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A New Database Facilitates Characterization of Flavonoid Intake, Sources, and Positive Associations with Diet Quality among US Adults[1,2]

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Abstract

Background: Epidemiologic studies demonstrate inverse associations between flavonoid intake and chronic disease risk. However, lack of comprehensive databases of the flavonoid content of foods has hindered efforts to fully characterize population intakes and determine associations with diet quality.

Objectives: Using a newly released database of flavonoid values, this study sought to describe intake and sources of total flavonoids and 6 flavonoid classes and identify associations between flavonoid intake and the Healthy Eating Index (HEI) 2010.

Methods: One day of 24-h dietary recall data from adults aged ≥20 y (n = 5420) collected in What We Eat in America (WWEIA), NHANES 2007–2008, were analyzed. Flavonoid intakes were calculated using the USDA Flavonoid Values for Survey Foods and Beverages 2007–2008. Regression analyses were conducted to provide adjusted estimates of flavonoid intake, and linear trends in total and component HEI scores by flavonoid intake were assessed using orthogonal polynomial contrasts. All analyses were weighted to be nationally representative.

Results: Mean intake of flavonoids was 251 mg/d, with flavan-3-ols accounting for 81% of intake. Non-Hispanic whites had significantly higher (P < 0.001) intakes of total flavonoids (275 mg/d) than non-Hispanic blacks (176 mg/d) and Hispanics (139 mg/d). Tea was the primary source (80%) of flavonoid intake. Regardless of whether the flavonoid contribution of tea was included, total HEI score and component scores for total fruit, whole fruit, total vegetables, greens and beans, seafood and plant proteins, refined grains, and empty calories increased (P < 0.001) across flavonoid intake quartiles.

Conclusions: A new database that permits comprehensive estimation of flavonoid intakes in WWEIA, NHANES 2007–2008; identification of their major food/beverage sources; and determination of associations with dietary quality will lead to advances in research on relations between flavonoid intake and health. Findings suggest that diet quality, as measured by HEI, is positively associated with flavonoid intake. *J Nutr* 2015;145:1239–48.

Keywords: USDA provisional flavonoid addendum, What We Eat in America, NHANES, flavonoid intake, flavonoid dietary sources, Healthy Eating Index

Introduction

Flavonoids, a large class of bioactive compounds that occur naturally in plants (1, 2), may play important roles in promoting health and preventing disease (3–5). They are the most abundant type of polyphenol in the diet, constituting approximately two-thirds of intake (6). Based on their chemical structure, they may be categorized into 6 classes: anthocyanidins, flavan-3-ols, flavanones, flavones, flavonols, and isoflavones (1, 2).

Flavonoids' biologic activities in vitro are well established (3, 7). They have a high capacity to limit oxidative damage to cells (3), although their effectiveness as direct antioxidants in the body has been questioned because of poor bioavailability (8, 9). Other in vitro effects of flavonoids include antiviral (3, 7) and anti-inflammatory (3, 10) activity, improvement of vascular

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endothelial function (7, 11), and inhibition of tumor development and angiogenesis (3, 12, 13). Numerous studies in animal models offer promising support for the occurrence of these effects of flavonoids in vivo (14, 15).

To determine whether flavonoids serve similar functions in humans, extensive research has studied relations between intake of flavonoids and/or flavonoid-rich foods and chronic disease. Inverse associations have been found between intake and incidence of coronary heart disease (16–20) and its risk factors (15, 21), cancer (22–24), type 2 diabetes (25–28), neuromuscular disorders (15, 29), and multiple other diseases and health conditions (4). Possibly because of structural differences among flavonoids (2), some studies have found associations between a given flavonoid or flavonoid class and development of a certain disease, while finding no associations with intake of total flavonoids, another class of flavonoids, or even another specific flavonoid within the same class (9, 27, 30, 31).

In epidemiologic studies such as these, measuring total, class, and individual flavonoid intake both accurately and comprehensively is paramount. Failure to do so could result in misclassification of individuals by flavonoid intake and lessen the likelihood of detecting associations between flavonoids and disease outcomes.

Over the past 2 decades, numerous databases have been designed to allow estimation of flavonoid intake for the study of flavonoid-health relations (17, 21, 32–46). However, a limitation common to all of them (and, therefore, the estimates they produce) was a shortage of information on the flavonoid content of foods available for their development. Databases applied in early studies included only a subset of the flavonoid classes (generally, flavones, flavonols, and flavanones) and contained composition data on a relatively small number of fruits, vegetables, and beverages (43–46). In later studies (39–41), researchers based their databases on the first USDA compilation of analytic flavonoid values for selected foods (47), which contained fewer than one-half as many foods as the most recent release by the USDA (48).

For a variety of reasons, many databases contain missing values for flavonoids in some foods (17, 34, 37, 39, 40), which could result in underestimates of flavonoid intake. To minimize this problem, some studies imputed flavonoid values from raw foods to the corresponding cooked version when analytic data were available only for the raw form (17, 32, 45). This lack of adjustment for processing losses could lead to overestimation of flavonoid intake. Other studies addressed this lack of data by either using default retention factors (40) or applying to flavonoid factors that had been calculated for other foods or food components (36), which could lead to over- or underestimation of intake.

