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Dietary Patterns Are Associated with Disease Risk among Participants in the Women's Health Initiative Observational Study[1–3]

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Abstract

Coronary heart disease (CHD) is the leading cause of death in women. A nested case-control study tested whether dietary patterns predicted CHD events among 1224 participants in the Women's Health Initiative-Observational Study (WHI-OS) with centrally confirmed CHD, fatal or nonfatal myocardial infarct compared to 1224 WHI-OS controls matched for age, enrollment date, race/ethnicity, and absence of CHD at baseline or follow-up. The first six principal components explained >75% of variation in dietary intakes and K-mean analysis based on these six components produced three clusters. Diet cluster 1 was rich in carbohydrate, vegetable protein, fiber, dietary vitamin K, folate, carotenoids, α-linolenic acid [18:3(n-3)], linoleic acid [18:2(n-6)], and supplemental calcium and vitamin D. Diet cluster 2 was rich in total and animal protein, arachidonic acid [20:4(n-6)], DHA [22:6(n-3)], vitamin D, and calcium. Diet cluster 3 was rich in energy, total fat, and *trans* fatty acids (all $P < 0.01$). Conditional logistic regression analysis demonstrated diet cluster 1 was associated with lower CHD risk than diet cluster 2 (reference group) adjusted for smoking, education, and physical activity [OR = 0.79 (95% CI = 0.64, 0.99); $P = 0.038$]. This difference was not significant after adjustment for BMI and systolic blood pressure. Diet cluster 3 was associated with higher CHD risk than diet cluster 2 [OR = 1.28 (95% CI = 1.04, 1.57); $P = 0.019$], but this difference did not remain significant after adjustment for smoking, education, and physical activity. Within this WHI-OS cohort, distinct dietary patterns may be associated with subsequent CHD outcomes. J. Nutr. 142: 284–291, 2012.

Introduction

Growing evidence suggests long-term influences from habitual food and beverage intake predict subsequent risk for chronic disease, including CHD[11], diabetes, and cancer (1–4). Few longitudinal studies have included detailed diet assessment methodology and adequate sample size to specify dietary factors and eating behaviors associated with more compared to less favorable outcomes.

Traditionally, studies of diet and chronic disease risk focused on isolated nutrients and results and, although helpful, were limited in translational applications. Recently, more sophisticated biostatistical approaches have used diet patterns as the exposure, thereby offering potential benefits for developing effective food-based interventions associated with reduced risk of cardiovascular and other chronic diseases. The WHI-OS offers this opportunity using a case-control study design to further assess eating patterns and CHD outcomes (5).

This approach of evaluating whole diet patterns, beyond individual nutrients or foods, was suggested as early as 1969 during the White House Conference on Food, Nutrition and Health, the intent of which was to evaluate diet and health relationships among the U.S. population (6,7). In the 1980s factor analysis was used to identify multiple eating patterns within a cohort, some of which were associated with better health outcomes (8–11). Since then, a number of studies have reported diet/disease associations using factor and principal component analyses or cluster analysis using data from a wide range of cohorts (12–32). The results of this work have supported the predictive value of using methodological approaches to summarize dietary data and identify relationships between diet patterns and health.

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[3] Supplemental Figure 1 is available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at jn.nutrition.org.

[11] Abbreviations used: ALA, α-linolenic acid; CHD, coronary heart disease; LA, linoleic acid; MI, myocardial infarct; WHI, Women's Health Initiative; WHI-OS, Women's Health Initiative-Observational Study.

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The purpose of these analyses was to assess baseline diet patterns reported by free-living, postmenopausal participants in the WHI-OS who had a subsequent CHD event compared to matched controls from the same cohort. It was hypothesized that distinct diet clusters would be identified within the dataset and that the distribution of these clusters between WHI-OS CHD cases and WHI-OS CHD controls would differ.

Materials and Methods

Study population

The WHI-OS is a prospective cohort study designed to assess the impact of biological, lifestyle, biochemical, and genetic factors on cancer and other major health events, including CHD. Enrolled were 93,676 postmenopausal women between the ages of 50 and 79 y who were recruited to the WHI-OS at 40 clinical centers in the United States. A detailed description of the WHI-OS design and analyses has been published elsewhere (33,34).

Exclusions were any medical condition associated with a predicted survival <3 y, participation in a clinical trial, alcohol or drug dependency, previous or existing breast or colorectal cancer, documented cardiovascular disease or type 1 diabetes mellitus, mental illness, dementia, or other inability to participate in the study. Demographic information and dietary data were obtained by self-report using standardized forms and validated WHI FFQ (35,36). Certified study staff measured blood pressure, height, and weight and took blood samples at the baseline clinic visit (33,34).

