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Original Research Article

Application of the Database of Flavonoid Values for USDA Food Codes 2007–2010 in assessing intake differences between the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study and What We Eat in America (WWEIA), NHANES

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ABSTRACT

Flavonoids are polyphenolic plant compounds whose biological activities may promote human health. It is worthwhile to examine whether flavonoid intake varies between populations with differing prevalence of diet-related diseases. This study compared flavonoid intakes in the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study with nationally representative estimates from What We Eat in America (WWEIA), NHANES stratified by sex, age (30−49, 50−64 years), and poverty status (income <125 %,>125 % of the 2004 HHS Poverty Guidelines). Flavonoid intakes from both surveys were estimated using the Database of Flavonoid Values for USDA Food Codes 2007–2010. Across all subpopulations analyzed, intake of anthocyanidins was lower in HANDLS ($p < 0.01$). Intakes of total flavonoids and all or most flavonoid classes were lower in HANDLS for men overall and in both age groups and for both men and women with poverty status <125 %. These findings of lower flavonoid intakes in HANDLS, particularly among men and those with the lowest incomes, suggest that flavonoid intake may be a factor in the high prevalence of diet-related disease in populations represented by HANDLS. This research illustrates how any survey using USDA's food codes can utilize the Flavonoid Database in comparing flavonoid intakes.

1. Introduction

Elimination of health disparities and achievement of health equity are among the overarching goals of Federal health research (Healthy People 2030 Framework, n.d.; U.S. Department of Health and Human Services, 2020). Since diet is one of the behavioral risk factors with the strongest impact on morbidity and mortality in the U.S. (US Burden of Disease Collaborators, 2018), it is worthwhile to examine whether intakes of specific food components vary between populations that experience differing levels of health outcomes.

Flavonoids are a group of dietary components found exclusively in plant foods that have generated a great deal of current interest with regard to human health. Some rich sources of these polyphenolic compounds include tea, berries, citrus fruits, and soy products (Beecher, 2003). Flavonoids exhibit many actions in vitro and in vivo, including anti-oxidant, anti-inflammatory, anti-neoplastic, and anti-microbial

Abbreviations: AMPM, Automated Multiple-Pass Method for the 24-h recall; Flavonoid Database, Database of Flavonoid Values for USDA Survey Food Codes 2007–2010; FNDDS, Food and Nutrient Database for Dietary Studies; HANDLS, Healthy Aging in Neighborhoods of Diversity across the Life Span; NHANES, U.S. National Health and Nutrition Examination Survey; USDA, U.S. Department of Agriculture; WWEIA, What We Eat in America.

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activity (Kozłowska and Szostak-Wegierek, 2014; Kumar and Pandey, 2013). Abundant research has identified inverse associations between flavonoid intake and cardiovascular disease (Cassidy et al., 2016; Wang et al., 2014), cancers (Cassidy et al., 2014; Woo and Kim, 2013), diabetes (Liu et al., 2014; Zamora-Ros et al., 2014), neurodegenerative diseases (Holland et al., 2020; Potì et al., 2019), and numerous other conditions (Grosso et al., 2017; Pandey and Rizvi, 2009).

Identifying dietary factors that are associated with health disparities is among the goals of the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study (HANDLS overall study protocol, 2004). HANDLS is a prospective fixed cohort of adults in Baltimore City, Maryland, with a design that incorporates several characteristics that are associated with cardiovascular and cerebrovascular health disparities, namely, income (operationalized as poverty status), race, sex, and age (Disparities, n.d.; Evans et al., 2010; Patnode et al., 2017).

Prevalence of chronic diseases among HANDLS participants is high. For example, in HANDLS at baseline in 2004 the prevalence of obesity was 42.1 % (Beydoun et al., 2018); diabetes, 16.5 % (Wright et al., 2017); and hypertension, 45.2 % (Cotugna et al., 2013). In comparison, national estimates among adults for a similar time frame were 32.2 % for obesity (Ogden et al., 2006), 10.3 % for diabetes (Palmer and Toth, 2019), and 29.3 % for hypertension (Ong et al., 2007).

