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RESEARCH ARTICLE

Ultra-Processed Foods and Excess Heart Age Among U.S. Adults

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Introduction: A high percentage of total calories from ultra-processed foods has been associated with several cardiovascular disease risk factors. No study has examined the association between ultra-processed foods and heart age. This study examines the association between ultra-processed foods and excess heart age (difference between estimated heart age and chronological age) among U.S. adults.

Methods: The National Health and Nutrition Examination Survey (2009−2016) data for participants aged 30−74 years without cardiovascular disease or stroke (n=12,640) was used. Ultra-processed food was assigned based on NOVA classification of food processing, with ultra-processed food being the highest level. This study estimated the usual percentage of calories from ultra-processed foods and used sex-specific Framingham heart age algorithms to calculate heart age. The multivariable linear or logistic regression was used to examine the association between ultra-processed foods and excess heart age or likelihood of excess heart age being ≥10 years. Data analyses were conducted in 2020.

Results: The median usual percentage of calories from ultra-processed foods was 54.5% (IQR=45.8%−63.1%). Adjusted excess heart age increased from 7.0 years (95% CI=6.4, 7.6) in the lowest quintile (Q1) to 9.9 years (95% CI=9.2, 10.5) in the highest quintile (Q5) (p<0.001). Compared with Q1, AORs for excess heart age of ≥10 years were 1.16 (95% CI=1.08, 1.25) in Q2, 1.29 (95% CI=1.14, 1.46) in Q3, 1.43 (95% CI=1.20, 1.71) in Q4, and 1.66 (95% CI=1.29, 2.14) in Q5 (p<0.001). The pattern of association was largely consistent across subgroups.

Conclusions: U.S. adults consumed more than half of total daily calories from ultra-processed foods. A higher percentage of calories from ultra-processed foods was associated with higher excess heart age and likelihood of excess heart age of ≥10 years.

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INTRODUCTION

Ultra-processed foods (UPFs) are industrial food products that contain multiple ingredients and are manufactured through multiple sequences of processes to create the final products.[1] UPFs are usually branded; ready-to-eat; high in added sugars, salt, and saturated fats; and often contain many food additives.[2,3] The consumption of UPFs has increased significantly during the past few decades, especially among developed countries.[1] UPFs represent an important part of food consumption in the U.S., providing more than half of total calories for U.S. adults, and these calories

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are typically nutritionally poor and inconsistent with diets recommended by U.S. nutrition guidelines.[4–8] A recent inpatient crossover randomized trial concluded that a diet with a large proportion of UPFs increased energy intake and caused weight gain among participants.[9] Many observational studies suggested that high consumption of UPFs is associated with several major cardiovascular disease (CVD) risk factors, such as obesity,[4,10–12] hypertension,[13] dyslipidemia,[14] and metabolic syndrome.[15] Several cohort studies showed that high consumption of UPFs was associated with increased risk of CVD[16] and early death from all-cause mortality.[2,17–19]

Reducing UPF intake may help to reduce risk factors and improve prevention of heart disease and stroke, the leading causes of death and serious disability in the U.S.[20] However, prevention of CVD through recommended lifestyle change is challenging, especially when few Americans meet guidelines for healthy diets.[20,21] During efforts to prevent and manage CVD, multivariable prediction models were developed that use the individual's CVD risk profile to estimate the absolute risk of developing a CVD event during the next 10 years.[22–24] Model-predicted absolute CVD risk can be difficult for patients to understand and may provide false assurances for people with high lifetime, but low short-term, CVD risk. Therefore, the effectiveness of predicted CVD risk in promoting lifestyle changes or adherence to recommended treatment may be limited.[25–27] To simplify risk communication, the Framingham Heart Study (FHS) introduced the concept of heart age (i.e., predicted age of a person's vascular system based on an individual's risk profile, which would be equal to the person's chronological age if their risk factor profile were ideal).[28] The difference between predicted heart age and one's chronological age was defined as excess heart age (EHA), which provides a simplified way to describe the risk of developing CVD.[25,28] This study assesses the association between percentage of total calories from UPFs and EHA using data from nationally representative samples of U.S. adults.

