Dose-Response Associations of Dietary Inflammatory Potential With Health Outcomes: A Prospective Cohort Study of 198,265 UK Biobank Participants

Frederick K. Ho, PhD[a], Michael D. Wirth, PhD[b,c], Solange Parra-Soto, MSc[a,d], Jirapitcha Boonpor, MSc[a,d,e], Ziyi Zhou, MPH[a], Fanny Petermann-Rocha, PhD[a,f], Shinya Nakada, MPH[a], Katherine M. Livingstone, PhD[g], John C. Mathers, PhD[h], Jill P. Pell, MD[a], James R. Hébert, ScD[c], and Carlos Celis-Morales, PhD[a,i*]

From the [a] School of Health and Wellbeing, University of Glasgow, Glasgow, UK, [b] College of Nursing, University of South Carolina, Columbia, SC, [c] Department of Epidemiology and Biostatistics, Cancer Prevention and Control Program, Arnold School of Public Health, University of South Carolina, Columbia, SC, [d] BHF Glasgow Cardiovascular Research Centre, Institute of Cardiovascular Medical Sciences, University of Glasgow, Glasgow, UK, [e] Faculty of Public Health, Chalermphrakiat Sakon Nakhon Province Campus, Kasetsart University, Sakon Nakhon, Thailand, [f] Facultad de Medicina, Universidad Diego Portales, Santiago, Chile, [g] Institute for Physical Activity and Nutrition, School of Exercise and Nutrition Sciences, Deakin University, Geelong, Victoria, Australia, [h] Human Nutrition Research Centre, Centre for Healthier Lives, Population Health Sciences Institute, Newcastle University, Newcastle, UK and [i] Human Performance Laboratory, Education, Physical Activity and Health Research Unit, Universidad Católica del Maule, Talca, Chile.

Objective: To investigate the dose-response associations of dietary inflammatory potential with all-cause mortality and incident cardiovascular disease (CVD) and cancer.

Data sharing statement: Data described in the manuscript, code book, and analytic code will be made available upon request to the UK Biobank https://www.ukbiobank.ac.uk/.
*Corresponding author. E-mail: Carlos.Celis@glasgow.ac.uk

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Methods: This was a prospective cohort study of 198,265 UK Biobank participants who completed at least 1 dietary assessment. A web based 24 hours recall questionnaire was used to derive the energy-adjusted dietary inflammatory index (E-DII). All-cause mortality and incident CVD and cancer ascertained from linked records.
Results: After adjusting for socio-demographic and lifestyle factors, there were J-shaped associations of E-DII with all-cause mortality and CVD, and a relatively linear association with cancer. When E-DII was <0, E-DII was not associated with any of the outcomes. When E-DII was ≥0, the linear associations were strongest in all-cause mortality (HR 1.09, 95% CI, 1.05-1.13), followed by CVD (HR 1.06, 95% CI, 1.03-1.09), and cancer (HR 1.03, 95%,CI, 1.01-1.05).
Conclusion: Dietary inflammatory potential was associated with mortality and CVD primarily when the diet is proinflammatory. (Curr Probl Cardiol 2023;48:101774.)

Introduction

Diet is a leading modifiable risk factor for the global burden of diseases.[1] However, diet is complex and multidimensional. Studies have variously shown that different levels of macronutrient intake,[2] diet quality,[3] and type of diet were all associated with mortality[4] and various major diseases, such as cardiovascular disease (CVD)[5] and cancer.[6] Identifying the underlying mechanism(s) linking diet and health outcomes may help to elucidate the key components or characteristics of diet that should form the basis of recommendations and interventions.

Since inflammation is a mechanistic driver of multiple noncommunicable diseases, the inflammatory potential of the whole diet may be associated with risk of such diseases. Some food items and macronutrients have been found to be associated with circulatory inflammatory markers, such as interleukin 6 and tumor necrosis factor alpha,[7] which could, in turn, cause major metabolic changes including insulin resistance and development of type 2 diabetes,[8] major risk factors for cardiovascular disease. Similarly, inflammation is found to be a critical component of cancer progression,[9] reinforcing the role of dietary inflammatory potential in health.

