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FUNCTIONAL DISORDERS

Association of Ultra-processed Food and Unprocessed or Minimally Processed Food Consumption With Bowel Habits Among U.S. Adults

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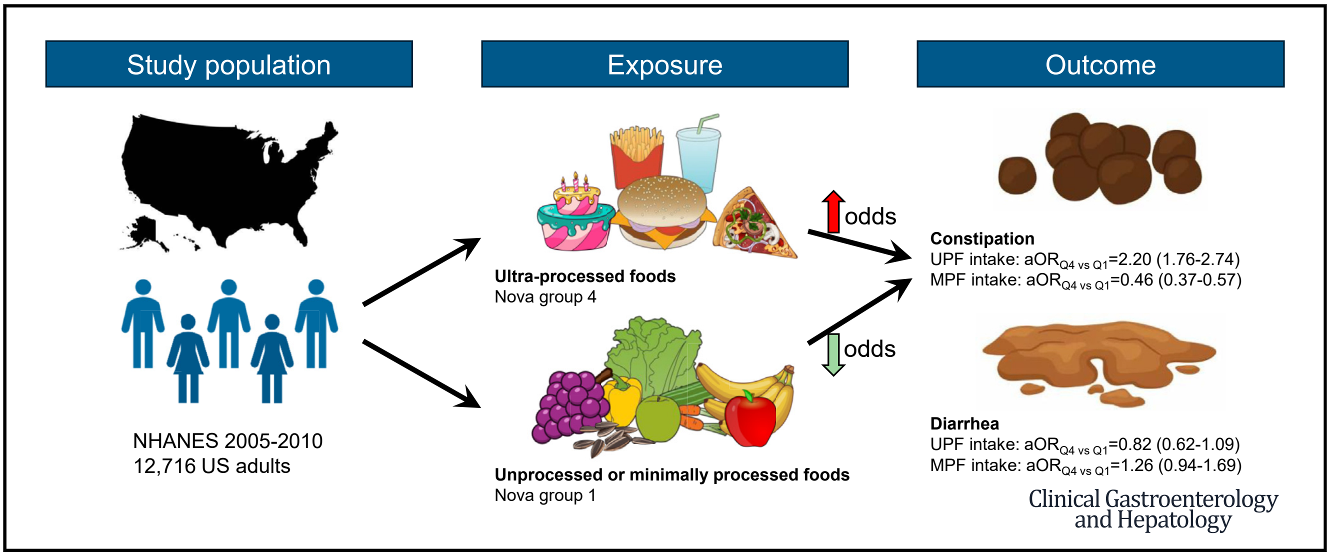

BACKGROUND & AIMS: **Ultra-processed foods (UPFs) may have a negative impact on bowel habits. We aimed to assess the association between UPF and unprocessed or minimally processed food (MPF) intake and bowel habits among adults in the United States (U.S.).**

METHODS: **We performed a cross-sectional study using data from the National Health and Nutrition Examination Survey (2005-2010). We used two 24-hour dietary recalls and, based on the Nova classification, calculated intakes of UPFs and MPFs. Constipation and diarrhea were defined using the Bristol Stool Form Scale and stool frequency. We performed survey-weighted logistic**

Abbreviations used in this paper: BMI, body mass index; BSFS, Bristol Stool Form Scale; CI, confidence interval; GI, gastrointestinal; HEI-2015, Healthy Eating Index-2015; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; MPF, unprocessed or minimally processed food; MVPA, moderate-to-vigorous physical activity; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; PIR, poverty-income ratio; UPF, ultra-processed food; US, United States.

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regression and substitution analysis to estimate the odds ratios (ORs) and 95% confidence intervals (CIs).

RESULTS: **Among 12,716 U.S. adults, there were 1290 cases of constipation and 1067 cases of diarrhea. Median UPF and MPF intakes were 26.5% and 66.2% of total grams per day, respectively. Greater UPF consumption (in % gram/d) was associated with higher odds of constipation (adjusted OR [$aOR_{Q4\ vs\ Q1}$], 2.20; 95% CI, 1.76–2.74) (P_{trend} < .001) but not diarrhea ($aOR_{Q4\ vs\ Q1}$, 0.82; 95% CI, 0.62–1.09) (P_{trend} = .12). Increased MPF consumption was associated with lower odds of constipation ($aOR_{Q4\ vs\ Q1}$, 0.46; 95% CI, 0.370–0.57) (P_{trend} < .001). Associations with constipation were attenuated after adjusting for diet quality ($aOR_{Q4\ vs\ Q1}$, UPF, 1.53; MPF, 0.69). Substituting 10% of UPF intake with an equivalent proportion of MPFs was associated with lower odds of constipation (aOR, 0.90; 95% CI, 0.87–0.93).**

CONCLUSIONS: **UPF intake was associated with higher odds of constipation, whereas the odds were lower with greater MPF consumption. The effect of food processing on bowel habits was independent of diet quality.**

Keywords: Colon; Epidemiology; Nova; Nutrition.

Constipation and diarrhea are common gastrointestinal (GI) symptoms in adults. The prevalence of chronic constipation has been estimated to be 16% (range, 0.7%–79%) in North America.[1] The prevalence of chronic diarrhea in the United States (U.S.) is reportedly 6.6% (95% confidence interval [CI], 5.8%–7.4%).[2] Both diarrhea and constipation are associated with large economic burden on the health care system. The estimated mean annual all-cause costs for chronic constipation and diarrhea measure close to $12,000 and $13,000 per patient per year, respectively.[3,4]

Diet appears to play a major role in constipation and diarrhea. Studies show that higher sodium and sugar intake increases the likelihood of constipation, whereas consuming a fiber-rich diet has the opposite effect.[5,6] High carbohydrate intake such as fructose has been associated with chronic diarrhea.[2] Consumption of various food items, macronutrients, and micronutrients are also well-established risk factors for gastrointestinal disorders that often present as chronic diarrhea. For example, dietary fat intake is associated with increased risk of inflammatory bowel disease (IBD).[7] Consuming gluten worsens diarrhea and malabsorption in celiac disease.[8]

There has been a worldwide shift towards greater consumption of ultra-processed foods (UPFs) in the past 2 decades.[9] These are foods defined under the Nova classification system, which categorizes foods by their degree of industrial processing.[10] Excess consumption of UPFs has been shown to cause disturbed intestinal motility.[11–13] Unprocessed or minimally processed foods (MPFs), on the other end of the food processing spectrum, are edible parts of plants, animals, fungi, and algae, either in their natural form or altered by methods and processes designed to preserve their content. Compared with UPFs, data on MPFs in disease processes are lacking and their role in bowel habits is unclear.

