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Change in the inflammatory potential of diet over 10 years and subsequent mortality: the Multiethnic Cohort Study

Song-Yi Park[1]*, Chloe P. Lozano[1,2], Yurii B. Shvetsov[1], Carol J. Boushey[1], Michael D. Wirth[3,4,5], Nitin Shivappa[4,5], James R. Hébert[4,5], Christopher A. Haiman[6], Lynne R. Wilkens[1] and Loïc Le Marchand[1]

[1]*Cancer Epidemiology Program, University of Hawaii Cancer Center, Honolulu, HI, USA*
[2]*Ingestive Behavior, Weight Management & Health Promotion Laboratory, Pennington Biomedical Research Center, Baton Rouge, LA, USA*
[3]*College of Nursing, University of South Carolina, Columbia, SC, USA*
[4]*Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC, USA*
[5]*Connecting Health Innovations LLC, Columbia, SC, USA*
[6]*Department of Population and Public Health Sciences, Keck School of Medicine and Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA, USA*

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Abstract

Dietary inflammatory potential assessed by the Dietary Inflammatory Index (DII®) has been associated with health outcomes. However, longitudinal changes in the DII in relation to health outcomes rarely have been studied. This study aimed to examine change in the DII score over 10 years and its association with subsequent mortality in the Multiethnic Cohort. The analysis included 56 263 African American, Japanese American, Latino, Native Hawaiian and White participants who completed baseline (45–75 years) and 10-year follow-up surveys, including a FFQ. Mean energy-adjusted DII (E-DII) decreased over 10 years in men (from −0·85 to −1·61) and women (from −1·80 to −2·47), reflecting changes towards a more anti-inflammatory diet. During an average follow-up of 13·0 years, 16 363 deaths were identified. In multivariable Cox models, compared with anti-inflammatory stable individuals, risk of all-cause mortality was increased with pro-inflammatory change in men (hazard ratio (HR) = 1·13, 95 % CI 1·03, 1·23) and women (HR = 1·22, 95 % CI 1·13, 1·32). Per one-point increase in E-DII score over time, HR was 1·02 (95 % CI 1·00, 1·03) for men and 1·06 (95 % CI 1·04, 1·07) for women (*P* for heterogeneity < 0·001). While no heterogeneity by race and ethnicity was observed for men, the increased risk per one-point increase among women was stronger in non-Whites than in Whites (*P* for heterogeneity = 0·004). Our findings suggest that a change towards a more pro-inflammatory diet is associated with an increased risk of mortality both in men and women, and that the association is stronger in women, especially non-White women, than in men.

Key words: **Cohort: Dietary change: Dietary Inflammatory Index: Mortality: Multiethnic population**

Chronic inflammation plays a role in the development of non-communicable diseases, including CVD and cancer[1]. Diet is recognised as an important modulator of chronic inflammation[2]. Thus, pro- or anti-inflammatory properties of dietary components have been examined in relation to disease outcomes[3,4]. Given the complexity of the food combinations people consume, evaluating the overall inflammatory potential of the diet provides more intuitive results compared with individual dietary components in terms of disease and mortality risk prediction[1]. The Dietary Inflammatory Index (DII®) is a literature-derived diet quality score, developed to assess the inflammatory potential of an individual's overall diet[5]. The evidence is growing that dietary inflammatory potential assessed by the DII is associated with health outcomes[6–12]. However, longitudinal changes in the DII in relation to disease and mortality rarely have been studied, especially in racially/ethnically diverse populations. In a cohort of women with a majority of White participants, studies examining DII change over 3 years reported no association for overall breast cancer risk[13] but an increased risk of proximal colon cancer with a pro-inflammatory change[14].

Previously, we found in the Multiethnic Cohort (MEC) that a higher inflammatory potential of diet at cohort entry, assessed

Abbreviations: DII, Dietary Inflammatory Index; E-DII, energy-adjusted Dietary Inflammatory Index; HR, hazard ratio; MEC, Multiethnic Cohort; QFFQ, quantitative FFQ.

* **Corresponding author:** Song-Yi Park, email spark@cc.hawaii.edu

using the DII, was associated with an elevated risk of all-cause, CVD and cancer mortality overall and in most racial and ethnic groups[15]. In the current study, we examined change in DII scores after reassessing diet at 10 years from baseline and its association with subsequent all-cause, CVD and cancer mortality by sex and race/ethnicity in the MEC.