In addition to studying relations between flavonoid intake and disease per se, it is also of interest to investigate associations with measures of health that may be related to development of disease, such as diet quality. Consumption of fruits and vegetables has been correlated with both flavonoid intake and overall diet quality. Murphy et al. (49) found that individuals who consumed the number of fruit and vegetable servings recommended for their dietary pattern had significantly higher phytonutrient intake, including flavonoid intake, than those who did not consume the recommended servings. Guenther et al. (50) found that, other than the total amount of empty calories consumed, intakes of whole fruit and total fruit are the second and third most correlated factors with the Healthy Eating Index (HEI)[3], which is a measure of an overall healthy eating pattern. However, no investigation has been conducted specifically to determine whether there is a relation between flavonoids and a measure of overall dietary quality that considers aspects of diet beyond intake of fruits and vegetables.

The USDA has created a special provisional database that allows calculation of nationally representative estimates of flavonoid intake using dietary data on all foods/beverages from What We Eat in America (WWEIA), NHANES 2007–2008. The objectives of this study were to apply this new database to (1) estimate intake of total flavonoids and 6 flavonoid classes and compare intakes by selected sociodemographic groups, (2) describe major sources of flavonoids in the US diet, and (3) identify associations, if any, between flavonoid intake and HEI total and component scores among US adults.

Methods

Development of a flavonoid composition database for USDA survey foods and beverages. The USDA Food and Nutrient Database for Dietary Studies (FNDDS) is a database of foods/beverages, their nutrient values, and weights for typical portions (51). Although it has many applications, the primary use of the FNDDS is for the calculation of nutrient intakes from WWEIA, NHANES, dietary recalls. Nutrient values for all FNDDS items are based on values in the USDA National Nutrient Database for Standard Reference (SR), the major source of food composition data in the United States (51, 52). FNDDS 4.1, the version that corresponds to WWEIA, NHANES 2007–2008, contains values for energy and 64 nutrients (51) but does not contain flavonoid values. To estimate flavonoid intakes for the same time period, we created a database addendum that includes flavonoid values for all 7174 foods in FNDDS 4.1.

Developing a complete database that allows estimation of US flavonoid intakes based on all foods/beverages reported in WWEIA, NHANES 2007–2008, was a 2-step process. First, the USDA Nutrient Data Laboratory created a database of values for 29 individual flavonoids in 6 classes for 2926 SR foods (53). Flavonoid values were assigned to SR foods by either matching analytic values from previously published sources (3% of all values), assigning logical zero values for items not expected to contain any flavonoids (~72%), or imputing flavonoid values by various methods (~25%) (54).

Next, the USDA Food Surveys Research Group used the applicable SR codes to develop flavonoid values for all FNDDS foods/beverages, in a manner similar to that used in developing FNDDS nutrient values (51). Each FNDDS food code was linked to a specified amount of one or more SR foods, and the summed flavonoid contributions of those amounts of SR foods became the flavonoid values for the FNDDS food/beverage. Appropriate factors were applied to account for losses in moisture (51) and flavonoid content associated with cooking and processing (54). Documentation of the steps taken to prepare this database is available elsewhere (55). On completion, 4314 (~60%) of the foods/beverages in the addendum had a nonzero value for one or more of the flavonoids studied.

Both the addendum and a set of intake files in SAS format that were generated by applying the addendum to WWEIA, NHANES 2007–2008, dietary intake data are available online (56). The dietary flavonoid intake files include values not only for 29 individual flavonoids, but also summative totals for 6 classes (anthocyanidins, flavan-3-ols, flavanones, flavones, flavonols, and isoflavones) and for total flavonoids (56). In the addendum, all values are standardized to milligrams of flavonoid per 100 g of food. As in the database of flavonoid values for SR foods, values in both the addendum and the intake files are reported as aglycone equivalents (48).

Sample. Estimates are based on dietary intake data from 2662 men and 2758 women aged ≥20 y interviewed in WWEIA, NHANES 2007–2008. The NHANES sample is designed to be representative of the civilian, noninstitutionalized US population, with oversampling of

[3] Abbreviations used: FNDDS, Food and Nutrient Database for Dietary Studies; HEI, Healthy Eating Index; SR, National Nutrient Database for Standard Reference; WWEIA, What We Eat in America.

Hispanics, adults ≥60 y of age, blacks, and low-income individuals (57). The survey protocol was approved by the National Center for Health Statistics Research Ethics Review Board. The current study was a secondary analysis and was deemed exempt from further review under Title 45 Code of Federal Regulations section 46.101(b).

Food intake. Dietary intake data were collected using the USDA Automated Multiple-Pass Method for the 24-h recall (58, 59). Recalls were conducted by trained interviewers fluent in English and Spanish (60). The first day of intake, which was analyzed in this study, was collected in person. WWEIA 2007–2008 dietary data are available online (61). Using the WWEIA Food Categories 2007–2008 (62) as a foundation, each food/beverage was classified into one of 51 mutually exclusive groups.