Here, we conducted a cross-sectional study among U.S. adults using data from the National Health and Nutrition Examination Survey (NHANES). This study aimed to examine the effects of UPF and MPF consumption on constipation and diarrhea.

Methods

Study Design and Participants

NHANES is a survey research program conducted by the National Center for Health Statistics of the U.S. Centers for Disease Control and Prevention.[14] Biannual cross-sectional surveys are designed to analyze a nationally representative sample of noninstitutionalized respondents in the U.S.. Participants are selected using a stratified multi-stage probability design with over-sampling of certain age and ethnic groups. Weighting is meant to compensate for differences in subject selection, sample design, and response rates, and is performed before univariable and multivariable analysis to adjust for sample frame.

Our study population consists of individuals 20 years old and older who responded to the bowel health questionnaires in the 2005 to 2006, 2007 to 2008, and 2009 to 2010 surveys and 2 24-hour dietary recalls.

Assessment of Dietary Intake and Nova Food Groups

For NHANES 2005 to 2010, two 24-hour dietary recalls are used to capture participants' dietary intake. The first dietary recall interviews are conducted in person by trained dietary interviewers in the Mobile Examination Center. Each Mobile Examination Center dietary interview room contains a standard set of measuring guides used to help the respondent report the volume and dimensions of the food items consumed. A second dietary interview is conducted by phone for all participants who completed the in-person recall 3 to 10 days later.

Based on the Nova classification, we categorized food items in the 24-hour dietary recall into 4 mutually exclusive food groups according to the extent and purpose of food processing—MPFs, processed culinary ingredients, processed foods, and UPFs (Supplementary Table 1). Details about the food categorization process in NHANES have been previously published.[15] Daily percentage intake of UPFs and MPFs in grams (% gram/d) are the main exposures of this study. UPF and MPF consumption were adjusted for total energy intake using the residual method. The residual method corrects for the effect of differences in total energy intakes.

Assessment of Bowel Habits

Bowel habits were assessed using the Bowel Health Questionnaire. Participants were asked to assess their usual or most common stool consistency using the Bristol Stool Form Scale (BSFS), which included various colorful cards and detailed descriptions of 7 stool types (Type 1: separate hard lumps, like nuts; Type 2: sausage-like, but lumpy; Type 3: like a sausage but with cracks in the surface; Type 4: like a sausage or snake, smooth and soft; Type 5: soft blobs with clear-cut edges; Type 6: fluffy pieces with ragged edges, a mushy stool; and Type 7: watery, no solid pieces). Participants' stool frequency was assessed with the following question: "How many times per week do you usually have a bowel movement?"

Constipation was defined as BSFS type 1 or 2 stools or less than three bowel movements per week. Diarrhea was defined as BSFS type 6 or 7 stools or more than 21 bowel movements per week.[16] We excluded a small number of participants who gave inconsistent answers—10 participants with BSFS type 1 or 2 stools AND more than 21 bowel movements per week and 35 participants with BSFS type 6 or 7 stools AND less than three bowel movements per week.

Covariates Assessment

Risk factors of constipation and diarrhea were identified as covariates from the literature. Details are included in the Supplementary Methods.

Demographic variables included age, sex, race/ethnicity, income, and educational attainment. Income was measured by the poverty-income ratio (PIR) as calculated by family income divided by the poverty threshold specific to family size and survey year.

Lifestyle variables included smoking, body mass index (BMI), physical activity, alcohol use, and total energy intake. Height and weight were measured to calculate BMI in kg/m^2. We calculated minutes of moderate-to-vigorous physical activity (MVPA). Participants who reported at least 150 minutes of MVPA per week met the Physical Activity Guidelines for Americans.[17]

Participants reported the number of prescription medications taken and laxative use during a 1-month period prior to the participant's interview date.

What You Need to Know

Background

Constipation and diarrhea are common gastrointestinal symptoms in the United States. Excess consumption of ultra-processed foods may have a negative impact on bowel habits.

Findings

Ultra-processed food consumption was associated with increased odds of constipation, whereas unprocessed or minimally processed food consumption was associated with decreased odds. Substituting ultra-processed foods with unprocessed or minimally processed foods was associated with reduced constipation.

Implications for patient care

Limiting ultra-processed food consumption and promoting the intake of unprocessed or minimally processed foods may serve as a management strategy to achieve healthy bowel habits.

The NHANES questionnaires provide self- and proxy-reported personal interview data on a broad range of health conditions and medical history. We selected a number of medical conditions that have been associated with bowel habits in the past which include cancer, congestive heart failure, chronic kidney disease, diabetes, thyroid disease, depression, and sleep disorder.

We used total fiber intake, total water intake, and the Healthy Eating Index-2015 (HEI-2015) to capture diet quality. Total fiber intake and total water intake were ascertained through 24-hour dietary recall interviews. Total water intake takes into account the water content from all foods and drinks. HEI-2015 is derived from the sum of 13 components, which included 9 adequacy components (total vegetables, greens and beans, total fruits, whole fruits, whole grains, dairy, total protein foods, seafood and plant proteins, and fatty acids) and 4 moderation components (sodium, refined grains, saturated fats, and added sugars).[18] A higher HEI-2015 indicates better diet quality.

Statistical Analysis

Due to the complex survey design applied by NHANES, we used appropriate sample weights, stratification, and clustering to ensure representative population-level data for the entire U.S. (Supplementary Methods). We examined daily percentage intakes of UPF and MPF in grams (% gram/d) in the primary analysis and kcal (% kcal/d) in a sensitivity analysis. To characterize study participants, we compared across quartiles of UPF/MPF consumption the distribution of mean (standard deviation) for continuous covariates and frequency for categorical covariates. *P* values for differences between quartiles of dietary intake were calculated by analysis of variance for means and the χ^2 test for frequencies.

We used survey-weighted logistic regressions with adjustment for potential confounding factors to calculate the odds ratios (ORs) and 95% CIs for constipation and diarrhea comparing quartiles of UPF and MPF consumption. Tests for trend were performed by assigning the median value of exposures to each quartile and modeling values as a continuous variable. We also calculated the ORs of constipation and diarrhea for every 10% increase in UPF and MPF intake. Age-adjusted models were adjusted for age group (20–39, 40–59, ≥60 years). Multivariable models were additionally adjusted for sex (male, female), race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, others), PIR (<1, 1–1.9, 2–4.9, ≥5), educational attainment (below college, college, above college), smoking status (never, former, current), BMI (<18.5, 18.5–24.9, 25–29.9, 30–39.9, ≥40 kg/m^2), physical activity (MVPA <150 min/wk, MVPA ≥150 min/wk), alcohol use (non-drinker, light drinker, heavy drinker), total energy intake (continuous, kcal/d), number of prescription medications (0, 1, 2–3, 4–7, ≥8), laxative use (no, yes), cancer (no, yes), congestive heart failure (no, yes), chronic kidney disease (no, yes), diabetes (no, yes), thyroid disease (no, yes), depression (no, yes), and sleep disorder (no, yes). We additionally adjusted for total fiber intake (continuous), total water intake (continuous), and HEI-2015 (continuous) to explore the independent effects of UPF and MPF consumption not mediated by diet quality.

