-Oxford cohort found a 28% lower risk of ischemic heart disease in those with higher adherence to EAT-Lancet diet (12-14 points) compared to the lowest adherence (4-9 points).[9] However, no association was found for stroke. Similarly, the EPIC-Netherlands cohort, found a14% and 12% lower risk of CVD and coronary heart disease, respectively, with higher adherence to EAT-Lancet diet, but not with total stroke[14] and a Swedish cohort a 20% lower risk of coronary events[25]. Regarding subtypes of stroke, a Danish cohort found a lower risk of subarachnoid stroke with higher adherence to diet[26]. We did not find any association with hemorrhagic stroke. Although the etiologies, and risk factors of each subtype of stroke differs there were a low number of hemorrhagic stroke cases, so the results for this subtype should be interpreted with caution.

However, not all studies have reported an inverse association with total CVD. In the NutriNet-Santé cohort with 62,382 participants and 786 cases of CVD events, no association was found between the EAT-Lancet diet and CVD.[13] More recently, another analyses of the UK biobank cohort, found no association between the EAT-Lancet diet and CVD[15]. Our study differs from

the latter in several aspects: the touchscreen questionnaire used in the previous study included only 29 questions and did not capture information on some significant foods (e.g., potatoes, pasta, rice, miscellaneous cereals, cakes, biscuits, buns). These foods can account for 22-25% of fiber intake[28 30] and may contribute to reducing the risk of CVD [31]. Also, this alternative PHDI did not include legumes or nuts, so it could underestimate the study association, given their recognized benefits on CVD[32]. Second, we analyzed a subsample of participants with at least two 24-h dietary assessments (n=118,469) in lieu of 447,000+ individuals with information in the touchscreen FFQ. Third, their scoring method to develop the PHDI differed considerably from ours. We used a continuous score that allowed us to capture the variation between the reference levels of the EAT-Lancet diet. In addition, the range of possible consumption levels for each food group allowed exchanges within a given total energy intake. Specifically, the scoring criteria were derived from the dose-response relationships between each food group and the risk of major chronic diseases[16], and the possible PHDI range was from 0 to130. However, in the previous UK Biobank study[24], the authors scored the consumption of the food groups dichotomously (possible range 0-11), which may limit the power to detect associations.

All the above-mentioned reasons, as well as differences in sample size, follow-up duration, and baseline characteristics of the cohorts, the definition of the food groups (including the combination of whole and refined grains in the same group), may contribute to the discrepancies in results between studies. A consensus is needed on how to operationalize the PHDI.

The EAT-Lancet diet is similar to other plant-based diets associated with improved health outcomes[23,33,34], although in our study comparing the results with a healthful plant-based diet

where somewhat weaker, possible due to differences in how these diets were defined. Nonetheless, the positive improved health outcomes found in all of them are in part due to the beneficial effects of their food components. Fruits, vegetables, nuts and whole grains are rich in antioxidants, phytochemicals with anti-inflammatory properties, and fiber, which can help control glucose and cholesterol levels[35,36,37]. The low amount of saturated fatty acids may help reduce LDL cholesterol and thus atherosclerosis development. This diet is also rich in potassium and low in sodium, which is beneficial for blood pressure[38]. Thus, the effects of this dietary pattern can be partly mediated through lowering CVD risk factors; indeed, the EAT-Lancet diet has been associated with lower BMI, non-HDL cholesterol, and systolic blood pressure[9,39,40]. In our study, the direction of the associations remained in all strata of BMI, diabetes, age, etc. However, we found three significant interactions between the PHDI and total CVD: first, the association was stronger in those more physically active (as expected, as physical activity could act synergically with diet in lowering CVD risk). In contrast, the strongest protective association was found among current smokers; this may be partly because former smokers often quitted smoking for health reasons, and they may have a higher accumulated risk of CVD and other chronic diseases from long-term tobacco exposure. However, these results, as well as the observed stronger association between the PHDI and CVD in non-hypertensive participants, required further research. Despite

Finally, upon examining the associations between the PHDI food groups and CVD, we observed a general trend towards lower risk of CVD, with higher consumption of whole grains, whole fruits, and fish, and lower consumption of added sugars showing the strongest associations. This confirms the health benefits of each individual component of the PHDI, but

also highlights the importance of their combined effects (note that the associations of the PHDI food groups were weaker than that of the PHDI as a whole).

