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Association between ultra-processed food and flavonoid intakes in a nationally representative sample of the US population

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Abstract

Consumption of ultra-processed food (UPF) has been associated with several chronic diseases and poor diet quality. It is reasonable to speculate that the consumption of UPF negatively associates with flavonoid dietary intake; however, this assumption has not been previously examined. The present study aims to assess association between the dietary contribution of UPF and flavonoid intake in the US population aged 0 years and above. We performed a cross-sectional analysis of dietary data collected by 24-h recalls from 7640 participants participating in the National Health and Nutrition Examination Survey 2017–2018. Foods were classified according to the Nova classification system. The updated US Department of Agriculture (USDA) Database for the Flavonoid Content of Selected Foods (Release 3.3) database was used to estimate total and six classes of flavonoid intakes. Flavonoid intakes were compared across quintiles of dietary contribution of UPF (% of total energy intake) using linear regression models. The total and five out of six class flavonoid intakes decreased between 50 and 70 % across extreme quintiles of the dietary contribution of UPF ($P_{\text{for linear trend}} < 0{\cdot}001$); only isoflavones increased by over 260 %. Our findings suggest that consumption of UPF is associated with lower total and five of six class flavonoid intakes and with higher isoflavone intakes, supporting previous evidence of the negative impact of UPF consumption on the overall quality of the diet and health outcomes.

Keywords: Flavonoid intake: Flavonoid classes: Ultra-processed foods: National Health and Nutrition Examination Survey

Ultra-processed foods (UPF) are defined by the Nova classification as industrial formulations of food-derived substances (such as oils, fats, sugars, starch and protein isolates) that contain little or no whole food and often include flavourings, colourings, emulsifiers and other additives with cosmetic functions(1). A considerable number of prospective observational studies have linked UPF intake with a higher risk of overweight, obesity, hypertension, diabetes, CVD, all-cause mortality, cancer as well mental disorders such as depression or cognitive decline(2–9).

A possible mechanism linking UPF with chronic diseases is its impact on diet quality. In fact, studies have shown an inverse association between dietary contribution of UPF and diet quality(10,11), which may be explained by the lower quality macro- and micronutrient profile of UPF and partitioning of higher-quality unprocessed/minimally processed foods.

Dietary flavonoids represent a diverse range of polyphenolic compounds present in fruits, vegetables, grains, herbs and tea(12) that have significant antioxidant protective effects against various pathologies such as obesity, cancer, CVD, hypertension, atherosclerosis, diabetes, dementia and Alzheimer's disease(13–16). Mechanistic studies have suggested various plausible means by which flavonoids may impact body fatness, such as decreasing energy intake, increasing energy expenditure and fat oxidation, influencing macronutrient absorption and uptake, and inhibiting adipogenesis(17–21). Evidence exists that the significant reduction in the incidence of chronic and degenerative diseases among those whose diets are high in cereals, fruits and vegetables may be, at least partially, explained by the higher intake of phenolic antioxidants(16).

Flavonoids have been classified into the following classes according to the position of the carbon in the chemical structure:

Abbreviations: NHANES, National Health and Nutrition Examination Survey; UPF, ultra-processed food; USDA, US Department of Agriculture.

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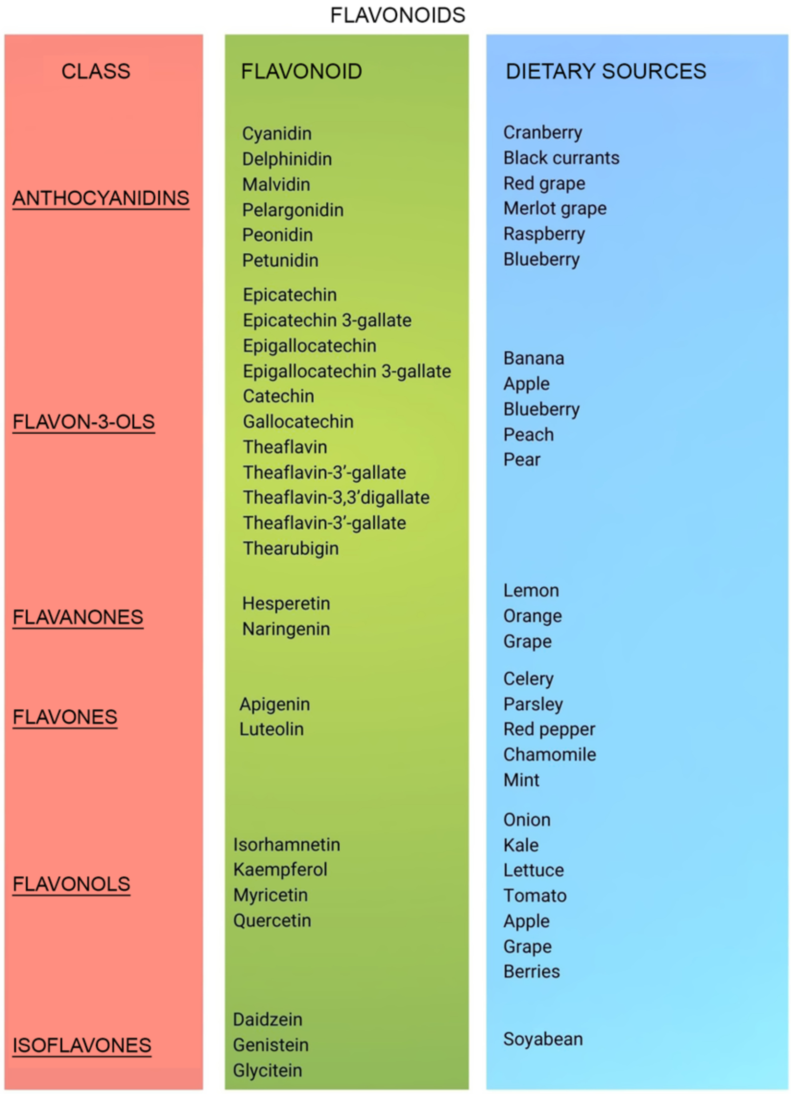