Measurement of diet quality. The HEI assesses diet quality in relation to national nutrition guidance provided in the *Dietary Guidelines for Americans* (63, 64). In the current HEI version, HEI 2010, 9 of the 12 components are scored based on their level of adequacy in the diet; higher scores indicate higher consumption (63). Four of these components are flavonoid-containing food groups (total fruit, whole fruit, vegetables, and greens and beans). The other 3 components are scored based on their level of moderation in the diet; higher scores indicate lower consumption (63).The total HEI score is the sum of the component scores and can range from 0 to 100 points, with higher scores indicating closer conformity with the dietary guidelines (63).

Statistical analysis. Analyses were performed using SAS, release 9.3 (2011; SAS Institute). SUDAAN, release 11.0 (2012; Research Triangle Institute) was used to adjust for survey design effects resulting from the NHANES' complex, multistage probability sampling (65). All analyses used dietary sample weights to produce nationally representative estimates.

The distribution of flavonoid intakes was highly positively skewed and required a Box-Cox transformation (66–69) before between-group statistical comparisons were conducted. Linear regression analyses produced adjusted estimates of flavonoid intake by sex, age, race/ethnicity, income, smoking status, weight status, and exercise level. Differences in estimates within demographic and lifestyle characteristic were evaluated using ANOVA. *P* values for demographic/lifestyle differences are results of parametric tests on data transformed to correct for the non-normal distributions.

To determine important contributors to dietary intakes of flavonoids for American adults, percentage contributions of each of the 51 food/beverage categories to intakes of total flavonoids and each flavonoid class were calculated. A category was considered an "important source" of flavonoids or a particular flavonoid class if it accounted for ≥5% of adults' total daily intake (70). Defining an "important" source of a flavonoid in this manner is an acknowledgment of the fact that some foods/beverages that are not particularly rich sources of a flavonoid are highly consumed and therefore provide notable proportions of overall intake (70).

To assess the relation between flavonoid intake and dietary quality, individuals were divided into quartiles of intake of total flavonoids from all foods/beverages. Mean total and component HEI scores were determined for each quartile of flavonoid intake, with adjustment via linear regression for selected characteristics, including those previously shown to be associated with HEI (viz., age, sex, and race/ethnicity) (71). Energy intake was not an adjustment variable, because HEI scores are determined on a density basis (63).

Because of the consumption of tea by ~29% of US adults on any given day (72), coupled with the very large difference in content of total flavonoids between tea and other foods (53), being classified in the highest quartile of total flavonoid intake was nearly synonymous with reporting tea. Therefore, we repeated the analysis, categorizing individuals into quartiles based on their flavonoid intakes from all foods/beverages other than tea. Linear trends between flavonoid intakes and mean total and component HEI scores were then assessed using orthogonal polynomial contrasts.

All results with a probability of occurrence of $P < 0.01$ were considered statistically significant.

Results

Flavonoid intakes. Intakes of anthocyanidins, flavan-3-ols, flavanones, flavones, flavonols, isoflavones, and their summative totals are presented in **Table 1**. On any given day in

TABLE 1 Dietary intake of flavonoids by adults aged ≥20 y in WWEIA, NHANES 2007–2008 (1 d)[1]

Flavonoid class	All adults (*n* = 5420)	Men (*n* = 2662)	Women (*n* = 2758)
Individuals with zero intakes,[2] %			
Anthocyanidins	31 ± 2	33 ± 2	29 ± 2
Flavan-3-ols	6 ± 1	5 ± 1	6 ± 1
Flavanones	37 ± 2	38 ± 3	35 ± 1
Flavones	10 ± 1	11 ± 1	10 ± 1
Flavonols	1 ± 0[3]	1 ± 0[3]	1 ± 0[3]
Isoflavones	60 ± 1	59 ± 2	62 ± 1
Total flavonoids	1 ± 0[4]	1 ± 0[4]	1 ± 0[4]
Intakes,[5] mg/d			
Anthocyanidins	11.6 ± 1.07 (0.00, 9.92)	10.5 ± 0.83 (0.00, 8.71)	12.6 ± 1.51 (0.00, 11.2)
Flavan-3-ols	204 ± 15.6 (3.07, 189)	214 ± 19.2 (3.51, 152)	196 ± 14.2 (2.62, 221)
Flavanones	13.1 ± 0.88 (0.00, 5.15)	14.4 ± 1.01 (0.00, 5.33)	11.9 ± 1.10 (0.00, 5.05)
Flavones	0.9 ± 0.1 (0.1, 1.1)	0.9 ± 0.1 (0.1, 1.2)	0.8 ± 0.1 (0.1, 1.0)
Flavonols	19.4 ± 0.91 (6.05, 25.4)	21.6 ± 1.06 (7.15, 28.7)	17.5 ± 0.85 (4.94, 23.4)
Isoflavones[6]	1.7 ± 0.3 (0.0, 0.0)[7]	1.8 ± 0.5 (0.0, 0.0)[7]	1.6 ± 0.3 (0.0, 0.0)[7]
Total flavonoids[8]	251 ± 16.8 (18.8, 272)	263 ± 20.4 (20.4, 271)	241 ± 15.2 (16.3, 272)

[1] WWEIA, What We Eat in America.
[2] Mean percentage ± SE.
[3] Value appears as zero because of rounding; actual value, SE = 0.2 for all adults and 0.3 for men and women.
[4] Value appears as zero because of rounding; actual value, SE = 0.2 for all adults and for women and 0.3 for men.
[5] Mean ± SE (IQR).
[6] Excludes some isoflavones contributed by functional ingredients added in small amounts to foods and beverages, as outlined in documentation for the provisional flavonoid addendum (55).
[7] Value appears as 0.0 because of rounding; actual value for 75th percentile, 0.03 for all adults and for women and 0.04 for men.
[8] Sum of dietary flavonoids in the 6 classes listed.

