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Ultra-processed food intake and mortality in the United States: Results from the Third National Health and Nutrition Examination Survey (NHANES III 1988-1994)

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Abstract

Objective—To evaluate the association between ultra-processed food intake and all-cause mortality and cardiovascular disease mortality in a nationally representative sample of U.S. adults.

Design—Prospective analyses of reported frequency of ultra-processed food intake in 1988-1994 and all-cause mortality and cardiovascular disease mortality through 2011

Setting—The Third National Health and Nutrition Examination Survey (NHANES III, 1988-1994)

Participants—Adult participants (≥20y, *n*=11,898)

Results—Over a median follow-up of 19 years, individuals in the highest quartile of frequency of ultra-processed food intake (e.g. sugar-sweetened or artificially-sweetened beverages, sweetened milk, sausage or other reconstructed meats, sweetened cereals, confectionery desserts) had a 31% higher risk of all-cause mortality, after adjusting for demographic and socioeconomic confounders, and health behaviors (adjusted HR: 1.31; 95% CI: 1.09, 1.58; *P*-trend=0.001). No association with cardiovascular disease mortality was observed (*P*-trend=0.86).

Conclusions—Higher frequency of ultra-processed food intake was associated with higher risk of all-cause mortality in a representative sample of U.S. adults. More longitudinal studies with dietary data reflecting the modern food supply are needed to confirm our results.

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Keywords

ultra-processed food; NOVA classification; nutritional characteristics; nutritional quality; mortality

INTRODUCTION

In the last few decades, the global food system has changed significantly. Ultra-processed foods, characterized as ready-to-eat foods that are manufactured with substances from industrial processing (chemical additives, colorants, flavoring) are more readily available in the food supplies of high- and middle-income countries[(1)]. Recent cross-sectional studies using individual-level consumption data reported that ultra-processed foods contribute 25-60% of total energy intake in the U.S.[(2)], Canada[(3)], Brazil[(4)], France[(5)], Mexico[(6)], and Chile[(7)]. In the U.S., these foods account for a strikingly high percent (90%) of energy from added sugar[(2)].

High consumption of ultra-processed foods raises health concerns. As ultra-processed foods contain little or no whole foods, these foods are nutritionally poor, with high amounts of fat, added sugar, and energy, and low amounts of micronutrients and fiber[(2,3,5,8)]. A systematic review reported a direct association between these types of foods, such as sugar-sweetened beverages, or sweetened/salted snacks and body fat in children and adolescents[(9)]. In addition to low nutritional quality, ultra-processed foods and their packaging contain compounds that can pose health risks[(10–12)]. Compounds such as acrylamide, polycyclic aromatic hydrocarbons, heterocyclic amines, and furanes may be present in ultra-processed foods as they can be generated during heating, a commonly used food processing technique[(13,14)]. Exposure to chemicals such as phthalates and bisphenol A, which are used in food packaging as plasticizers is also possible[(15,16)].

Furthermore, previous studies which classified foods using pre-defined criteria on degree of processing have shown elevated risk of chronic diseases with high consumption of ultra-processed food. A longitudinal study of Brazilian children showed that ultra-processed food intake was associated with dyslipidemia[(17)]. In adults, cross-sectional studies have shown an increased odds of obesity with higher consumption of ultra-processed foods[(18–20)]. A prospective cohort of university students in Spain reported a dose-response relationship between ultra-processed food consumption and a higher risk of incident obesity and hypertension[(21,22)]. In addition, a recent population-based study from France found that a 10% increase in ultra-processed foods in the diet was associated with a higher risk of overall cancer and breast cancer[(23)]. These studies suggest that there are adverse health outcomes associated with ultra-processed food intake, but all of these studies are limited in that they are either cross-sectional or had a relatively short follow-up period (5-9 years).

To address these gaps, we investigated the association between ultra-processed food intake and all-cause mortality and cardiovascular disease mortality using data from a nationally representative sample of U.S. adults with over 20 years of follow-up. We focused on cardiovascular disease mortality given the previously reported associations between ultra-processed foods and cardiovascular disease risk factors[(21,22)]. We also aimed to examine socio-demographic and nutritional characteristics according to different levels of ultra-processed food consumption.