On stratified analysis, associations between UPF and MPF intake and odds of constipation and diarrhea were examined according to strata of covariates. We selected these covariates based on their significant associations with either constipation or diarrhea in the main models. To test for multiplicative interaction, we conducted the Wald test and evaluated the coefficient for the cross-product term representing the main effect of food consumption and stratification factors.

We performed a substitution analysis and estimated the odds of constipation and diarrhea when substituting 5%, 10%, and 20% of UPF intake with an equivalent proportion of MPFs. Both variables in continuous form were included in the same multivariable model described above. The differences between regression β coefficients were used to derive the ORs and 95% CIs for the substitution effects.

All statistical analyses were performed using SAS software (version 9.4; SAS Institute Inc). Statistical significance was evaluated using a 2-sided test at .05.

Results

Participants' Characteristics

We included 12,716 participants in the current analysis—1290 with constipation (weighted prevalence, 9.7%) and 1067 with diarrhea (weighted prevalence, 7.5%). The median intakes of UPFs and MPFs in % gram/d were 26.5% (interquartile range [IQR], 15.7%–41.6%) and 66.2% (IQR, 50.5%–78.6%), respectively (Table 1). Median UPF intake accounted for 53.7% (IQR, 42.5%–64.8%) of daily total energy intake (% kcal/d), whereas MPF intake accounted for 32.3% (IQR, 23.1%–42.5%).

Greater UPF consumption (in % gram/d) was associated with younger age, male sex, lower socioeconomic status, and unhealthy lifestyle such as smoking and high BMI. Non-Hispanic Black participants consumed greater amounts of UPFs compared with other racial/ethnic groups. Participants who consumed more UPFs were more likely to use prescription medications and laxatives. Rates of chronic diseases, such as cancer, diabetes, thyroid disease, and depression, were also higher with greater UPF consumption.

Diets high in UPFs were associated with poor diet quality and nutritional profile. Participants who consumed more UPFs had lower water intake (Table 1); lower intakes of fruits, vegetables, and whole grains; and higher intakes of saturated fats, sodium, and added sugars (Supplementary Table 2).

For MPF intake, trends of the above characteristics were largely in the opposite direction (Table 1; Supplementary Table 2).

UPF Consumption

Greater daily percentage intake of UPFs in grams (% gram/d) was associated with increased odds of constipation even after adjusting for potential confounders (adjusted OR [$aOR_{Q4\ vs\ Q1}$], 2.20; 95% CI, 1.76–2.74) (Table 2). This association was accompanied by a linear trend (P_{trend} < .001), and the odds of constipation became greater with every 10% increase in daily UPF consumption (aOR, 1.31; 95% CI, 1.23–1.40). We further adjusted for total fiber intake, total water intake, and HEI-2015 and found attenuated associations between UPF consumption and constipation ($aOR_{Q4\ vs\ Q1}$, 1.53; 95% CI, 1.23–1.90; P_{trend} < .001).

On the other hand, consumption of UPFs was not associated with odds of diarrhea in age-adjusted or multivariable models. The aOR for diarrhea comparing the highest with the lowest quartile of UPF intake in the multivariable model was 0.82 (95% CI, 0.62–1.09; P_{trend} = .12).

These findings were largely similar when we assessed UPF consumption in % kcal/d (Supplementary Table 3). UPF consumption in % kcal/d was also significantly associated with constipation ($aOR_{Q4\ vs\ Q1}$, 1.51; 95% CI, 1.19–1.92; P_{trend} < .001). Stratified analysis did not reveal significant differences in associations by age, sex, race, and other covariates (Supplementary Table 4).

MPF Consumption

Greater consumption of MPFs in % gram/d was associated with lower odds of constipation ($aOR_{Q4\ vs\ Q1}$,

Table 1. Characteristics of Study Participants According to Quartiles of UPF and MPF Consumption

Variable	UPF consumption, % *gram/d* Quartile 1 (n = 3179)	Quartile 2 (n = 3179)	Quartile 3 (n = 3179)	Quartile 4 (n = 3179)	*P* value
UPF consumption, % *gram/d*	10.3 (7.2–13.1)	20.7 (18.3–23.6)	33.1 (29.7–37.0)	54.6 (46.9–65.0)	
Age, *years*	50.7 (0.6)	49.5 (0.5)	46.3 (0.4)	41.8 (0.4)	< .001
Male sex	42.5	45.7	51.6	50.6	< .001
Race/ethnicity					< .001
Non-Hispanic White	72.9	73.1	69.9	70.6	
Non-Hispanic Black	7.8	9.0	12.4	14.5	
Mexican American	11.6	12.5	13.5	11.3	
Others	7.7	5.4	4.2	3.6	
Poverty-income ratio					< .001
<1	10.7	9.6	11.7	15.3	
1–1.9	23.5	25.5	23.7	24.5	
2–4.9	37.3	38.2	38.1	40.8	
≥5	28.5	26.7	26.5	19.4	
Educational attainment					< .001
Below college	35.6	39.5	41.9	49.0	
College	30.7	30.2	31.1	31.3	
Above college	33.7	30.3	27.0	19.7	
Smoking status					< .001
Never	54.8	53.6	54.3	50.6	
Former	27.9	28.8	24.1	20.3	
Current	17.3	17.6	21.6	29.1	
Body mass index, *kg/m²*					< .001
<18.5	1.4	1.4	1.0	2.1	
18.5–24.9	31.7	30.6	29.1	25.2	
25.0–29.9	35.5	34.5	34.3	33.1	
30.0–39.9	26.4	28.2	29.5	31.5	
≥40	5.0	5.3	6.1	8.1	
MVPA ≥150 min/wk	43.3	41.9	44.2	41.1	.36
Alcohol use					< .001
Non-drinker	27.0	27.7	26.0	30.5	
Light drinker	61.4	63.4	66.9	63.6	
Heavy drinker	11.6	8.9	7.1	5.9	
Total energy intake, kcal/d	1890 (21.3)	2065 (24.5)	2205 (26.5)	2255 (22.7)	< .001
Number of prescription medications					< .001
0	49.5	43.2	38.4	35.7	
1	16.5	16.8	18.3	16.3	
2–3	17.7	19.7	21.0	22.6	
4–7	12.6	15.8	17.0	18.3	
≥8	3.7	4.5	5.3	7.1	
Laxative use	2.3	3.9	3.5	4.0	.02
Cancer	6.1	7.4	11.1	12.5	< .001
Congestive heart failure	1.6	1.9	2.2	3.3	.002
Chronic kidney disease	1.6	1.6	2.5	2.2	.13
Diabetes	5.9	7.6	8.1	10.4	< .001
Thyroid disease	7.3	9.8	11.9	12.6	< .001
Depression	5.6	6.6	7.9	10.0	< .001
Sleep disorder	7.9	6.2	8.5	8.9	.06
Total fiber intake, *mg/d*	17.9 (0.3)	17.6 (0.3)	16.7 (0.3)	14.3 (0.2)	< .001