Dietary Inflammatory Index (DII) has been validated and is the most commonly used tool in assessing the inflammatory potential of diets.[10] Empirical studies were used to derive the inflammatory potential of dietary parameters, based on associations of those parameters with 6 inflammatory biomarkers. Numerous studies have shown the associations

between DII and various health outcomes, including all-cause mortality, CVD, and cancer.[11–14] However, most of the existing studies did not, or did not have sufficient power to, investigate dose-response relationships. This hinders our understanding of the optimal level of DII in relation to health risk. The existing studies also are subject to residual confounding due to socioeconomic status and/or overadjustment for potential mediators. To provide more robust evidence on whether, and to which extent, dietary inflammatory potential is associated with major health outcomes, we conducted this prospective cohort study using data from UK Biobank.

Material and Methods

UK Biobank is a prospective cohort study. A total of over 500,000 participants aged 37 to 73 years at baseline were enrolled, from the general population (representing 5.5% of those invited).[15] In brief, between 2006 and 2010, participants attended 1 of 22 assessment centers across Scotland, England and Wales.[16] All participants completed a touch-screen questionnaire, had physical measurements taken, and provided blood, urine, and saliva samples at baseline. More information about the UK Biobank protocol can be found online (http://www.ukbiobank.ac.uk).

Energy-Adjusted Dietary Inflammatory Index (E-DII)

Dietary data were collected through the Oxford WebQ, a web-based 24 hours dietary assessment tool that collects information on 206 foods and 32 beverages consumed during the past 24 hours.[17] The assessment tool asked for the previous day's intake using questions such as: "did you have any of these yesterday?" or "how much of the following did you drink yesterday?" Energy and nutrient intake were calculated using McCance and Widdowson's The Composition of Food, 5th edition.[18] Participants were invited to complete the Oxford WebQ 5 times and the average of the assessments completed was used.

The original DII includes 45 different dietary factors based on their pro- or anti-inflammatory potential, as it is described elsewhere.[10] Following the proposed scoring algorithm,[10] the 18 relevant foods and nutrients available in the UK Biobank dataset (Table S1) were used to create the DII. Overall DII score is calculated by summating all the DII scores for each of the 18 items. For E-DII, intakes are expressed per 1000 kcal/day, rather than as absolute amounts per day, and the global comparative database also uses energy-adjusted values.[19] The E-DII was

used for all the analyses in this study to avoid confounding due to energy intake and/or obesity.

Outcomes

All-cause mortality and incident (fatal and nonfatal) CVD and cancer were the outcomes of this study. Dates and causes of death were 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 admissions were identified via record linkage to Health Episode Statistics (England and Wales) and the Scottish Morbidity Record 01 (SMR01) (Scotland). Details of the linkage procedure can be found at http://content.digital.nhs.uk/services. Hospital admissions data were available until the end of September 2021 in England, July 2021 in Scotland and the February 2018 in Wales. Mortality data were available until the end of September 2021. Therefore, follow-up was censored on these dates. CVD was defined as ischemic heart disease (International Classification of Diseases, 10th revision [ICD-10]: I20-25), stroke (ICD-10: I60-64), heart failure (ICD-10: I11.0, I42.0, I42.6, I42.7, I42.9, I50), and peripheral vascular diseases (I70-73). Cancer was defined as C00-C97, excluding nonmelanoma skin cancer (C44).

Covariates

Age at baseline was determined from dates of birth and baseline assessment. Sex was self-reported at baseline. Deprivation (area-based socioeconomic status) was derived from the postcode of residence, using the Townsend score.[20] Ethnicity was self-reported and categorized as: White, Black, South Asian, Chinese, Mixed, and others. Self-reported smoking status was categorized as never, former or current smoker. Chronic conditions were self-reported in a nurse-led interview at baseline. Finally, total physical activity was self-reported using the International Physical Activity Questionnaire short form.[21] TV viewing was self-reported as the number of hours per day. Body height measured to the nearest 1 cm and weight to the nearest 0.1 kg were measured by trained nurses. Body mass index (BMI) was calculated as weight (kg) divided by height (cm) squared. Additional information on the measurements is available on the UK Biobank website (http://www.ukbiobank.ac.uk).

Ethical Approval

UK Biobank was approved by the North-West Multi-Centre Research Ethics Committee (Ref: 11/NW/0382). All participants provided written informed consent. This work was conducted under the UK Biobank application number 7155.

Statistical Analyses

Descriptive baseline characteristics by Energy-adjusted DII (E-DII)[19] quartile are presented as means with standard deviations (SD) for quantitative variables and as frequencies and percentages for categorical variables. Associations between E-DII score and outcomes were investigated using Cox proportional hazard models with penalized cubic splines to capture nonlinearity in the exposure-outcome relationship.[22] The reference point of the splines was set at E-DII = 0; that is, neutral in terms of inflammatory potential. The ranges of the E-DII values associated with the lowest HR for each outcome was identified based on when the lower boundary of the 95% confidence intervals (CI) crossed the lowest hazard ratio (HR). Based on the shape of the associations, the E-DIIs were recategorized and the HRs associated with a per-unit increase in E-DII score were estimated for the applicable ranges of E-DII.