Ethics

The WHI protocol was approved by the Institutional Review Boards at the Clinical Coordinating Center at the Fred Hutchinson Cancer Research Center and the 40 clinical centers. Separate approval to use deidentified data for these analyses was obtained from the Tufts University/Tufts Medical Center Institutional Review Board.

WHI cases/controls

CHD event data in WHI-OS participants were ascertained annually. A nested case-control design was used in following women during the first 8 y of the WHI. To compare potential dietary differences between cases and controls, a total of 1224 cases (WHI-OS CHD cases) with centrally confirmed CHD, fatal MI, or nonfatal MI were first identified. An equal number of control participants (WHI-OS CHD controls) was selected who were free of CHD or MI, angina, coronary artery by-pass graft/percutaneous transluminal coronary angioplasty, congestive heart failure, stroke, or peripheral vascular disease during the study period and were matched to the WHI-OS CHD cases on the basis of age, date of enrollment, and race/ethnicity.

Dietary data assessment

During screening, participants completed a validated FFQ developed by the WHI to estimate mean daily nutrient intakes during the previous 3-mo period (35,36). These data served as the baseline measurement. The FFQ was based on instruments used in the WHI feasibility studies (33,35,36) and the original National Cancer Institute/Block FFQ (35,37). The three sections of WHI FFQ included 19 adjustment questions related to type of fat intake, 122 composite and single food line items asking about frequency of consumption and portion size, and 4 summary questions asking about the usual intake of fruits and vegetables and added fats for comparison with information gathered from the line items. The nutrient database used to calculate intakes was linked to the University of Minnesota Nutrition Coordinating Center Nutrition Data System for Research and is based on the USDA standard reference releases and manufacturer information (35). Details of the algorithms used to derive nutrient intake from the FFQ at the Fred Hutchinson Cancer Research Center have been discussed elsewhere (35). Total dietary energy and 25 diet components known to be associated with CHD, including total protein, animal protein, vegetable protein, carbohydrate, fiber, total fat, SFA, MUFA, PUFA, LA [18:2(n-6)], arachidonic acid [20:4(n-6)], ALA [18:3(n-3)], EPA [20:5(n-3)], DHA [22:6(n-3)], total (n-3) fatty acids, total *trans* fatty acids, cholesterol, dietary vitamin D, supplemental vitamin D, dietary calcium, supplemental calcium, dietary vitamin K, dietary folate equivalents, alcohol, and total carotenoids, were selected a priori based on current diet and CHD-related associations (1,25,32,38), as the set of variables of interest and calculated based on the FFQ. The WHI FFQ has demonstrated reasonably good validity as a measurement of dietary intake compared with 24-h dietary recall interviews and food records (35,36).

Statistical methods

Confounders/covariates: age, BMI, smoking, diabetes. Sociodemographic variables were measured by interview or self-report at baseline using standardized questionnaires [age, race/ethnicity, income, marital status, education (high school and below vs. college vs. postgraduate or professional)]. Traditional CHD risk factors were measured by self-report at baseline using questionnaires (smoking status, family history of MI, and frequency, intensity, and duration of physical activity) as well as by trained, certified staff at the baseline exam (height, weight, BMI, waist:hip ratio). Height was measured using a stadiometer, weight was measured with participants wearing light clothing, and BMI was calculated as weight in kilograms divided by height in meters squared. Diabetes and abnormal lipid level were defined as self-report of physician diagnosis and self-report of taking medication at baseline.

Data analyses. Principal component analysis on the correlation matrix was used to identify dietary patterns based on total dietary energy and the 25 potentially CHD-relevant diet components selected a priori (39). Based on the main principal components, each of which are linear combinations of the original data (25 diet components), K-mean analysis was performed to cluster participants with similar dietary patterns into the same cluster (40). The number of clusters was selected by examining the within-cluster sum of squares with different numbers of clusters in the K-mean analysis. The principal component analysis aims to identify underlying patterns of CHD-relevant diet component in the WHI-OS population. When the number of principal components needed to account for the majority of variation in the data are not small (6 in our analysis), it may be difficult to directly seek a clinically meaningful interpretation of the constructed components. Nevertheless, the K-mean clustering based on selected principal components often can better summarize and distinguish underlying dietary patterns in the population (41). The CHD risk was then compared across the formed clusters with conditional logistic regression analysis, conditioned on the matching factors of age, date of enrollment, and race/ethnicity. Additional conditional logistic regression analyses were sequentially performed adjusting for potential confounding factors, including smoking status, education level, sedentary behavior (time spent sitting or lying), physical activity (number of episodes of moderate or strenuous activity), baseline BMI, systolic blood pressure, total energy intake, and lipid-lowering and/or diabetic medication use in 4 separate models according to their potentials to be confounding factors for the association of interest, i.e., the likelihood that the factors are in the causal pathway between dietary intakes and CHD risk. Lastly, to further characterize the constructed clusters, various food and nutrient intakes and cardiovascular risk factors were compared across clusters in cases and controls with separate ANOVA. In all the analyses, the significance level was set at $P < 0.05$ and analyses were performed on R-2.10.1.