2007–2008, nearly all adults aged ≥20 y consumed some flavonoids. Because of large variations in the flavonoid content of foods, zero intakes were more common for some flavonoid classes, especially isoflavones (60% of adults), flavanones (37%), and anthocyanidins (31%). Mean intake of total flavonoids by adults was 251 mg, with flavan-3-ols providing the largest share (81%), followed by flavonols (8%), flavanones (5%), anthocyanidins (5%), isoflavones (1%), and flavones (<1%). For 4 of the flavonoid classes, the mean was larger than the 75th percentile (Table 1), which highlights the extreme positive skewness of the intake distributions.

No significant differences in intake of total flavonoids were found by sex, age, income level, smoking status, weight status, or exercise status (**Table 2**). However, intakes differed significantly by race/ethnicity (P < 0.001). Mean intake of total flavonoids was higher for non-Hispanic whites (275 mg) than for non-Hispanic blacks (176 mg) or Hispanics (139 mg).

Dietary sources of flavonoids. Important sources (i.e., contributors of ≥5% of total intake) of each flavonoid class and total flavonoids are shown in **Table 3**. Some foods were among the top contributors because they were highly concentrated sources of a particular flavonoid class (e.g., for anthocyanidins, berries; for isoflavones, soy-based protein powder), whereas others were top contributors because of being highly consumed by the US population (e.g., for anthocyanidins, bananas; for flavonols, beer). Tea was the only important source of total flavonoids and flavan-3-ols, and it was also the highest contributor to flavonol intake. Mixed dishes was the only other food group that was included in the

TABLE 2 Flavonoid intakes by demographic and lifestyle factors for adults aged ≥20 y in WWEIA, NHANES 2007–2008 (1 d)[1]

		Flavonoid class, mg/d							
Demographic/lifestyle factor	Sample size	Anthocyanidins	Flavan-3-ols	Flavanones	Flavones	Flavonols	Isoflavones	Total[2]	P[3]
Sex									
Male	2662	9.46 ± 0.77	197 ± 16.9	13.5 ± 0.72	0.9 ± 0.1	19.6 ± 0.89	1.5 ± 0.3	242 ± 17.7	0.25
Female	2758	13.5 ± 1.61	211 ± 12.5	12.8 ± 1.16	0.9 ± 0.1	19.3 ± 0.75	1.9 ± 0.4	259 ± 13.2	
Age (y)									
20–39	1751	9.32 ± 0.95	177 ± 19.2	13.0 ± 1.33	0.8 ± 0.1	17.8 ± 0.91	2.4 ± 0.5	220 ± 20.8	0.09
40–59	1722	11.9 ± 1.65	238 ± 22.8	12.3 ± 1.34	0.9 ± 0.1	21.1 ± 1.13	1.3 ± 0.3	286 ± 23.8	
≥60	1947	14.6 ± 1.23	193 ± 14.5	14.6 ± 1.07	0.9 ± 0.1	19.3 ± 0.89	1.3 ± 0.3	243 ± 15.8	
Race/ethnicity[4]									
Non-Hispanic white	2548	12.5 ± 1.30	228 ± 18.0	11.8 ± 0.78	0.9 ± 0.1	20.4 ± 1.03	1.7 ± 0.3	275 ± 19.6[a]	<0.001
Non-Hispanic black	1136	8.89 ± 0.92	134 ± 10.0	16.1 ± 1.51	0.6 ± 0.0[5]	15.3 ± 0.51	1.2 ± 0.3	176 ± 10.9[b]	
Hispanic[6]	1525	10.1 ± 1.16	94.5 ± 14.1	16.3 ± 1.49	0.9 ± 0.1	15.5 ± 0.76	1.4 ± 0.3	139 ± 14.3[b]	
Income (%PIR)[7]									
0–130	1506	12.4 ± 3.03	203 ± 15.8	11.8 ± 1.09	0.8 ± 0.1	18.3 ± 0.66	0.8 ± 0.2	247 ± 15.7	0.08
131–300	1682	9.36 ± 0.82	170 ± 17.8	13.1 ± 1.34	0.8 ± 0.1	17.9 ± 0.97	1.7 ± 0.5	213 ± 19.1	
>300	1747	12.2 ± 1.18	228 ± 18.5	13.8 ± 0.82	0.9 ± 0.1	20.8 ± 0.93	2.2 ± 0.5	278 ± 19.8	
Smoking status[8]									
Never	2854	14.1 ± 1.50	204 ± 13.2	15.3 ± 0.95	0.9 ± 0.1	19.9 ± 0.82	1.9 ± 0.4	256 ± 14.4	0.77
Former	1363	12.4 ± 1.25	195 ± 22.4	12.2 ± 1.46	0.9 ± 0.1	19.1 ± 0.94	2.4 ± 0.9	242 ± 24.1	
Current	1201	5.09 ± 1.03	215 ± 23.1	9.01 ± 0.96	0.7 ± 0.1	18.8 ± 1.07	0.6 ± 0.4	249 ± 24.1	
Weight status[9]									
Normal	1536	14.2 ± 1.64	196 ± 13.7	13.3 ± 0.85	0.9 ± 0.1	19.3 ± 0.82	2.4 ± 0.6	246 ± 15.8	0.36
Overweight	1852	12.4 ± 1.60	216 ± 12.9	14.8 ± 1.12	0.8 ± 0.1	20.0 ± 0.73	1.8 ± 0.3	265 ± 13.4	
Obese	1963	8.29 ± 0.71	204 ± 22.4	10.5 ± 0.96	0.9 ± 0.1	19.2 ± 1.16	1.0 ± 0.3	244 ± 23.1	
Exercise level[10]									
Inactive/low	3865	10.5 ± 1.01	210 ± 16.4	12.5 ± 1.05	0.8 ± 0.0[11]	19.4 ± 0.90	1.3 ± 0.2	255 ± 17.6	0.26
Moderate	539	12.1 ± 1.41	229 ± 23.7	14.3 ± 2.03	1.0 ± 0.1	20.3 ± 1.21	1.7 ± 0.6	278 ± 25.7	
Active	1016	14.5 ± 1.68	176 ± 17.1	14.2 ± 1.26	1.1 ± 0.1	19.1 ± 0.85	3.0 ± 0.8	227 ± 17.6	