METHODS

Study Population

The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional assessment of the U.S. population's health with information gathered through interviews, medical examinations, and laboratory tests. The survey provides demographic and laboratory data for a nationally representative sample of non-institutionalized U.S. residents.[29] This study pooled NHANES 2009–2016 data for stable estimates by demographic subgroups. Adults aged 30–74 years were included in accordance with the age range used in the FHS heart age calculation.[28] Among 16,835 adults aged 30–74 years, this study excluded 108 pregnant women; 1,329 participants who reported a history of heart attack, stroke, or congestive heart failure; 1,679 with incomplete or unreliable data on first-day 24-hour dietary recall; 975 who had missing information on risk factors used in heart age calculation; and 104 who had missing values on covariates. This left 12,640 participants for analysis.

Measures

This study used 24-hour dietary recall to estimate intake of UPFs.[30] All NHANES participants who received physical examinations provided first-day 24-hour dietary recall through in-person interviews at the mobile examination center, and 88.7% provided a second recall via telephone interview 3–10 days later. NHANES estimated participants' nutrient intake from foods by using U.S. Department of Agriculture Food and Nutrient Databases for Dietary Studies for each 2-year NHANES cycle.

This study used the NOVA foods classification system that considers the nature, extent, and purpose of processing when categorizing foods and beverages into 4 groups: (1) unprocessed or minimally processed foods, (2) processed culinary ingredients, (3) processed foods, and (4) UPFs.[1] This study focused on UPFs, the highest level of food processing. Examples of UPFs include sugar-sweetened beverages, breads, packaged salty snacks, packaged cakes, and processed meats. Briefly, the U.S. Department of Agriculture Food and Nutrient Databases for Dietary Studies converts foods and beverages (consumed among participants) into gram amounts and determines their nutrient values by using 8-digit food codes. The NOVA system was applied to this classification to classify all foods and beverages into 4 groups. The classification procedures of the NOVA system have been described in detail elsewhere.[4,6]

Dietary data from a single 24-hour recall may not represent a participant's usual intake because of day-to-day variations in diet, and use of such data may bias estimate of the association between nutrient intake and health outcomes because of the measurement errors.[31] Therefore, the methods developed by the National Cancer Institute were used to estimate the usual percentage of total calories from UPFs.[31,32] These methods require that some of the participants have multiple days of nutrient values to estimate the within- and between-individual variations; 88.7% of participants in this study had second-day recalls.[31] The models for estimating usual UPFs included the following: age, sex, race/ethnicity (white, non-Hispanic; black, non-Hispanic; Mexican American; and others), educational level (less than high school, high school graduate, and more than high school), leisure-time physical activity (inactive, insufficient, and met recommended physical activity),[33] poverty–income ratio (PIR, the ratio of household income to poverty threshold after accounting for inflation and family size [<1.3, 1.3–3.49, ≥3.5, missing, n=1,034]),[34] total calorie intake (first-day recall), and day of the week recall (weekday vs weekend [Friday–Sunday]).

FHS provided the sex-specific laboratory-based and nonlaboratory-based Framingham Risk Score (FRS) to estimate 10-year risk of developing CVD for each participant.[28] This study used the sex-specific nonlaboratory-based FRS, and the parameters from FRS models were used to calculate predicted heart age.[28] Heart age is the age of a person's heart based on their risk factor profile for heart attack and stroke. For example, a 50-year-old woman who smokes and has uncontrolled high blood pressure could have

a heart age of 75 years and EHA of 25 years, whereas the same woman without smoking and with optimal blood pressure and normal weight could have a heart age of 47 years, that is, 3 years younger than her chronologic age. EHA represents an alternative way to express a person's risk for developing CVD that may simplify CVD risk communication.[25] Because most U.S. adults have 1 or more CVD risk factors, the average adult has a positive EHA (i.e., heart age is greater than chronological age).[20,35] The nonlaboratory-based FRS model included the following 7 variables: age, sex, systolic blood pressure, hypertension treatment status (yes/no), smoking status (current/no), diabetes (yes/no),[36] and BMI. The average systolic blood pressure with up to 3 measurements (98.8% had 3 measurements) was used. Hypertension treatment, smoking status, and diabetes were self-reported. BMI was calculated as measured weight in kilograms divided by height in meters squared. For sensitivity analysis, this study calculated the heart age by using the laboratory-based FRS (replacing BMI with total cholesterol and high-density lipoprotein cholesterol) (Appendix Tables 1 and 2, available online).