Methods

Study population

The MEC was designed to study lifestyle and genetic factors in relation to cancer and other chronic diseases[16]. Between 1993 and 1996, more than 215 000 men and women aged 45–75 years and living in Hawaii or California were enrolled in MEC by completing a twenty-six-page mailed questionnaire on diet, medical history and lifestyle. Participants were mainly African American, Japanese American, Latino, Native Hawaiian or White and were recruited through targeted strategies. This study was conducted according to guidelines in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Institutional Review Boards at the University of Hawaii and the University of Southern California. The Institutional Review Boards considered that informed consent was implied by the return of the baseline questionnaire that was mailed to potential participants along with a cover letter explaining the study. Between 2003 and 2008, all participants who were alive (~89 %) were contacted for the 10-year follow-up and 98 214 of them repeated the comprehensive questionnaire. For the current analysis, we excluded participants who did not self-identify as one of the five major racial and ethnic groups (n 5265) or who reported implausible dietary data based on total energy intake or its components at cohort entry or follow-up survey (n 5928). Specifically, we calculated a robust standard deviation (SD) for the truncated normal distribution for the middle 80 % of the log energy distribution (after excluding the top and bottom 10 % tails). Then, we excluded all individuals with energy values beyond the ranges of the mean ± 3 robust SD. We applied similar approaches to exclude individuals with extreme fat, protein or carbohydrate intakes[17]. We further excluded participants who had prior heart disease or cancer at either survey (n 23 833) or had missing data on BMI or smoking at the follow-up survey (n 6925). Thus, data from a total of 56 263 men and women were included in this analysis. Online Supplementary Fig. S1 shows a flow diagram of study population and sample size.

Dietary assessment

Dietary intake was assessed at baseline and 10-year follow-up by a quantitative FFQ (QFFQ) as part of the comprehensive twenty-six-page questionnaire (available at https://www.uhcancercenter.org/mec). To estimate usual intake for over 180 food items during the past 12 months, the baseline QFFQ was developed from 3-d measured food records completed by approximately sixty men and women from each main racial/ethnic group[16]. Daily intakes of foods and nutrients were calculated using a food composition table specific to the MEC. A calibration study within the MEC showed satisfactory Pearson Product Moment correlations for nutrients as energy densities (0·57–0·74) between the QFFQ and three 24-h recalls for all ethnic and sex groups being studied[18]. For the 10-year follow-up survey, the QFFQ was updated with new food products and written examples for each food item. In a second calibration study, correlations between the baseline and 10-year follow-up QFFQ were high for nutrient densities (0·70–0·74).

Dietary Inflammatory Index

The DII was developed and validated to determine an inflammatory effect score, based on nearly 2000 peer-reviewed articles published through 2010 on the association between diet and six inflammatory markers (i.e. C-reactive protein, IL-1β, IL-4, IL-6, IL-10 and TNF-α)[5,19]. A total of forty-five food components were identified as having sufficiently robust evidence linking them to at least one of the six markers. For the MEC, twenty-eight of the forty-five components were available for inclusion in the DII calculation: carbohydrate; protein; total fat; saturated, monounsaturated, and polyunsaturated fats; ω-3 and ω-6 FA; alcohol; fibre; cholesterol; vitamins A, B_6, B_{12}, C, D and E; thiamin; riboflavin; niacin; Fe; Mg; Zn; Se; folate; β-carotene; isoflavones; and caffeine[20]. Intake from foods only, not from supplements, was used in the DII calculation. The DII was standardised to its current range with the use of dietary intake from surveys or studies conducted in eleven countries. A z-score was created for each component for each participant and then converted to a centred proportion score. For these analyses, DII calculations are based on the energy density of each component (intake per 4184 kJ (1000 kcal)), also known as the energy-adjusted DII (E-DII™)[20]. As for the DII, a higher E-DII score indicates a more pro-inflammatory diet, and a lower score indicates a more anti-inflammatory diet.

To determine the role of patterns of change in the inflammatory potential of diet over time in mortality risk, we applied Tabung *et al.*'s categorisation, first used in the Women's Health Initiative[13,14], to facilitate comparison of results across studies. We categorised E-DII scores at cohort entry and the 10-year follow-up surveys into sex-specific quintiles based on the distribution at cohort entry. We then further categorised change in E-DII scores between surveys based on change between sex-specific quintiles as follows:

1. Anti-inflammatory stable: quintile 1 or 2 at both surveys, or change from quintile 3 to quintile 2.
2. Anti-inflammatory change: downward change of at least 2 quintiles.
3. Neutral inflammation stable: changes from quintile 2 to quintile 3 or from quintile 4 to quintile 3 or stable at quintile 3 at both surveys.
4. Pro-inflammatory change: upward change of at least 2 quintiles.
5. Pro-inflammatory stable: quintile 4 or quintile 5 at both surveys, or change from quintile 3 to quintile 4.

We also examined change in E-DII scores as a continuous variable, which was computed by subtracting E-DII at cohort entry from E-DII at 10-year follow-up.