[1] Flavonoid intakes, means ± SEs. Estimates adjusted for sex, age, race/ethnicity, smoking status, weight status, and energy intake (except when characteristic was being tested). %PIR, Poverty Income Ratio; WWEIA, What We Eat in America.
[2] Sum of dietary flavonoids in the 6 classes listed. Total flavonoid means with different superscript letters are significantly different, $P < 0.01$.
[3] For each health/demographic characteristic, P value from t test or ANOVA for differences in intake of total flavonoids. Although nontransformed estimates are presented, significance results are based on transformed data.
[4] Excludes individuals who were of other races or multiracial (n = 211).
[5] Value appears as 0.0 because of rounding; actual value, SE = 0.04.
[6] Includes Mexican Americans and other Hispanics.
[7] The %PIR variable is an index for the ratio of family income to poverty. The Department of Health and Human Services poverty guidelines were used as the poverty measure to calculate this index (73).
[8] Participants who reported smoking <100 cigarettes in their lives were classified as ''never smokers.'' Respondents who had smoked ≥100 cigarettes but did not smoke at all at the time of the survey were classified as ''former smokers,'' and those who smoked cigarettes every day or some days at the time of the survey were classified as ''current smokers'' (74).
[9] A few underweight individuals (n = 83) are included in the normal weight category.
[10] Includes only recreational activity, with each vigorous-intensity minute counted as the equivalent of 2 moderate-intensity minutes; levels correspond to those in the 2008 Physical Activity Guidelines for Americans (75).
[11] Value appears as 0.0 because of rounding; actual value, SE = 0.05.

TABLE 3 Important dietary sources of flavonoids for adults aged ≥20 y in WWEIA, NHANES 2007–2008 (1 d)[1]

Flavonoid class and important sources	Rank	Percentage contribution
Anthocyanidins		78
Berries	1	20
Wine	2	16
Bananas	3	11
Grapes	4	11
Red/purple vegetables[2]	5	8
100% juice, noncitrus	6	6
Yogurt	7	6
Flavan-3-ols		95
Tea	1	95
Flavanones		88
100% juice, citrus	1	60
Citrus fruit	2	26
Flavones		79
Mixed dishes	1	28
Condiments and sauces	2	12
Tea	3	10
Sweet peppers	4	9
Celery, squash	5	8
Melons	6	7
Lettuce	7	5
Flavonols		68
Tea	1	39
Mixed dishes	2	13
Beer	3	6
Onions	4	5
White potatoes	5	5
Isoflavones[3]		88
Soy-based protein powder	1	32
Milk substitutes	2	15
Mixed dishes	3	15
Processed soy products	4	13
Snack/meal bars	5	8
Beans, peas, legumes	6	5
Total[4]		80
Tea	1	80

[1] An "important" source is defined as a food/beverage category that contributes ≥5% of the intake of a flavonoid class or total flavonoids (70). WWEIA, What We Eat in America.
[2] Includes eggplant, red cabbage, and radish.
[3] Determination of important dietary sources of isoflavones excluded isoflavones contributed by functional ingredients added in small amounts to foods and beverages, because those ingredients were omitted from calculation of flavonoid values in the provisional flavonoid addendum (55).
[4] Sum of dietary flavonoids in the 6 classes listed.

list of important contributors for more than one flavonoid class.

Associations between flavonoids and dietary quality. In **Table 4**, mean total and component HEI scores are presented by quartile of flavonoid intake. There were significant ($P < 0.001$) positive linear trends in HEI total score by quartile of flavonoid intake from all foods and beverages. Positive associations with total flavonoid intake were also demonstrated for 9 of the 12 component scores, including all fruit and vegetable components, as well as total protein foods, seafood and plant proteins, FAs, refined grains, and empty calories. Most of the positive trends identified when the flavonoid contribution of tea was excluded from the analysis were the same as when tea was included, except no trends were found in scores for total protein foods or FAs and a significant positive trend was found in sodium score.