FLAVONOIDS

CLASS	FLAVONOID	DIETARY SOURCES
ANTHOCYANIDINS	Cyanidin Delphinidin Malvidin Pelargonidin Peonidin Petunidin	Cranberry Black currants Red grape Merlot grape Raspberry Blueberry
FLAVON-3-OLS	Epicatechin Epicatechin 3-gallate Epigallocatechin Epigallocatechin 3-gallate Catechin Gallocatechin Theaflavin Theaflavin-3′-gallate Theaflavin-3,3′digallate Theaflavin-3′-gallate Thearubigin	Banana Apple Blueberry Peach Pear
FLAVANONES	Hesperetin Naringenin	Lemon Orange Grape
FLAVONES	Apigenin Luteolin	Celery Parsley Red pepper Chamomile Mint
FLAVONOLS	Isorhamnetin Kaempferol Myricetin Quercetin	Onion Kale Lettuce Tomato Apple Grape Berries
ISOFLAVONES	Daidzein Genistein Glycitein	Soyabean

Fig. 1. Classes of flavonoids and dietary sources.

flavan-3-ols (including catechins), flavanones, flavonols, anthocyanidins, flavones and isoflavones (Fig. 1). Though few studies have analysed the health effects of each class separately, available evidence(13) suggests that flavonols regulate systolic blood pressure, glycemic levels, and BMI, flavones regulate blood glucose levels, flavanones lower risk of ischemic stroke, flavanols reduce mean arterial pressure and improve insulin resistance and LDL-cholesterol, HDL-cholesterol levels, anthocyanidins and catechins lower risk of myocardial infarctions, and isoflavones are beneficial for type 2 diabetes and menopause symptoms.

As flavonoids typically occur in unprocessed or minimally processed foods, it is reasonable to suggest that diets higher in UPF would be associated with lower consumption of flavonoids. To our knowledge, no previous studies have assessed the association between UPF consumption and flavonoid intakes. The present study aimed to assess possible associations between dietary relative contribution of UPF to total energy and flavonoid intake (total and six classes) in a representative sample of the US population.

Methods

Data source and dietary assessment

For this cross-sectional study, we used publicly available data from the 2017–2018 National Health and Nutrition Examination Survey (NHANES). NHANES is a nationally representative, multistage, complex survey of the civilian, non-institutionalised US population providing health and nutrition data, conducted by the National Center for Health Statistics (NCHS), CDC. Study protocols for NHANES were approved by the NCHS ethics review board. Signed informed consent was obtained from all participants; parents or guardians provided consent for participants < 18 years of age. Detailed descriptions of NHANES methods are published elsewhere(22). Participants were first interviewed in their homes to collect background information, such as socio-demographic, medical and family histories. Participants subsequently visited a mobile examination centre where a health examination and a dietary recall interview were performed. A second dietary recall

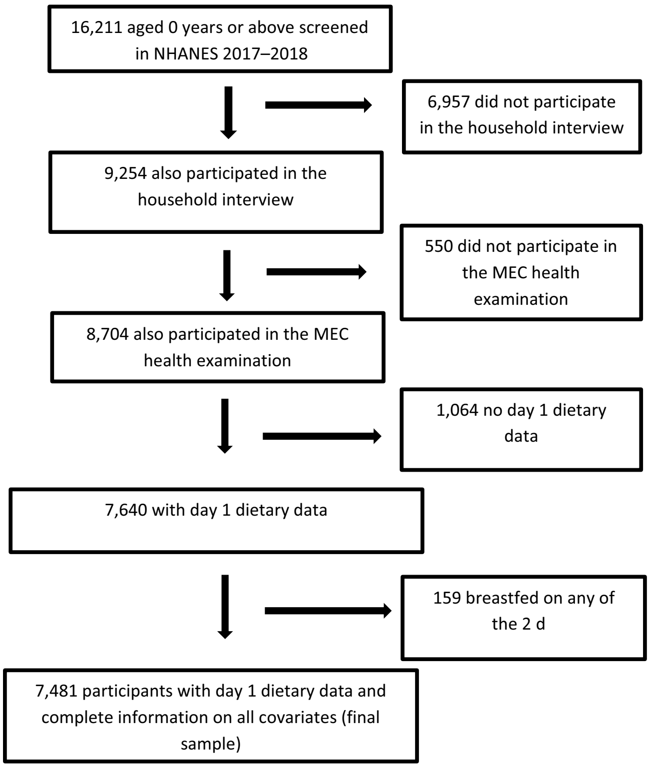

Fig. 2. Study flow chart. NHANES 2017–2018. NHANES, National Health and Nutrition Examination Survey.

was collected by telephone 3–10 d later in a different day of the week.