To gain insight into these high rates of diet-related diseases in HANDLS, determining whether intakes of beneficial dietary components such as flavonoids in that study differ from those in the U.S. population is of interest. One previous study has compared flavonoid intakes between participants in HANDLS and the nationally representative survey What We Eat in America (WWEIA), NHANES overall and by race (Fanelli Kuczmarski et al., 2018); however, the same comparisons have not been conducted by the other characteristics that together define HANDLS study's factorial design.

The objective of this study was to determine if flavonoid intakes (total and six classes: anthocyanidins, flavan-3-ols, flavanones, flavones, flavonols, and isoflavones) differed between HANDLS and WWEIA, NHANES in groups stratified by sex, and by age and poverty status within sex. In light of the evidence regarding health benefits of flavonoids, a difference in intake could contribute to the high prevalence of diet-related disease observed in the HANDLS population.

2. Methods

2.1. Study samples

2.1.1. HANDLS

The HANDLS study design (Evans et al., 2010; HANDLS overall study protocol, 2004) was a 4-way factorial cross of age (seven five-year age bands from 30 through 64 years), sex (men and women), race (self-reported; non-Hispanic African American and non-Hispanic White), and socioeconomic status operationalized as poverty status (self-reported household income <125 % or >125 % of the 2004 Health and Human Services poverty guidelines; 2004 HHS Poverty Guidelines, 2004). Details regarding the HANDLS sample, design, and methods are available elsewhere (Evans et al., 2010; HANDLS main page, n.d.; HANDLS overall study protocol, 2004). Data collection in Wave 1, which was analyzed in this study, began in 2004 and was completed in 2009 (Raffensperger et al., 2010). Participants were recruited from 13 pre-determined neighborhoods (groups of contiguous census tracts) in Baltimore City. Neighborhoods were selected based on the likelihood of being able to enlist adult men and women in the target racial, poverty status, and age groups. Additional inclusion criteria were the ability to give informed consent and the ability to perform at least 5 measures; exclusion criteria were pregnancy and active cancer treatment within the last 6 months (HANDLS overall study protocol, 2004).

Wave 1 data collection was conducted in two phases. Phase 1 took place in the home and included household screening, recruitment, completion of a household questionnaire, and conduct of a 24 -h dietary recall with each participant (maximum 2 per household). Phase 2 took place in a Mobile Research Vehicle stationed in the neighborhood, where participants underwent comprehensive health examinations, answered computer-assisted questionnaires, and completed a second 24 -h dietary recall interview.

The Wave 1 sample consisted of 3720 participants. Most (91.9 %) completed the in-home 24 -h recall, but fewer (59.2 %) completed both 24 -h recalls. As there was potential non-response bias in Phase 2 participation with respect to demographic variables of interest (Evans et al., 2010), only 1 day of dietary intake data was analyzed, yielding a final sample size of 3418.

The study protocol was approved by the human investigation institutional review board at MedStar Health Research Institute. All participants provided informed consent.

2.1.2. WWEIA, NHANES 2007–2010 subsample

WWEIA is the dietary intake interview component of NHANES; details regarding the sample, design, and methods are available elsewhere (NHANES questionnaires, datasets, and related documentation, 2020). In brief, NHANES is a nationally representative sample of the noninstitutionalized U.S. population. For comparability with HANDLS, a subsample of individuals from WWEIA, NHANES 2007–2010 who resembled HANDLS participants in demographic characteristics related to dietary, and thus also flavonoid, intake was selected. Inclusion criteria were (1) age 30–64 years, (2) non-Hispanic White or non-Hispanic Black race, and (3) annual household income <$75,000. Pregnant and lactating females were excluded, yielding a final sample of 2598 adults.

Informed consent was obtained from all participants. The survey protocol was approved by the National Center for Health Statistics Research Ethics Review Board. This study was a secondary analysis and was deemed exempt from further review under federal regulation 45 CFR 46.101(b).

Characteristics of participants in the HANDLS Wave 1 sample and the WWEIA, NHANES 2007–2010 subsample are shown in Table 1.