METHODS

Study Population

We conducted prospective analyses on adult participants (≥20y) from the Third National Health and Nutrition Examination Survey (NHANES III, 1988-1994). NHANES III used a multi-stage, stratified, clustered, probability sampling design to identify a nationally representative sample of non-institutionalized civilians in the U.S.[(24)]. Participants completed a household interview, laboratory measurements, and physical examinations[(24)]. Details of the survey design have been published previously[(24)].

In this study, we included adults with no missing information on ultra-processed food intake and mortality (*n*=18,779). Since dietary intake often changes after diagnosis of a clinical condition, we excluded adults with a chronic disease, such as heart disease (self-reported diagnosis of heart attack, stroke, or ischemic heart disease, *n*=1,728), cancer (self-reported diagnosis of cancer, *n*=609), diabetes (self-reported diagnosis of diabetes, diabetes medication use, or fasting glucose ≥126 mg/dL, *n*=3,701), or chronic kidney disease (estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2, *n*=843) at baseline. The final sample size was 11,898 (Supplemental Figure 1).

Dietary Assessment and Classification of Ultra-Processed Food

At baseline, trained interviewers administered an 81-item food frequency questionnaire, which assessed participants' usual intake of foods and beverages consumed in the past month, and a 24-hour dietary recall[(24)]. Since portion size was not assessed on the food frequency questionnaire, we used data from participants' 24-hour dietary recalls to examine intake of total energy, macronutrients, and micronutrients. The NHANES III Nutrition Methodology Working group, which is comprised of a group of experts from academia, government agencies, and industry, recommended the use of an food frequency questionnaire to rank participants by their food intake[(24)].

We used the NOVA classification to categorize each reported food item on the food frequency questionnaire into one of the following categories representing levels of processing: 1) fresh or minimally processed foods; 2) processed culinary ingredients; 3) processed foods with salt, sugar, or oil; or 4) ultra-processed foods containing predominantly industrial substances and few whole foods (Supplemental Table 1)[(3,25,26)]. The first category represents foods that are obtained directly from plants or animals that have undergone alterations to increase shelf life or storage. These types of alterations can range from removing inedible parts, refrigerating, freezing, vacuum packaging, drying, crushing, grinding, filtering to pasteurizing. The second category represents substances that are extracted from nature or foods from the first category, which may be used in the kitchen as culinary ingredients. The third category represents foods that have undergone simple alterations such as adding oil, sugar, salt, or other items in the second category to foods in the first category. These alterations are usually made to improve sensorial qualities or extend the durability of foods in the first category. The fourth category represents foods containing substances that are not typically used in culinary preparation such as hydrogenated oils, hydrolyzed protein, or emulsifiers, and have few whole foods. Ultra-processed foods contain industrial substances to mimic sensorial qualities of whole foods and create foods that are highly palatable.

The focus of our study was on the fourth level of processing. After food items were classified by NOVA category, we summed the frequency of ultra-processed food intake per day for each participant and then divided the participants into quartiles based on their frequency of consumption per day.

Nutrient Analyses

We used three methods to examine the nutritional characteristics of individuals reporting different frequencies of ultra-processed food. For all methods, we used participants' 24-hour dietary recall data. First, we examined nutrient density across quartiles of frequency of ultra-processed food intake. We expressed macronutrients (protein, carbohydrates, total fat, saturated fat, monounsaturated fat, and polyunsaturated fat) and added sugars as percent of energy, and fiber, cholesterol, and micronutrients as grams, milligrams, or micrograms per 1,000 kcal. All nutrient estimates except for added sugars were assigned by the National Center for Health Statistics using the USDA food composition database[24]. To derive estimates on added sugar intake, we used the Pyramid Servings Database developed by the National Cancer Institute. This database provides estimates of added sugars in all food items reported in NHANES III dietary recalls[27].