Strengths and limitations

Strengths of this study include the prospective design, the large sample size, the moderately long follow-up, the use of repeated 24-hour dietary assessments, and the high reliability and completeness of ascertainment of incident CVD. However, this study also has some limitations. First, because lifestyle and diet are self-reported, some measurement error is inevitable, potentially biasing the true association in any direction[40]. Additionally, our study could not account for potential changes in diet over time, which may affect long-term health outcomes. Also, two dietary assessments may not perfectly reflect usual food consumption; however, we obtained similar results when we used three or more assessments. Second, we could not estimate the consumption of unsaturated oils, and as it was one of the food groups that drove most of the association with mortality in another study[16], we may be underestimating the true association of the PHDI with lower CVD risk. Additionally, the PHDI has a limited capacity to accurately assess the intake of ultra-processed foods. Although some components of the index, such as the consumption of added sugars and fruit juices, may indirectly relate to the intake of ultra-processed foods, it does not explicitly account for the degree of food processing that have been previously associated with increased risk CVD[42]. Third, as in all observational studies, residual and unmeasured confounding cannot be ruled out, despite that we adjusted for a number of potential confounders. Fourth, generalizability might be limited because participants were recruited voluntarily[43], and participants with more dietary assessments tended to have a higher educational attainment than the general participants in

the UK biobank[44]. However, previous studies support that results remain barely unchanged among those with 3 or more dietary assessments[45,46]

CONCLUSION

In a large cohort of middle-aged and older British adults, higher adherence to a planetary dietary pattern proposed by the EAT-Lancet Commission — designed to benefit both human health and environmental sustainability —, was associated with lower risk of total CVD, myocardial infarction and stroke Future research should confirm whether this dietary pattern yields similar results in other populations, and specifically assess if the protective association between PHDI and CVD risk reaches a plateau at the highest level of adherence to this dietary pattern.

Funding:

This work was supported by the Carlos III Health Institute, the Secretary of R+D+I, and the European Regional Development Fund/European Social Fund (FIS grants 20/00896; 23/00079); National Agency of Research (CNS2022-135623); Ministry of Science and Innovation (RYC 2018-02069I) to M.S.P.); Universidad Autónoma de Madrid (FPI contract) to J.M.R.; and Comunidad de Madrid and European Regional Development Fund ("FACINGLCOVID-CM" project. Funding REACT EU Program).

The funding agencies had no role in study design, data collection and analysis, interpretation of results, manuscript preparation or in the decision to submit this manuscript for publication.

Data Availability: The data used in this study are available from the UK Biobank, subject to their data access policies. Interested researchers can apply for access at https://www.ukbiobank.ac.uk and are required to cover the access fees.

Disclosures:

Authors declare no conflict of interest.

Acknowledgments

This research has been conducted using the UK Biobank Resource under Application Number 80773.

Authorship: MSP and FRA contributed to the conception or design of the work. MSP contributed to the acquisition, analysis, or interpretation of data for the work. RO reviewed analysis for accuracy. MSP drafted the manuscript. FRA critically revised the manuscript. All gave final approval, reviewed the manuscript and agree to be accountable for all aspects of work ensuring integrity and accuracy

BIBLIOGRAPHY

1. Afshin A, Sur PJ, Fay KA, et al. Health effects of dietary risks in 195 countries, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet* 2019; 393: 1958–1972.

2. Ivanovich CC, Sun T, Gordon DR, et al. Future warming from global food consumption. *Nat Clim Chang* 2023; 13: 297–302.