This study used dietary data obtained via the first of the two 24-h dietary recalls administered in-person by trained interviewers using the validated automated multi-pass method(23). Because the mean of a population's intake can be appropriately derived from a sample of 1 d individuals' 24-h recalls (provided the data are collected evenly throughout the year and the days of the week are evenly represented as is the case of NHANES), only the first dietary recall was used in the current study. For participants aged 5 years or younger, proxies/assistants familiar with the usual dietary intake of the child responded to the 24-h dietary recall. Participants aged 6–11 years were assisted by a proxy/assistant, and the participants aged ≥ 12 years completed the 24-h dietary recall interview on their own.

During the 2017–2018 NHANES cycle, 16 211 participants aged ≥ 0 year were screened; of those, 7640 had a complete first 24-h dietary recall. We sequentially excluded 159 infants breastfed on any of the 2 d (due to lack of data on the amount of breast milk consumed), leaving 7481 participants for analysis (Fig. 2). The socio-demographic distribution did not change between participants completing the first 24-h dietary recall and the final sample.

Food classification according to processing and assessment of ultra-processed food intake

We used the Nova system(1) to classify all foods and beverages (food codes) into four groups on the basis of nature, extent and purpose of industrial food processing. Nova includes four groups: 'unprocessed or minimally processed foods' (such as fresh, dry or frozen fruits or vegetables; packaged grains and pulses; grits, flakes or flours made from maize, wheat or cassava; pasta, fresh or dry, made from flours and water; eggs; fresh or frozen meat and fish and fresh or pasteurised milk), 'processed culinary ingredients' (including sugar, oils, fats, salt, and other substances extracted from foods or nature and used in kitchens to season and cook unprocessed or minimally processed foods and to make culinary preparations), 'processed foods' (including canned foods, salted meat products, cheeses and other products manufactured with the addition of salt or sugar or other processed culinary ingredients to unprocessed or minimally processed foods) and 'UPF' (defined as food formulations made up from several ingredients including sugar, oils, fats, and salt and food substances that are rarely used in homemade recipes such as high-fructose corn syrup, hydrogenated oils and protein isolates). Industrial techniques used to manufacture UPF include extrusion, moulding and pre-frying; application of additives including those whose function is to make the final product palatable or hyper-palatable such as flavours, colorants, non-sugar sweeteners and emulsifiers; and sophisticated packaging, usually with synthetic materials. This category includes soft drinks, sweet or savoury packaged snacks, confectionery, and industrialised desserts, mass-produced packaged bread and buns, poultry and fish nuggets and other reconstituted meat products, instant noodles and soups, and many other ready-to-consume formulations of several ingredients.

For food codes judged to be handmade recipes, the classification was applied to the underlying ingredient codes obtained from the US Department of Agriculture (USDA) Food and Nutrient Database for Dietary Studies (FNDDS) 2017–2018(24).

Energy values were assigned to food codes by NHANES using the USDA FNDDS (2017–2018)(24). For potential handmade recipes, we calculated the underlying ingredient code energy values using variables from both FNDDS 2017–2018 and USDA National Nutrient Database for Standard Reference, Release 28 (SR28)(25). The detailed procedures to classify food items according to Nova and estimate Nova energy contributions have been described elsewhere(26). The relative contribution of UPF to total daily energy intake was calculated for each participant.

Flavonoid intake assessment

We used the Database of Flavonoid Values for USDA Food Codes 2017–2018(27) which provides twenty-nine flavonoid values (in mg) in six flavonoid classes (flavan-3-ols (including catechins), flavanones, flavonols, anthocyanidins, flavones and isoflavones) present in 100 (edible) grams of each food code included in FNDDS 2017–2018, to estimate the total and six classes of flavonoid daily intakes (mg) for each participant. Further details are provided in online Supplementary Tables 1–3.

Covariates

Potential confounders were identified from the literature. Socio-demographic covariates included sex, age, race/ethnicity, family income and education. Sex was coded as male or female. Age was grouped into three categories (0–11 years, 12–19 years, and 20 years of age and over). Race/ethnicity was categorised as Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black and Other Races including Multi-Racial. In regard to family income, ratio of family income to poverty was established and categorised based on Supplemental Nutrition Assistance Program (SNAP) eligibility as 0·00–1·30, > 1·30–3·50, 3·50 and above, and missing[28]. Education attainment was categorised into four categories (< 12 years, 12 years, > 12 years of education and missing); household reference person education was used for participants aged 20 years or below.

Data analysis

First, we evaluated mean daily dietary contribution of UPF (% of total energy), and total and classes of flavonoid intakes (mg) overall and across socio-demographic characteristics. Wald test with Bonferroni inequality adjustment for multiple comparisons was used to determine differences across categorical variables.

As flavonoid intakes had skewed distributions, variables were log-transformed using natural logarithms and geometric means were presented. Flavonoid intakes were compared across quintiles of dietary contribution of UPF (% of total energy intake) using linear regression models. Tests of linear trend were performed to evaluate the effect of quintiles as a single continuous variable. These associations were explored using two models: (1) crude (mg) and (2) adjusted for socio-demographic variables: sex, age group, race/ethnicity, ratio of family income to poverty and educational attainment. Results were shown as geometric means and standard errors. We performed additional analyses to test the association between quintiles of dietary energy contribution of unprocessed/minimally processed foods and flavonoid intakes.

Effect modification by sex and age group was tested by including a one-by-one multiplicative interaction term in the multivariable socio-demographic adjusted model. Analyses were stratified according to sex and age group.

We also used the restricted cubic spline in the multivariable linear regression models with five knots (5th, 27·5th, 50th, 72·5th and 95th) following Harrell's recommendations[29] to examine the shape of the dose–response relationship curve between daily percent of energy from UPF and total and each class flavonoid intakes.