Results

When matched on the basis of age and ethnicity, compared to WHI-OS CHD controls, WHI-OS CHD cases reported higher rates of ever having smoked as well as lipid-lowering medication use and lower attained level of education and had higher BMI and mean systolic and diastolic blood pressures (**Table 1**) (all $P < 0.01$).

Of the 25 diet components entered into the model, the first 6 principal components explained >75% of the variation in dietary intakes. K-mean analysis clustered WHI-OS participants into 3 diet clusters based on these 6 principal components. A graphic representation of diet clusters in the space spanned by the first 2 principal components is presented in **Supplemental**

TABLE 1 Characteristics of the matched CHD case-control cohorts in the WHI-OS[1]

	WHI-OS Cases (n = 1224)	WHI-OS Control (n = 1224)	P
Age at screening,[2] *y*	67.8 ± 6.8	67.8 ± 6.8	
Ethnicity,[2] *% white*	89.3	89.3	
Diabetic medication use, *%*	8.7	1.9	<0.01
Antihyperlipidemic medication use, *%*	10.5	7.8	0.01
BMI, *kg/m²*	28.1 ± 6.3	27.0 ± 5.7	<0.01
Ever smoked, *% yes*	52.3	46.3	<0.01
College degree or above, %	35.5	41.9	<0.01
Systolic blood pressure, *mm Hg*	136 ± 21	129 ± 18	<0.01
Diastolic blood pressure, *mm Hg*	76 ± 10	74 ± 9	<0.01

[1] Values are mean ± SD or percent. CHD, coronary heart disease; Hg, hemoglobin; WHI-OS, Women's Health Initiative-Observational Study.
[2] Cases and controls were matched on these characteristics.

Figure 1. The first and second principal components explained 30 and 15% variation, respectively. Participants in the same cluster shared the similar values of the principal components, i.e., similar patterns of dietary intakes.

All the diet variables in the model were distributed differently across the 3 diet clusters for both the WHI-OS CHD cases and controls (all $P < 0.01$), with the exception of alcohol (**Table 2**). This confirms that the K-mean analysis identified clusters of participants with different dietary intakes. Specifically, relative to the other diet clusters, participants in diet cluster 1 reported eating diets rich in carbohydrate, vegetable protein, fiber, dietary vitamin K, folate, carotenoids, total (n-3) fatty acids, ALA, LA, and supplemental calcium and vitamin D. Participants in diet cluster 2 reported eating diets rich in total and animal protein, arachidonic acid, DHA, vitamin D, and calcium. Participants in diet cluster 3 reported eating diets higher in energy, total fat, and *trans* fatty acids.

When the data were assessed on the basis of selected food items, rather than nutrients, a majority of the food categories were differently distributed across the three diet clusters (all $P < 0.01$ except that for meals eaten outside the home) (**Table 3**). Diet cluster 1 was characterized as being rich in vegetables, fruits, and soy and low in sources of animal protein (meat and dairy). Diet cluster 2 was characterized as being rich in fish (all kinds) and poultry. Diet cluster 3 was characterized as being rich in red meat and fried foods, use of added fat, and low in soy. When patient characteristics and cardiovascular disease risk factors in WHI-OS CHD cases and controls were assessed across the three diet clusters, an interesting pattern emerged (**Table 4**). Both case and control participants in the diet cluster 1 had a lower BMI ($P < 0.01$) and engaged in more episodes of moderate to strenuous physical activity ($P < 0.01$). Participants in diet cluster 3 attained a lower level of education ($P < 0.01$). For both cases and controls, there was no significant difference in blood pressure, either systolic or diastolic, nor time spent sitting or lying down among diet clusters. Cases in diet cluster 1 were older than those in the other clusters, a difference that was not observed in the controls in diet cluster 1.

Control participants more often reported consuming diets classified as diet cluster 1 (38.0 vs. 30.1%, controls and cases, respectively) and fewer reported consuming diets classified as diet cluster 3 (35.3 vs. 43.5%, controls and cases, respectively). A similar number of control and case participants reported consuming diets classified as the reference group, diet cluster 2 (26.3 and 26.7%, controls and cases, respectively).