Table 1. Continued

Variable	UPF consumption, % *gram/d* Quartile 1 (n = 3179)	Quartile 2 (n = 3179)	Quartile 3 (n = 3179)	Quartile 4 (n = 3179)	*P* value
Total water intake, *mL/d*	5013 (64.1)	4151 (55.5)	3665 (57.1)	2926 (35.6)	
Healthy Eating Index-2015	60.9 (0.4)	55.9 (0.4)	51.9 (0.3)	45.7 (0.3)	

Variable	MPF consumption, % *gram/d* Quartile 1 (n = 3179)	Quartile 2 (n = 3179)	Quartile 3 (n = 3179)	Quartile 4 (n = 3179)	*P* value
MPF consumption, % *gram/d*	37.0 (27.6-44.7)	59.2 (55.3-62.9)	72.6 (69.5-75.7)	84.8 (81.6-88.9)	
Age, *years*	41.5 (0.4)	46.3 (0.5)	48.9 (0.6)	51.8 (0.6)	< .001
Male sex	56.0	53.3	45.8	34.1	< .001
Race/ethnicity					< .001
Non-Hispanic White	71.1	70.9	73.8	70.8	
Non-Hispanic Black	14.4	11.7	9.1	8.4	
Mexican American	11.5	12.4	12.5	12.4	
Others	3.0	5.0	4.6	8.4	
Poverty-income ratio					< .001
<1	15.7	11.6	10.0	9.9	
1–1.9	24.6	22.8	23.5	26.5	
2–4.9	40.0	38.5	37.5	38.4	
≥5	19.7	27.1	29.0	25.2	
Educational attainment					< .001
Below college	50.1	41.8	37.2	36.7	
College	31.4	29.2	31.3	31.5	
Above college	18.5	29.0	31.5	31.8	
Smoking status					< .001
Never	47.0	52.0	56.6	58.3	
Former	20.4	26.2	26.7	27.8	
Current	32.6	21.8	16.7	13.9	
Body mass index, kg/m^2					< .001
<18.5	1.5	1.7	1.5	1.2	
18.5–24.9	26.6	29.8	30.1	29.9	
25.0–29.9	34.4	34.3	33.7	35.1	
30.0–39.9	30.2	28.3	30.0	27.1	
≥40	7.3	5.9	4.7	6.7	
MVPA ≥150 min/wk	24.7	23.6	28.6	35.1	< .001
Alcohol use					< .001
Non-drinker	24.7	23.6	28.6	35.1	
Light drinker	61.3	67.5	65.4	61.1	
Heavy drinker	14.0	8.9	6.0	3.8	
Total energy intake, *kcal/d*	2364 (28.2)	2224 (27.3)	2036 (24.1)	1764 (19.8)	< .001
Number of prescription medications					< .001
0	38.9	38.7	43.8	45.8	
1	16.8	18.1	15.7	17.4	
2–3	21.4	21.8	18.6	19.2	
4–7	17.5	16.0	16.6	13.4	
≥8	5.4	5.4	5.3	4.2	
Laxative use	3.6	3.7	3.8	2.6	.13
Cancer	12.2	10.6	7.9	6.2	< .001
Congestive heart failure	2.6	2.6	1.9	1.8	.15
Chronic kidney disease	1.4	2.6	1.7	2.0	.04

Table 1. Continued

Variable	MPF consumption, *% gram/d* Quartile 1 (n = 3179)	Quartile 2 (n = 3179)	Quartile 3 (n = 3179)	Quartile 4 (n = 3179)	*P* value
Diabetes	8.7	8.6	8.3	6.9	.09
Thyroid disease	11.3	11.6	9.8	8.7	.01
Depression	9.4	7.9	6.7	5.9	< .001
Sleep disorder	8.0	8.1	7.4	8.0	.88
Total fiber intake, *mg/d*	14.2 (0.2)	16.9 (0.3)	17.6 (0.3)	17.8 (0.3)	< .001
Total water intake, *mL/d*	3064 (39.4)	3664 (50.0)	4146 (66.8)	4926 (61.7)	< .001
Healthy Eating Index-2015	46.3 (0.3)	51.9 (0.3)	55.8 (0.4)	60.7 (0.4)	< .001

Note: Data are presented as percentage, mean (standard deviation), or median (interquartile range).
IQR, interquartile range; MPF, unprocessed or minimally processed food; MVPA, moderate-to-vigorous physical activity; SD, standard deviation; UPF, ultra-processed food.

0.46; 95% CI, 0.37–0.57; $P_{trend} < .001$) (Table 3), and the odds became lower with every 10% increase in MPF consumption (aOR, 0.77; 95% CI, 0.72–0.83; $P_{trend} < .001$). These associations were attenuated after adjusting for total fiber intake, total water intake, and HEI-2015 (aOR, 0.69; 95 CI, 0.56–0.84; $P_{trend} < .001$). We did not find an association between consumption of MPFs and diarrhea (aOR, 1.26; 95% CI, 0.94–1.69; $P_{trend} = .07$).

Substitution Analysis

In a substitution analysis, replacing UPFs in diet with an equivalent proportion of MPFs was associated with lower odds of constipation. Replacing higher amount was accompanied by larger reduction in odds (aOR 5%, 0.95; 95% CI, 0.93–0.96; 10%, 0.90; 95% CI, 0.87–0.93; 20%, 0.81; 95% CI, 0.76–0.86) (Table 4). The same substitution analysis yielded null results for diarrhea.