Statistical Analysis

This study estimated the weighted prevalence and means (95% CIs) of selected covariates and CVD risk factors used in FRS by sex and tested for significance between men and women based on *t*-tests for continuous variables and Wald *F*-tests for categorical variables. Multivariable linear regression was used to examine the association between EHA and UPFs. It is not recommended to classify the predicted usual percentage of calories from UPFs into categories (e.g., quintiles, because of potential misclassifications at the quintile boundaries).[37] To present the results in quintile format, this study first used the restricted cubic spline in multivariable linear regression models with 4 knots (20th, 40th, 60th, and 80th percentiles) to examine the departure from a linear relationship between UPFs and EHA,[38] and there was no evidence of departure from a linear relationship (p=0.16 for nonlinearity). Second, this study calculated the 10th, 30th, 50th, 70th, and 90th percentile distribution of the percentage of calories from UPFs as the middle value of each quintile,[32] and then estimated the adjusted mean EHA associated with these UPF percentiles by multiplying the regression coefficient (β-coefficient) by the middle value of each quintile. This study estimated mean EHA adjusted for age, age squared, sex, and race/ethnicity and fully adjusted models, including additional covariates of education, physical activity, PIR, and total calorie intake. Multivariable logistic regression was used to examine the association between usual percentage of calories from UPFs and likelihood for an EHA of ≥10 years (1/0). Similar to the linear regression models, this study first examined the linear relationship between UPFs and EHA of ≥10 years (p=0.28 for nonlinearity) and then estimated the AORs by comparing the middle values of each quintile with the first quintile as reference (Q5, Q4, Q3, and Q2 vs Q1). This study also presented the stratified analyses by age group (<60 years vs ≥60 years), sex, race/ethnicity, educational level, physical activity, and PIR. This study tested for interactions between UPFs and selected covariates by including cross-product terms in the multivariable regression models based on Wald *F*-tests and presented false discovery rate adjusted *p*-values to account for multiple comparisons.[39] All analyses were conducted in 2020 using SAS, version 9.4 and SUDAAN, version 11, which accounted for the survey's complex sampling design.

RESULTS

Participant information is provided in Table 1. The mean age was 50 (range=30–74) years; the percentage of participants aged 30–44 years was higher among men than among women (p<0.001); more men than women met the recommended amount of physical activity (p<0.001); more women had a PIR <1.3 (p<0.001) and had more than high school education (p=0.026); and the percentage of black, non-Hispanic women was higher than that of men (p=0.002). For CVD risk factors, the mean systolic blood pressure, prevalence of diabetes, and current smoking were significantly higher among men than women (p<0.05), but the percentage of hypertension treatment was higher among women than men (p<0.001). The mean usual percentage of calories from UPFs was 54.5% (IQR=45.8%–63.1%) and was similar between men and women.

Table 2 presents the results for the linear regression models. Adjusted EHA increased from 7.0 (95% CI=6.4, 7.6) in the lowest quintile of UPF (Q1) to 9.9 (95% CI=9.2, 10.5) in Q5 (p<0.001). The association appeared to be stronger among women, increasing from 5.2 (95% CI=4.2, 6.2) in Q1 to 9.4 (95% CI=8.6, 10.3) in Q5 (p<0.001), but increased from 8.7 (95% CI=7.8, 9.6) in Q1 to 10.2 (95% CI=9.3, 11.1) in Q5 among men (p=0.064; false discovery rate adjusted p=0.067 for interaction between men and women). The pattern of association was largely consistent by age group, race/ethnicity, education, and PIR (p>0.05 for all interactions) (Figure 1A).

Table 3 presents the results for the logistic regression models. Compared with those with the lowest intake of UPFs (Q1, 38.1% of calories from UPFs), AORs for an EHA of ≥10 years increased 29% for those with average consumption (Q3, 54.5% calories from UPFs) and 66% among those with the highest intake (Q5, 71% calories from UPFs) (p<0.001). Among men, having an EHA of ≥10 years increased 19% in Q3 to 41% in Q5 (p=0.088), and among women the corresponding numbers were 42% and 101%, respectively (p<0.001; false discovery rate adjusted p=0.785 for interaction between men and women). These associations were similar by age group, race/ethnicity, education, and PIR (p>0.05 for all interactions) (Figure 1B).

In sensitivity analysis using the laboratory-based FRS to estimate heart age, adjusted EHA increased from 3.3 years in Q1 to 5.5 years in Q5 (a 2.2-year difference in EHA) (p=0.001) (Appendix Table 1, available online), and adjusted likelihoods for an EHA of ≥10 years were 15% and 32% higher comparing Q3 and Q5 with Q1 UPF intake (p=0.019) (Appendix Table 2, available online).