Outcome ascertainment

Deaths among MEC participants were identified through linkage to death certificate files in Hawaii and California and the National Death Index through 31 December 2019. Causes of death were classified according to the International Classification of Diseases, 9th (ICD-9) and 10th revision (ICD-10) into CVD (ICD-9 codes 390–434, 436–448; ICD-10 codes I00-I78) and cancer (ICD-9 codes 140–208; ICD-10 codes C00-C97). During a mean follow-up of 13·0 (SD 3·5) years since the 10-year follow-up survey, a total of 16 363 deaths, including 3807 CVD and 3650 cancer deaths, were identified among the eligible participants.

Statistical analysis

A Cox proportional hazards model, with age as the time metric, was used to estimate hazard ratios (HR) and 95 % confidence intervals (CI) of mortality risk according to the E-DII change in men and women separately. For the E-DII change patterns, the anti-inflammatory stable group served as a reference category. The E-DII change also was modelled as a continuous variable to estimate HR of mortality per one-point increase in the E-DII score change. Basic models were adjusted for age at 10-year follow-up and race/ethnicity as covariates. The E-DII change was also fit as a continuous variable with adjustment for baseline E-DII score. For fully adjusted models, we used a comprehensive smoking model developed for lung cancer studies in the MEC[21], because smoking is related to both diet quality and mortality outcome. The model included smoking status (never, former, current), average number of cigarettes, squared average number of cigarettes, number of years smoked (time dependent), number of years since quitting (time dependent) and interactions of race/ethnicity with smoking status, with average number of cigarettes, with squared average number of cigarettes and with number of years smoked. We further adjusted for BMI (< 25, 25–29·9, ≥ 30 kg/m^2) and history of diabetes (yes, no) as strata variables, education (≤ 12, 13–15, ≥ 16 years, missing), marital status (married, not married, missing), moderate-to-vigorous physical activity (< 0·5, 0·5–< 1·3, ≥ 1·3 h/d, missing), alcohol intake (g/d), total energy intake (kcal/d) and menopausal hormone therapy use (never, ever, missing) for women only as covariates. The proportional hazards assumption was verified by Schoenfeld residuals[22]. We also ran the models for each race/ethnicity separately. Tests for heterogeneity by sex and race/ethnicity were based on Wald statistics for interaction terms of the E-DII change (continuous) and subgroup indicator. In sensitivity analyses, we removed deaths (*n* 910) that occurred within 2 years after the 10-year follow-up survey. We also examined a possible non-linear relationship between E-DII change and subsequent mortality non-parametrically with restricted cubic splines[23]. All analyses were performed using SAS statistical software version 9.4 (SAS Institute Inc.).

Results

Over 10 years, mean E-DII scores decreased in both men (–0·85 to −1·61) and women (–1·80 to −2·47) and in all racial/ethnic groups within sexes reflecting changes towards a more anti-inflammatory diet (Table 1). Among men, Whites had the lowest E-DII scores at both the baseline and 10-year follow-up surveys ($P < 0·001$). In women, Japanese Americans had the lowest mean scores at both surveys ($P < 0·001$). Japanese Americans and Native Hawaiians showed the largest decrease over time in both men and women ($P < 0·001$).

Compared with anti-inflammatory stable participants over the 10 years, pro-inflammatory stable individuals were more likely at baseline to be younger, Latino or Native Hawaiian, less educated, current smokers, be less physically active, have a higher BMI and to drink more alcoholic beverages. Results were consistent across both sexes, and women with higher E-DII scores were less likely to use menopausal hormone therapy (Table 2). Compared to participants with anti-inflammatory change in diet over time, those with pro-inflammatory change were more likely to be older, African American or White, less physically active and to drink more alcoholic beverages, findings that were consistent in both men and women.