Second, we used the Nutrient-Rich Foods (NRF) index, a score which ranks the nutritional quality of a food. NRF scores has been associated with overall diet quality[28] and has been inversely associated with all-cause mortality in a European cohort[29]. Details on development, validation, and calculation of the score have been published previously[28,30]. Briefly, NRF9.3 is calculated based on 9 nutrients to encourage (protein, fiber, vitamin A, C, and E, calcium, iron, magnesium, and potassium) and 3 nutrients to limit (saturated fat, added sugar, and sodium). A higher NRF9.3 food score indicates higher nutritional quality of a food. We additionally excluded pregnant and lactating women for this analysis (n=267), as intake of micronutrients differ during this period. For each participant, we summed the NRF9.3 food scores, divided by total energy intake, and expressed the NRF9.3 index score per 100 kcals.

Lastly, we used the Healthy Eating Index (HEI)-2000, a 100-point score based on the U.S. Dietary Guidelines for Americans[31], to assess diet quality across quartiles of ultra-processed food intake.

Outcome Ascertainment

From baseline through December 31, 2011, participants' vital status and cause-of-death information were followed by the National Center for Health Statistics. Vital status was determined by probabilistic matching of participants to the National Death Index based on identifying information, including social security number, name, sex, and date of birth[32]. Thus, only participants with insufficient information on these matching criteria were lost to follow-up. Details of the linkage methods have been reported previously[32]. We calculated follow-up time (number of days) as the time from NHANES examination until the date of death or the end of follow-up on December 31, 2011. We defined death due to cardiovascular disease as those with a primary cause of death listed as International Classification of Diseases 10th edition I00-I69[33].

Covariates

Participants self-reported the following covariates: age (continuous), sex (male or female), race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, or other), total energy intake (continuous), education level (<high school, high school, or > high school), income (poverty-income ratio <130%, 130-<350%, ≥350%), health behaviors including smoking (current smoker, former smoker, or never smoker), alcohol consumption (quartiles), and physical activity (continuous).

Participants reported frequency of engaging in any moderate or vigorous physical activity such as walking, jogging, running, bicycling, swimming, aerobics, lifting weights, dancing, or gardening in the past week. For each activity, an intensity rating (a metabolic equivalent of task, MET) was assigned[34]. We multiplied the frequency and intensity of any physical activity performed in the past week.

Participants' height (centimeters) and weight (kilograms) were measured using standardized methods[24]. We calculated body mass index (BMI in kg/m^2) from this information, and categorized it as underweight (<18.5), normal weight (18.5-<25), overweight (25-<30), or obese (≥30). Baseline hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or self-reported use of antihypertensive medication. Total serum cholesterol was assessed using enzymatic methods that were previously described[35]. We calculated eGFR using the 2009 Chronic Kidney Disease Epidemiology Collaboration equation after calibrating serum creatinine measurements to reference values at the Cleveland Clinic Research Laboratory[36,37]. We used total serum cholesterol and eGFR as continuous variables. The percentages of participants with missing covariates were low (range: 0-8%). We conducted the analyses among participants with no missing information.

Statistical Analyses

We examined participants' baseline characteristics and nutritional characteristics according to quartiles of frequency of ultra-processed food intake. We used weighted chi-square tests for categorical variables and weighted analysis of variance (ANOVA) for continuous variables[38].

We performed three Cox proportional hazards models, with length of follow-up time as the time-metric to calculate hazard ratios (HR) and 95% confidence intervals (CIs) for the association between frequency of ultra-processed food intake and all-cause mortality and cardiovascular disease mortality. Model 1 adjusted for demographic characteristics (age, sex, race/ethnicity), and total energy intake. Model 2 adjusted for covariates in model 1 as well as socioeconomic factors (poverty level, education level), and health behaviors (smoking status, physical activity, and alcohol intake). In order to test the mediating effect of body mass index, hypertension status, total cholesterol, and eGFR, secondary analysis was carried out adjusting for these variables in addition to covariates in model 2 (model 3). We considered model 2 as our main result because model 3 includes factors that may be along the causal pathway. We tested for a linear trend across quartiles using median value within each quartile.