Table 1. Characteristics of Participants Aged 30–74 Years by Sex, NHANES 2009–2016

Characteristics	Total *n*=12,640	Men *n*=6,059	Women *n*=6,581	*p*-value[a]
Demographics and covariates				
Age, years, mean (95% CI)	49.7 (49.2, 50.1)	49.0 (48.6, 49.5)	50.2 (49.7, 50.7)	**<0.001**
Age group in years, % (95% CI)				
30–44	36.9 (35.1, 38.7)	38.7 (36.7, 40.7)	35.3 (33.2, 37.4)	**<0.001**
45–59	39.9 (38.3, 41.4)	39.8 (37.8, 41.8)	39.9 (38.0, 41.8)	
60–74	23.3 (22.0, 24.4)	21.5 (19.9, 23.1)	24.8 (23.4, 26.2)	
Race or ethnicity, % (95% CI)				
White, non-Hispanic	68.8 (64.6, 71.7)	68.9 (65.4, 72.4)	67.4 (63.6, 71.3)	**0.002**
Black, non-Hispanic	10.3 (8.7, 12.0)	9.5 (8.0, 11.0)	11.1 (9.2, 12.9)	
Mexican American	8.4 (6.4, 10.3)	8.7 (6.6, 10.7)	8.1 (6.1, 10.1)	
Other	13.2 (11.6, 14.8)	13.0 (11.2, 14.7)	13.4 (11.8, 15.1)	
Education, % (95% CI)				
Less than high school	14.7 (13.1, 16.4)	15.0 (13.2, 16.9)	14.4 (12.7, 16.2)	**0.026**
High school graduate	20.6 (19.2, 22.0)	22.0 (20.2, 23.7)	19.3 (17.7, 20.9)	
More than high school	64.7 (62.3, 67.1)	63.0 (60.4, 65.6)	66.3 (63.6, 68.9)	
Physical activity, % (95% CI)[b]				
Met recommendation	32.6 (30.8, 34.3)	34.1 (32.0, 36.2)	31.2 (29.1, 33.2)	**<0.001**
Insufficient	15.6 (14.5, 16.8)	13.9 (12.2, 15.6)	17.2 (15.9, 18.5)	
Inactive	51.8 (49.8, 53.7)	52.0 (49.4, 54.6)	51.6 (49.4, 53.8)	
PIR, % (95% CI)[c]				
<1.3	18.1 (16.2, 20.0)	16.8 (14.8, 18.8)	19.3 (17.3, 21.3)	**<0.001**
1.3–3.49	30.8 (28.9, 32.7)	30.3 (28.3, 32.3)	31.3 (29.2, 33.4)	
≥3.5	44.8 (42.1, 47.6)	46.8 (44.0, 49.6)	43.1 (40.1, 46.10)	
CVD risk factors				
SBP, mmHg, mean (95% CI)	122.3 (121.7, 122.9)	124.3 (123.6, 124.9)	120.4 (119.8, 121.1)	**<0.001**
BMI, kg/m^2, mean (95% CI)	29.4 (29.2, 29.6)	29.3 (29.0, 29.5)	29.5 (29.3, 29.8)	0.066
Hypertension, % (95% CI)				
No	67.6 (66.2, 69.0)	67.5 (65.6, 69.5)	67.7 (66.2, 69.2)	0.898
Yes	32.4 (31.0, 33.8)	32.5 (30.5, 34.3)	32.3 (30.8, 33.8)	
Participants taking medications for hypertension	71.0 (68.8, 73.1) (*n*=4,474)	65.2 (62.1, 68.2) (*n*=2,084)	76.3 (73.6, 79.1) (*n*=2,390)	**<0.001**
Diabetes, % (95% CI)[d]				
No	86.9 (86.0, 87.8)	86.0 (84.6, 87.3)	87.7 (86.7, 88.7)	**0.024**
Yes	13.1 (12.2, 14.0)	14.0 (12.7, 15.4)	12.3 (11.3, 13.3)	
Smoke, % (95% CI)				
Nonsmoker	80.8 (79.6, 82.0)	79.1 (77.6, 80.5)	82.4 (80.8, 84.0)	**0.001**
Current	19.2 (18.0, 20.4)	20.9 (19.5, 22.4)	17.6 (16.0, 19.2)	
Calories from UPFs, median % (IQR)[e]	54.5 (45.8–63.1)	55.0 (48.4–61.7)	54.8 (47.8–61.4)	0.325[f]