Discussion

Global increases in the production and consumption of UPFs prompted our investigations into their effects on bowel health. In this nationally representative cohort of the U.S. adult population, UPF consumption was associated with increased odds of constipation. The positive

Table 2. ORs (95% CIs) of Constipation and Diarrhea Comparing Quartiles of UPF Consumption

	UPF consumption, *% gram/d* Quartile 1 (n = 3179)	Quartile 2 (n = 3179)	Quartile 3 (n = 3179)	Quartile 4 (n = 3179)	P_{trend}[c]	Per 10% increase
UPF consumption, *% gram/d*, median (IQR)	10.3 (7.2–13.1)	20.7 (18.3–23.6)	33.1 (29.7–37.0)	54.6 (46.9–65.0)		
Constipation						
No. of cases/controls	270/2909	282/2897	317/2862	421/2758		
Age-adjusted model	1 (reference)	1.15 (0.85–1.54)	1.41 (1.09–1.82)	1.97 (1.56–2.49)	< .001	1.26 (1.18–1.35)
Multivariable model 1[a]	1 (reference)	1.19 (0.88–1.59)	1.59 (1.26–2.00)	2.20 (1.76–2.74)	< .001	1.31 (1.23–1.40)
multivariable model 2[b]	1 (reference)	1.04 (0.78–1.38)	1.26 (1.03–1.55)	1.53 (1.23–1.90)	< .001	1.17 (1.09–1.25)
Diarrhea						
No. of cases/controls	284/2895	271/2908	266/2913	246/2933		
Age-adjusted model	1 (reference)	0.99 (0.79–1.23)	0.92 (0.73–1.16)	0.94 (0.72–1.24)	.58	0.98 (0.89–1.07)
Multivariable model 1[a]	1 (reference)	0.96 (0.76–1.21)	0.85 (0.67–1.09)	0.82 (0.62–1.09)	.12	0.93 (0.85–1.02)
multivariable model 2[b]	1 (reference)	1.00 (0.77–1.30)	0.91 (0.69–1.21)	0.91 (0.65–1.29)	.50	0.96 (0.87–1.07)

CI, Confidence interval; HEI-2015, Health Eating Index-2015; IQR, interquartile range; OR, odds ratio; UPF, ultra-processed food.
[a]Adjusted for age group, sex, race/ethnicity, poverty-income ratio, educational attainment, smoking status, body mass index, physical activity, alcohol use, total energy intake, number of prescription medications, laxative use, cancer, congestive heart failure, chronic kidney disease, diabetes, thyroid disease, depression, and sleep disorder.
[b]Multivariable model 1 additionally adjusted for total fiber intake, total water intake, and HEI-2015.
[c]Tests for trend were performed by assigning the median value of exposures to each quartile and modeling exposures as a continuous variable.

Table 3. ORs (95% CIs) of Constipation and Diarrhea Comparing Quartiles of MPF Consumption

	MPF consumption, % *gram/d*					
	Quartile 1 (n = 3179)	Quartile 2 (n = 3179)	Quartile 3 (n = 3179)	Quartile 4 (n = 3179)	P_{trend}[c]	Per 10% increase
MPF consumption, % gram/d, median (IQR)	37.0 (27.6–44.7)	59.2 (55.3–62.9)	72.6 (69.5–75.7)	84.8 (81.6–88.9)		
Constipation						
No. of cases/controls	378/2801	316/2863	298/2881	298/2881		
Age-adjusted model	1 (reference)	0.78 (0.60–1.00)	0.69 (0.55–0.87)	0.64 (0.51–0.80)	< .001	0.86 (0.80–0.92)
Multivariable model 1[a]	1 (reference)	0.74 (0.57–0.96)	0.59 (0.47–0.76)	0.46 (0.37–0.57)	< .001	0.77 (0.72–0.83)
Multivariable model 2[b]	1 (reference)	0.85 (0.66–1.09)	0.76 (0.59–0.96)	0.69 (0.56–0.84)	< .001	0.88 (0.83–0.94)
Diarrhea						
No. of cases/controls	258/2921	253/2926	263/2916	293/2886		
Age-adjusted model	1 (reference)	0.91 (0.67–1.25)	0.99 (0.73–1.33)	1.09 (0.82–1.46)	.43	1.04 (0.95–1.13)
Multivariable model 1[a]	1 (reference)	1.00 (0.74–1.35)	1.13 (0.85–1.50)	1.26 (0.94–1.69)	.07	1.09 (0.99–1.19)
Multivariable model 2[b]	1 (reference)	0.96 (0.71–1.31)	1.06 (0.78–1.44)	1.14 (0.83–1.56)	.33	1.05 (0.95–1.16)

CI, confidence interval; HEI-2015, Health Eating Index-2015; IQR, interquartile range; MPF, unprocessed or minimally processed food; OR, odds ratio.
[a]Adjusted for age group, sex, race/ethnicity, poverty-income ratio, educational attainment, smoking status, body mass index, physical activity, alcohol use, total energy intake, number of prescription medications, laxative use, cancer, congestive heart failure, chronic kidney disease, diabetes, thyroid disease, depression, and sleep disorder.
[b]Multivariable model 1 additionally adjusted for total fiber intake, total water intake, and HEI-2015.
[c]Tests for trend were performed by assigning the median value of exposures to each quartile and modeling exposures as a continuous variable.

associations between UPF consumption and constipation were observed even after adjusting for diet quality, highlighting food processing as an independent factor in regulating gut motility. Higher intake of MPFs, on the other hand, was accompanied by decreased odds of constipation. Replacing UPFs with an equivalent proportion of MPFs could lead to a substantially lower odds of constipation. There were no statistically significant associations between consumption of either Nova food group and odds of diarrhea.

The findings related to UPF and MPF consumption and constipation may be partially explained by the foods' diet quality. Greater UPF consumption was associated with higher intakes of added sugar and saturated fat. Sugary products have been shown to cause prolonged gut transit and confirmed to be associated with increased risk of constipation in epidemiologic studies.[5,6,13] Similar positive associations were found for intake of saturated fatty acids,[19] which may be related to loss of nitrergic myenteric neurons and enterochromaffin cells.[11,12] MPFs consist of foods rich in fiber such as fruits, vegetables, and whole grains. Short-chain fatty acids in fiber-rich foods have been shown to accelerate intestinal transit by promoting the secretion of colonic hormones.[20] The Mediterranean diet contains abundant fiber contents and a variety of MPFs. Greater adherence to the Mediterranean diet has been associated with reduced constipation.[21,22] The role of hydration in the prevention or treatment of constipation has been controversial. Increasing fluid intake appears to be only useful in individuals in a dehydrated state.[23] Nonetheless, we observed a significant disparity in water intake across levels of UPF consumption. HEI-2015 has often been used as an indicator of diet quality by nutritional studies. One prior study shows an inverse association between HEI-2015 and risk of constipation.[5] We found that after adjusting for HEI-2015 along with fiber and water intake, the association between UPF and MPF consumption and

Table 4. ORs (95% CIs) of Constipation and Diarrhea Associated With Substituting UPFs With MPFs

	Constipation		Diarrhea	
Substitute UPFs with MPFs, % *gram/d*	aOR (95% CI)[a]	*P*	aOR (95% CI)[a]	*P*
Replacing 5% of UPF in diet with an equivalent proportion of MPFs	0.95 (0.93–0.96)	< .001	1.00 (0.99–1.02)	.67
Replacing 10% of UPF in diet with an equivalent proportion of MPFs	0.90 (0.87–0.93)	< .001	1.01 (0.97–1.05)	.67
Replacing 20% of UPF in diet with an equivalent proportion of MPFs	0.81 (0.76–0.86)	< .001	1.02 (0.94–1.09)	.67

aOR, Adjusted odds ratio; CI, confidence interval; MPF, unprocessed or minimally processed food; UPF, ultra-processed food.
[a]Multivariable model includes the following variables: UPF intake, MPF intake, age group, sex, race/ethnicity, poverty-income ratio, educational attainment, smoking status, body mass index, physical activity, alcohol use, total energy intake, number of prescription medications, laxative use, cancer, congestive heart failure, chronic kidney disease, diabetes, thyroid disease, depression, and sleep disorder.

constipation, though attenuated, remained statistically significant. This suggests that diet quality only partially explains the role of UPFs and MPFs in constipation.