The models were run initially adjusting for socioeconomic confounders (age, sex, ethnicity and deprivation). They were then also adjusted for lifestyle confounders factors: smoking, physical activity, and TV viewing. Finally, BMI and number of prevalent morbidities were included as covariates because they could potentially be confounders or mediators and therefore their inclusion may underestimate the true association.

Several sensitivity analyses were conducted. Firstly, the 20,565 participants in whom the outcomes of interest occurred during the first 2 years of follow-up were excluded in a landmark analysis to reduce the risk of reverse causation due to preclinical disease. Secondly, the 75,148 participants who had only 1 dietary assessment were excluded as since multiple assessments is likely to provide a more robust measure of habitual diet. Finally, the 50,666 participants who had hypertension, type 2 diabetes, chronic liver and kidney diseases, and/or inflammatory bowel disease at baseline were excluded as these conditions could alter participants' dietary intake.

The consistency of the associations also was examined across subgroups: age ($<$ or $\geq$ 60 years), sex (female or male), ethnicity (White or non-White), Townsend deprivation score ($<$ or $\geq$ median). All analyses were conducted using R 4.2.0 with the survival package. The proportional

hazard assumption was checked using Schoenfeld residuals. A *P*-value below 0.05 was considered statistically significant.

Results

Of the 502,413 participants in UK Biobank, 201,984 were excluded as they had not completed any of the 5 dietary assessments. A further 3719 were excluded as their reported dietary data were not plausible, defined as a total energy intake <1.1 or >2.5 times basal metabolic rate, estimated using the Henry equation.[23] Therefore, 198,265 participants were included in the primary analyses. In sensitivity analyses, 20,565, 76,148, and 50,666 were excluded due to events in the first 2 years, completing only 1 dietary assessment, and having prevalent chronic conditions at baseline respectively (Fig 1).

Participants characteristics are shown in Table 1. Generally proinflammatory diets were more common in participants who were younger, male, lived in neighborhoods with higher deprivation index, and who smoked at baseline. They also tend to have less physical activity, viewed more TV, and had higher BMI and slightly higher prevalence of the chronic conditions at baseline.

Crude incidence rates are shown in Supplementary Table 2. Compared to participants who had anti-inflammatory diets, those with proinflammatory diets had a higher all-cause mortality rate (39.9 vs 47.6 per 10,000), and CVD (79.0 vs 92.0 per 10,000) and cancer (116.8 vs 121.3 per 10,000) incidence.

The findings from the primary analyses are shown in Figure 2. After adjusting for socio-demographic and lifestyle factors, there were nonlinear associations of E-DII with all-cause mortality and incident CVD, and a relatively linear association with cancer. The minimum risk were observed for E-DII < -1 for all-cause mortality, E-DII <0.5 for incident CVD and E-DII < -2 for incident cancer. Across all-cause-mortality and incident CVD, the associations were strongest for E-DII ≥0. In fact, for E-DII <0, the associations across all outcomes were not significant (Table 2). When E-DII ≥0, the linear associations were strongest for all-cause mortality (HR 1.09, 95% CI, 1.05-1.13), followed by incident CVD (HR 1.06, 95% CI, 1.03-1.09), and incident cancer (HR 1.03, 95% CI, 1.01-1.05).

The linear associations for E-DII ≥0 were broadly consistent when total energy intake, BMI, and number of chronic conditions were included as covariates, in the 2 years landmark analysis, and when participants with only 1 dietary assessment or any chronic conditions were excluded (Table 3). They also were consistent across age and deprivation subgroups. The associations with mortality and incident CVD appeared