Note: Boldface indicates statistical significance ($p<0.05$).
[a]*p*-value for testing significance between men and women based on *t*-test for continuous variable and Ward-*F*-test for categorical variables.
[b]Definition of physical activity: inactive, defined as <10 minutes per week; insufficient, defined as some activity but not enough to meet the recommended amount; met recommendation, defined as ≥150 minutes per week moderate or ≥75 minutes per week vigorous or an equivalent combination. Minutes of vigorous-intensity activity were given twice the credit of minutes of moderate-intensity activity to calculate the equivalent combination.
[c]There were 1,034 participants with missing PIR.
[d]Definition of diabetes: self-reported or healthcare provider diagnosis or fasting glucose ≥126 mg/dL or HbA1c concentration ≥6.5%.
[e]Estimated usual percentage of calories from UPFs.
[f]*p*-value for testing significance in median calories from UPFs between men and women based on Wilcoxon test.
CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; PIR, poverty—income ratio; SBP, systolic blood pressure; UPF, ultra-processed food.

Table 2. Adjusted Mean EHA According to Usual Percentage of Calories From UPFs—NHANES 2009–2016

Characteristic	Mid-value of quintiles of usual percentage of calories from UPFs among U.S. adults					p-value[a]
	Q1 38.1%	Q2 47.8%	Q3 54.5%	Q4 61.2%	Q5 70.9%	
Range/usual percent, %	0 to <43.7	43.7 to <51.3	51.3 to <57.7	57.7 to <65.3	≥65.3	
Total						
Mean EHA adjusted for age, age squared, sex, and race or ethnicity only	5.4 (4.7, 6.0)	7.0 (6.6, 7.4)	8.1 (7.8, 8.5)	9.3 (8.9, 9.7)	10.9 (10.3, 11.5)	**<0.001**
Fully adjusted EHA[b]	7.0 (6.4, 7.6)	7.8 (7.5, 8.2)	8.4 (8.1, 8.7)	9.0 (8.6, 9.4)	9.9 (9.2, 10.5)	**<0.001**
Men[c]						
Mean EHA adjusted for age, age suared, sex, and race or ethnicity only	7.4 (6.6, 8.2)	8.4 (7.9, 8.9)	9.1 (8.7, 9.5)	9.8 (9.3, 10.3)	10.8 (10.0, 11.7)	**<0.001**
Fully adjusted EHA[b]	8.7 (7.8, 9.6)	9.1 (8.6, 9.7)	9.4 (9.0, 9.9)	9.7 (9.2, 10.3)	10.2 (9.3, 11.1)	0.064
Women[c]						
Mean EHA adjusted for age, age squared, sex, and race or ethnicity only	3.2 (2.4, 4.1)	5.5 (4.9, 6.0)	7.0 (6.5, 7.5)	8.5 (8.0, 9.1)	10.8 (10.0, 11.7)	**<0.001**
Fully adjusted EHA[b]	5.2 (4.2, 6.2)	6.4 (5.8, 7.1)	7.3 (6.8, 7.8)	8.2 (7.7, 8.7)	9.4 (8.6, 10.3)	**<0.001**

Note: Boldface indicates statistical significance ($p<0.05$). Data presented as mean (95% CI) unless otherwise noted.
[a]*p*-value for testing significant association between the usual percentage of calories from UPFs and EHA based on *t*-test (β-coefficient); all tests are 2-tailed.
[b]Adjusted for age, age squared, sex, race or ethnicity, educational attainment, physical activity level, poverty–income ratio, and total calorie.
[c]FDR-adjusted $p=0.067$ for interaction between usual percentage of calories from UPFs and sex for association with EHA based on Wald *F*-test; all tests are 2-tailed.
EHA, excess heart age; FDR, false discovery rate; NHANES, National Health and Nutrition Examination Survey; Q, quintile; UPF, ultra-processed food.