As sensitivity analyses, we additionally controlled for diet quality scores, as ultra-processed food consumption can be a marker of an unhealthy dietary pattern and to examine the mediating role of diet quality on ultra-processed food and mortality. In addition, we excluded the first 2 years of follow-up for all participants to minimize the possibility that deaths were due to an underlying health condition at baseline. We repeated the analyses excluding processed meats (bacon, sausage, and processed meats) from ultra-processed food intake to confirm if the observed associations were not due to consumption of processed meat, which has a strong and direct association with mortality[39]. Analyses were conducted using Stata version 13.0 (StataCorp, College Station, Texas).

RESULTS

In the overall sample, participants consumed a mean of 4 times of ultra-processed food per day (range: 0-29.8). A total of 0.06% of the analytic sample consumed no ultra-processed food on a daily basis. Those in the highest quartile consumed more than 5 times of ultra-processed food per day.

Those in the highest quartile of frequency of ultra-processed food intake were more likely to be younger, male, non-Hispanic white, and current smokers and were less likely to have less than a high school education or to have a household income more than 350% of poverty level ($P \leq 0.01$ for all comparisons) (Table 1). Those in the highest quartile were more likely to have lower total cholesterol ($P=0.02$) and higher eGFR ($P<0.001$).

Participants in the highest quartile of frequency of ultra-processed food intake had significantly higher intake of total energy, total fat, saturated fat, monounsaturated fat, and added sugar, and lower intake of protein ($P<0.001$ for all comparisons) (Table 2). Intakes of fiber, cholesterol, and almost all micronutrients were significantly lower among participants in the highest quartile. Those in the highest quartile had lower scores for nutritional quality using NRF9.3 ($P<0.001$) and diet quality using HEI-2000 ($P=0.001$).

Over a median follow-up of 19 years, 2,451 deaths due to any cause occurred and 648 deaths were due to cardiovascular disease. In model 2, those in the highest quartile of frequency of ultra-processed food had a 31% higher risk of death compared to those in the lowest quartile (HR: 1.31; 95% CI: 1.09, 1.58, *P*-trend across quartiles = 0.001) (Table 3). When potential mediating variables were included in the model (Model 3), the association did not change substantially (HR: 1.30; 95% CI: 1.08, 1.57, *P*-trend: 0.001).

No significant associations were observed for frequency of ultra-processed food intake and cardiovascular disease mortality in model 2 or model 3 (Table 4).

Results were similar in sensitivity analyses after additionally adjusting for diet quality scores (all-cause mortality: *P*-trend=0.001; cardiovascular disease mortality: *P*-trend=0.54), after excluding the first two years of follow-up (all-cause mortality: *P*-trend=0.007; cardiovascular disease mortality: *P*-trend=0.88), and after excluding bacon, sausage, and processed meats from ultra-processed food intake (all-cause mortality: *P*-trend=0.02; cardiovascular disease mortality: *P*-trend=0.45) in model 3.

DISCUSSION

Among U.S. adults without chronic disease at baseline, we observed a significant association between higher frequency of ultra-processed food intake and higher risk of all-cause mortality over a median follow-up of 19 years. This association remained significant after adjusting for sociodemographic factors, health behaviors, and clinical factors. We found that a diet that is high in ultra-processed food consists of a high amount of fat, added sugar, and total energy and is low in overall diet quality, protein, fiber, and micronutrients.

Our study builds on previous longitudinal studies which used the NOVA framework to study the association between ultra-processed food intake and chronic conditions. These studies reported adverse health outcomes in association with ultra-processed food consumption including obesity, hypertension, and cancer at mid-life (40 years of age or older at follow-up)[21–23]. To the best of our knowledge, this is the first study which examined the association between ultra-processed food intake and mortality. Our findings suggest that the adverse health risks associated with ultra-processed food consumption, which was observed in previous studies in mid-life, may lead to a shorter lifespan.