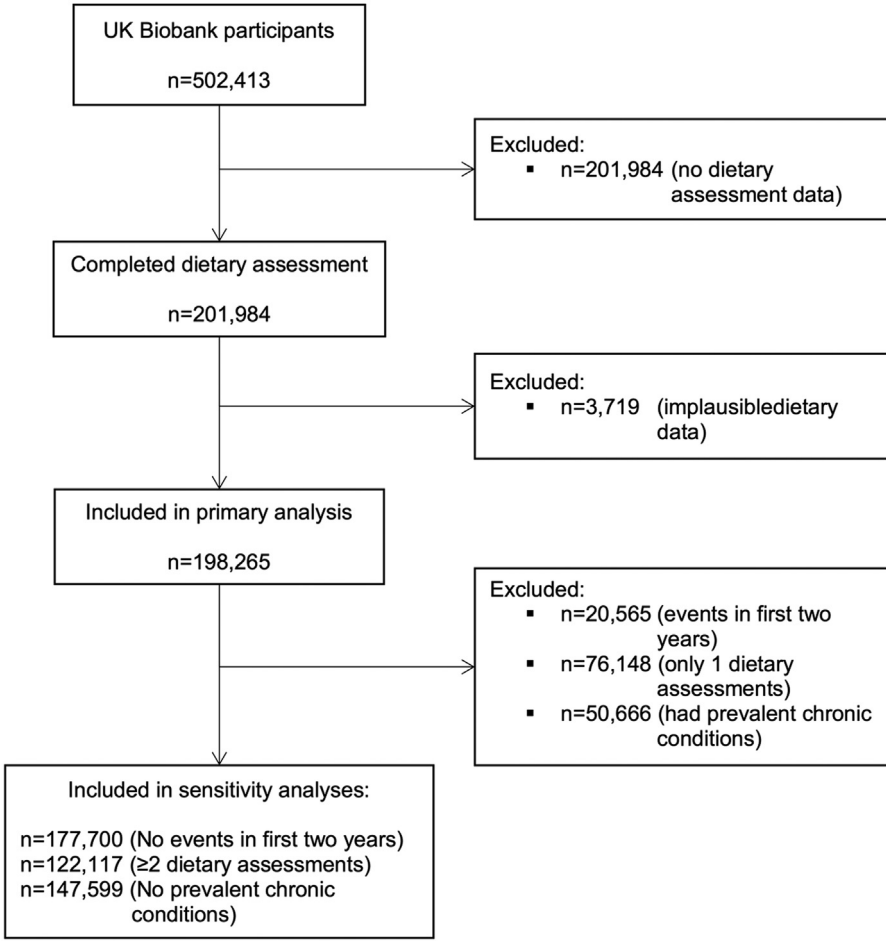

FIG 1. Flowchart of participant inclusion. Chronic conditions include hypertension, type-2 diabetes, chronic liver disease, chronic kidney disease, inflammatory bowel disease.

stronger in women and were nonsignificant in non-White participants. The nonlinear associations were also consistent in different adjustment and sensitivity analysis (Supplementary Fig 1).

Discussion

Principal Findings

This prospective cohort study showed consistent associations between dietary inflammatory potential and mortality, incident CVD and cancer.