The WHI-OS participants in diet cluster 1 had a lower CHD risk than those in diet cluster 2, designated as the reference group [OR = 0.80 (95% CI = 0.67, 0.99); $P = 0.036$] (**Table 5**). The difference remained significant after adjusting for current smoking status, education level, and physical activity (model 2) [OR = 0.79 (95% CI = 0.64, 0.99); $P = 0.038$]. After adjustment for baseline BMI and systolic blood pressure (model 3) [OR = 0.82 (95% CI = 0.65, 1.03); $P = 0.085$], the difference was no longer significant. The WHI-OS participants in diet cluster 3 had a higher risk than did diet cluster 2 [OR = 1.28 (95% CI = 1.04, 1.57); $P = 0.019$]. However, this difference was no longer significant after adjusting for current smoking status, education level, and physical activity [OR = 1.18 (95% CI = 0.95, 1.47); $P = 0.13$].

The K-mean clustering is mainly driven by the value of the first 2 principal components based on total dietary energy and 25 diet components. The first principal component (first dietary pattern factor) explained 30% of the variation. In the first dietary pattern factor, the loading of dietary total carbohydrate, total fiber, vegetable protein, dietary folate equivalents, dietary carotenoids, and dietary calcium were the most positive and the loading of total fat, MUFA, SFA, PUFA, LA, *trans* fatty acids, ALA, total (n-3) fatty acids, and cholesterol were the most negative. Therefore, a higher value of the first dietary factor represents higher intakes of total carbohydrate, total fiber, vegetable protein, dietary folate equivalents, dietary carotenoids, and dietary calcium, and lower intakes of total fat, MUFA, SFA, PUFA, LA, *trans* fatty acids, ALA, total (n-3) fatty acids, and cholesterol. The conditional logistic regression confirms that the WHI-OS participants with the highest values for the first dietary pattern factors were at lower CHD risk. Specifically, the OR were 0.61 (95% CI = 0.48, 0.76), 0.64 (95% CI = (0.51, 0.81), and 0.79 (95% CI = 0.64, 0.99) for the fourth, third, and second quintiles compared to the first quintile, respectively.

Discussion

This WHI-OS case-control analysis assessed baseline dietary patterns and subsequent CHD events. The principal component analysis, followed by K-means clustering, was used to identify specific dietary patterns based on total dietary energy and 25 diet components. Three dietary patterns were identified and designated diet clusters 1, 2 and 3, suggesting that the cohort can be naturally divided into three subpopulations in which the participants share similar dietary patterns. The occurrence of these diet clusters was compared between WHI-OS CHD case and control participants. The proportion of women in diet cluster 1 was significantly higher in the WHI controls and was associated with marginally lower CHD risk ($P = 0.20$) before and after adjusting for baseline BMI, systolic blood pressure, current smoking status, education level, and physical activity. The point estimator of the OR changed from 0.79 to 0.82 after the additional adjustment of BMI and systolic blood pressure, which indicates that these two variables only partially account for the difference between the two diet clusters. In contrast, the proportion of women in diet cluster 3 was significantly higher in the WHI-OS CHD cases than in the controls and was associated with higher CHD risk. However, the difference became nonsignificant after adjusting for the aforementioned factors. This confirms prior work indicating that dietary intake is an important determinant of CHD risk, along with conventional risk factors (1,42). Of note, the significance of the difference in CHD risk between diet clusters 1 and 2 disappeared completely after additional adjustment for total energy intake and lipid-lowering and diabetic medication use. We cannot rule out the possibility that diabetic and lipid status should not be

TABLE 2 Intakes of selected nutrients by cluster group for WHI-OS CHD cases and controls[1]