In men, compared with anti-inflammatory stable individuals, those in all other groups showed a significantly higher risk of all-cause mortality, after adjustment for age and race/ethnicity (Table 3). After considering all potential confounders, the increased risk remained significant for the pro-inflammatory change (HR = 1·13, 95 % CI 1·03, 1·23) and pro-inflammatory stable (HR = 1·09, 95 % CI 1·02, 1·16) groups. Similarly, in women, pro-inflammatory change (HR = 1·22, 95 % CI 1·13, 1·32) and pro-inflammatory stable (HR = 1·12, 95 % CI 1·06, 1·20) groups had an increased risk in all-cause mortality in the fully adjusted model. Per one-point increase in E-DII scores over 10 years (change towards a more pro-inflammatory diet), the risk of all-cause mortality was higher in women (HR = 1·06, 95 % CI 1·04, 1·07) than in men (HR = 1·02, 95 % CI 1·00, 1·03, *P* for heterogeneity by sex < 0·001). This pattern also was observed for CVD mortality. Pro-inflammatory change in both men and women and being in the pro-inflammatory stable group in women were associated with an increased risk in CVD mortality in the fully adjusted model. The increase in risk in CVD mortality per one-point increase was higher in women than in men (*P* for heterogeneity by sex = 0·021). For cancer mortality, after adjusting for covariates, women in the pro-inflammatory stable group showed an increased risk. In the sensitivity analysis excluding deaths within the first 2 years of follow-up, the results remained similar. Based on non-parametric restricted cubic splines (online Supplementary Fig. S2), the relationship between E-DII change in score and subsequent mortality in men was linear for all-cause mortality (*P* for linearity = 0·013), while the non-linear components were not significant; there was no significant non-linear or linear relationship for CVD and cancer mortality. Among women, the relationship was non-linear for all-cause mortality (*P* for non-linearity = 0·005) with a J-shaped curve, while it was linear for CVD (*P* for linearity < 0·001) and cancer (*P* for linearity = 0·029) mortality (online Supplementary Fig. 2).

In race- and ethnicity-specific analysis among men, a statistically significant increase in all-cause mortality was observed in Whites (HR = 1·17, 95 % CI 1·00, 1·37) with pro-inflammatory change and in Latinos for the pro-inflammatory stable group (HR = 1·17, 95 % CI 1·02, 1·35) (Table 4). However, there was

Table 1. Energy-adjusted Dietary Inflammatory Index (E-DII) scores at cohort entry (1993–1996) and 10-year follow-up (2003–2008) (Mean values and standard deviations)

	Men (*n* 24 072)						Women (*n* 32 191)					
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Race/ethnicity	Cohort entry		Follow-up		Change*		Cohort entry		Follow-up		Change*	
African American	−0·96	1·97	−1·47	1·98	−0·51	1·86	−1·74	1·90	−2·26	1·88	−0·52	1·79
Japanese American	−0·71	1·99	−1·70	2·01	−0·99	1·84	−1·91	1·87	−2·72	1·76	−0·81	1·69
Latino	−0·75	1·78	−1·39	1·84	−0·64	1·75	−1·53	1·72	−2·20	1·78	−0·67	1·73
Native Hawaiian	−0·47	1·99	−1·33	2·08	−0·87	1·81	−1·42	2·03	−2·16	2·01	−0·75	1·80
White	−1·17	1·96	−1·75	1·99	−0·58	1·75	−1·95	1·82	−2·50	1·84	−0·55	1·70
Total	−0·85	1·95	−1·61	1·98	−0·76	1·81	−1·80	1·86	−2·47	1·84	−0·67	1·72

* E-DII change = E-DII at 10-year follow-up − E-DII at cohort entry.

Table 2. Characteristics of participants at 10-year follow-up (2003–2008) by E-DII change pattern* (Mean values and standard deviations; numbers and percentages)

	Anti-inflammatory stable		Anti-inflammatory change		Neutral inflammatory stable		Pro-inflammatory change		Pro-inflammatory stable	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Men										
Participants (n)	8537		5104		3234		1427		5770	
Age at cohort entry (years)										
Mean	58·5		55·6		57·2		58·3		55·0	
SD	8·4		7·7		8·1		8·5		7·7	
Age at 10-year follow-up (years)										
Mean	69·5		66·7		68·2		69·4		65·9	
SD	8·3		7·7		8·1		8·4		7·7	
Race/ethnicity										
African American	643	7·5	309	6·1	245	7·6	159	11·1	414	7·2
Japanese American	2977	34·9	2254	44·2	1058	32·7	421	29·5	2182	37·8
Latino	1418	16·6	929	18·2	787	24·3	291	20·4	1146	19·9
Native Hawaiian	519	6·1	408	8·0	223	6·9	86	6·0	550	9·5
White	2980	34·9	1204	23·6	921	28·5	470	32·9	1478	25·6
Education†										
≤ High school graduate	2053	24·0	1483	29·1	938	29·0	441	30·9	1834	31·8
Vocational school/some college	2365	27·7	1582	31·0	1024	31·7	420	29·4	1948	33·8
≥ College graduate	4062	47·6	2004	39·3	1253	38·7	551	38·6	1954	33·9
Smoking										
Never	3758	44·0	1832	35·9	1186	36·7	510	35·7	1674	29·0
Former	4506	52·8	2963	58·1	1822	56·3	821	57·5	3181	55·1
Current	273	3·2	309	6·1	226	7·0	96	6·7	915	15·9
BMI										
< 25 kg/m^2	3602	42·2	1702	33·3	1039	32·1	485	34·0	1864	32·3
25–< 30 kg/m^2	3700	43·3	2435	47·7	1509	46·7	649	45·5	2614	45·3
≥ 30 kg/m^2	1235	14·5	967	18·9	686	21·2	293	20·5	1292	22·4
Diabetes history	1477	17·3	1026	20·1	552	17·1	258	18·1	878	15·2
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Physical activity (h/d)‡	1·77	1·66	1·71	1·68	1·62	1·60	1·52	1·66	1·55	1·62
Total energy intake (kcal/d)	2023	826	1942	807	2045	867	2025	909	2109	892
Alcohol intake (g/d)	8·6	14·1	9·2	15·1	11·7	18·8	13·7	26·5	16·2	28·3
E-DII at cohort entry	−2·68	1·12	0·47	1·15	−0·75	1·02	−2·49	1·11	1·03	1·15
E-DII at 10-year follow-up	−3·23	1·04	−2·67	1·21	−0·96	0·35	0·23	1·10	0·91	0·90
E-DII change	−0·56	1·11	−3·14	1·08	−0·21	1·05	2·72	0·89	−0·12	1·12
	n	%	n	%	n	%	n	%	n	%
Women										
Participants (*n*)	11 467		7084		4033		2244		7363	
Age at cohort entry (years)										
Mean	59·1		55·4		57·7		59·7		55·2	
SD	8·3		7·8		8·1		8·5		8·0	
Age at 10-year follow-up (years)										
Mean	70·0		66·4		68·7		70·8		66·2	
SD	8·3		7·8		8·2		8·6		8·1	