TABLE 1. Participant characteristics

		Energy-adjusted Dietary Inflammatory Index			
	Overall	**Q1: −3.0 to −1.2**	**Q2: >−1.2 to −0.2**	**Q3: >−0.2 to 0.7**	**Q4 >0.7**
Number of participants	198,265	49,567	49,566	49,566	49,566
Age, mean (SD), years	56.14 (7.94)	56.98 (7.62)	56.54 (7.84)	55.90 (8.01)	55.14 (8.16)
Male	87,340 (44.1)	15,881 (32.0)	20,799 (42.0)	23,812 (48.0)	26,848 (54.2)
Ethnicity					
White	189,863 (95.8)	47,326 (95.5)	47,712 (96.3)	47,538 (95.9)	47,287 (95.4)
South Asian	2515 (1.3)	751 (1.5)	568 (1.1)	574 (1.2)	622 (1.3)
Black	2145 (1.1)	551 (1.1)	425 (0.9)	513 (1.0)	656 (1.3)
Chinese	538 (0.3)	137 (0.3)	130 (0.3)	130 (0.3)	141 (0.3)
Mixed	1167 (0.6)	262 (0.5)	252 (0.5)	310 (0.6)	343 (0.7)
Others	2037 (1.0)	540 (1.1)	479 (1.0)	501 (1.0)	517 (1.0)
Deprivation index, mean (SD)	−1.61 (2.85)	−1.69 (2.81)	−1.72 (2.78)	−1.64 (2.83)	−1.37 (2.97)
Smoking					
Never	112,628 (56.8)	28,934 (58.4)	28,884 (58.3)	28,067 (56.6)	26,743 (54.0)
Previous	70,405 (35.5)	18,088 (36.5)	17,637 (35.6)	17,636 (35.6)	17,044 (34.4)
Current	15,232 (7.7)	2545 (5.1)	3045 (6.1)	3863 (7.8)	5779 (11.7)
Physical activity, mean (SD), MET-min/week	2507.08 (2109.52)	2703.97 (2156.90)	2497.36 (2058.64)	2428.00 (2068.54)	2398.98 (2138.85)
TV viewing, mean (SD), hr/d	2.54 (1.46)	2.42 (1.40)	2.47 (1.41)	2.55 (1.44)	2.72 (1.56)
Total energy intake, mean (SD), kcal	2116.26 (549.70)	1924.63 (486.85)	2081.26 (508.64)	2184.85 (540.20)	2274.29 (594.56)
BMI, mean (SD), kg/m^2	26.83 (4.54)	26.35 (4.43)	26.62 (4.39)	26.91 (4.50)	27.44 (4.76)
Underweight	316 (0.2)	100 (0.2)	69 (0.1)	73 (0.1)	74 (0.1)
Normal weight	75,146 (37.9)	21,135 (42.7)	19,616 (39.6)	18,250 (36.8)	16,145 (32.6)
Overweight	82,769 (41.8)	19,736 (39.8)	20,683 (41.7)	21,093 (42.6)	21,257 (42.9)
Obese	39,969 (20.2)	8579 (17.3)	9188 (18.5)	10,132 (20.4)	12,070 (24.4)
Chronic conditions at baseline					
Total number, mean (SD)	1.09 (1.13)	1.09 (1.13)	1.08 (1.13)	1.07 (1.12)	1.11 (1.16)
Hypertension	46,459 (23.4)	11,492 (23.2)	11,565 (23.3)	11,651 (23.5)	11,751 (23.7)
Type 2 diabetes	7119 (3.6)	1764 (3.6)	1742 (3.5)	1773 (3.6)	1840 (3.7)
Chronic liver disease	328 (0.2)	70 (0.1)	92 (0.2)	78 (0.2)	88 (0.2)
Chronic kidney disease	474 (0.2)	120 (0.2)	112 (0.2)	106 (0.2)	136 (0.3)
Inflammatory bowel disease	1640 (0.8)	293 (0.6)	409 (0.8)	400 (0.8)	538 (1.1)

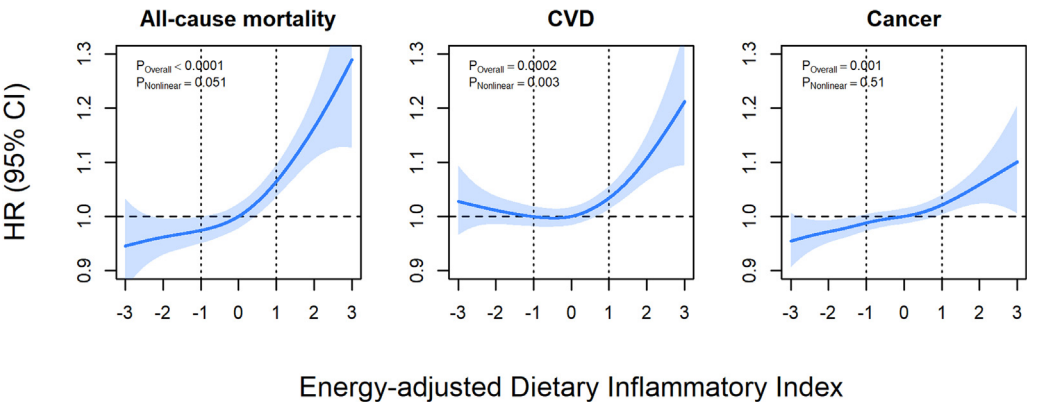

FIG 2. Association between E-DII and health outcomes. Adjusted for age, sex, ethnicity, deprivation, smoking, physical activity, and TV viewing Vertical dotted lines indicate the previous categorization on anti-inflammatory (E-DII < -1), neutral (-1 ≤ E-DII ≤ 1), and proinflammatory (E-DII > 1) Blue-shaded area indicates 95% confidence band Grey-shaded polygons indicate the ranges of E-DII where the associated HRs were the lowest.

TABLE 2. Linear association between E-DII and health outcomes by ranges of E-DII

	E-DII < 0		E-DII ≥ 0	
	HR (95% CI)	***P***	**HR (95% CI)**	***P***
All cause-mortality	1.01 (0.98-1.04)	0.44	1.09 (1.05-1.13)	<0.0001
CVD	0.99 (0.97-1.01)	0.15	1.06 (1.03-1.09)	<0.0001
Cancer	1.01 (1.00-1.03)	0.17	1.03 (1.01-1.05)	0.01

Adjusted for age, sex, ethnicity, deprivation, smoking, physical activity, and TV viewing.