3. Emissions due to agriculture. Global, regional and country trends 2000–2018 |Policy Support and Governance| Food and Agriculture Organization of the United Nations, https://www.fao.org/policy-support/tools-and-publications/resources-details/en/c/1382716/ (accessed 9 January 2024).

4. Foley JA, DeFries R, Asner GP, et al. Global Consequences of Land Use. *Science* 2005; 309: 570–574.

5. Willett W, Rockström J, Loken B, et al. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. *Lancet* 2019; 393: 447–492.

6. Willett WC, Hu FB, Rimm EB, et al. Building better guidelines for healthy and sustainable diets. *Am J Clin Nutr* 2021; nqab079.

7. Springmann M, Spajic L, Clark MA, et al. The healthiness and sustainability of national and global food based dietary guidelines: modelling study. *BMJ* 2020; 370: m2322.

8. Springmann M, Wiebe K, Mason-D'Croz D, et al. Health and nutritional aspects of sustainable diet strategies and their association with environmental impacts: a global modelling analysis with country-level detail. *Lancet Planet Health* 2018; 2: e451–e461.

9. Knuppel A, Papier K, Key TJ, et al. EAT-Lancet score and major health outcomes: the EPIC-Oxford study. *Lancet* 2019; 394: 213–214.

10. López GE, Batis C, González C, et al. EAT-Lancet Healthy Reference Diet score and diabetes incidence in a cohort of Mexican women. *Eur J Clin Nutr* 2022; 1–8.

11. Xu C, Cao Z, Yang H, et al. Association Between the EAT-Lancet Diet Pattern and Risk of Type 2 Diabetes: A Prospective Cohort Study. *Front Nutr* 2021; 8: 784018.

12. Stubbendorff A, Sonestedt E, Ramne S, et al. Development of an EAT-Lancet index and its relation to mortality in a Swedish population. *Am J Clin Nutr* 2022; 115: 705–716.

13. Berthy F, Brunin J, Allès B, et al. Association between adherence to the EAT-Lancet diet and risk of cancer and cardiovascular outcomes in the prospective NutriNet-Santé cohort. *Am J Clin Nutr* 2022; 116: 980–991.

14. Colizzi C, Harbers MC, Vellinga RE, et al. Adherence to the EAT-Lancet Healthy Reference Diet in Relation to Risk of Cardiovascular Events and Environmental Impact: Results From the EPIC-NL Cohort. *J Am Heart Assoc* 2023; 12: e026318.

15. Karavasiloglou N, Thompson AS, Pestoni G, et al. Adherence to the EAT-Lancet reference diet is associated with a reduced risk of incident cancer and all-cause mortality in UK adults. *One Earth* 2023; 6: 1726–1734.

16. Bui LP, Pham TT, Wang F, et al. Planetary Health Diet Index and risk of total and cause-specific mortality in three prospective cohorts. *Am J Clin Nutr* 2024; 120: 80–91.

17. Sudlow C, Gallacher J, Allen N, et al. 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.

18. UK Biobank: Protocol for a large-scale prospective epidemiological resource. *UK Biobank*, https://www.ukbiobank.ac.uk/media/gnkeyh2q/study-rationale.pdf.

19. Liu B, Young H, Crowe FL, et al. Development and evaluation of the Oxford WebQ, a low-cost, web-based method for assessment of previous 24 h dietary intakes in large-scale prospective studies. *Public Health Nutr* 2011; 14: 1998–2005.

20. Perez-Cornago A, Pollard Z, Young H, et al. Description of the updated nutrition calculation of the Oxford WebQ questionnaire and comparison with the previous version among 207,144 participants in UK Biobank. *Eur J Nutr* 2021; 60: 4019–4030.

21. Piernas C, Perez-Cornago A, Gao M, et al. Describing a new food group classification system for UK biobank: analysis of food groups and sources of macro- and micronutrients in 208,200 participants. *Eur J Nutr* 2021; 60: 2879–2890.