Statistical hypotheses were tested using a two-tailed $P < 0{\cdot}05$ level of significance. Data were analysed using Stata statistical software package version 14.

Results

Mean dietary energy contribution of UPF and flavonoid intakes, overall and according to characteristics of respondents of the US population aged 0 years and above in 2017–2018, are displayed in Table 1. Mean daily energy contribution of UPF was 58 % and was higher among men, Non-Hispanic Black, lower income level and younger age groups.

The geometric mean intake of total flavonoids was 45·7 mg/d. Total flavonoids intake was higher among women, adults, other races, highest income and highest education level.

Geometric mean flavonoid intakes (mg/d) according to quintiles of dietary contribution of UPF are presented in Table 2. In both crude and adjusted models, total flavonoid intakes decreased by 70 % across extreme quintiles ($P_{\text{for linear trend}} < 0{\cdot}001$). Decreases were also observed in five out of six classes of flavonoid intakes ($P_{\text{for linear trend}} < 0{\cdot}001$), with decreases across extreme quintiles of UPF intake ranging between 50 and 70 %. The consumption of isoflavones was positively associated with quintiles of UPF consumption ($P_{\text{for linear trend}} < 0{\cdot}001$), with an increase of more than 260 % observed across extreme quintiles.

Curves using restricted cubic splines showed no evidence of a linear dose–response association between dietary contribution of UPF and flavonoid intakes (online Supplementary Fig. 1).

Opposite trends were observed for the association between quintiles of unprocessed/minimally processed foods and total and classes of flavonoid intakes (online Supplementary Table 1). Thus, total and class flavonoid intakes increased across quintiles of unprocessed/minimally processed foods ($P_{\text{for linear trend}} < 0{\cdot}001$) except for isoflavone, with increases ranging between 180 and 270 % across extreme quintiles. Isoflavone intakes decreased by 60 % between the first and fifth quintiles.

The association between total flavonoid intake and quintiles of UPF consumption were not modified by sex or age group ($P_{\text{for interaction}} > 0{\cdot}05$) (Table 3). The associations with isoflavone and flavonol intakes were both slightly stronger among women when compared with men ($P_{\text{for interaction}} < 0{\cdot}05$). For isoflavone intakes, 270 % and 450 % increases across extreme quintiles of UPF consumption were observed for men and women, respectively. As for flavonol, 57 % and 59 % decreases were observed for men and women, respectively (Table 3).

Discussion

In this nationally representative US study, a strong inverse association was observed between dietary contribution of UPF and total and six class flavonoid intakes. Isoflavones, however, showed a strong positive association with UPF intake. Opposite trends were observed for the association between unprocessed/minimally processed foods and total and class flavonoid intakes.

The inverse association between UPF and flavonoid intakes is likely explained by the fact that UPF are devoid of flavonoids (because UPF are formulations with minimal amounts of fruits, vegetables, grains, herbs and tea) and because the consumption of UPF likely implicates in partitioning of the consumption of flavonoid-rich unprocessed or minimally processed foods. As a matter of fact, a previous study carried out in the US population observed that across extreme quintiles of UPF consumption, both unprocessed/minimally processed fruit and vegetable consumption decreased by over 70 % each[30]. Besides this, these compounds tend to be unstable due to interference with other compounds and sensitivity to heat, light, pH, or temperature, and metabolic transformations (methylation, glucuronidation and sulfation), which will result in a loss of their efficiency and effectiveness when consumed as part of UPF[31].

Studies suggest that flavonoids have beneficial anti-inflammatory effects, protecting cells from oxidative damage that can

Table 1. Dietary contribution of ultra-processed foods and flavonoid intakes according to characteristics of respondents. US population aged 0 years and above (NHANES 2017–2018) (*n* 7481) (using day 1 dietary data)