There are several pathways through which ultra-processed foods may increase the risk of all-cause mortality. Participants in the highest quartile of frequency of ultra-processed food intake consumed higher amounts of total energy, total fat, saturated fat, and added sugar, and lower amounts of protein, micronutrients, and fiber. Low dietary fiber and micronutrients may contribute to earlier death by increasing the risk of major chronic conditions and damaging mitochondrial function[40,41]. In addition, those in the highest quartile had poor overall diet quality and nutritional quality. In epidemiological studies, diet quality has been shown to be a strong predictor of incident chronic conditions, such as diabetes, cardiovascular disease, cancer, and all-cause mortality[29,42–44]. However, when we further adjusted for diet quality scores, the results on ultra-processed food and all-cause mortality did not change. This suggests that diet quality may not be a strong mediator of the association between ultra-processed food intake and mortality and there may be other bioactive compounds in ultra-processed foods that can increase the risk of death[23].

Ultra-processed food intake may elevate the risk of all-cause mortality by increasing exposure to contaminants and environmental chemicals. For example, acrylamide is formed during heating [13], and this compound is considered by the U.S. Environmental Protection Agency and the National Toxicology Program as a neurotoxin and carcinogenic[45]. Furthermore, environmental chemicals that are present in food packaging, such as phthalates and bisphenol A have been shown to be associated with adverse health outcomes[11,46,47]. Phthalates and bisphenol A are endocrine disruptors that are associated with diabetes and obesity in cross-sectional studies[15,16,48]. Examining environmental chemicals in ultra-processed food was beyond the scope of our study, and chemical exposure biomarkers were not available at NHANES III. Further investigation on environmental chemicals in ultra-processed food and health outcomes is necessary to test these hypotheses.

Given the association between ultra-processed food consumption and cardiovascular disease risk factors[21,22], the null association with cardiovascular disease mortality in our study was surprising. However, it is known that cause-of-death information is often inaccurate on death certificates for cardiovascular disease[49,50]. In our dataset, the most common cause of death was other causes. It is possible that deaths were coded as “other” if the underlying cause of death was not apparent. In addition, individuals with cardiovascular disease may be less likely to die from this condition since there are many effective treatments for reducing cardiovascular disease risk factors such as blood pressure and cholesterol. We had a smaller number of cause-specific (cardiovascular) deaths, and therefore less power to detect significant associations. Additional research investigating the association between ultra-processed food intake with cardiovascular disease events and mortality are needed.

Another surprising result was a lower intake of sodium at higher reported frequency of ultra-processed food intake. Given the common notion that processed foods are the largest sources of sodium intake[51], we expected to find higher sodium intake in this group. However, similar to our results, a cross-sectional study which used two dietary recalls from NHANES 2009-2010 found lower sodium intake among those in the highest quintile of ultra-processed food[8]. In contrast, the study in France which used a specific module to include sodium naturally present in foods, salt added during food preparation and at the table, and validated it against urinary sodium excretion showed that sodium intake was the highest among those in the highest quartile of ultra-processed food[23]. Lower sodium intake observed in our study may be due to not accounting for salt added during preparation or at the table in NHANES III or possibly underestimation of this nutrient in the food composition database.

Strengths of our study include the use of nationally representative data of U.S. adults, long-term follow-up period, minimal loss to follow-up (0.1%), pre-defined criteria to classify food items by degree of processing, and comprehensive nutrient analyses considering overall nutritional quality and diet quality.

Several limitations need to be considered. The food frequency questionnaire that was used in this study was not designed to answer the research question on food processing. Thus, several ultra-processed foods such as mass-produced breads were not included. Further, there is potential for misclassification. For example, we classified breads as processed foods, but consumption of mass-produced breads, which is considered ultra-processed food, may be more common than consumption of artisanal breads or handmade breads. We did not use participants’ 24-hour dietary recall data to rank participants by ultra-processed food consumption because the 24-hour dietary recall does not represent usual intake of foods and beverages[52]. Only 5% of the participants completed a second 24-hour dietary recall in this dataset, making it difficult to reliably distinguish between those who consume ultra-processed frequently, infrequently, and never[53,54]. Moreover, in NHANES III, the 24-hour dietary recall does not provide detailed descriptions of foods and beverages. This is problematic, particularly for recipe foods, because the dataset does not have detailed ingredient lists and focuses mainly on fats used for cooking, and fat content of protein foods. Unfortunately, the 24-hour dietary recall does not provide better information than the food frequency questionnaire in NHANES III to classify foods according to different levels of processing. The classification of foods by processing level using the 24-hour dietary recall would require making assumptions about ingredients, which would be subjective and may lead to misclassification.