	Cases				Controls			
	Diet cluster 1	Dietcluster 2	Diet cluster 3	*P*	Diet cluster 1	Diet cluster 2	Diet cluster 3	*P*
n (%)	369 (30.1)	322 (26.3)	533 (43.5)		465 (38.0)	327 (26.7)	432 (35.3)	
Energy intake, *kcal/d*	1430 ± 5	1530 ± 6	1750 ± 7	<0.01	1430 ± 5	1540 ± 5	1730 ± 6	<0.01
Protein, *% energy*	15.7 ± 2.5	20.2 ± 2.6	15.9 ± 2.7	<0.01	15.9 ± 2.4	20.1 ± 2.7	15.6 ± 2.7	<0.01
Animal protein, *g/kcal*	23.7 ± 6.4	38.2 ± 6.6	28.8 ± 7.1	<0.01	24.2 ± 6.6	38.0 ± 6.8	27.6 ± 6.9	<0.01
Vegetable protein, *g/kcal*	15.5 ± 3.7	12.2 ± 2.6	11.0 ± 2.4	<0.01	15.6 ± 3.9	12.3 ± 2.6	11.3 ± 2.7	<0.01
Carbohydrate, *% energy*	60.9 ± 7.2	52.0 ± 6.8	44.0 ± 7.0	<0.01	60.4 ± 6.7	52.2 ± 6.9	45.1 ± 6.7	<0.01
Fiber, *g/kcal*	13.8 ± 4.0	10.4 ± 2.7	8.2 ± 2.4	<0.01	13.9 ± 3.9	10.8 ± 2.8	8.5 ± 2.3	<0.01
Fat, *% energy*	24.1 ± 5.4	27.6 ± 5.8	38.9 ± 5.9	<0.01	24.3 ± 5.5	27.2 ± 5.3	38.2 ± 5.2	<0.01
SFA, *% total fat*	32.1 ± 4.7	34.5 ± 4.9	33.0 ± 4.9	<0.01	31.8 ± 4.9	34.1 ± 4.4	33.3 ± 4.9	<0.01
MUFA, *% total fat*	37.2 ± 3.0	37.0 ± 2.8	38.4 ± 2.8	<0.01	37.1 ± 3.1	37.3 ± 2.7	38.3 ± 3.0	<0.01
PUFA, *% total fat*	22.1 ± 4.1	20.3 ± 4.2	20.9 ± 4.2	<0.01	22.4 ± 4.4	20.4 ± 4.1	20.8 ± 4.3	<0.01
18:2(n-6), *% total fat*	19.3 ± 3.6	17.4 ± 3.5	18.4 ± 3.8	<0.01	19.5 ± 3.8	17.4 ± 3.5	18.3 ± 3.8	<0.01
20:4(n-6), *% total fat*	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1	<0.01	0.2 ± 0.1	0.3 ± 0.1	0.1 ± 0.1	<0.01
(n-3) Fatty acids, *% total fat*	2.8 ± 1.1	2.6 ± 1.0	2.3 ± 0.6	<0.01	2.9 ± 1.3	2.8 ± 1.0	2.3 ± 0.7	<0.01
18:3(n-3), *% total fat*	2.5 ± 1.0	2.1 ± 0.7	2.1 ± 0.6	<0.01	2.5 ± 1.2	2.2 ± 0.7	2.1 ± 0.6	<0.01
20:5(n-3), *% total fat*	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.0	<0.01	0.1 ± 0.1	0.2 ± 0.1	0.0 ± 0.0	<0.01
22:6(n-3), *% total fat*	0.2 ± 0.2	0.3 ± 0.3	0.1 ± 0.1	<0.01	0.2 ± 0.2	0.3 ± 0.3	0.1 ± 0.1	<0.01
Trans fatty acids, *% total fat*	6.9 ± 2.7	6.3 ± 2.0	7.6 ± 2.9	<0.01	6.4 ± 2.4	6.2 ± 2.1	7.6 ± 2.9	<0.01
Cholesterol, *mg/kcal*	93 ± 36	148 ± 55	152 ± 60	<0.01	96 ± 36	146 ± 70	143 ± 54	<0.01
Alcohol, *% energy*	2.3 ± 4.4	2.10 ± 4.17	2.64 ± 5.18	0.21	2.33 ± 3.89	2.49 ± 4.07	2.76 ± 5.33	0.35
Dietary vitamin D, *μg/kcal*	2.4 ± 1.3	4.31 ± 2.13	2.31 ± 1.10	<0.01	2.31 ± 1.27	4.36 ± 2.11	2.29 ± 1.06	<0.01
Dietary calcium, *mg/kcal*	540 ± 18	691 ± 27	418 ± 14	<0.01	523 ± 18	690 ± 27	440 ± 14	<0.01
Dietary vitamin K, *μg/kcal*	76.0 ± 61.5	57.1 ± 34.2	51.7 ± 28.4	<0.01	76.7 ± 62.4	62.9 ± 44.0	52.0 ± 26.2	<0.01
Dietary folate, *μg/kcal*	375 ± 11	333 ± 12	263 ± 72	<0.01	367 ± 10	342 ± 11	266 ± 69	<0.01
Dietary carotenoids, *mg/kcal*	9.40 ± 5.1	7.40 ± 3.5	5.31 ± 2.4	<0.01	9.83 ± 5.5	7.72 ± 3.4	5.65 ± 2.5	<0.01
Supplemental vitamin D, *μg/kcal*	4.80 ± 5.9	3.96 ± 4.7	2.96 ± 4.0	<0.01	4.92 ± 6.4	4.22 ± 4.5	3.08 ± 4.4	<0.01
Supplemental calcium, *mg/kcal*	377 ± 514	291 ± 431	191 ± 345	<0.01	414 ± 645	297 ± 379	243 ± 380	<0.01