		Dietary contribution of ultra-processed foods (% total daily energy intake)		Flavonoids (mg/d)															
				ΣTotal flavonoids		ΣIsoflavones		ΣAnthocyanidins		ΣFlavan-3-ols (total)		ΣCatechin [Flavan-3-ols] (subtotal)		ΣFlavanones		ΣFlavones		ΣFlavonols	
		Mean	SE	GM*	GSE	GM	GSE	GM	GSE	GM	GSE	GM	GSE	GM	GSE	GM	GSE	GM	GSE
Sex†	Men (*n* 3676)	59·3	0·9^{A}	42·7	1·1^{A}	0·4	1·9^{A}	1·9	1·1^{A}	12·2	1·1^{A}	9·2	1·1^{A}	1·4	1·0^{A}	0·4	1·1^{A}	8·7	1·0^{A}
	Women (*n* 3805)	57·5	0·9^{B}	48·8	1·1^{B}	0·4	1·1^{A}	2·3	1·1^{B}	13·7	1·1^{B}	9·8	1·1^{A}	1·3	1·1^{A}	0·4	1·1^{A}	8·6	1·0^{A}
Age groups (years)†	0–11 (*n* 1695)	64·7	0·7^{A}	27·3	1·1^{A}	0·5	1·1^{AB}	2·1	1·1^{A}	8·8	1·1^{A}	7·7	1·1^{A}	1·5	1·1^{A}	0·3	1·1^{A}	4·1	1·1^{A}
	12–19 (*n* 1045)	67·7	0·7^{B}	25·3	1·1^{A}	0·6	1·1^{A}	1·3	1·1^{B}	7·7	1·1^{A}	5·6	1·1^{B}	1·3	1·1^{A}	0·3	1·1^{A}	5·2	1·1^{B}
	20 or above (*n* 4741)	55·8	1·0^{C}	54·8	1·1^{B}	0·4	1·1^{B}	2·3	1·1^{A}	15·0	1·1^{B}	10·7	1·1^{C}	1·3	1·0^{A}	0·4	1·1^{B}	10·7	1·0^{C}
Race/ethnicity†	Mexican American (*n* 1087)	57·7	1·0^{B}	36·5	1·1^{AB}	0·4	1·1^{A}	1·8	1·1^{A}	8·2	1·1^{A}	7·0	1·1^{AB}	2·0	1·1^{C}	0·5	1·1^{C}	7·4	1·1^{AB}
	Other Hispanic (*n* 628)	53·0	1·8^{A}	40·9	1·1^{AB}	0·5	1·1^{A}	2·4	1·1^{A}	10·4	1·1^{AB}	8·4	1·1^{BC}	1·8	1·1^{BC}	0·4	1·1^{ABC}	8·4	1·1^{BC}
	Non-Hispanic White (*n* 2632)	59·5	1·1^{B}	49·6	1·1^{B}	0·4	1·1^{A}	2·2	1·1^{A}	15·0	1·1^{BC}	10·6	1·1^{CD}	1·2	1·1^{AB}	0·4	1·1^{AB}	9·1	1·1^{CD}
	Non-Hispanic Black (*n* 1745)	63·1	1·2^{C}	28·4	1·1^{A}	0·5	1·1^{A}	1·7	1·1^{A}	7·5	1·1^{A}	5·7	1·1^{A}	1·3	1·1^{A}	0·3	1·1^{A}	6·4	1·1^{A}
	Other Race (including Multi-Racial) (*n* 1389)	51·1	1·2^{A}	65·4	1·1^{C}	0·4	1·1^{A}	2·6	1·1^{A}	18·8	1·1^{C}	13·2	1·1^{D}	1·3	1·1^{ABC}	0·5	1·1^{BC}	10·5	1·1^{D}
Income to poverty†	0·00–1·30 (*n* 2190)	59·9	1·2^{B}	34·7	1·1^{A}	0·5	1·1^{A}	1·7	1·1^{A}	10·5	1·1^{A}	7·8	1·1^{A}	1·2	1·1^{A}	0·3	1·1^{A}	7·0	1·1^{A}
	>1·30–3·50 (*n* 2667)	59·8	0·8^{B}	37·8	1·1^{A}	0·4	1·1^{A}	1·8	1·1^{A}	10·2	1·1^{A}	7·8	1·1^{A}	1·3	1·0^{A}	0·4	1·1^{AB}	7·7	1·0^{A}
	>3·50 and above (*n* 1796)	56·6	1·1^{A}	64·5	1·1^{B}	0·4	1·1^{A}	2·9	1·1^{B}	18·6	1·1^{B}	12·9	1·1^{B}	1·4	1·1^{A}	0·5	1·1^{B}	11·1	1·0^{B}
	Missing (*n* 828)	56·2	(1·2^{A}	43·9	1·2^{AB}	0·4	1·2^{A}	2·0	1·1^{AB}	12·0	1·2^{AB}	9·1	1·2^{AB}	1·5	1·1^{A}	0·4	1·1^{AB}	8·0	1·1^{A}
Educational attainment†	<12 years (*n* 1341)	57·8	1·2^{AB}	33·7	1·1^{A}	0·5	1·1^{AB}	1·7	1·1^{A}	9·9	1·1^{A}	7·9	1·1^{A}	1·6	1·1^{A}	0·4	1·1^{B}	6·7	1·1^{A}
	12 years (*n* 2732)	62·2	0·8^{C}	33·3	1·1^{A}	0·5	1·1^{B}	1·6	1·1^{A}	9·3	1·1^{A}	7·1	1·1^{A}	1·3	1·1^{A}	0·3	1·0^{A}	6·8	1·1^{A}
	>12 years (*n* 3255)	55·9	0·9^{A}	60·9	1·1^{B}	0·4	1·1^{A}	2·7	1·1^{B}	17·3	1·1^{B}	12·2	1·1^{B}	1·3	1·1^{A}	0·4	1·1^{B}	10·9	1·0^{B}
	Missing (*n* 153)	62·7	2·5^{BC}	30·3	1·2^{A}	0·4	1·2^{AB}	1·7	1·5^{AB}	8·1	1·3^{AB}	6·5	1·3^{AB}	2·4	1·3^{A}	0·4	1·2^{AB}	5·3	1·2^{A}
Total		58·3	0·9	45·7	1·1	0·4	1·1	2·1	1·1	12·9	1·1	9·5	1·1	1·4	1·0	0·4	1·0	8·6	1·0

GM, geometric means; GSE, geometric standard error.

* GM.

† Values sharing a letter in the group label are not significantly different at the $P < 0.05$ level (using Bonferroni inequality adjustment for multiple comparisons).