22. Townsend P, Phillimore P, Beattie A. *Health and Deprivation: Inequality and the North.* London: Croom Helm, 1988.

23. Sotos-Prieto M, Struijk EA, Fung TT, et al. Association between the quality of plant-based diets and risk of frailty. *J Cachexia Sarcopenia Muscle* 2022; 13: 2854–2862.

24. Adherence to the EAT-Lancet reference diet is associated with a reduced risk of incident cancer and all-cause mortality in UK adults - PMC, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10731983/ (accessed 9 January 2024).

25. Zhang S, Dukuzimana J, Stubbendorff A, et al. Adherence to the EAT-Lancet diet and risk of coronary events in the Malmö Diet and Cancer cohort study. *Am J Clin Nutr* 2023; 117: 903–909.

26. Ibsen DB, Christiansen AH, Olsen A, et al. Adherence to the EAT-Lancet Diet and Risk of Stroke and Stroke Subtypes: A Cohort Study. *Stroke* 2022; 53: 154–163.

27. Lin X, Wang S, Huang J. The Association between the EAT-Lancet Diet and Diabetes: A Systematic Review. *Nutrients* 2023; 15: 4462.

28. Zhang S, Stubbendorff A, Olsson K, et al. Adherence to the EAT-Lancet diet, genetic susceptibility, and risk of type 2 diabetes in Swedish adults. *Metabolism* 2023; 141: 155401.

29. Langmann F, Ibsen DB, Tjønneland A, et al. Adherence to the EAT-Lancet diet is associated with a lower risk of type 2 diabetes: the Danish Diet, Cancer and Health cohort. *Eur J Nutr* 2023; 62: 1493–1502.

30. NDNS: results from Years 1 to 4 (combined). *GOV.UK*, 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 (2017, accessed 24 January 2024).

31. Ramezani F, Pourghazi F, Eslami M, et al. Dietary fiber intake and all-cause and cause-specific mortality: An updated systematic review and meta-analysis of prospective cohort studies. *Clin Nutr* 2024; 43: 65–83.

32. Houston L, Probst YC, Chandra Singh M, et al. Tree Nut and Peanut Consumption and Risk of Cardiovascular Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Adv Nutr* 2023; 14: 1029–1049.

33. Satija A, Malik V, Rimm EB, et al. Changes in intake of plant-based diets and weight change: results from 3 prospective cohort studies. *Am J Clin Nutr* 2019; 110: 574–582.

34. Estruch R, Ros E, Salas-Salvadó J, et al. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. *N Engl J Med* 2018; 378: e34.

35. Albuquerque TG, Nunes MA, Bessada SMF, et al. 14 - Biologically active and health promoting food components of nuts, oilseeds, fruits, vegetables, cereals, and legumes. In: Pico Y (ed) *Chemical Analysis of Food (Second Edition)*. Academic Press, pp. 609–656.

36. Kris-Etherton PM, Hu FB, Ros E, et al. The role of tree nuts and peanuts in the prevention of coronary heart disease: multiple potential mechanisms. *J Nutr* 2008; 138: 1746S-1751S.

37. Kumar A, Chidambaram V, Mehta JL. Vegetarianism, microbiota, and cardiovascular health: looking back, and forward. *Eur J Prev Cardiol*. 2022;29(14):1895-1910.

38. Satija A, Hu FB. Plant-based diets and cardiovascular health. *Trends Cardiovasc Med* 2018; 28: 437–441.

39. Montejano Vallejo R, Schulz C-A, van de Locht K, et al. Associations of Adherence to a Dietary Index Based on the EAT-Lancet Reference Diet with Nutritional, Anthropometric,

and Ecological Sustainability Parameters: Results from the German DONALD Cohort Study. *J Nutr* 2022; 152: 1763–1772.

40. Cacau LT, Benseñor IM, Goulart AC, et al. Adherence to the EAT-Lancet sustainable reference diet and cardiometabolic risk profile: cross-sectional results from the ELSA-Brasil cohort study. *Eur J Nutr* 2023; 62: 807–817.