2.2. Assessment of flavonoid intake

Dietary data in both HANDLS and WWEIA, NHANES were collected using the USDA Automated Multiple-Pass Method (AMPM) for the 24 -h recall (Steinfeldt et al., 2013). All foods and beverages reported were assigned USDA food codes using the USDA Food and Nutrient Database for Dietary Studies (FNDDS): HANDLS was coded using FNDDS 3.0, and WWEIA, NHANES 2007–2008 and 2009–2010 were coded using FNDDS 4.1 and 5.0, respectively (FNDDS documentation and databases, 2021).

The USDA food codes served as the link between the dietary data and the source of flavonoid values, the Database of Flavonoid Values for USDA Survey Food Codes 2007–2010 (or "Flavonoid Database" for short; Flavonoid database, 2021; Sebastian et al., 2016). Although the Flavonoid Database was designed primarily for use in studies analyzing WWEIA, NHANES data, it can also be used to estimate flavonoid intakes in other studies (Sebastian et al., 2017b), and in fact both NHANES and non-NHANES analyses using the Flavonoid Database have been published (Fanelli Kuczmarski et al., 2018; Goetz et al., 2016a, 2016b; Sebastian et al., 2017a). The source of values for the Flavonoid Database is USDA's Expanded Flavonoid Database for the Assessment of Dietary Intakes (USDA's Expanded Flavonoid Database for the Assessment of Dietary Intakes, Release 1.1 – December 2015 [database, codebook, and documentation], 2015). FDB-EXP contains values for 29 selected commonly occurring flavonoid compounds in 6 flavonoid classes (anthocyanidins, flavan-3-ols, flavanones, flavones, flavonols, and isoflavones) and excludes proanthocyanidins. Approximately 73 % of all values in FDB-EXP are assumed zero values; 24 %, calculated values; and 3%, analytic values.

The Flavonoid Database provides flavonoid values per 100 g for all foods/beverages in FNDDS 5.0, as well as for 20 items that had been

Table 1
Characteristics of participants, WWEIA, NHANES 2007-2010 subsample[a] and HANDLS Wave1[b] sample.

Characteristic	WWEIA, NHANES		HANDLS	
	N	Percent[c]	N	Percent[c]
All	2598	100	3418	100
Sex:				
Male	1231	47	1550	45
Female	1367	53	1868	55
Age:				
30−49 y	1487	57	1887	55
50−64 y	1111	43	1531	45
Poverty status:				
<125 % poverty	981	38	1421	42
>125 % poverty	1617	62	1997	58
Race[d]:				
African American	895	34	2029	59
White	1703	66	1389	41
Educational level:				
<High school diploma/GED	640	25	1143	33
High school diploma/GED	775	30	1145	33
Post-secondary education	1181	45	1064	31
Not available[e]	2	[f]	66	2
Employed last week/month[g]:				
Yes	1495	58	1911	56
No	1103	42	1444	42
Not available[e]	0	–	63	2
Weight status:				
Normal weight[h]	681	26	763	22
Overweight	783	30	751	22
Obese	1110	43	1129	33
Not available[e]	24	1	775	23
Cigarette smoking status:				
Currently smoking	1622	62	1159	34
Not currently smoking	975	38	1228	36
Not available[e]	1	[f]	1031	30
Health status:				
Excellent/very good	911	35	1128	33
Good	947	36	1376	40
Fair/poor	739	28	912	27
Not available[e]	1	[f]	2	[f]
Day of week of dietary intake:				
Weekday (Monday-Thursday)	993	38	1823	53
Weekend (Friday-Sunday)	1605	62	1595	47

[a] Unweighted counts and percentages for all. For WWEIA, NHANES participants, inclusion criteria were non-Hispanic origin, Black or White race, age 30–64 years, and household income <$75,000. Women who were pregnant or lactating were excluded.
[b] Data collection for HANDLS Wave 1 took place from August 2004 to March 2009.
[c] Within a characteristic, percentages may not add to 100 due to rounding.
[d] HANDLS terminology presented; comparable classifications in NHANES were "non-Hispanic Black" and "non-Hispanic White.".
[e] For most characteristics, the "not available" category is comprised mainly of "don't know" responses. For weight status and cigarette smoking status in HANDLS, the "not available" category primarily reflects refusal to participate in the second (examination) phase, when these data were to be collected, by a subject who had already completed a dietary recall during the first (household) phase. For weight status in NHANES, some respondents in the "not available" category refused to be measured and others could not be measured due to functional reasons.
[f] Percentage too small to report (<0.5 % of reports).
[g] The timeframe used to determine employment status differed between HANDLS (last month) and NHANES (last week).
[h] "Normal" includes a small number of individuals who were underweight - 82 (2% of the sample) in HANDLS and 60 (2%) in NHANES.