Table 2. Flavonoid intakes (mg per d) according to the quintiles of the dietary share of ultra-processed foods. US population aged 0 years and above (NHANES 2017–2018) (*n* 7481)

		Quintile of dietary share of ultra-processed foods (% of total energy intake)*					
		Q1	Q2	Q3	Q4	Q5	$P_{\text{for trend}}$
ΣTotal flavonoids (GM†)	Crude (mg)	72·0	57·9	52·4	44·0	20·7	<0·001
	Adjusted for socio-demographic variables (mg)‡	64·8	55·2	51·5	45·6	23·7	<0·001
ΣIsoflavones (GM)	Crude (mg)	0·3	0·3	0·4	0·5	0·9	<0·001
	Adjusted for socio-demographic variables (mg)‡	0·3	0·3	0·4	0·5	0·8	<0·001
ΣAnthocyanidins (GM)	Crude (mg)	3·8	2·7	1·9	1·9	1·2	<0·001
	Adjusted for socio-demographic variables (mg)‡	3·6	2·7	1·9	1·9	1·3	<0·001
ΣFlavan-3-ols (total) (GM)	Crude (mg)	19·1	13·6	14·6	13·8	6·9	<0·001
	Adjusted for socio-demographic variables (mg)‡	17·5	13·1	14·4	14·1	7·8	0·001
ΣCatechin [flavan-3-ols] (subtotal) (GM)	Crude (mg)	14·2	10·5	10·7	9·9	4·9	<0·001
	Adjusted for socio-demographic variables (mg)‡	13·3	10·2	10·5	10·0	5·5	<0·001
ΣFlavanones (GM)	Crude (mg)	1·7	1·8	1·5	1·1	0·9	<0·001
	Adjusted for socio-demographic variables (mg)‡	1·7	1·8	1·5	1·1	0·9	<0·001
ΣFlavones (GM)	Crude (mg)	0·6	0·5	0·4	0·3	0·2	<0·001
	Adjusted for socio-demographic variables (mg)‡	0·6	0·5	0·4	0·3	0·2	<0·001
ΣFlavonols (GM)	Crude (mg)	13·3	10·2	9·8	8·0	4·5	<0·001
	Adjusted for socio-demographic variables (mg)‡	12·0	9·8	9·8	8·4	5·0	<0·001

NHANES, National Health and Nutrition Examination Survey; GM, geometric means.

* Mean (range) dietary share of ultra-processed foods per quintile: 1st = 26·8 (0 to 39·3); 2nd = 46·3 (39·3 to 53·0); 3rd = 59·1 (53·0 to 65·2); 4th = 71·1 (65·3 to 78·0); 5th = 88·1 (78·0 to 100).

† GM presented in all cases.

‡ Adjusted for sex, age group (0 to 11, 12 to 19, +20), race/ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black and Other Race), ratio of family.

Table 3. Flavonoid intakes (mg) according to the quintiles of the dietary share of unprocessed/minimally processed foods. US population aged 0 years and above (NHANES 2017–2018) (*n* 7481)

		Quintile of dietary share of ultra-processed foods (% of total energy intake)*					
		Q1	Q2	Q3	Q4	Q5	$P_{\text{for trend}}$
ΣTotal flavonoids (GM†)	Crude (mg)	23·4	40·0	60·5	54·0	64·9	<0·001
	Adjusted for socio-demographic variables (mg)‡	25·9	40·2	59·8	51·9	61·6	<0·001
ΣIsoflavones (GM)	Crude (mg)	0·7	0·5	0·4	0·3	0·3	<0·001
	Adjusted for socio-demographic variables (mg)‡	0·7	0·5	0·4	0·3	0·3	<0·001
ΣAnthocyanidins (GM)	Crude (mg)	1·2	1·7	2·4	2·7	3·3	<0·001
	Adjusted for socio-demographic variables (mg)‡	1·2	1·7	2·4	2·6	3·2	<0·001
ΣFlavan-3-ols (total) (GM)	Crude (mg)	7·9	12·4	16·8	13·2	16·6	0·002
	Adjusted for socio-demographic variables (mg)‡	8·7	12·3	16·6	12·8	16·0	0·007
ΣCatechin [flavan-3-ols] (subtotal) (GM)	Crude (mg)	5·5	9·2	12·4	9·8	12·6	<0·001
	Adjusted for socio-demographic variables (mg)‡	6·0	9·2	12·2	9·5	12·2	0·001
ΣFlavanones (GM)	Crude (mg)	0·8	1·0	1·7	1·8	1·7	<0·001
	Adjusted for socio-demographic variables (mg)‡	0·9	1·0	1·7	1·8	1·7	<0·001
ΣFlavones (GM)	Crude (mg)	0·3	0·3	0·4	0·5	0·6	<0·001
	Adjusted for socio-demographic variables (mg)‡	0·3	0·3	0·4	0·4	0·6	<0·001
ΣFlavonols (GM)	Crude (mg)	5·2	8·1	9·9	10·3	11·1	<0·001
	Adjusted for socio-demographic variables (mg)‡	5·6	8·2	9·8	10·0	10·6	<0·001

NHANES, National Health and Nutrition Examination Survey; GM, geometric means.

* Mean (range) dietary share of unprocessed/minimally processed foods per quintile: 1st = 5·1 (0 to 11·5); 2nd = 15·8 (11·5 to 20·2); 3rd = 25·0 (20·2 to 29·8); 4th = 35·6 (29·8 to 42·4); 5th = 55·9 (42·4 to 100).

† GM presented in all cases.