Discussion

Until now, although flavonoids have been shown to have beneficial health associations, comprehensive quantification of intake by Americans has been difficult because of incomplete databases of the flavonoid content of foods. Using a newly available addendum to the USDA FNDDS, this study is the first to fully characterize flavonoid intake from all foods and beverages, its sources, and its associations with dietary quality in a representative sample of US adults.

The literature contains limited comparable estimates of flavonoid intake in large, heterogeneous populations. Studies that reported mean flavonoid intake in the United States, Europe, Asia, and Australia are listed in **Table 5**. Most similar to our study in study population and dietary assessment method is research conducted by Chun and colleagues (39) with data from NHANES 1999–2002. Their estimates of total flavonoid intake and 4 of the flavonoid classes are lower than those in the present study—as expected, considering the missing data, dated analytic sources, and limited amount of imputation performed in their study. Although it is unclear why the estimate of flavone intake appears higher in the study by Chun et al. (39), the apparent difference in flavanone intake is likely due to a correction first applied in the USDA Database for the Flavonoid Content of Selected Foods, Release 3.1 (48), to the conversion factor used in calculating the flavanone content of orange juice. Relative to the current study, the other US studies (21, 36, 42) also had higher flavones and flavanone estimates [with the exception of flavones intake in Fink et al. (42)], suggesting that the discrepancies seen for both of these flavonoid classes are due to the flavonoid databases applied.

Arguably, the best-known studies investigating flavonoid intakes in countries other than the United States are those that used dietary data collected in the European Prospective Investigation into Cancer and Nutrition (34, 79). Total (34, 79) and flavon-3-ol (79) estimates are not comparable with the present study, however, because the European Prospective Investigation into Cancer and Nutrition analyses included proanthocyanidins but excluded thearubigins, contrary to our methodology. In general, estimates for the other classes appear lower than those in this study, although flavone intakes were higher (79).

Our finding of differences by race/ethnicity aligns with results of previous studies in which, in general, individuals classified as white had higher intakes of total flavonoids than their nonwhite counterparts (32, 39, 80). These findings imply that benefits attributable to flavonoid consumption may not be experienced equally by persons of all racial/ethnic groups.

Other than race/ethnicity, we found no significant differences by demographic or health characteristics. Considering only variables we analyzed, previous research found differences not only by race/ethnicity, but also sex (34, 37, 79), age (32, 34, 39, 77, 79, 80), income (32, 39, 79), BMI (32, 34, 77, 80), smoking status (34, 40, 77, 79, 80), and exercise level (32, 34, 40, 77, 80).

In addition to differences in sample, dietary data collection, and flavonoid databases applied, the data transformations we conducted may help to account for the fewer significant findings in this study relative to other studies. The flavonoid data from WWEIA, NHANES, were highly skewed, and simple

TABLE 4 HEI total and component scores by quartile of total flavonoid intake for adults aged ≥20 y in WWEIA, NHANES 2007–2008 (1 d)[1]