Another limitation is that no validation study was conducted for this specific food frequency questionnaire used in NHANES III. However, similar questionnaires of varying length have been validated[55,56]. In addition, there was a similar trend of demographic characteristics, and macro- and micronutrient intakes according to quartiles of ultra-processed food intake when we compared them with studies which used a semi-quantitative food frequency questionnaire and series of 24 hour dietary recalls[21–23]. This suggests that the food frequency questionnaire used in our study ranked participants to different quartiles reasonably well. Because frequency of ultra-processed food consumption is not necessarily the only or best proxy for dietary contribution of ultra-processed foods, it is important for future studies to confirm our findings using quantitative estimates of absolute intake instead of frequency of consumption of ultra-processed food. Next, information bias may be a limitation. Participants may have underreported ultra-processed food intake at baseline because of social stigma, and this could have led to an underestimation of the associations. However, information bias may not be a concern in our data because participants were not specifically asked about consumption of ultra-processed food. Participants reported their dietary intakes using a food frequency questionnaire, and we used pre-specified criteria to classify foods according to different levels of processing. Another limitation is that the NHANES III was conducted several decades ago, and thus food intake assessed in this cycle does not reflect the current U.S. food supply. Participants' dietary intake was measured only at baseline, because repeated assessment was not available in this dataset. Considering that the modern food supply has shifted to include more ultra-processed foods than 1988-94s[1], it is important to replicate our findings in more recent settings where there were repeated measurements of diet to better understand the association between ultra-processed food and long-term health outcomes. Lastly, even though we controlled for the most important confounders including socio-demographic characteristics, health behaviors, and potential risk factors for mortality, there is a possibility of residual confounding due to unmeasured or incorrectly measured covariates.

In addition to these considerations, it may be important to consider the issue of self-selection in future studies, because it is possible that those who were more at-risk for death had poorer self-care in general, beyond their dietary choices. However, when we examined additional variables in the NHANES III, we did not find evidence that those in the highest quartile of ultra-processed food intake have poorer self-care. The NHANES III did not assess factors that may have influenced participants to consume ultra-processed food (i.e., knowledge of potential adverse health outcomes associated with ultra-processed food consumption, perceived convenience, taste, and price of ultra-processed food, or food environment), which can provide important information to address self-selection. Future studies on ultra-processed food and health outcomes should consider collecting this information.

In conclusion, we found an elevated risk of all-cause mortality in association with higher frequency of ultra-processed food intake in a nationally representative sample of U.S. adults. Given the consistent results on elevated health risk of ultra-processed food intake, future dietary guidelines might consider making a recommendation about degree of food processing. More longitudinal studies with dietary data reflecting the modern food supply are needed to confirm our results.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Baseline Participant Characteristics According to Quartiles of Frequency of Ultra-Processed Food Intake[a]

	Quartiles of Frequency of Ultra-Processed Food Intake				
Characteristic	**Quartile 1: (*n*=2982)**	**Quartile 2: (*n*=2989)**	**Quartile 3: (*n*=2985)**	**Quartile 4: (*n*=2942)**	***P*-value[b]**
Ultra-processed food intake, times/day (range)	0-<2.6	2.6-<3.8	3.8-<5.2	5.2-<29.8	<0.001
Age, years	43±0.5	42±0.5	41±0.5	38±0.5	<0.001
Female sex	59	52	51	45	<0.001
Race/ethnicity					
Non-Hispanic white	65	77	81	80	
Non-Hispanic black	11	9	9	12	<0.001
Mexican American	8	6	5	4	
Other	16	8	5	4	
Poverty level					
<130%	20	16	15	18	
130-<350%	40	43	47	49	<0.001
≥350%	40	40	38	33	
Education level					
Less than high school	25	20	20	21	
High school	31	35	34	35	<0.001
More than high school	44	45	46	44	
Smoking status					
Current	28	28	28	34	
Former	22	25	24	22	0.01
Never	50	47	47	44	
Physical activity, MET/wk	29±5.5	24±1.0	25±0.9	27±0.9	0.08
Alcohol intake, drinks/mo	8±0.6	9±0.6	9±0.4	10±0.7	0.09
Body mass index, kg/m^2	26.2±0.1	26.3±0.1	26.1±0.2	26.2±0.2	0.95
Hypertension status	26	25	26	24	0.71
Total cholesterol, mg/dL	203±1.5	202±1.2	201±1.3	197±1.4	0.02
eGFR, mL/min/1.73 m^2	101±0.5	102±0.6	102±0.6	105±0.5	<0.001