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Table 2. (*Continued*)

	Anti-inflammatory stable		Anti-inflammatory change		Neutral inflammatory stable		Pro-inflammatory change		Pro-inflammatory stable	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Race/ethnicity										
African American	1304	11·4	772	10·9	544	13·5	321	14·3	993	13·5
Japanese American	4299	37·5	2715	38·3	1229	30·5	651	29·0	2144	29·1
Latino	1534	13·4	1232	17·4	796	19·7	382	17·0	1485	20·2
Native Hawaiian	736	6·4	560	7·9	241	6·0	156	7·0	770	10·5
White	3594	31·3	1805	25·5	1223	30·3	734	32·7	1971	26·8
Education†										
≤ High school graduate	3620	31·6	2299	32·5	1407	34·9	879	39·2	2884	39·2
Vocational school/some college	3497	30·5	2301	32·5	1258	31·2	682	30·4	2401	32·6
≥ College graduate	4268	37·2	2425	34·2	1329	33·0	664	29·6	2022	27·5
Smoking										
Never	7664	66·8	4449	62·8	2494	61·8	1355	60·4	4115	55·9
Former	3486	30·4	2268	32·0	1333	33·1	749	33·4	2386	32·4
Current	317	2·8	367	5·2	206	5·1	140	6·2	862	11·7
BMI										
< 25 kg/m^2	6447	56·2	3517	49·6	1869	46·3	995	44·3	2881	39·1
25–< 30 kg/m^2	3396	29·6	2207	31·2	1315	32·6	725	32·3	2397	32·6
≥ 30 kg/m^2	1624	14·2	1360	19·2	849	21·1	524	23·4	2085	28·3
Diabetes history	1525	13·3	1067	15·1	613	15·2	329	14·7	1100	14·9
Menopausal hormone therapy ever use	8045	70·2	4795	67·7	2751	68·2	1553	69·2	4754	64·6
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Physical activity (h/d)‡	1·57	1·54	1·44	1·46	1·32	1·37	1·19	1·33	1·24	1·43
Total energy intake (kcal/d)	1693	706	1635	712	1673	732	1634	735	1715	786
Alcohol intake (g/d)	3·1	7·6	3·2	7·7	3·4	8·7	5·2	15·5	4·4	12·7
E-DII at cohort entry	−3·43	0·84	−0·66	1·25	−1·88	0·91	−3·29	0·86	0·14	1·42
E-DII at 10-year follow-up	−3·87	0·81	−3·49	0·94	−2·09	0·29	−0·77	1·22	−0·03	1·16
E-DII change	−0·44	0·89	−2·83	1·05	−0·21	0·94	2·51	0·96	−0·16	1·37

E-DII, energy-adjusted Dietary Inflammatory Index.
* See text for definition of the E-DII change categories.
† Due to missing data, the percentages did not sum up to 100%.
‡ Hours spent in moderate or vigorous activity.

no indication of heterogeneity across the five groups ($P = 0{\cdot}65$). In women, a significant increase in all-cause mortality was found among Japanese American, Latino and Native Hawaiian groups with pro-inflammatory change and Japanese American and White women who were pro-inflammatory stable. E-DII increase over time was associated with a higher risk of all-cause mortality in women more strongly among African American, Japanese American, Latino and Native Hawaiian women than among White women (P for heterogeneity = 0·014 across five racial and ethnic groups; 0·004 between non-White *v.* White groups).