‡ Adjusted for sex, age group (0 to 11, 12 to 19, +20), race/ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black and Other Race), ratio of family income to poverty (Supplemental Nutrition Assistance Program 0·00–1·30, > 1·30–3·50 and > 3·50 and over, missing) and educational attainment (< 12, 12, > 12 years, missing).

lead to disease(32). These dietary antioxidants can prevent the development of CVD, diabetes, cancer, and cognitive diseases like Alzheimer's and dementia(13–16). A meta-analysis performed on eight cohorts showed a linear decreased risk of CVD as a function of increased intake of flavonoid, with intakes of up to 500 mg/d of total flavonoids being associated with a 27 % lower risk of CVD(14). On the other hand, prior studies have associated high UPF consumption with an increased risk of several chronic diseases, including CVD, diabetes, cancer, depression and cognitive decline(4,5,7–9). Our analysis revealed a negative association between UPF and total and five out of six classes of flavonoid intakes, indicating that decreased flavonoid intake

Table 4. Adjusted* flavonoid intakes (mg per d) according to the quintiles of the dietary share of ultra-processed foods, stratified by covariates with statistically significant interaction. US population aged 0 + years (NHANES 2017–2018) (*n* 7481)

		Quintile of dietary share of ultra-processed foods (% of total energy intake)‡						
		Q1	Q2	Q3	Q4	Q5	$P_{\text{for trend}}$	$P_{\text{for interaction}}$
ΣTotal flavonoids (mg/d)†	Sex							
	Men	59·3	48·2	50·8	44·5	21·9	<0·001	0·427
	Women	71·1	61·1	51·5	49·5	24·9	<0·001	
	Age group							
	0–11	30·1	38·4	25·6	31·8	16·2	0·001	
	12–19	38·6	35·0	31·7	24·4	9·9	<0·001	0·674
	20 or above	79·4	64·6	64·2	49·8	30·1	<0·001	
ΣIsoflavones (GM)	Sex							
	Men	0·3	0·4	0·4	0·4	0·8	0·001	0·036
	Women	0·2	0·2	0·4	0·5	0·9	<0·001	
	Age group							
	0–11	0·3	0·3	0·5	0·6	0·9	<0·001	0·877
	12–19	0·4	0·4	0·5	0·8	1·0	<0·001	
	20 or above	0·3	0·3	0·4	0·4	0·7	<0·001	
ΣAnthocyanidins (GM)	Sex							
	Men	2·6	2·3	1·9	1·9	1·2	<0·001	0·12
	Women	4·3	3·1	2·1	1·9	1·3	<0·001	
	Age group							
	0–11	2·5	2·7	2·0	1·7	1·8	0·062	0·532
	12–19	2·2	1·8	1·3	1·0	0·9	0·001	
	20 or above	4·0	2·7	2·1	2·0	1·3	<0·001	
ΣFlavan-3-ols (total) (GM)	Sex							
	Men	15·9	11·3	14·0	14·0	7·6	0·044	0·32
	Women	19·9	14·8	14·4	14·2	8·0	<0·001	
	Age group							
	0–11	7·8	10·8	8·8	11·0	6·3	0·113	0·213
	12–19	11·8	9·7	7·6	8·1	3·9	<0·001	
	20 or above	22·0	14·4	16·7	15·3	9·3	0·004	
ΣCatechin [flavan-3-ols] (subtotal) (GM)	Sex							
	Men	12·2	9·2	10·7	10·0	5·4	0·01	0·274
	Women	15·0	10·9	10·1	10·3	5·4	<0·001	
	Age group							
	0–11	7·3	9·9	8·1	8·8	5·4	0·011	0·218
	12–19	9·5	7·0	6·2	4·6	2·9	<0·001	
	20 or above	16·3	10·3	11·8	11·0	6·3	0·001	
ΣFlavanones (GM)	Sex							
	Men	2·0	1·9	1·6	1·0	0·9	<0·001	0·663
	Women	1·5	1·6	1·5	1·2	0·8	0·001	
	Age group							
	0–11	1·7	1·9	1·3	1·5	1·2	0·068	0·393
	12–19	1·4	1·9	1·4	0·9	1·1	0·068	
	20 or above	1·6	1·9	1·6	1·1	0·8	<0·001	
ΣFlavones (GM)	Sex							
	Men	0·6	0·5	0·4	0·3	0·2	<0·001	0·621
	Women	0·5	0·5	0·3	0·4	0·2	<0·001	
	Age group							
	0–11	0·3	0·3	0·3	0·2	0·2	<0·001	0·115
	12–19	0·6	0·4	0·3	0·3	0·2	<0·001	
	20 or above	0·6	0·6	0·5	0·4	0·3	<0·001	
ΣFlavonols (GM)	Sex							
	Men	11·9	8·9	10·0	9·0	5·1	<0·001	0·022
	Women	12·0	10·7	9·1	8·3	4·9	<0·001	
	Age group							
	0–11	4·8	5·3	4·0	4·3	2·7	<0·001	0·815
	12–19	8·3	6·1	6·1	4·6	2·7	<0·001	
	20 or above	14·5	12·6	11·9	9·8	6·5	<0·001	

NHANES, National Health and Nutrition Examination Survey; GM, geometric means.

* Adjusted for sex, age group (0 to 11, 12 to 19, +20), race/ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black and Other Race), ratio of family income to poverty (Supplemental Nutrition Assistance Program 0·00–1·30, > 1·30–3·50 and > 3·50 and over, and missing) and education (< 12 years, 12 years, > 12 years and missing).

† GM.

‡ Mean (range) dietary share of ultra-processed foods per quintile in men: 1st = 28·3 (0 to 40·6); 2nd = 47·3 (40·6 to 54·0); 3rd = 59·6 (54·0 to 65·9); 4th = 72·5 (65·9 to 79·0); 5th = 88·8 (79·0 to 100).