HEI component by source	Quartile of total flavonoid intake				*P*-trend[2]
	1	2	3	4	
From all foods and beverages					
Total vegetables	2.5 (2.4, 2.7)	3.1 (2.9, 3.4)	3.1 (2.9, 3.4)	3.3 (3.0, 3.5)	<0.001
Greens and beans	0.7 (0.5, 0.8)	1.3 (1.1, 1.5)	1.5 (1.3, 1.7)	1.4 (1.0, 1.7)	<0.001
Total fruit	0.6 (0.4, 0.7)	2.1 (1.9, 2.3)	3.5 (3.3, 3.7)	2.3 (2.0, 2.7)	<0.001
Whole fruit	0.7 (0.6, 0.9)	2.3 (2.1, 2.5)	3.1 (2.9, 3.3)	2.3 (1.9, 2.6)	<0.001
Whole grains	1.9 (1.6, 2.2)	2.3 (1.8, 2.8)	2.5 (2.0, 3.1)	2.1 (1.7, 2.5)	0.23
Dairy	5.3 (4.8, 5.8)	5.3 (4.8, 5.7)	5.1 (4.7, 5.5)	4.9 (4.4, 5.3)	0.05
Total protein foods	4.1 (4.0, 4.3)	4.2 (4.0, 4.4)	4.2 (4.0, 4.4)	4.3 (4.2, 4.4)	<0.001
Seafood and plant proteins	1.5 (1.2, 1.8)	1.9 (1.6, 2.2)	2.2 (2.0, 2.5)	2.1 (1.8, 2.3)	<0.001
FAs	4.4 (4.0, 4.8)	5.0 (4.6, 5.3)	5.0 (4.6, 5.4)	5.2 (4.8, 5.5)	<0.001
Refined grains[3]	5.3 (4.9, 5.7)	6.3 (5.9, 6.8)	6.8 (6.4, 7.1)	6.4 (6.0, 6.8)	<0.001
Sodium[3]	4.2 (3.7, 4.7)	4.6 (4.3, 4.9)	5.2 (4.8, 5.7)	4.5 (4.2, 4.8)	0.06
Empty calories[3]	10.2 (9.48, 11.0)	11.9 (11.1, 12.7)	13.3 (12.4, 14.2)	11.8 (10.9, 12.7)	<0.001
Total HEI	41.5 (40.1, 42.9)	50.4 (48.3, 52.5)	55.5 (53.6, 57.4)	50.5 (48.0, 53.0)	<0.001
From all foods and beverages except tea					
Total vegetables	2.3 (2.2, 2.5)	3.1 (2.9, 3.3)	3.3 (3.0, 3.6)	3.3 (3.1, 3.5)	<0.001
Greens and beans	0.5 (0.4, 0.7)	1.2 (1.0, 1.4)	1.6 (1.2, 1.9)	1.6 (1.4, 1.8)	<0.001
Total fruit	0.4 (0.3, 0.5)	1.3 (1.1, 1.5)	2.8 (2.6, 3.0)	3.9 (3.7, 4.1)	<0.001
Whole fruit	0.5 (0.4, 0.7)	1.6 (1.4, 1.8)	2.9 (2.6, 3.1)	3.4 (3.2, 3.6)	<0.001
Whole grain	1.9 (1.6, 2.3)	2.0 (1.7, 2.4)	2.5 (2.0, 2.9)	2.4 (1.9, 2.9)	0.01
Dairy	5.2 (4.7, 5.7)	5.0 (4.6, 5.4)	5.3 (4.9, 5.6)	5.1 (4.6, 5.6)	0.89
Total protein foods	4.1 (4.0, 4.3)	4.3 (4.2, 4.3)	4.3 (4.1, 4.5)	4.2 (4.1, 4.3)	0.47
Seafood and plant proteins	1.5 (1.3, 1.7)	1.8 (1.6, 2.0)	2.1 (1.7, 2.5)	2.3 (2.2, 2.5)	<0.001
FAs	4.7 (4.2, 5.1)	4.9 4.5, 5.2)	4.8 (4.4, 5.2)	5.2 (4.8, 5.6)	0.02
Refined grains[3]	5.1 (4.7, 5.5)	6.2 (5.6, 6.7)	6.4 (6.0, 6.9)	7.1 (6.7, 7.5)	<0.001
Sodium[3]	4.1 (3.5, 4.7)	4.5 (4.2, 4.9)	4.6 (4.2, 5.0)	5.3 (5.0, 5.6)	<0.001
Empty calories[3]	9.94 (9.24, 10.6)	11.1 (10.2, 12.1)	12.3 (11.6, 13.1)	13.8 (13.0, 14.7)	<0.001
Total HEI	40.4 (38.8, 42.1)	47.0 (45.0, 49.0)	52.9 (50.7, 55.1)	57.6 (55.9, 59.3)	<0.001

[1] Mean (99% CI). Estimates adjusted for sex, age, race/ethnicity, smoking status, and weight status. HEI, Healthy Eating Index; WWEIA, What We Eat in America.

[2] Results based on polynomial orthogonal linear contrast.

[3] Reverse scored, i.e., the higher the score, the lower the intake.

transformations (e.g., log transformations) did not normalize the distributions. Modeling of total flavonoids was required to meet statistical assumptions before testing the point estimates for significant differences. Researchers who apply these data for inferential purposes must address the inherent nonnormality of the flavonoid intake distributions, either by transforming the data or limiting analyses to nonparametric statistical tests.

Dietary sources varied tremendously by flavonoid class. Tea was identified as the primary source of flavonoids in the US diet, in accordance with other studies (32, 36, 39). Some food groups found to be important sources of flavonoids were not intuitive. Yogurt, for example, was a top contributor to anthocyanidin intake; however, it is an animal-based product. The anthocyanidin contribution of yogurt is due to the fact that fruit-flavored yogurts, many with berries as ingredients, comprise the majority of yogurt consumption in the United States (81). Likewise, mixed dishes were important sources of flavones and flavonols because of their frequent inclusion of vegetable ingredients such as onions, sweet and hot peppers, celery, and potatoes. Researchers who use food frequency data to quantify flavonoid intake should be mindful of these hidden—but not inconsequential—sources of flavonoids and account for them in their methodology to obtain comprehensive results.

Our finding of a positive association between flavonoid intake and dietary quality suggests that a diet high in flavonoids is synonymous with greater compliance with national dietary guidance. By re-examining the relation between the flavonoid intake category and HEI without the contribution of tea, we showed that flavonoid intake was not simply a proxy for tea intake, i.e., that total HEI score and component scores were positively associated with flavonoid intake independent of the flavonoid contribution of tea. Although our finding that scores for fruit and vegetable HEI components are associated with flavonoid intake was predictable, associations were also found for other HEI components not directly related to fruit or vegetable intake, including components for which moderation is recommended, i.e., refined grain, sodium, and empty calories. These 3 components account for 40% of the total composite score (63), indicating their comparative importance. Of all the HEI components, the empty calories score has been shown to share the largest positive correlation with total HEI score (50). The current study's finding of positive associations with moderation components suggests that individuals with higher flavonoid intakes not only consume more fruits and vegetables but also eat more healthfully in other ways.