[1] Values are mean ± SD or percent. WHI-OS, Women's Health Initiative-Observational Study.

treated as confounding factors because of their direct relationship to CHD and that the differences identified are valid for this cohort prior to those corrections (model 4). We also cannot rule out the possibility that this finding could be due to the limited sample size.

An alternate approach to analyzing dietary data and performing principal component analysis is to calculate a diet score using a qualitative ranking system, such as the Healthy Eating Index developed from the Dietary Guidelines for Americans, with or without weighing of the individual components (24,43–59). This approach has likewise identified relationships between diet quality and health outcomes that may offer different outcomes than those reported here. The merits of one system over another have yet to be fully explored.

There are a number of advantages to summarizing habitual food intake in terms of diet clusters rather than individual foods or nutrients (60). Data derived from self-reported FFQ or diet

TABLE 3 Comparison of selected foods by diet cluster for WHI-OS CHD cases and controls[1]

	Cases				Controls			
	Diet cluster 1	Diet cluster 2	Diet cluster 3	*P*	Diet cluster 1	Diet cluster 2	Diet cluster 3	*P*
n (%)	370 (30.1)	320 (26.3)	530 (43.5)		470 (38.0)	330 (26.7)	430 (35.3)	
		servings/d				*servings/d*		
Yellow and green vegetables	2.33 ± 1.7	2.25 ± 1.4	1.79 ± 1.1	<0.01	2.47 ± 1.7	2.49 ± 1.4	1.84 ± 1.1	<0.01
Fruits	1.75 ± 1.3	1.58 ± 1.1	1.16 ± 0.9	<0.01	1.69 ± 1.3	1.53 ± 1.1	1.28 ± 0.9	<0.01
Soy	0.042 ± 0.2	0.017 ± 0.1	0.005 ± 0.0	<0.01	0.056 ± 0.2	0.020 ± 0.1	0.007 ± 0.0	<0.01
Fish	0.092 ± 0.1	0.16 ± 0.2	0.11 ± 0.1	<0.01	0.10 ± 0.1	0.18 ± 0.2	0.10 ± 0.1	<0.01
Dark fish	0.027 ± 0.1	0.059 ± 0.1	0.021 ± 0.0	<0.01	0.029 ± 0.1	0.078 ± 0.1	0.022 ± 0.0	<0.01
Tuna	0.065 ± 0.1	0.10 ± 0.1	0.086 ± 0.1	<0.01	0.074 ± 0.1	0.10 ± 0.1	0.078 ± 0.1	<0.01
Poultry	0.27 ± 0.2	0.43 ± 0.3	0.38 ± 0.3	<0.01	0.29 ± 0.2	0.46 ± 0.3	0.36 ± 0.3	<0.01
Red meat	0.35 ± 0.3	0.63 ± 0.4	0.96 ± 0.7	<0.01	0.37 ± 0.3	0.60 ± 0.4	0.83 ± 0.7	<0.01
Dairy products	1.29 ± 0.8	1.79 ± 1.3	1.26 ± 0.8	<0.01	1.24 ± 0.8	1.77 ± 1.3	1.38 ± 0.8	<0.01
Fat added	0.65 ± 0.6	0.78 ± 0.7	1.82 ± 1.4	<0.01	0.66 ± 0.6	0.78 ± 0.7	1.75 ± 1.4	<0.01
Fried food	0.24 ± 0.2	0.29 ± 0.3	0.50 ± 0.5	<0.01	0.24 ± 0.2	0.27 ± 0.3	0.42 ± 0.5	<0.01
Meals eaten outside the home >10 times, %	3.0	2.5	3.4	0.76	1.7	5.2	3.5	0.02

[1] Values are mean ± SD or percent. WHI-OS, Women's Health Initiative-Observational Study.