Discussion

In this multiethnic population, for both men and women, pro-inflammatory change in diet over 10 years was associated with an increased risk of subsequent mortality from all causes and CVD. Compared with men, the association with increasing E-DII score and all-cause mortality was stronger in women overall and in African American, Japanese American, Latino and Native Hawaiian, than White, women.

The inflammatory potential of the diet, as estimated by the E-DII, has been consistently associated with disease outcomes and mortality[6–12]. However, there are only few studies that have contributed additional evidence by examining longitudinal changes in the inflammatory potential of diet[13,14,24–26]. In the Women's Health Initiative Observational Study where FFQ were repeated among postmenopausal women (aged 50–79 years at baseline), mean E-DII score decreased modestly from −1·14 at baseline to −1·50 at Year 3 representing a transition towards an anti-inflammatory diet[24]. In that cohort of women, of whom the majority were White, patterns of E-DII change over 3 years, as defined by Tabung *et al.* and described in the 'Methods' section, were not associated with risk of overall invasive breast cancer[13]. However, for ER–, PR– and HER2+ subtypes, the pro-inflammatory stable group showed an increase in risk compared with the anti-inflammatory stable group (HR = 1·85, 95 % CI 1·06, 3·13), suggesting that dietary inflammatory potential may differentially influence the development of breast cancer by phenotype[13]. In the same cohort, women with dietary changes towards, or a history of, pro-inflammatory diets had a higher risk of colon cancer compared with those in the anti-inflammatory stable group, particularly for proximal colon cancer (for pro-inflammatory change, HR = 1·32, 95 % CI 1·01, 1·74) and among non-users of non-steroidal anti-inflammatory drugs (for pro-inflammatory stable, HR = 1·42, 95 % CI 1·01, 2·03)[14]. Pro-inflammatory change in diet has been reported in a small cohort of Australian women (aged 51–62 years at baseline, −0·60 to −0·46 over 14 years)[25] and in rural postmenopausal women (55 years or older) in Nebraska over 4 years, which was larger in participants who developed cancer than in those without cancer[26].

Table 3. E-DII change over 10 years and subsequent mortality from all causes, CVD and cancer, 2003–2019 (Hazard ratios and 95 % confidence intervals)

	Men (*n* 24 072)					Women (*n* 32 191)					
	Deaths	HR*	95 % CI*	HR†	95 % CI†	Deaths	HR*	95 % CI*	HR†	95 % CI†	*P* for heterogeneity‡
All causes											
Anti-inflammatory stable	3011	1·00	(ref)	1·00	(ref)	3176	1·00	(ref)	1·00	(ref)	
Anti-inflammatory change	1443	1·10	1·04, 1·18	1·00	0·94, 1·07	1417	1·05	0·98, 1·11	0·97	0·91, 1·03	
Neutral inflammatory stable	1085	1·11	1·04, 1·19	1·01	0·94, 1·08	1116	1·15	1·07, 1·23	1·07	1·00, 1·14	
Pro-inflammatory change	578	1·27	1·16, 1·39	1·13	1·03, 1·23	833	1·33	1·23, 1·44	1·22	1·13, 1·32	
Pro-inflammatory stable	1855	1·39	1·31, 1·47	1·09	1·02, 1·16	1849	1·35	1·28, 1·44	1·12	1·06, 1·20	
Per one-point increase§	7972	1·05	1·04, 1·07	1·02	1·00, 1·03	8391	1·08	1·07, 1·10	1·06	1·04, 1·07	< 0·001
CVD											
Anti-inflammatory stable	727	1·00	(ref)	1·00	(ref)	712	1·00	(ref)	1·00	(ref)	
Anti-inflammatory change	341	1·15	1·01, 1·31	1·07	0·93, 1·22	303	1·06	0·93, 1·22	0·97	0·85, 1·11	
Neutral inflammatory stable	258	1·10	0·96, 1·27	1·01	0·87, 1·17	269	1·23	1·07, 1·42	1·14	0·99, 1·31	
Pro-inflammatory change	153	1·33	1·12, 1·59	1·19	1·00, 1·42	210	1·40	1·20, 1·64	1·27	1·09, 1·49	
Pro-inflammatory stable	404	1·32	1·17, 1·50	1·10	0·96, 1·25	430	1·44	1·27, 1·63	1·20	1·06, 1·36	
Per one-point increase§	1883	1·04	1·01, 1·07	1·01	0·98, 1·04	1924	1·09	1·06, 1·13	1·07	1·04, 1·10	0·021
Cancer											
Anti-inflammatory stable	637	1·00	(ref)	1·00	(ref)	607	1·00	(ref)	1·00	(ref)	
Anti-inflammatory change	375	1·23	1·08, 1·40	1·07	0·94, 1·22	341	1·13	0·98, 1·29	1·02	0·89, 1·17	
Neutral inflammatory stable	268	1·24	1·07, 1·43	1·07	0·93, 1·24	220	1·12	0·96, 1·30	1·03	0·88, 1·21	
Pro-inflammatory change	134	1·37	1·14, 1·65	1·17	0·97, 1·41	137	1·16	0·96, 1·40	1·05	0·87, 1·26	
Pro-inflammatory stable	483	1·51	1·34, 1·71	1·04	0·92, 1·19	448	1·45	1·28, 1·65	1·15	1·01, 1·31	
Per one-point increase§	1897	1·05	1·02, 1·08	1·00	0·97, 1·03	1753	1·07	1·03, 1·10	1·04	1·00, 1·07	0·53