Mean (range) dietary share of ultra-processed foods per quintile in women: 1st = 25·6 (0 to 38·0); 2nd = 45·3 (38·0 to 51·9); 3rd = 58·5 (51·9 to 64·9); 4th = 70·7 (64·9 to 77·0); 5th = 87·3 (77·0 to 100).

Mean (range) dietary share of ultra-processed foods per quintile in age group 0 to 11 years: 1st = 35·6 (1·0 to 48·3); 2nd = 55·0 (48·3 to 60·8); 3rd = 66·3 (60·8 to 71·7); 4th = 76·4 (71·7 to 81·6); 5th = 90 (81·7 to 100).

Mean (range) dietary share of ultra-processed foods per quintile in age group 12 to 19 years: 1st = 35·4 (0 to 49·6); 2nd = 56·5 (49·8 to 63·9); 3rd = 70·7 (64·0 to 76·2); 4th = 81·5 (76·2 to 86·9); 5th = 94·5 (87·0 to 100).

Mean (range) dietary share of ultra-processed foods per quintile in age group 20 years and above: 1st = 25·0 (0 to 36·8); 2nd = 43·5 (36·8 to 50·1); 3rd = 56·1 (50·1 to 62·2); 4th = 68·6 (62·2 to 75·0); 5th = 85·8 (75·0 to 100).

may be a potential mechanism to explain the positive association between UPF and several chronic diseases.

A positive association was observed between UPF and isoflavone intakes. This is likely explained by the fact that the main sources of isoflavones are soy-based products, milk substitutes, processed soya products, snack/meal bars, and beans, peas, and legumes(33), many of which are likely to be part of UPF. Isoflavones are phytoestrogens associated with diverse positive outcomes for human health(34,35). They are used as alternative therapies for a range of hormone-dependent conditions, such as cancer, menopausal symptoms, CVD and osteoporosis(36). However, in most of UPF soybean products, the isoflavones are conjugated with sugars or sweeteners and other flavour enhancers and/or food preservatives, minimising the protective action of this phytoestrogen(36). Interestingly, a previous US study that observed an inverse association between UPF consumption and urinary enterodiol concentrations failed to observe any significant associations with isoflavone concentrations(37). If urinary concentrations of isoflavones reflect both their food content (as measured in the current study) and bioavailability after gut microbiota metabolisation (not captured in the current study), we might speculate that food processing may affect how food isoflavones are metabolised by the gut microbiota, potentially decreasing their bioavailability. Evidence exists that the final flavonoid content and bioavailability in processed foods depend on factors such as the nature of the process, duration of treatment and food matrix(38).

The associations of UPF with isoflavone and flavonol intakes were both slightly stronger among women when compared with men. Women in the lowest UPF quintile consumed less isoflavones and more flavonols when compared with men, whereas women in the highest UPF quintile consumed more isoflavones and less flavonols. The reason for these differences by sex remains unclear.

There are several strengths of this study. First, the use of the Flavonoid Database for USDA Food Codes which is a comprehensive database that includes flavonoid values on a large number of foods derived from both the most (e.g. tea, fruits, vegetables) and the less obvious sources (e.g. amounts consumed as ingredients of mixed dishes) permitted a comprehensive estimation of flavonoid intake with minimal imputations of missing food flavonoid profiles(27). Second, the study used a nationally representative sample, increasing the external validity of the results.

Our study had some limitations. Though dietary data obtained through 24-h recalls are considered the least biased self-report instrument available, they can suffer from measurement error(39). Additionally, while NHANES collects some information about food processing (such as the place of meals and product brands), these data are not consistently available for all food items and may not provide up-to-date nutrient information that accurately reflects market conditions, which may over- or underestimate the dietary contribution of UPF or dilute the studied association towards the null. The fact that NHANES was not specifically designed to capture flavonoid intake may have led to the assignment of the same food code, and thus flavonoid composition, to foods that vary significantly in flavonoid content. In addition to this, the Flavonoid Database for USDA Food Codes imputed the flavonoid values for most of its foods because of missing analytical data. Logical zeros, however, were the most imputed values and the foods/beverages that did have analytical values accounted for a large proportion of flavonoid intake overall(27). Furthermore, the application of retention factors according to processing (cooking, storage, etc.) and flavonoid classes across all foods in the Flavonoid Database for USDA Food Codes likely fails to account for variations across specific flavonoids and particular foods(27). All the aforementioned limitations may contribute to under- or overestimation of flavonoid intakes or may bias their association with UPF consumption towards the null. On the other hand, the conservative approach used in the Flavonoid Database for USDA Food Codes of setting to zero the non-zero isoflavone values provided by a functional ingredient that may not be present in all brands or types of a certain food code(27) may have underestimated isoflavone intakes and their positive association with UPF intakes. Lastly, the calculated flavonoid intakes estimated using the Flavonoid Database for USDA Food Codes could have different bioavailability depending on the food matrix, the dietary pattern and how they both impact the microbiota(40). Thus, based on the results from this study, no conclusions can be drawn regarding the association between UPF consumption and flavonoid bioavailability.

Conclusion

Total and five classes of flavonoid intakes were inversely associated with UPF consumption. Conversely, isoflavones intake was positively associated with UPF consumption. This finding reinforces the existing evidence regarding the negative impact of UPF consumption on the overall quality of the diet(10,11).

Further research is warranted to investigate the association between UPF consumption and flavonoid bioavailability and the long-term impact of this association on health outcomes.

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The authors declare no conflict of interests.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114523002568

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