TABLE 4 Analysis of selected characteristics of WHI-OS cases and controls by diet cluster group[1]

	Cases				Controls			
	Diet cluster 1	Diet cluster 2	Diet cluster 3	*P*	Diet cluster 1	Diet cluster 2	Diet cluster 3	*P*
n (%)	369 (30.1)	322 (26.3)	533 (43.5)		465 (38.0)	327 (26.7)	432 (35.3)	
Age,[2] *y*	68.3 ± 7.0	68.0 ± 6.5	67.2 ± 6.7	0.01	67.7 ± 6.9	67.8 ± 6.9	68.0 ± 6.5	0.91
Ethnicity,[2] *% white*	89.9	91.0	87.9	0.30	88.1	92.9	88.8	0.09
BMI, *kg/m²*	26.7 ± 5.2	28.6 ± 6.6	29.0 ± 6.6	<0.01	26.2 ± 5.7	27.2 ± 5.2	27.7 ± 6.1	<0.01
Ever smoked, *% yes*	46.8	51.8	55.4	0.05	42.9	46.8	50.2	0.09
Education, *% college degree or above*	42.0	40.5	27.9	<0.01	46.5	47.8	32.4	<0.01
Systolic blood pressure, *mm Hg*	137 ± 21	136 ± 19	135 ± 19	0.56	129 ± 19	127 ± 16	129 ± 18	0.41
Diastolic blood pressure, *mm Hg*	76 ± 10	75 ± 9	76 ± 10	0.39	74 ± 10	74 ± 8	74 ± 9	0.68
Time spent on sitting or lying down, *h/d*	14.9 ± 4.1	15.4 ± 4.3	15.5 ± 4.1	0.12	15.0 ± 3.8	15.1 ± 4.3	15.2 ± 4.0	0.69
Episodes of moderate or strenuous activity ≥20 min, *n/wk*	2.66 ± 1.07	2.57 ± 1.04	2.25 ± 0.97	<0.01	2.85 ± 1.01	2.70 ± 0.99	2.44 ± 1.02	<0.01

[1] Values are mean ± SD or percent.
[2] Cases and controls were matched on these characteristics.

recalls are an estimate rather than a precise quantization of absolute intake. Sources of uncertainty include recollection of actual foods and specific amounts eaten, completeness and accuracy of nutrient databases, inaccuracies in linking mixed-dishes to items in the database, and systematic measurement error. Analysis of individual nutrients or foods cannot capture potential synergistic or antagonistic interactions among dietary components. Food processing and preparation techniques can alter nutrient availability and are somewhat variable across foods in standard nutrient databases. Bioactive compounds are not typically a component in current food and nutrient databases. It is not yet possible to account for the potential interaction of background diets or gene-environment factors on health outcomes. Within a stable energy intake, if consumption of one category of food is high, another by definition is low. Only simultaneous assessment of the whole diet can allow for inter-individual comparisons.

This study was designed to take a food-/nutrient-based approach toward characterizing the relation between food intake and CHD risk in postmenopausal women who participated in the WHI-OS. Those who had a CHD event (WHI-OS CHD cases) were matched with controls (WHI-OS CHD controls) who remained event free during the 8-y observational period. Three distinct dietary patterns emerged. None contained all the elements of what would be considered a heart-healthy diet by current definitions and 30% of cases reported consuming a dietary pattern consistent with diet cluster 1, whereas 35% of controls reported consuming a dietary pattern consistent with diet cluster 3, so these associations were not completely distinct. This simply reflects the fact that people typically consume a variety of foods, some considered especially nutritious and others less so. Approaching this assessment using a sophisticated statistical methodology rather than qualitatively ranking dietary adherence may offer new or different insights for consideration.

Notably, a higher proportion of WHI-OS CHD cases than controls reported consuming a diet consistent with diet cluster 1, a diet characterized by lower fat. The low-fat diets are not consistent with dietary guidance after the year 2000, starting with the 2000 Dietary Guidelines for Americans, 2000 AHA (61), and National Cholesterol Education Panel ATP III (42). The current recommendations for a cardioprotective diet (62) are more consistent with the pattern presented in diet cluster 1. The majority of saturated fat in the American diet is contributed by cheese and meat products. Not surprisingly, the lower reported total fat intake was associated with greater reliance on plant-based foods. Although the distribution of the major types of dietary fat, SFA, MUFA, and PUFA, was significantly different among diet clusters, the absolute differences were modest. WHI-OS CHD cases reporting consuming diet cluster 1 also had a lower BMI and were older, less likely to have ever smoked, reported spending less time sitting or lying down, and reported more episodes of moderate or strenuous activity than the other diet clusters. A similar pattern was observed in the WHI-OS CHD controls, although the differences among diet clusters were not significant for all the variables. In general, we are reluctant to emphasize distinctions or individual differences among the three diet clusters identified beyond describing them, because that would violate the underlying premise of the work that dietary intake must be viewed and interpreted as the sum of its parts, not individual components.