eGFR, estimated glomerular filtration rate; MET, metabolic equivalent of task

[a]Values are means ± standard errors for continuous variables and % for categorical variables.

[b]We tested for differences in baseline characteristics using weighted chi-square tests for categorical variables and weighted analysis of variance (ANOVA) for continuous variables.

Table 2.

Nutritional Characteristics According to Quartiles of Frequency of Ultra-Processed Food (times/day) from participants' 24-hour recalls[a]

	Quartiles of Frequency of Ultra-Processed Food Intake				
Nutrient	**Quartile 1: (*n*=2982)**	**Quartile 2: (*n*=2989)**	**Quartile 3: (*n*=2985)**	**Quartile 4: (*n*=2942)**	***P*-value[b]**
Total energy intake, kcal/d	1970±33.3	2174±35	2312±33.9	2573±34	<0.001
Protein, % of energy	16.2±0.2	15.2±0.1	15.0±0.1	14.7±0.1	<0.001
Carbohydrates, % of energy	49.3±0.5	49.8±0.4	49.5±0.4	49.9±0.4	0.31
Fat, % of energy	25.1±0.3	25.9±0.3	26.5±0.2	26.7±0.2	<0.001
SFA, % of energy	8.4±0.1	8.7±0.1	8.9±0.1	9.1±0.1	<0.001
MUFA, % of energy	9.3±0.1	9.7±0.1	9.9±0.1	10.1±0.1	<0.001
PUFA, % of energy	5.4±0.1	5.5±0.1	5.7±0.1	5.5±0.1	0.15
Added sugars, % of energy	11.3±0.4	13.1±0.4	14.0±0.3	16.4±0.3	<0.001
Fiber, g/1000 kcal	8.6±0.2	8.2±0.1	7.9±0.1	7.1±0.1	<0.001
Cholesterol, mg/1000 kcal	137±3.2	124±2.2	126±2.7	124±2.4	<0.001
Sodium, mg/1000 kcal	1702±23.2	1637±17.8	1607±15.4	1620±18.8	0.02
Phosphorus, mg/1000 kcal	620 ±5.5	606±6.7	604±3.9	593±5.0	0.01
Potassium, mg/1000 kcal	1465±24.7	1395±17	1367±11.7	1249 ±12.6	<0.001
Magnesium, mg/1000 kcal	153±2.4	145±1.9	143±1.1	133±1.5	<0.001
Calcium, mg/1000 kcal	382±7.0	390±7.6	394.6±5.2	383±6.5	0.10
Iron, mg/1000 kcal	7.3±0.1	7.6±0.2	7.4±0.1	6.9±0.1	<0.001
Zinc, mg/1000 kcal	5.5±0.1	5.5±0.1	5.5±0.1	5.3±0.1	0.15
Vitamin A, μg RAE/1000 kcal	561±26.1	510±26.6	501±13.9	429±16.2	0.001
Thiamin, mg/1000 kcal	0.8±0.01	0.8±0.01	0.8±0.01	0.8±0.01	0.04
Riboflavin, mg/1000 kcal	0.9±0.01	0.9±0.01	0.9±0.01	0.9±0.01	0.004
Niacin, mg/1000 kcal	11.7±0.2	11.5±0.2	11.4±0.1	10.8±0.1	<0.001
Vitamin B6, mg/1000 kcal	0.9±0.01	0.9±0.01	0.9±0.01	0.8±0.01	<0.001
Vitamin B12, μg/1000 kcal	2.5±0.1	2.5±0.2	2.3±0.1	2.2±0.1	0.22
Vitamin C, mg/1000 kcal	51.2±1.2	51.4±1.6	53.3±1.5	47.7±1.4	0.04
Vitamin E, mg AT/1000 kcal	4.4±0.1	4.3±0.1	4.5±0.1	4.2±0.1	0.01
Folate, μg/1000 kcal	136.7±2.5	138.3±4.1	141.4±2.8	123.9±2.3	<0.001
Nutrient-Rich Foods Index[c]	23.2±0.6	20.9±0.6	20.2±0.4	16.0±0.4	<0.001
Healthy Eating Index-2000[d]	63.0±0.4	63.9±0.4	63.8±0.4	62.6±0.4	0.001