41. Greenland S. The effect of misclassification in the presence of covariates. *Am J Epidemiol* 1980; 112: 564–569.

42. Lane MM, Gamage E, Du S, et al. Ultra-processed food exposure and adverse health outcomes: umbrella review of epidemiological meta-analyses. *BMJ* 2024; 384: e077310.

43. Hernán MA, Hernández-Díaz S, Robins JM. A structural approach to selection bias. *Epidemiology* 2004; 15: 615–625.

44. Galante J, Adamska L, Young A, et al. The acceptability of repeat Internet-based hybrid diet assessment of previous 24-h dietary intake: administration of the Oxford WebQ in UK Biobank. *British Journal of Nutrition* 2016; 115: 681–686.

45. Maroto-Rodriguez J, Ortolá R, Carballo-Casla A, et al. Association between a mediterranean lifestyle and Type 2 diabetes incidence: a prospective UK biobank study. *Cardiovasc Diabetol* 2023; 22: 271.

46. Maroto-Rodriguez J, Delgado-Velandia M, Ortolá R, et al. Association of a Mediterranean Lifestyle With All-Cause and Cause-Specific Mortality: A Prospective Study from the UK Biobank. *Mayo Clin Proc* 2023; S0025-6196(23)00305–1.

Table 1. Baseline characteristics of the UK Biobank participants by quartiles of the Planetary Health Diet index

	Quartile 1 21.1-71.1 points	**Quartile 2 71.1-80.7 points**	**Quartile 3 80.7-89.9 points**	**Quartile 4 89.9-128.5 points**
N	29,617	29,617	29,617	29,618
Sex, female, *n* (%)	12,696 (42.9)	16,052 (54.2)	18,079 (61.0)	20,703 (69.9)
Age, years, mean (SD)	57.9 (8.04)	58.8 (7.92)	59.2 (7.75)	59.2 (7.62)
Ethnicity, non-white, *n* (%)	811 (2.7)	879 (3.0)	914 (3.1)	1,092 (3.7)
Region of assessment, *n* (%)				
England	26,891 (90.8)	27,212 (91.8)	27,114 (91.6)	27,226 (91.9)
Wales	1,049 (3.26)	909 (3.14)	910 (3.01)	826 (2.83)
Scotland	1,677 (5.7)	1,496 (5.1)	1,593 (5.4)	1,566 (5.3)
Education, non-university, *n* (%)	18,245 (60.6)	16,139 (54.5)	14,683 (49.6)	12,888 (43.5)
Deprivation index, mean (SD)	-1.58 (2.89)	-1.73 (2.77)	-1.74 (2.78)	-1.64 (2.84)
Smoking status, *n* (%)				
Never	16,170 (54.6)	17,105 (57.8)	17,702 (59.8)	17,807 (60.1)
Former	10,172 (34.4)	10,443 (35.3)	10,372 (35.0)	10,584 (35.7)
Current	3,275 (11.1)	2,069 (7.0)	1,543 (5.2)	1,227 (4.1)
Energy intake, kcal/day, mean (SD)	2,149 (529)	2,079 (495)	2,026 (482)	2,001 (466)
Alcohol, g/day, mean (SD)	1.89 (2.22)	1.72 (1.95)	1.56 (1.77)	1.37 (1.58)
Physical activity, MET minutes per week				
Tertile 1	10,883 (36.8)	9,555 (32.3)	8,751 (29.6)	7,782 (26.3)
Tertile 2	9,490 (32.0)	10,242 (34.6)	10,328 (34.9)	10,351 (35.0)
Tertile 3	9,244 (31.2)	9,820 (33.2)	10,538 (35.6)	11,485 (38.8)
Body mass index , *n* (%)				
< 25 kg/m^2	9,346 (31.6)	10,955 (37.0)	12,554 (42.4)	15,181 (51.3)
25 – 29.9 kg/m^2	12,915 (43.6)	12,500 (42.2)	12,013 (40.6)	10,730 (36.2)
≥ 30 kg/m^2	7,356 (24.8)	6,162 (20.8)	5,050 (17.1)	3,707 (12.5)