E-DII, energy-adjusted Dietary Inflammatory Index; HR, hazard ratio.

* Adjusted for age and race/ethnicity.

† Further adjusted for BMI, history of diabetes, education, marital status, physical activity, alcohol intake, energy intake and menopausal hormone therapy use (for women only) in the smoking model, which included smoking status, average number of cigarettes, squared average number of cigarettes, number of years smoked (time dependent), number of years since quitting (time dependent) and interactions between race/ethnicity and smoking status, average number of cigarettes, squared average number of cigarettes and number of years smoked.

‡ Based on per one-point increase in the multivariable-adjusted model.

§ Additionally adjusted for E-DII at cohort entry.

Table 4. E-DII change over 10 years and subsequent all-cause mortality by race/ethnicity, 2003–2019
(Hazard ratios and 95 % confidence intervals)

	African American			Japanese American			Latino			Native Hawaiian			White			*P* for hetero-geneity†
	Deaths	HR*	95 % CI*	Deaths	HR*	95 % CI*	Deaths	HR*	95 % CI*	Deaths	HR*	95 % CI *	Deaths	HR*	95 % CI*	
Men		(*n* 1770)			(*n* 8892)			(*n* 4571)			(*n* 1786)			(*n* 7053)		
Anti-inflammatory stable	299	1·00	(ref)	1135	1·00	(ref)	463	1·00	(ref)	182	1·00	(ref)	932	1·00	(ref)	
Anti-inflammatory change	124	0·99	0·79, 1·23	580	0·99	0·89, 1·10	309	1·21	1·04, 1·40	119	0·94	0·73, 1·20	311	0·96	0·85, 1·10	
Neutral inflammatory stable	123	1·10	0·89, 1·37	338	1·02	0·90, 1·15	270	1·03	0·88, 1·20	59	0·73	0·54, 0·99	295	1·09	0·95, 1·24	
Pro-inflammatory change	82	1·09	0·84, 1·40	175	1·15	0·98, 1·35	107	1·15	0·93, 1·42	24	0·96	0·62, 1·49	190	1·17	1·00, 1·37	
Pro-inflammatory stable	185	1·05	0·85, 1·28	602	1·08	0·97, 1·20	391	1·17	1·02, 1·35	180	1·00	0·80, 1·27	497	1·09	0·97, 1·23	
Per one-point increase‡	813	1·03	0·98, 1·08	2830	1·00	0·98, 1·02	1540	1·02	0·99, 1·06	564	1·01	0·96, 1·07	2225	1·03	1·00, 1·06	0·65
Women		(*n* 3934)			(*n* 11 038)			(*n* 5429)			(*n* 2463)			(*n* 9327)		
Anti-inflammatory stable	451	1·00	(ref)	1250	1·00	(ref)	362	1·00	(ref)	189	1·00	(ref)	924	1·00	(ref)	
Anti-inflammatory change	202	0·93	0·78, 1·10	490	0·96	0·86, 1·07	237	0·92	0·78, 1·09	103	0·85	0·66, 1·09	385	1·06	0·94, 1·19	
Neutral inflammatory stable	211	1·16	0·98, 1·37	299	1·01	0·89, 1·15	223	1·15	0·97, 1·36	57	0·94	0·70, 1·28	326	1·04	0·91, 1·18	
Pro-inflammatory change	148	1·20	0·99, 1·45	240	1·25	1·09, 1·44	144	1·48	1·21, 1·79	55	1·44	1·06, 1·97	246	1·08	0·94, 1·25	
Pro-inflammatory stable	323	1·05	0·91, 1·23	433	1·21	1·08, 1·36	371	1·08	0·93, 1·25	167	0·98	0·78, 1·23	555	1·16	1·04, 1·30	
Per one-point increase‡	1335	1·06	1·02, 1·09	2712	1·08	1·05, 1·11	1337	1·08	1·04, 1·12	571	1·07	1·02, 1·13	2436	1·03	1·00, 1·06	0·014§