DISCUSSION

The main findings from this nationally representative survey are that U.S. adults aged 30–74 years consumed on average more than half of their total daily calories from UPFs, and higher consumption of UPFs was associated with significantly increased EHA (increased EHA represents increased risk of developing CVD). U.S. adults in the highest quintile of UPF consumption had approximately 3 additional years of EHA compared with those in the lowest quintile and 66% increased risk for having an EHA ≥10 years. The pattern of association was largely consistent across age groups, sex, race/ethnicity, education, physical activity, and PIR.

Many studies have suggested that high consumption of UPFs is associated with several major CVD risk factors, including overweight and obesity,[4,7,10–12] hypertension,[13] increased total cholesterol, low-density lipoprotein cholesterol among children,[14] and metabolic syndrome among children and adults.[15,40] Numerous studies have reported that dietary factors play significant roles in the incidence and mortality of CVD and other noncommunicable diseases with an estimate of 33% to >40% of incidence or deaths from these conditions associated with unhealthy diets.[41,42] Heart-healthy diets consist of fruits and vegetables; whole grains; legumes; nuts; fish; poultry; and limited intake of added sugars, sodium, and saturated fat.[8] By contrast, UPFs are typically energy-dense; high in added sugar, sodium, saturated or trans-fats; and low in dietary fiber and micronutrients.[2,6,43,44] In addition, UPFs contain classes of food additives to make the final food products palatable or more appealing and to extend shelf-life. Several animal and observational studies have indicated that cumulative exposure and interactions of multiple food additives may be associated with increased CVD risk factors,[16] such as lipid profiles in mice[45] and humans,[46] inflammation and metabolic syndrome in mice,[47] and glucose intolerance and insulin resistance in humans.[48] Other studies suggest that the highly refined carbohydrate, added sugar, or fat content of UPFs might produce changes in reward neurocircuitry, leading to addictive-like eating behaviors and overconsumption.[49,50] A recent trial revealed that a diet with a large proportion of UPFs significantly increased energy intake and caused weight gain among the adult participants.[9] This study showed that high consumption of UPFs was associated with increased EHA, consistent with the findings of other studies on the association between UPFs and CVD risk factors[4,7,10–15,40]