Number of medications, mean (SD)	2.02 (2.30)	1.99 (2.25)	1.93 (2.21)	1.90 (2.17)
Vitamin use, n (%)	8,256 (27.9)	9,195 (31.1)	9,978 (33.7)	11,678 (39.4)
Hypertension, *n* (%)	7,339 (24.8)	6,905 (23.3)	6,381 (21.6)	5,732 (19. 4)
Cholesterol-lowering medication, *n* (%)	3,942 (13.3)	3,631 (12.3)	3,316 (11.2)	2,853 (9.6)
Diabetes, n (%)	1,155 (3.9)	1,041 (3.5)	965 (3.3)	741 (2.5)
Cancer, n (%)	2,023 (6.8)	2,150 (7.3)	2,290 (7.7)	2,422 (8.2)

1 Abbreviations: *N*, total number of participants; *n*, number of participants included in the category; SD, standard deviation.

Table 2. Hazard ratios (95% confidence interval) of cardiovascular disease risk by adherence to the PHDI(quartiles).

	Planetary Health Diet index					
Median (IQR)	Quartile 1 64.6 (8.8)	Quartile 2 76.2 (4.72)	Quartile 3 85.1 (4.54)	Quartile 4 96.0 (8.05)	*p*-trend	Per 20-point increment
Total CVD						
cases/n	1,580/ 29,618	1,372/ 29,617	1,228/ 29,617	1,077/ 29,617		5257/118,469
Model 1	Ref.	**0.89 (0.83, 0.96)**	**0.81 (0.75, 0.88)**	**0.78 (0.72, 0.85)**	**< 0.001**	**0.85 (0.82 – 0.89)**
Model 2	Ref.	**0.91 (0.85, 0.99)**	**0.84 (0.78, 0.91)**	**0.81 (0.75, 0.88)**	**< 0.001**	**0.87 (0.84 – 0.91)**
Model 3	Ref.	0.93 (0.86, 1.00)	**0.87 (0.80, 0.94)**	**0.86 (0.79, 0.94)**	**< 0.001**	**0.90 (0.86, 0.95)**
Myocardial infarction						
cases/n	1,256/ 29,618	1,076/ 29,617	942/ 29,617	838/ 29,617		4,112/118,469
Model 1	Ref.	**0.90 (0.83, 0.98)**	**0.80 (0.73, 0.88)**	**0.79 (0.72, 0.86)**	**< 0.001**	**0.85 (0.81, 0.90)**
Model 2	Ref.	0.92 (0.85, 1.00)	**0.83 (0.76, 0.91)**	**0.82 (0.75, 0.90)**	**< 0.001**	**0.88 (0.83, 0.92)**
Model 3	Ref.	0.93 (0.86, 1.02)	**0.86 (0.79, 0.95)**	**0.88 (0.80, 0.97)**	**0.001**	**0.91 (0.86, 0.96)**
Stroke						
cases/n	365/ 29,618	318/ 29,617	316/ 29,617	269/ 29,617		1,268/118,469
Model 1	Ref.	**0.85 (0.72, 0.99)**	**0.84 (0.72, 0.99)**	**0.76 (0.65, 0.90)**	**0.002**	**0.85 (0.78, 0.93)**
Model 2	Ref.	0.86 (0.74, 1.00)	0.87 (0.74, 1.02)	**0.79 (0.67, 0.94)**	**0.010**	**0.88 (0.80, 0.96)**
Model 3	Ref.	0.87 (0.74, 1.01)	0.89 (0.76, 1.04)	**0.82 (0.70, 0.97)**	**0.036**	**0.89 (0.82, 0.98)**

Abbreviations: PHDI, Planetary Health Diet Index,; CVD, Cardiovascular disease, *n*, number of participants in the category.