Intervention studies have reported improved CHD outcomes and/or risk factors based on defined dietary patterns or comparisons among dietary patterns (63–74). Although the effect has been attributed, at times, to a single putative component of the diet, a careful review of the data reveals that when energy-containing variables were changed, in all cases there was a displacement of one for the other to avoid confounding by changes in body weight.

TABLE 5 Association of dietary patterns with CHD in WHI-OS cases and controls[1]

	Diet cluster 1 Case:control (*n* =369:465)		Diet cluster 2 Case:control (*n* =322:327)	Diet cluster 3 Case:control (*n* =533:432)	
	OR	(95% CI)	Reference	OR	(95% CI)
Model 1[2]	0.80	(0.65, 0.99)	1.0	1.28	(1.04, 1.57)
Model 2[3]	0.78	(0.64, 0.99)	1.0	1.18	(0.95, 1.47)
Model 3[4]	0.82	(0.65, 1.03)	1.0	1.14	(0.91, 1.44)
Model 4[5]	0.81	(0.65, 1.03)	1.0	1.14	(0.91, 1.45)
Model 5[6]	0.85	(0.67, 1.08)	1.0	1.15	(0.91, 1.46)

[1] CHD, coronary heart disease; WHI-OS, Women's Health Initiative-Observational Study.
[2] Model 1: Adjusted for matching factors: age, date of enrollment, race/ethnicity, absence of relevant disease at baseline (conditional logistic regression was performed on matched pairs, thus automatically these results are adjusted for the effect due to matching factors).
[3] Model 2: adjusted model 1 + smoking + education + physical activity.
[4] Model 3: adjusted models 1 and 2 + BMI + systolic blood pressure.
[5] Model 4: adjusted models 1, 2, and 3 + total energy intake.
[6] Model 5: adjusted models 1, 2, 3, and 4 + lipid medication use+ diabetic treatment.

Principal component and factor analyses have been reported in several other observational studies that have likewise reported dietary patterns associated with CHD outcomes (46,75–81). Direct comparisons are difficult due to different approaches used to model the data and inherent cross-cultural differences in food availability and cultural practices. Temporal changes in the food supply, e.g., increased availability of nonfat and reduced-fat dairy products and leaner cuts of meat, and the inherent delay in detecting these changes in standardized nutrient databases may also confound such comparisons. Due to the modest differences in the reported macronutrient intake among the diet clusters, it is difficult to attribute the differences in CHD odds ratios to the fatty acid profile of the diet, fiber content, use of supplemental nutrients, or dietary micronutrient intakes, all factors that have individually been associated with CHD risk (1,32,44). Type of dietary fat, a variable associated with CHD risk, was addressed in recent meta-analyses and one concluded there was insufficient evidence to support the hypothesis that SFA was associated with CHD (82–84). Using pooled analysis of cohort studies, the second concluded that displacing SFA with PUFA rather than carbohydrate was associated with decreased CHD risk (84,85). Although we were not able to address this issue directly, results showed participants in diet clusters 1, 2, and 3 reported consuming 24, 28, and 39% of energy as fat, respectively, and 61, 52, and 44% of energy as carbohydrate, respectively. Quality of the dietary carbohydrate is likely an additional confounding factor deserving further exploration (86–88).

Limitations to this work include the absence of individual, prospective blood lipid-lipoprotein and other risk factor data that would be especially relevant to CHD. Known limitations in the FFQ methodology include under-reporting, especially among overweight participants, with regard to dietary energy intake (36,89). Of note, although it is difficult to identify and quantify misreporting based on the available data, it is likely that misreporting such as under-reporting dilutes rather than exaggerates the association under examination. Also, during the study period, dietary messages in the lay press and proliferation of fat-free products may have changed long-term dietary behaviors or subliminally suggested "right" answers to the FFQ. The principal component analysis may itself have limitations related to accurate characterization of dietary behavior (90). Both principal component analysis and K-mean clustering are dependent on subjective choice of tuning parameters, such as the number of principal components and clusters. The reproducibility of the current finding therefore needs to be examined in other independent data sets and is beyond the scope of the current paper. Regardless, the large sample size, understudied age group, and standardized diet assessment methodology in a case-control format offer certain advantages not available in smaller studies with limited dietary data.

This study blends novel statistical methodology not used in the field of nutrition with careful and standardized dietary data collection among a large population of postmenopausal women with adjudicated outcomes. Findings suggest there are potential dietary patterns and behaviors that may be predictive of CHD. Studies are needed to further quantify and integrate eating patterns with physical activity and other lifestyle behaviors to further characterize heart-healthy behaviors.

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