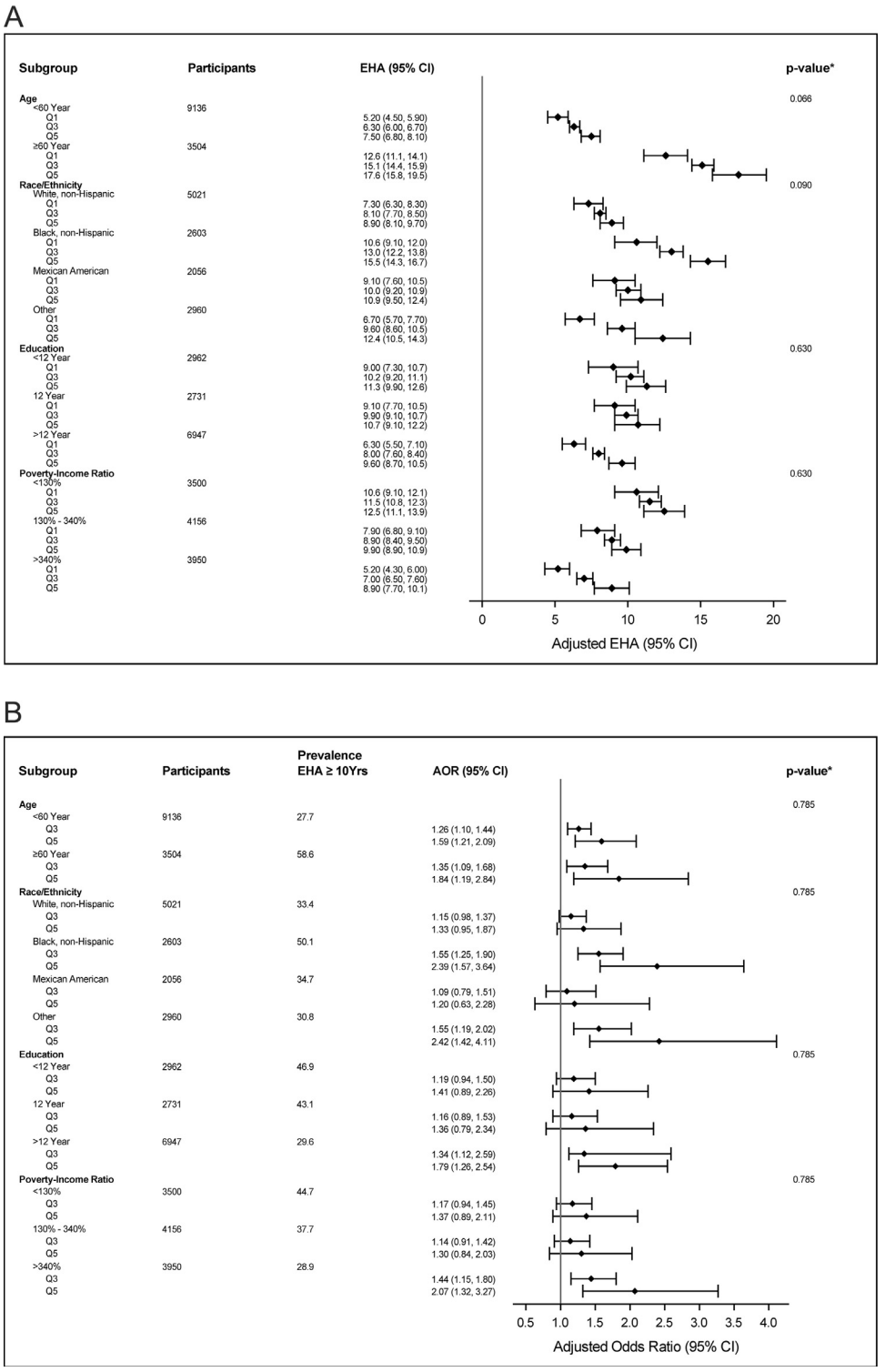

Figure 1. Adjusted mean EHA (panel A) and AOR of risk for EHA ≥10 years (panel B) according to usual percentage of calories from UPFs by selected subgroups—NHANES 2009–2016. Q1 usual percentage of calories from UPFs serves as reference group. *FDR adjusted *p*-value for interaction by subgroups. EHA, excess heart age; FDR, false discovery rate; NHANES, National Health and Nutrition Examination Survey; Q, quintile; UPF, ultra-processed food.

Table 3. AOR of EHA ≥10 Years According to Usual Percentage of Calories From UPFs—NHANES 2009–2016

Characteristic	Mid-value of quintiles of usual percentage of calories from UPFs among U.S. adults					p-value[a]
	Q1 38.1%	Q2 47.8%	Q3 54.5%	Q4 61.2%	Q5 70.9%	
Range/usual percent, %	0 to <43.7	43.7 to <51.3	51.3 to <57.7	57.7 to <65.3	≥65.3	
Total						
Mean EHA adjusted for age, age squared, sex, and race or ethnicity only	1.00	1.34 (1.25, 1.43)	1.63 (1.45, 1.83)	1.99 (1.69, 2.35)	2.66 (2.10, 3.36)	**<0.001**
Fully adjusted EHA[b]	1.00	1.16 (1.08, 1.25)	1.29 (1.13, 1.46)	1.43 (1.19, 1.70)	1.66 (1.29, 2.13)	**<0.001**
Men[c]						
Mean EHA adjusted for age, age squared, sex, and race or ethnicity only	1.00	1.25 (1.12, 1.40)	1.47 (1.22, 1.77)	1.72 (1.32, 2.24)	2.16 (1.48, 3.14)	**<0.001**
Fully adjusted EHA[b]	1.00	1.11 (0.98, 1.24)	1.19 (0.97, 1.45)	1.27 (0.96, 1.69)	1.41 (0.94, 2.11)	0.088
Women[c]						
Mean EHA adjusted for age, age squared, sex, and race or ethnicity only	1.00	1.42 (1.30, 1.55)	1.81 (1.56, 2.11)	2.32 (1.87, 2.86)	3.30 (2.44, 4.46)	**<0.001**
Fully adjusted EHA[b]	1.00	1.23 (1.12, 1.35)	1.42 (1.21, 1.66)	1.64 (1.31, 2.04)	2.01 (1.47, 2.75)	**<0.001**

Note: Boldface indicates statistical significance ($p<0.05$). Data presented as AOR (95% CI) unless otherwise noted.
[a]*p*-value for testing significant association between the usual percentage of calories from UPFs and an EHA of ≥10 years based on *t*-test (β-coefficient); all tests are 2-tailed.
[b]Adjusted for age, age squared, sex, race or ethnicity, educational attainment, physical activity level, poverty–income ratio, and total calorie.
[c]FDR-adjusted $p=0.785$ for interaction between usual percentage of calories from UPFs and sex on risk of an EHA of ≥10 years based on Wald *F*-test; all tests are 2-tailed.
EHA, excess heart age; FDR, false discovery rate; NHANES, National Health and Nutrition Examination Survey; Q, quintile; UPF, ultra-processed food.