Model 1: Adjusted for sex (male, female), age (continuous), ethnicity(White, Asian, Black, Chinese, other) , education (College or University degree, A levels/AS levels or equivalent, O levels/GCSEs or equivalent, CSEs or equivalent, NVQ or HND or HNC or equivalent, other professional qualifications).), deprivation index (continuous), and region of assessment ((England, Wales, Scotland).
Model 2: Adjusted as Model 1 + for smoking status (never, former, current), energy intake (quintiles), alcohol intake (g/day) , and physical activity (tertiles).
Model 3: Adjusted as in Model 2 + BMI (<25 Kg/m^2, 25-29.9 Kg/m^2, ≥ 30 kg/m^2), diabetes (yes/no), cancer (yes/no), hypertension (yes/no), cholesterol-lowering medication (yes/no), number of medications, and vitamin supplement use (yes/no).

Legends Figures:

Figure 1. Hazard ratios (95% confidence interval) for CVD risk per 2-point increment of each PHDI food group in the UK Biobank.

Multivariable-adjusted model: for sex, age, ethnicity, education, deprivation index, region of assessment, smoking status, energy intake, physical activity, BMI, diabetes, cancer, hypertension, cholesterol-lowering medication, number of medications, and vitamin supplement use.

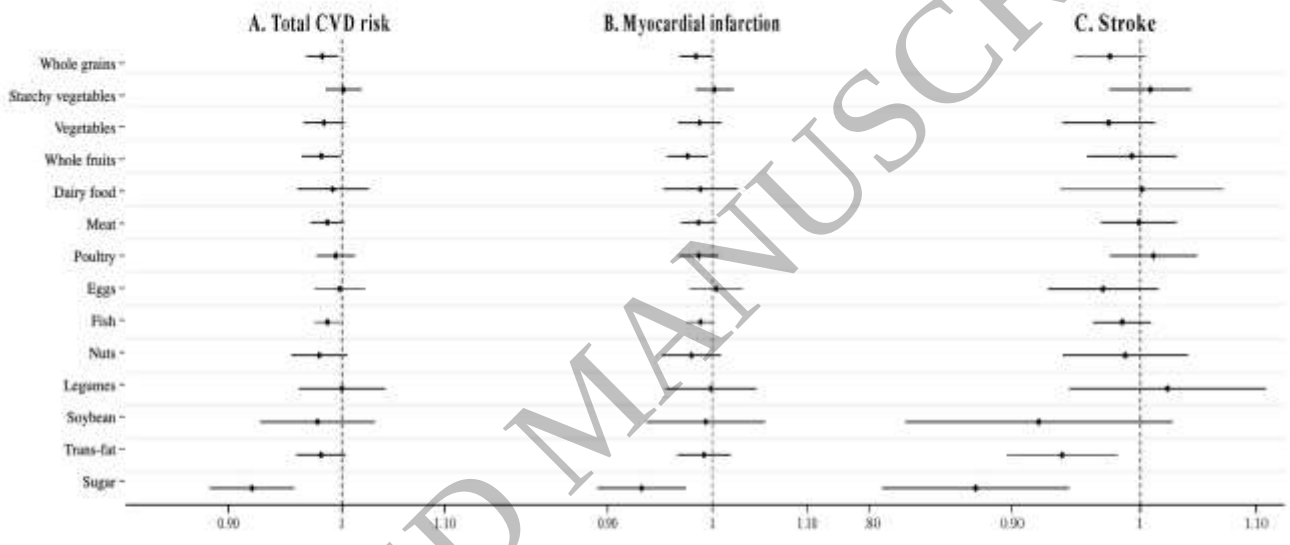
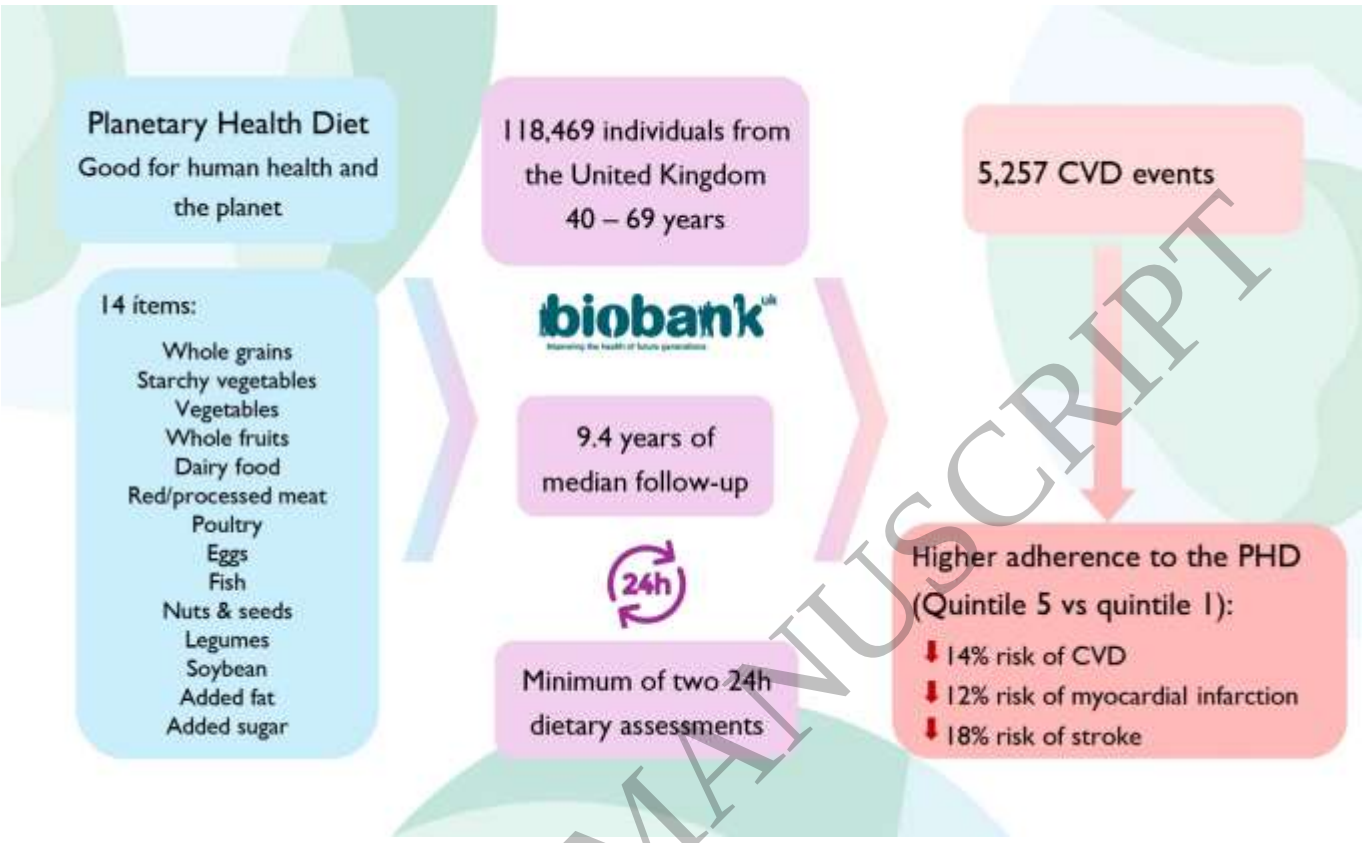


Figure 1. Hazard ratios (95% CI) for CVD risk per 2-point increment of each PHDI food group.

PHDI: Planetary Health Diet Index, CI: confidence interval, CVD: cardiovascular disease. Multivariable-adjusted model: for sex, age, ethnicity, education, deprivation index, region of assessment, smoking status, energy intake, physical activity, BMI, diabetes, cancer, hypertension, cholesterol-lowering medication, number of medications, and vitamin supplement use.

Figure 1
297x210 mm (x DPI)



Graphical Abstract
180x110 mm (x DPI)