The Nova classification system is unique in that it identifies food groups based on the nature and extent of food processing. Although UPFs and MPFs can both contain fruits, grains, dairy, seafood, and plant proteins, they undergo distinct levels of food processing and differ in the proportion of natural food content and additives. The persistently strong associations with UMP and MPF consumption despite adjustment for diet quality suggest that food processing plays a unique role in constipation. Many published prospective studies on the relationship between UPF consumption and various health outcomes adjusted for nutrient content and overall dietary patterns.[24] In line with our findings, these adjustments do not explain the observed associations. Gut microbiota composition has been implicated in chronic constipation[25,26] and may partially explain the adverse effects of UPFs on gut motility. Studies showed that commonly used emulsifiers such as carboxymethyl cellulose and polysorbate 80 promote intestinal inflammation and microbiota dysbiosis, which may lead to disturbed gut transit.[27] Further studies are needed to investigate the role of food processing in regulating bowel function.

Interestingly, we did not find an association with diarrhea. UPF consumption has been associated with increased risks of GI disorders that can cause chronic diarrhea including IBD[28] and irritable bowel syndrome (IBS).[29] This was thought to be related to alteration of the gut barrier integrity and activation of the immune response in the setting of microbial dysbiosis.[30] The overall effect induces a pro-inflammatory micro-environment in the intestine and alterations in bowel function. However, the amount of UPFs needed to be consumed by individuals such that the risk of diarrhea would be higher is unknown and likely varies between individuals. The duration of UPF intake associated with increased diarrhea is also unknown. We did not have data on the duration of dietary intake. If such data were present, it could be used to stratify individuals and assess the risks of developing diarrhea with long-term consumption of UPFs. Lastly, any associations with diarrhea would be biased towards the null if individuals change their diet after they experience diarrhea. Prospective studies may help minimize this bias.

The major strength of the present study is the use of a nationally representative multi-ethnic cohort of the U.S. adult population equipped with standardized data-gathering methods and rigorous data quality control, all of which improve the generalizability of the study findings. Nonetheless, one of the major limitations is the method by which dietary intake was assessed. We assessed dietary intake using 2 24-hour dietary recalls. Such a method does not allow assessment of dietary changes over time. Participants' responses to dietary recalls may vary between weekdays and weekends (Supplementary Table 5), although such variability may be reduced by averaging 2 dietary recalls. Additionally, misclassification may occur in exposures and outcomes. Each food product was categorized into the most likely Nova group, but we cannot rule out misclassification of food items at the individual level due to varying degrees of food processing across brands of the same foods. Participants with constipation may take laxatives for relief and be captured as having normal bowel habits. To account for this, we adjusted for laxative use in our models. There may be discrepancies in exposure and outcome definitions between studies. For instance, Schnabel et al utilized a Rome III questionnaire and found significant associations between UPF intake and IBS-C but not functional constipation.[29] The authors' categorization of UPFs might also differ from our studies. Lastly, as with any observational study, we could not fully account for unmeasured confounders. Reverse causation is also a concern in this cross-sectional study, as individuals may change their diet after they experience abnormal bowel habits, thus diluting the studied association towards the null.

Conclusion

In conclusion, UPF consumption was associated with increased odds of constipation in the general U.S. adult population, whereas MPF consumption was associated with decreased odds. Substituting UPFs with MPFs could lead to reduced constipation. Adjustment for diet quality did not alter these associations, highlighting the important role of food processing in regulating gut motility, though further studies are needed for confirmation. Our analysis supports current public health recommendations on limiting UPF consumption and promoting the intake of fresh or minimally processed foods to achieve healthy bowel habits.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2024.04.036.

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Conflicts of interest
The authors disclose no conflicts.

Supplementary Methods

This study did not require institutional review board approval per institutional policy at the University of Nevada, Las Vegas (UNLV) as the analysis used publicly available aggregated data without individually identifiable information.

Covariates Assessment

Risk factors of constipation and diarrhea were identified as covariates from the literature.[1–5] Demographic variables included age, sex, race/ethnicity, income, and educational attainment. Participants' race/ethnicity were identified as non-Hispanic White, non-Hispanic Black, Mexican American, and others. Income was measured by the poverty-income ratio (PIR) as calculated by family income divided by the poverty threshold specific to family size and survey year. Income was categorized into four PIR groups: PIR <1, PIR 1–1.9, PIR 2–4.9, and PIR ≥5. Educational attainment was categorized into below college, college, and above college.

Lifestyle variables included smoking, body mass index (BMI), physical activity, alcohol use, and total energy intake. Height and weight were measured to calculate BMI in kg/m^2, which was then categorized into the following groups: <18.5, 18.5–24.9, 25–29.9, 30–39.9, ≥40 kg/m^2. We calculated minutes of work-related activity, transportation activity, and leisure time activity per week. Minutes of vigorous-intensity activity were doubled and added to moderate-intensity minutes to calculate minutes of moderate-to-vigorous-intensity physical activity (MVPA). We classified participants reporting at least 150 minutes of MVPA per week as meeting the Physical Activity Guidelines for Americans (PAGA).[6] Participants were grouped into nondrinkers, light drinkers, and heavy drinkers according to their alcohol use. Heavy drinkers were defined as participants who drank eight or more drinks per week for women or 15 or more drinks per week for men. Light drinkers were defined as those who drink less than the above cutoff for the respective sex.

Participants reported the number of prescription medications taken and laxative use during a 1-month period prior to the participant's interview date.