and increased risk of developing CVD or all-cause mortality.[2,16–19] High intake of UPFs appears to be associated with multiple CVD risk factors and pathways to increase CVD risk; however, the exact biological mechanisms remain unclear. The clinical and policy implications regarding UPF consumption depend on better understanding of these pathways.

The major strengths of the study include use of a large, nationally representative sample of the U.S. population with comprehensive measurements of major CVD risk factors and sociodemographic data. This study used a measurement error model to estimate usual percentage of calories from UPFs accounting for within-person day-to-day variation.[31] The NOVA is a novel food classification system, and UPF is a promising dietary quality indicator that is relatively simple to understand. In addition, heart age is an alternative and simplified way to express the predicted risk of developing CVD. Risk prediction has played an important role in the prevention of CVD.[22] However, identifying effective approaches to communicate CVD risk to patients for lifestyle changes and to support the recommended treatments for CVD prevention remains a challenge.[51,52] Studies suggest that heart age might be an effective way to communicate individual-level risk for developing CVD and encourage actions to adopt heart-healthy lifestyles.[26,53] Expressing increased heart age in association with high consumption of UPFs may simplify CVD risk communication and motivate more people to adopt heart-healthy diets and lifestyles.

Limitations

First, although NHANES 24-hour dietary recall databases contain some information indicative of food processing, the degree of processing could not be determined consistently for all food items and may result in errors in NOVA classification. This study used a conservative approach, such that the lower level of processing was assigned in case of uncertainty. Therefore, potential misclassifications would lead to underestimation of UPF consumption. Second, studies showed that intake of total calories is under-reported in NHANES,[54,55] with different levels of under-reporting by BMI status (i.e., approximately 3%, 15%, and 20% by normal, overweight, and

people with obesity, respectively).[55] Using the percentage of energy contribution of UPF as the exposure variable may reduce the bias introduced by misreporting as long as the participants nondifferentially misreported calorie intakes from all foods. However, differential under-reporting of calorie intakes by NOVA groups could result in underestimating UPF consumption and attenuating the strength of association. Third, FHS consisted of predominantly white, non-Hispanic adults, and the heart age algorithm may not apply to other racial or ethnic groups. Although the Pooled Cohort Risk Equations included white, non-Hispanic and black, non-Hispanic adults in CVD risk prediction, the parameters for calculating heart age were not available.[22] Fourth, FHS developed the general CVD risk score for heart age on the basis of 1967 to 1987 cohorts.[28] This study used nonlaboratory-based FRS to estimate heart age to be consistent with previous publications.[25,56,57] The laboratory-based FRS provided different estimated heart age in this population because of the declining trend of total cholesterol, increasing trend of statin use,[58–60] and increasing trend of obesity and diabetes since the 1980s.[61–63] In sensitivity analyses, although the pattern of associations remained unchanged, the magnitude of EHA by using laboratory-based FRS was less than the nonlaboratory-based FRS. Fifth, NHANES consists of cross-sectional representative surveys that are subject to the potential for reverse causality between UPF consumption and CVD risk factors, should patients improve their diet after developing symptoms or disease. Sixth, as lifestyle risk factors tend to cluster,[64] higher UPF consumption could be a proxy of an overall unhealthy diet or lifestyle, and subsequent residual confounding could overestimate the strength of the association. Furthermore, as a cross-sectional analysis without follow-up CVD outcomes, causal association between UPF and CVD could not be determined. However, the results of this study are consistent with several cohort studies suggesting that high consumption of UPFs was associated with increased incidence of CVD and all-cause mortality.[16–19]

CONCLUSIONS

U.S. adults aged 30–74 years consumed more than half of total daily calories from UPFs, and a high percentage of calories from UPFs was associated with higher estimated EHA and likelihood of an EHA of ≥10 years. Discussing consumption of UPFs in the context of elevated EHA may be an effective approach for clinicians to communicate CVD risk with patients and to enhance motivation for preventing CVD.

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SUPPLEMENTAL MATERIAL

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