E-DII, energy-adjusted Dietary Inflammatory Index; HR, hazard ratio.
* Adjusted for age, BMI, history of diabetes, education, marital status, physical activity, alcohol intake, energy intake and menopausal hormone therapy use (for women only) in the smoking model, which included smoking status, average number of cigarettes, squared average number of cigarettes, number of years smoked (time dependent) and number of years since quitting (time dependent).
† Based on per one-point increase.
‡ Additionally adjusted for E-DII at cohort entry.
§ *P* for heterogeneity between non-White *v.* White women = 0·004.

In the MEC, mean E-DII scores decreased over 10 years in both men (from −0·85 to −1·61) and women (from −1·80 to −2·47). Improvement in the inflammatory potential of the diet with age is consistent with previous research that found diet quality improves with age among MEC participants as assessed with the Healthy Eating Index-2015, the Alternative Healthy Eating Index-2010, the alternate Mediterranean diet score and the Dietary Approaches to Stop Hypertension score[27]. These diet quality indexes were developed based on adherence to dietary recommendations or on their relation to reduced risk of chronic disease and mortality[28], while the DII, and by logical extension the E-DII, was developed to characterise the inflammatory potential of the diet.

In the present study, the association between increase in dietary inflammation potential over time and subsequent all-cause and CVD mortality was stronger in women than in men. Women tended to have more anti-inflammatory diets at both cohort entry and 10-year follow-up and showed less changes in E-DII scores compared with men. A meta-analysis showed that increased risk of CVD incidence or mortality in individuals with the highest *v.* lowest DII score was significant in women but not in men[8]. However, within studies, no heterogeneity by sex was found for CVD mortality in the MEC[15] and for CVD risk in other large US cohorts[29]. Men and women undergo different ageing-related changes including changes in body weight and composition and hormonal changes in sex hormones. However, in the present study, when we further adjusted for change in body weight over 10 years, the associations remained unchanged. Also, the associations were similar between menopausal hormone therapy ever users *v.* never users in women. Among MEC female participants, the association between increase in E-DII score and all-cause mortality was weaker in Whites, compared with other racial/ethnic groups. This may be due to White women having the lowest E-DII scores at cohort entry and one of the smallest changes in E-DII scores over time. Our research complements previous findings that the relationship between food consumption, diet quality and chronic inflammation may vary by sex and race/ethnicity[30–33]. However, potential differences in the E-DII change-mortality association by sex and race/ethnicity warrant further investigation.

This study has notable strengths including a population-based prospective design, a large sample size with participants from various racial/ethnic backgrounds, a validated FFQ and a wide range of covariates for diet-mortality analyses. However, dietary assessments based on a self-administered FFQ are subject to measurement error, which is most likely non-differential in a cohort study leading to attenuated risk estimates[34]. The sample size might be limited for some subgroup analyses. Despite the comprehensive information on lifestyle factors and careful adjustment for covariates, there is still the possibility of residual confounding by unmeasured or incompletely controlled variables that might be related to both diet and mortality. To compute the E-DII scores for the MEC, only twenty-eight of the forty-five components originally included for the DII development were available on our questionnaire. However, DII/E-DII scores based on fewer components have been demonstrated to adequately predict inflammatory markers and health outcomes in several studies[19,35,36] including the previous reports from the MEC[15,20]. Because the current findings are from MEC participants who completed the 10-year follow-up survey (45 % of total) with further restriction to those (~56 000) without prior heart disease or cancer, generalisability may be limited.

In conclusions, our findings suggest that pro-inflammatory change in diet in mid- to late adult life is associated with increased risk of mortality from all causes and CVD in both men and women, and that the association is stronger in women, especially non-White women, than in men.

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All authors declare no conflict of interest. We wish to disclose that Dr. Hébert owns controlling interest in Connecting Health Innovations LLC (CHI), a company that has licensed the right to his invention of the Dietary Inflammatory Index™ (DII®) from the University of South Carolina in order to develop computer and smartphone applications for patient counselling and dietary intervention in clinical settings. Drs. Wirth and Shivappa are employees of CHI. The subject matter of this paper will not have any direct bearing on that work, nor has that activity exerted any influence on this project.

Supplementary material

For supplementary material referred to in this article, please visit https://doi.org/10.1017/S0007114522000861

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