The NHANES questionnaires provide self- and proxy-reported personal interview data on a broad range of health conditions and medical history. We selected a number of medical conditions that have been associated with bowel habits in the past, which include cancer, congestive heart failure, chronic kidney disease, diabetes, thyroid disease, depression, and sleep disorder.[7–9] Participants were screened for depression using the Patient Health Questionnaire 9 (PHQ-9)—a 9-item validated depression questionnaire.[10] We defined depression as a score of 10 or higher.[8]

We used total fiber intake, total water intake, and the Healthy Eating Index-2015 (HEI-2015) to capture diet quality. Total fiber intake and total water intake were ascertained through 24-hour dietary recall interviews. Total intake of fiber was calculated by summing the amounts in mg from all food sources. Total water intake takes into account the water content from all foods and drinks reported by participants, including plain tap and bottled water and water used as an ingredient in preparations. Details about HEI-2015 have been described previously.[11] Briefly, HEI-2015 is derived from the sum of 13 components, which included 9 adequacy components (total vegetables, greens and beans, total fruits, whole fruits, whole grains, dairy, total protein foods, seafood and plant proteins, and fatty acids) and 4 moderation components (sodium, refined grains, saturated fats, and added sugars). A higher HEI-2015 indicates better diet quality.

Weighting

To represent the complex, multi-stage, stratified, and probability sampling design, NHANES provides the clustering and stratification adjustment for each participant. A sample weight is assigned to each sample person and can be considered as a measure of the number of people represented by that sampled person. In the current analysis, we combined 3 continuous NHANES cycles (2005–2006, 2007–2008, 2009–2010). We constructed 6-year weight by dividing the 3 2-year sample weights by 3 (number of 2-year cycles) in the analysis. More details about the study design and analytic guidelines for the NHANES could be found elsewhere.[12]

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Supplementary Table 1. List of Food Items in UPFs

UPF subgroup	Food items
Ultra-processed breads and breakfast foods	Bread, sugared breakfast cereals, sandwiches, hamburgers on bun
Beverages	Sugared milk drinks, soft drinks (carbonated), other sweetened beverages
Packaged sweet snacks and desserts	Cakes/cookies/pies/pancakes and pastries, desserts and other sugary products
Frozen or shelf-stable ready-to-eat/heat meals	Frozen and shelf-stable plate meals, pizza, French fries and potato products, instant and canned soups
Others	Others
Packaged savory snacks	Salty-snacks (crackers, chips, popcorn), sweet-snacks
Sauces, cheese spreads, and gravies	Sauces, dressings, gravies
Meat and meat-substitute-based products	Reconstituted meat or fish products
Dairy-based desserts	Ice cream, ice pops, frozen yogurts

UPF, Ultra-processed food.

Supplementary Table 2. Components of HEI-2015 According to Quartiles of UPF and MPF Consumption

	UPF consumption, % *gram/d*				
Variable[a]	Quartile 1 (n = 3179)	Quartile 2 (n = 3179)	Quartile 3 (n = 3179)	Quartile 4 (n = 3179)	*P* value
UPF consumption, % gram/d, median (IQR)	10.3 (7.2–13.1)	20.7 (18.3–23.6)	33.1 (29.7–37.0)	54.6 (46.9–65.0)	
Healthy Eating Index-2015, mean (SD)	60.9 (0.4)	55.9 (0.4)	51.9 (0.3)	45.7 (0.3)	< .001
Total fruits, cup equiv per 1000 kcal	0.8 (0.0)	0.6 (0.0)	0.5 (0.0)	0.3 (0.0)	< .001
Whole fruits, cup equiv per 1000 kcal	0.6 (0.0)	0.4 (0.0)	0.3 (0.0)	0.2 (0.0)	< .001
Total vegetables, cup equiv per 1000 kcal	1.1 (0.0)	0.9 (0.0)	0.8 (0.0)	0.7 (0.0)	< .001
Greens and beans, cup equiv per 1000 kcal	0.2 (0.0)	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	< .001
Whole grains, oz equiv per 1000 kcal	0.6 (0.0)	0.5 (0.0)	0.4 (0.0)	0.3 (0.0)	< .001
Dairy, cup equiv per 1000 kcal	0.8 (0.0)	0.8 (0.0)	0.8 (0.0)	0.7 (0.0)	< .001
Total protein foods, oz equiv per 1000 kcal	3.6 (0.0)	3.3 (0.0)	3.1 (0.0)	2.9 (0.0)	< .001
Seafood and plant proteins, oz equiv per 1000 kcal	1.2 (0.0)	0.9 (0.0)	0.8 (0.0)	0.6 (0.0)	< .001
Fatty acids	2.0 (0.0)	1.9 (0.0)	1.8 (0.0)	1.8 (0.0)	< .001
Refined grains, oz equiv per 1000 kcal	2.4 (0.0)	2.7 (0.0)	2.8 (0.0)	2.8 (0.0)	< .001
Sodium, g per 1000 kcal	1.7 (0.0)	1.7 (0.0)	1.7 (0.0)	1.6 (0.0)	< .001
Added sugars, % energy	7.8 (0.1)	11.1 (0.2)	13.7 (0.2)	19.2 (0.3)	< .001
Saturated fats, % energy	10.7 (0.1)	11.1 (0.1)	11.3 (0.1)	11.2 (0.1)	.001

	MPF consumption, % *gram/d*				
Variable[a]	Quartile 1 (n = 3179)	Quartile 2 (n = 3179)	Quartile 3 (n = 3179)	Quartile 4 (n = 3179)	*P* value
MPF consumption, % *gram/d*, median (IQR)	37.0 (27.6–44.7)	59.2 (55.3–62.9)	72.6 (69.5–75.7)	84.8 (81.6–88.9)	
Healthy Eating Index-2015, mean (SD)	46.3 (0.3)	51.9 (0.3)	55.8 (0.4)	60.7 (0.4)	< .001
Total fruits, *cup equiv per 1000 kcal*	0.3 (0.0)	0.4 (0.0)	0.6 (0.0)	0.9 (0.0)	< .001
Whole fruits, *cup equiv per 1000 kcal*	0.2 (0.0)	0.3 (0.0)	0.4 (0.0)	0.6 (0.0)	< .001
Total vegetables, *cup equiv per 1000 kcal*	0.7 (0.0)	0.8 (0.0)	0.9 (0.0)	1.1 (0.0)	< .001
Greens and beans, *cup equiv per 1000 kcal*	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	0.2 (0.0)	< .001
Whole grains, *oz equiv per 1000 kcal*	0.2 (0.0)	0.4 (0.0)	0.5 (0.0)	0.6 (0.0)	< .001
Dairy, *cup equiv per 1000 kcal*	0.7 (0.0)	0.8 (0.0)	0.8 (0.0)	0.9 (0.0)	< .001
Total protein foods, *oz equiv per 1000 kcal*	2.9 (0.0)	3.1 (0.0)	3.3 (0.0)	3.6 (0.1)	< .001
Seafood and plant proteins, *oz equiv per 1000 kcal*	0.6 (0.0)	0.8 (0.0)	0.9 (0.0)	1.2 (0.0)	< .001
Fatty acids	1.8 (0.0)	1.9 (0.0)	1.9 (0.0)	1.9 (0.0)	< .001
Refined grains, *oz equiv per 1000 kcal*	2.7 (0.0)	2.8 (0.0)	2.7 (0.0)	2.5 (0.0)	< .001
Sodium, *g per 1000 kcal*	1.6 (0.0)	1.7 (0.0)	1.7 (0.0)	1.7 (0.0)	< .001
Added sugars, *% energy*	18.0 (0.3)	13.5 (0.2)	11.3 (0.2)	8.8 (0.1)	< .001
Saturated fats, *% energy*	11.0 (0.1)	11.2 (0.1)	11.2 (0.1)	10.9 (0.1)	.52

HEI-2015, Healthy Eating Index-2015; IQR, interquartile range; MPF, unprocessed or minimally processed food; SD, standard deviation; UPF, ultra-processed food.
[a]Dietary intakes are presented in mean (standard deviation).