The associations with all-cause mortality and incident CVD were observed only for diets that were more proinflammatory than the global average (E-DII = 0). In contrast, the association with incident cancer was broadly linear. These associations were consistent across a wide range of sensitivity analyses, adding confidence in their robustness. If these associations are indeed causal, anti-inflammatory or, at least, neutral diets may minimize diet-related disease risk.

Strengths and Limitations

There are several key strengths of the current study. To our knowledge, this is the first study that illustrated the nonlinearity in the associations between dietary inflammatory potential and mortality and incident CVD. The findings demonstrated that the differences in risk were strongest between a proinflammatory diet (E-DII > 1) and a neutral diet (-1 ≤ E-DII ≤1), whilst the differences between a neutral and anti-inflammatory diet (E-DII < -1) were very small for mortality, and nonsignificant for incident CVD.

More importantly, utilizing the wealth of variables available in UK Biobank, we were able to conduct a comprehensive set of sensitivity analyses, showing that the findings were robust regardless of adjustment and exclusion. Reverse causation was minimized by using a 2 years landmark analysis. However, as with any observational study, we could not confirm causality due to potential residual confounding and reverse causation. Future randomized controlled trials would be required. It should be noted that UK Biobank is not representative of the UK population in relation to lifestyle, and prevalent diseases. However, previous studies have shown exposure-outcome associations estimated from UK Biobank to be consistent with population representative cohorts.[24] Last but not least, the E-DII was based on self-reported dietary data with only a limited number of food items, so inaccuracies are possible. The number of food parameters used to generate the E-DII was also fewer than most previous

TABLE 3. Sensitivity and subgroup analyses for the association between E-DII and all-cause mortality in the range of E-DII $\geq$ 0

	All-cause mortality		CVD incidence		Cancer incidence	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Primary analysis	1.09 (1.05-1.13)	<0.0001	1.06 (1.03-1.09)	< 0.0001	1.03 (1.01-1.05)	0.01
Additionally adjusted for:						
Total energy intake	1.09 (1.05-1.13)	<0.0001	1.06 (1.03-1.09)	< 0.0001	1.03 (1.00-1.05)	0.02
BMI	1.08 (1.04-1.12)	<0.0001	1.05 (1.02-1.07)	0.0006	1.03 (1.00-1.05)	0.02
Number of chronic conditions	1.08 (1.04-1.12)	<0.0001	1.05 (1.02-1.08)	0.0002	1.03 (1.00-1.05)	0.02
Excluded participants with:						
Events in the first 2 years	1.08 (1.04-1.12)	<0.0001	1.05 (1.03-1.08)	0.0002	1.03 (1.00-1.05)	0.02
Only 1 dietary assessment	1.10 (1.04-1.15)	0.0002	1.05 (1.01-1.09)	0.007	1.04 (1.01-1.07)	0.02
Chronic conditions	1.10 (1.05-1.15)	<0.0001	1.07 (1.03-1.11)	< 0.0001	1.03 (1.00-1.06)	0.048
Subgroup analyses						
Age <60 years	1.10 (1.04-1.17)	0.002	1.07 (1.02-1.11)	0.002	1.03 (0.99-1.07)	0.10
Age ≥60 years	1.08 (1.03-1.13)	0.0004	1.05 (1.02-1.09)	0.002	1.03 (1.00-1.06)	0.03
Male	1.07 (1.02-1.12)	0.003	1.04 (1.01-1.07)	0.02	1.03 (1.00-1.06)	0.05
Female	1.13 (1.06-1.19)	<0.0001	1.10 (1.05-1.15)	< 0.0001	1.03 (1.00-1.07)	0.07
Ethnic White	1.09 (1.06-1.13)	<0.0001	1.06 (1.03-1.09)	< 0.0001	1.03 (1.00-1.05)	0.02
Ethnic non-White	0.89 (0.72-1.10)	0.28	0.98 (0.86-1.11)	0.74	1.12 (0.98-1.27)	0.10
Less deprived	1.07 (1.02-1.13)	0.007	1.06 (1.02-1.10)	0.003	1.03 (1.00-1.07)	0.04
More deprived	1.09 (1.05-1.15)	0.0001	1.06 (1.02-1.10)	0.002	1.02 (0.99-1.06)	0.13

Adjusted for age, sex, ethnicity, deprivation, smoking, physical activity, and TV viewing unless otherwise specified.
Chronic conditions include hypertension, type-2 diabetes, chronic liver disease, chronic kidney disease, inflammatory bowel disease

studies,[25,26] which could reduce precision of the estimates. These factors appear to be more likely to cause nondifferential misclassification bias (i.e. no systematic factor linking reporting error and E-DII), resulting in a more conservative estimate.