This study has a few limitations. Two limitations concern data in the flavonoid database for SR foods, on which the

TABLE 5 Estimated flavonoid intakes by country[1]

Country (reference)	Study sample, *n*	Age (y), gender[2]	Dietary assessment method	Flavonoid intake, mg/d Total	Anthocyanidins	Flavan-3-ols	Flavanones	Flavones	Flavonols	Isoflavones
Australia (76)	10,851	≥19	24HR	454	2.9	420	6.9	0.5	21	—
China (33)	1393	35–75	FFQ	—	28[3]	—	—	11	120[4]	3.7
Europe, multiple countries (34)	35,628	35–74	24HR	204–549[5]	—	—	—	—	—	—
Finland (77)	1950	42–60, M	4-d Food record	139	6.2	120	3.1	0.3	10	—
Finland (38)	2007	25–64	48HR	—	47	12[6]	27	—	5.4	—
France (37)	4942	45–60	≥6 24HRs	—	35	87[6]	13	18	34	—
South Korea (78)	4186	40–59	24HR	—	—	—	21–29	0.4–0.5	16–17[4]	—
Spain (79)	40,683	35–64	Diet history	—	19	30[6]	51	3.4	19	0.1
United Kingdom (25)	1997	18–76, F	FFQ	1170[5]	18	230,[6] 840[7]	30	2.0	46	—
United States (32)	17,900	≥19	24HR	345[5]	9.2	190	22	1.2	18	2.4
United States (21)	46,672	30–55, F	Multiple FFQs	358[5]	12	55,[6] 230[7]	37	1.7	18	—
	87,242	25–42, F	—	413[5]	14	62,[6] 280[7]	33	1.5	18	—
	23,043	40–75, M	—	376[5]	15	50,[6] 240[7]	52	2.2	19	—
United States (36)	366	68.9 ± 14.7	7-d Diet records	280	27	110	23	1.5	16	6.4
	609	63.2 ± 15.4	—	280	18	120	27	1.7	14	4.1
	663	62.5 ± 16.5	—	250	14	120	25	1.4	12	1.5
United States (39)	8809	>19	24HR	190	3.1	160	14	1.6	13	1.2
United States (42)	1500	20–95, F	FFQ	—	3.5	170	31	0.2	10	0.7[8]

[1] 24H, 24-h recall; 48HR, 48-h recall.
[2] Gender is specified only when both are not included.
[3] Excludes malvidin and petunidin.
[4] Excludes isorhamnetin.
[5] Includes proanthocyanidin estimates.
[6] Monomers only.
[7] Polymers (including proanthocyanidins) only.
[8] Excludes glycitein.

FNDDS addendum is based. First, the flavonoid content of foods can vary widely, depending on many factors (48). Although only one value is assigned for each individual flavonoid for each specific food, Harnly et al. (82) noted an average relative SD of 168% in flavonoid values across >60 fruits, vegetables, and nuts. Second, many of the flavonoid values in the database produced by the Nutrient Data Laboratory, and thus in the addendum, are imputed rather than analytic. Other limitations are related to the survey methods and sample. Because assessing flavonoid intake was not a focus of WWEIA, NHANES 2007–2008, questions in the survey instrument were not tailored to elicit information about flavonoid-containing foods. Consequently, considerable variation in the use and amount of some flavonoid-contributing ingredients in mixed foods may not have been captured. Although some studies have found distinct flavonoid intake patterns, particularly of isoflavones and flavonoids present in tea, in Asians (33, 83, 84), the number of Asian Americans in the NHANES 2007–2008 sample did not permit analysis of intakes by this group.

Several strengths of this study hinge on the databases used. The flavonoid addendum allowed estimation of total flavonoids, 6 classes, and 29 individual flavonoids from all dietary sources. The large number of foods (7174) in the FNDDS makes the corresponding flavonoid addendum the most extensive database of flavonoid values for commonly consumed foods. By design, the addendum to the FNDDS includes not only flavonoids provided by primary sources (e.g., tea, fruits, and vegetables) but also incidental amounts from flavonoid-containing ingredients of more complex foods. Some researchers have postulated that omission of the flavonoid contribution of mixed foods may result in underestimation of flavonoid intake (36). Another strength of this study is the representativeness of its sample, which allows our findings to be generalized to all American adults. Finally, although under-reporting can be an issue with self-reported dietary data, the dietary intake instrument used in collecting WWEIA data has undergone extensive methodologic testing to enhance food recall and minimize forgotten food items (58) and has been validated for both energy and sodium intakes (59, 85).

The new, publicly released flavonoids addendum to the FNDDS, along with further efforts to improve the values contained in it (e.g., more analytic values and studies measuring the effect of processing on retention of flavonoids), will facilitate research to delineate relations between flavonoid intake and health. Its application permits comprehensive estimation of flavonoid intakes in WWEIA, NHANES 2007–2008; identification of their major food and beverage sources; and determinations of associations with dietary quality, as demonstrated in this study. Findings suggest that compliance to national dietary guidance, as measured by HEI, is positively associated with flavonoid intake and that aspects of the diet not limited to fruit and vegetable intake contribute to this association.

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