AT, alpha-tocopherol equivalent; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated; SFA, saturated fat.

[a]Values are means ± standard errors

[b]We tested for differences in nutritional characteristics using weighted analysis of variance (ANOVA).

[c]After excluding pregnant and lactating women, the Nutrient-Rich Foods Index was calculated based on 9 nutrients to encourage (protein, fiber, vitamin A, vitamin C, vitamin E, calcium, iron, potassium, magnesium) and 3 nutrients to discourage (saturated fat, added sugar, sodium); $\Sigma_{i=1\text{-}9}$ (nutrient i/ recommended daily values for nutrient i)* 100 – $\Sigma_{i=1\text{-}3}$ (nutrient i/ maximum daily values for nutrient i)* 100

[d]Healthy Eating Index-2000 can range from 0 to 100.

Table 3.

Hazard Ratios and 95% Confidence Intervals for All-Cause Mortality According to Quartiles of Frequency of Ultra-Processed Food (times/day)

	Quartile of Frequency of Ultra Processed Food Intake				
	Quartile 1: (*n*=2982)	**Quartile 2: (*n*=2989)**	**Quartile 3: (*n*=2985)**	**Quartile 4: (*n*=2942)**	***P*-trend**
Deaths, *n*	625	588	617	621	
Model 1[a]	1 [Reference]	0.98 (0.82, 1.16)	1.02 (0.83, 1.24)	1.29 (1.09, 1.53)	0.002
Model 2[b]	1 [Reference]	0.98 (0.83, 1.17)	1.06 (0.85, 1.29)	1.31 (1.09, 1.58)	0.001
Model 3[c]	1 [Reference]	0.99 (0.83, 1.18)	1.06 (0.87, 1.30)	1.30 (1.08, 1.57)	0.001

[a]Model 1 was adjusted for age, sex, race/ethnicity, and total energy intake.

[b]Model 2 was adjusted for the variables in Model 1 plus poverty level, education level, smoking status, physical activity, and alcohol intake.

[c]Model 3 was adjusted for the variables in Model 2 plus body mass index, hypertension status, total cholesterol, and estimated glomerular filtration rate.

Table 4.

Hazard Ratios and 95% Confidence Intervals for Cardiovascular Disease Mortality According to Quartiles of Frequency of Ultra-Processed Food (times/day)

	Quartile of Frequency of Ultra Processed Food Intake				
	Quartile 1: (*n*=2982)	**Quartile 2: (*n*=2989)**	**Quartile 3: (*n*=2985)**	**Quartile 4: (*n*=2942)**	***P*-trend**
Deaths due to cardiovascular disease, *n*	174	172	151	151	
Model 1[a]	1 [Reference]	1.04 (0.70, 1.54)	0.85 (0.56, 1.28)	1.04 (0.73, 1.50)	0.88
Model 2[b]	1 [Reference]	1.09 (0.69, 1.74)	0.92 (0.60, 1.41)	1.10 (0.74, 1.67)	0.86
Model 3[c]	1 [Reference]	1.10 (0.69, 1.76)	0.94 (0.61, 1.45)	1.13 (0.74, 1.71)	0.78

[a]Model 1 was adjusted for age, sex, race/ethnicity, and total energy intake.

[b]Model 2 was adjusted for the variables in Model 1 plus poverty level, education level, smoking status, physical activity, and alcohol intake.

[c]Model 3 was adjusted for the variables in Model 2 plus body mass index, hypertension status, total cholesterol, and estimated glomerular filtration rate.