Comparison With Other Studies

An association between dietary inflammatory potential and CVD has been consistently reported in previous studies. A 2018 meta-analysis of 14 studies conducted on 152,986 participants demonstrated a significant higher CVD risk (OR 1.36, 95% CI, 1.19-1.57) among individuals in the lowest DII category compared to those in the highest DII category.[13] However, heterogeneity was high ($I^2 = 65\%$) and many studies were subject to residual confounding (eg, no adjustment for socioeconomic status) or overadjustment (eg, adjustment for biomarkers of disease).[27] A subgroup analysis of the meta-analysis confirmed that adjustment for socioeconomic status substantially attenuated the effect size. Another, slightly more recent, meta-analysis focused on cohort studies reported similar findings,[12] but there was significant asymmetry in the funnel plot, suggesting publication bias.

Similarly there have been meta-analyses of the association between DII and cancer outcomes[14,28] but only 6 of the included studies were based on prospective data and only 1 smaller (n = 6542) prospective study reported overall cancer as an outcome. Interestingly, the meta-analyses did not include tests for publication bias. One meta-analysis reported a nonlinear association between DII and colorectal cancer.[11] In contrast to our findings, they showed that the association was relatively flat when DII $<$ -1. However, it should be noted that dose-response estimation from meta-analysis is subject to both within- and between-study confounding.

Another meta-analysis of prospective studies examined the association between DII and all-cause mortality.[29] The investigators used the data from 2 cohorts (25,356 participants and 532 deaths) to explore the dose-response relationship. The meta-analysis using categorized DII data showed again a significant association between DII and all-cause mortality, albeit from a pooled estimate derived from highly heterogeneous studies ($I^2 = 71.3\%$).

The current study meaningfully extends the existing evidence base with a larger sample size than some of the meta-analyses, comprehensive and carefully considered adjustment models, and a set of rigorous sensitivity analyses, all of which reduce the risk of bias. More importantly,

none of the previous studies have investigated the nonlinearity of the association, and identified the potential optimal level of DII, with regard to CVD risk. This study showed that a neutral diet ($-1 \leq$ E-DII ≤ 1) may be sufficient to minimize CVD risk. As a single study, there would also be no between-study confounding in estimating dose-response association.

Conclusions

Our findings corroborate existing meta-analyses that suggest proinflammatory diets are associated with higher risk of all-cause mortality, and incident CVD and cancer. However, our findings also suggest that adoption of a highly anti-inflammatory diet – difficult to achieve and maintain at the population level – may not be necessary to reduce the risk of all-cause mortality and incident CVD. A slightly anti-inflammatory diet might be sufficient to minimize the risk of all-cause death, whilst avoidance of a proinflammatory diet might be sufficient to minimize the risk of CVD. These findings need to be corroborated in future randomized controlled trials.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cpcardiol.2023.101774.