Supplementary Table 3. ORs (95% CIs) of Constipation and Diarrhea Comparing Quartiles of UPF Consumption in % kcal/d

	UPF consumption, % *kcal/d*					
	Quartile 1 (n = 3179)	Quartile 2 (n = 3179)	Quartile 3 (n = 3179)	Quartile 4 (n = 3179)	P_{trend}[b]	Per 10% increase
UPF consumption, % kcal/d, median (IQR)	34.5 (28.5-38.9)	48.5 (45.6-51.1)	59.2 (56.3-62.0)	72.4 (68.2-78.6)		
Constipation						
Cases/controls	279/2900	278/2901	339/2840	394/2785		
Age-adjusted model	1 (reference)	0.94 (0.72–1.23)	1.28 (0.94–1.75)	1.56 (1.23–1.97)	< .001	1.19 (1.09–1.29)
Multivariable model[a]	1 (reference)	0.98 (0.77–1.26)	1.24 (0.94–1.65)	1.51 (1.19–1.92)	< .001	1.17 (1.07–1.27)
Diarrhea						
Cases/controls	301/2878	267/2912	225/2954	274/2905		
Age-adjusted model	1 (reference)	0.92 (0.72–1.18)	0.85 (0.65–1.11)	0.99 (0.77–1.29)	.82	0.99 (0.91–1.07)
Multivariable model[a]	1 (reference)	0.93 (0.72–1.19)	0.81 (0.61–1.07)	0.92 (0.72–1.17)	.33	0.96 (0.89–1.04)

CI, Confidence interval; IQR, interquartile range; UPF, ultra-processed food.
[a]Adjusted for age group, sex, race/ethnicity, poverty-income ratio, educational attainment, smoking status, body mass index, physical activity, alcohol use, total energy intake, number of prescription medications, laxative use, cancer, congestive heart failure, chronic kidney disease, diabetes, thyroid disease, depression, and sleep disorder.
[b]Tests for trend were performed by assigning the median value of exposures to each quartile and modeling exposures as a continuous variable.

Supplementary Table 4. Stratified Analysis for Associations Between UPF Consumption and Constipation and Diarrhea

	Constipation		Diarrhea	
Variable	aOR (95% CI)[a]	$P_{interaction}$[b]	aOR (95% CI)[a]	$P_{interaction}$[b]
Age, *years*		.75		.25
<60	1.18 (1.13–1.24)		0.95 (0.89–1.02)	
≥60	1.14 (1.03–1.26)		1.03 (0.93–1.13)	
Sex		.35		.87
Male	1.21 (1.13–1.30)		0.97 (0.90–1.04)	
Female	1.15 (1.10–1.21)		0.98 (0.92–1.04)	
Race/ethnicity		.13		.17
Non-Hispanic White	1.20 (1.14–1.27)		0.98 (0.93–1.04)	
Others	1.12 (1.05–1.18)		0.94 (0.87–1.02)	
Educational attainment		.90		.63
Below college	1.16 (1.09–1.23)		1.00 (0.93–1.08)	
College and above	1.19 (1.10–1.27)		0.94 (0.87–1.01)	
Smoking status		.44		.29
Never smoker	1.18 (1.11–1.26)		0.99 (0.91–1.08)	
Ever smoker	1.15 (1.09–1.21)		0.95 (0.88–1.02)	
Total energy intake, kcal		.63		.23
<2000	1.18 (1.12–1.24)		0.99 (0.92–1.07)	
≥2000	1.16 (1.08–1.24)		0.96 (0.89–1.03)	
Laxative use		.99		.95
No	1.17 (1.12–1.22)		0.97 (0.92–1.02)	
Yes	1.20 (0.94–1.53)		0.97 (0.76–1.23)	
Depression		.60		.07
No	1.16 (1.11–1.22)		0.95 (0.90–1.00)	
Yes	1.20 (1.09–1.33)		1.04 (0.93–1.16)	
Total fiber intake, g		.12		.05
<25	1.16 (1.11–1.21)		1.00 (0.95–1.05)	
≥25	1.34 (1.15–1.57)		0.82 (0.68–0.98)	
Total water intake, L		.41		.98
<3	1.14 (1.07–1.21)		0.98 (0.91–1.06)	
3	1.18 (1.11–1.25)		0.97 (0.89–1.05)	
HEI-2015		.99		.93
<50	1.16 (1.08–1.25)		0.97 (0.90–1.03)	
≥50	1.14 (1.08–1.21)		0.96 (0.88–1.05)	

aOR, Adjusted odds ratio; CI, confidence interval; HEI-2015, Health Eating Index-2015; UPF, ultra-processed food.
[a]OR per 10% gram/d increase. Model were adjusted for age group, sex, race/ethnicity, poverty-income ratio, educational attainment, smoking status, body mass index, physical activity, alcohol use, total energy intake, number of prescription medications, laxative use, cancer, congestive heart failure, chronic kidney disease, diabetes, thyroid disease, depression, and sleep disorder.
[b]Tests for interaction were performed by including the multiplicative term (cross-product term) of the exposure and each stratification variable in the model and using a Wald test to assess statistical significance.

Supplementary Table 5. Comparison of UPF and MPF Consumption Between Weekdays and Weekends

	Weekdays			Weekends		
	%	UPF consumption, *% gram/d*	MPF consumption, *% gram/d*	%	UPF consumption, *% gram/d*	MPF consumption, *% gram/d*
Day 1	59.6	33.9 (0.5)	60.4 (0.4)	40.4	35.7 (0.6)	57.3 (0.6)
Day 2	79.7	33.1 (0.4)	61.3 (0.4)	20.3	34.5 (0.7)	59.5 (0.7)

Note: Data are presented as mean (standard deviation).
MPF, Unprocessed or minimally processed food; UPF, ultra-processed food.