REFERENCES

1. Murray CJ, Aravkin AY, Zheng P, et al. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020;396(10258):1223–49.

2. Ho FK, Gray SR, Welsh P, et al. Associations of fat and carbohydrate intake with cardiovascular disease and mortality: prospective cohort study of UK Biobank participants. *BMJ* 2020:368.
3. Petermann-Rocha F, Ho FK, Foster H, et al. Nonlinear associations between cumulative dietary risk factors and cardiovascular diseases, cancer, and all-cause mortality: a prospective cohort study from UK Biobank. *Mayo Clin Proc* 2021;96(9):2418–31.
4. Dehghan M, Mente A, Zhang X, et al. Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. *The Lancet* 2017;390(10107):2050–62.
5. Petermann-Rocha F, Parra-Soto S, Gray S, et al. Vegetarians, fish, poultry, and meat-eaters: who has higher risk of cardiovascular disease incidence and mortality? A prospective study from UK Biobank. *Eur Heart J* 2021;42(12):1136–43.
6. Parra-Soto S, Ahumada D, Petermann-Rocha F, et al. Association of meat, vegetarian, pescatarian and fish-poultry diets with risk of 19 cancer sites and all cancer: findings from the UK Biobank prospective cohort study and meta-analysis. *BMC Med* 2022;20(1):1–16.
7. Esposito K, Giugliano D. Diet and inflammation: a link to metabolic and cardiovascular diseases. *Eur Heart J* 2006;27(1):15–20.
8. Kern PA, Ranganathan S, Li C, Wood L, Ranganathan G. Adipose tissue tumor necrosis factor and interleukin-6 expression in human obesity and insulin resistance. *Am J Physiol Endocrinol Metab* 2001;280:E745–51.
9. Hanahan D. Hallmarks of cancer: new dimensions. *Cancer Discov* 2022;12(1):31–46.
10. Shivappa N, Steck SE, Hurley TG, Hussey JR, Hébert JR. Designing and developing a literature-derived, population-based dietary inflammatory index. *Public Health Nutr* 2014;17(8):1689–96.
11. Jayedi A, Emadi A, Shab-Bidar S. Dietary inflammatory index and site-specific cancer risk: a systematic review and dose-response meta-analysis. *Adv Nutr* 2018;9 (4):388–403.
12. Ji M, Hong X, Chen M, Chen T, Wang J, Zhang N. Dietary inflammatory index and cardiovascular risk and mortality: a meta-analysis of cohort studies. *Medicine* 2020;99(20).
13. Shivappa N, Godos J, Hébert JR, et al. Dietary inflammatory index and cardiovascular risk and mortality—a meta-analysis. *Nutrients* 2018;10(2):200.
14. Syed Soffian SS, Mohammed Nawi A, Hod R, et al. Meta-analysis of the association between dietary inflammatory index (DII) and colorectal cancer. *Nutrients* 2022;14 (8):1555.
15. Collins R. What makes UK Biobank special? *Lancet* 2012;379(9822):1173–4.
16. 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(3):e1001779.
17. Greenwood DC, Hardie LJ, Frost GS, et al. Validation of the Oxford WebQ online 24-hour dietary questionnaire using biomarkers. *Am J Epidemiol* 2019;188(10):1858–67.
18. McCance RA, Widdowson EM. McCance and Widdowson's the Composition of Foods. London: Royal Society of Chemistry; 2014.

19. Hebert JR, Shivappa N, Wirth MD, Hussey JR, Hurley TG. Perspective: the Dietary Inflammatory Index (DII®): lessons learned, improvements made and future directions. *Adv Nutr* 2019;10(2):185–95.
20. Townsend P PM, Beattie A. Health and deprivation. Inequality and the North. *Health Policy (New York)* 1988;10(207).
21. Guo W, Bradbury KE, Reeves GK, Key TJ. Physical activity in relation to body size and composition in women in UK Biobank. *Ann Epidemiol* 2015;25(6):406–13.e6.
22. Govindarajulu US, Malloy EJ, Ganguli B, Spiegelman D, Eisen EA. The comparison of alternative smoothing methods for fitting non-linear exposure-response relationships with Cox models in a simulation study. *Int J Biostat* 2009;5(1):Article 2.
23. Henry C. Basal metabolic rate studies in humans: measurement and development of new equations. *Public Health Nutr* 2005;8(7a):1133–52.
24. Fry A, Littlejohns TJ, Sudlow C, et al. Comparison of Sociodemographic and health-related characteristics of UK Biobank participants with those of the general population. *Am J Epidemiol* 2017;186(9):1026–34.
25. Shivappa N, Wirth MD, Murphy EA, Hurley TG, Hébert JR. Association between the Dietary Inflammatory Index (DII) and urinary enterolignans and C-reactive protein from the National Health and Nutrition Examination Survey-2003−2008. *Eur J Nutr* 2019;58(2):797–805.
26. Mazidi M, Shivappa N, Wirth MD, et al. Dietary inflammatory index and cardiometabolic risk in US adults. *Atherosclerosis* 2018;276:23–7.
27. Schisterman EF, Cole SR, Platt RW. Overadjustment bias and unnecessary adjustment in epidemiologic studies. *Epidemiology* 2009;20(4):488.
28. Fowler ME, Akinyemiju TF. Meta-analysis of the association between dietary inflammatory index (DII) and cancer outcomes. *Int J Cancer* 2017;141(11):2215–27.
29. Garcia-Arellano A, Martínez-González MA, Ramallal R, et al. Dietary inflammatory index and all-cause mortality in large cohorts: the SUN and PREDIMED studies. *Clin Nutr* 2019;38(3):1221–31.