discontinued after FNDDS 4.1 (Sebastian et al., 2016). Due to discontinuation of 4 of the FNDDS 3.0 food codes used for HANDLS foods (3 pizzas and 1 cereal), flavonoid values for those items were imputed, based on the flavonoid profile of the food code most similar in content of flavonoid-containing ingredients.

For this study, dietary intakes of flavonoids were estimated based on food and beverage intake alone. Any contribution to flavonoid intake from dietary supplements was not assessed.

To determine top contributors to flavonoid intakes (total and class), each food or beverage reported was classified into one of 78 mutually exclusive groups.

2.3. Statistical analysis

SAS® 9.4 (2012, SAS Institute Inc., Cary, NC, USA) and SAS®/STAT 14.2 (2016, SAS Institute Inc., Cary, NC, USA) were used in data preparation and analysis. SAS-callable SUDAAN®, release 11.0 (2012, RTI International, Research Triangle Park, NC, USA), was used to account for the HANDLS and WWEIA, NHANES sample designs in statistical testing. Sample weights were applied to HANDLS data to permit calculation of estimates representative of the Baltimore City adult population with the targeted demographics. Likewise, sample weights applied to the WWEIA, NHANES data permitted calculation of nationally representative estimates for those same groups.

The intake distributions of many nutrients and food components are skewed (Dietary assessment primer, n.d.) and thus are unlikely to meet assumptions for parametric testing. This is the case for the intake distributions of total flavonoids and flavonoid classes in both WWEIA, NHANES and HANDLS, due in large part to the uneven occurrence of flavonoids in foods (i.e., a limited number of foods having high concentrations and many foods having little or none). The Markov chain Monte Carlo hierarchical predictive modeling transformation was used to normalize the flavonoid intake distributions (Albert, 2009). Following its application, Kolmogorov-Smirnov normality test statistics for all transformed flavonoid intake distributions were non-significant ($p > 0.05$), indicating the distributions did not depart from normality. The transformed flavonoid intake means closely mirrored their corresponding medians, with mean:median ratios ranging from 0.95 to 1.04.

Ordinary least squares linear regression performed on the transformed data produced adjusted estimates of total flavonoid and flavonoid class intake for men and women overall in HANDLS and the WWEIA, NHANES subsample and for age and poverty status groups within sex. Adjustment variables included in the analyses were energy, race, and, as appropriate, poverty status and/or age. Though differences in flavonoid intake between the two survey samples were tested by age category (30–49 years and 50–64 years), age was entered as a centered, continuous variable when applied in adjustment. However, information on poverty status for HANDLS participants was limited to the dichotomous classification <125 % of poverty or >125 % of poverty and was entered as such when used in adjustment. Flavonoid intake estimates of participants in HANDLS and WWEIA, NHANES by sex and by age and poverty status within sex were compared, and differences were identified based on results of t-tests on the transformed data.

To account for the large number of comparisons performed, results with $p < 0.01$ were considered statistically significant in all analyses.

3. Results

3.1. Major food group contributors of flavonoids by class

Table 2 describes the main food group contributors (defined as those providing ≥10 % of overall intake) to total flavonoids and six flavonoid classes. For each food group, the table lists examples of specific foods included in the group along with their content (mg/100 g) of the applicable flavonoid class. The percent contribution of each food group to total intake of the specified flavonoid class is presented by survey within sex.

Total flavonoids and flavan-3-ols each had only one major food/ beverage group contributor (tea), while other flavonoid classes had multiple main contributors. Columns 3 through 5 show examples of one or more specific foods within the food group. Where it is possible to do so, two contrasting foods from within a given food group are listed to

Table 2
Food/beverage groups contributing ≥10 % of intake[a] of total flavonoids and six flavonoid classes, WWEIA, NHANES 2007-2010 subsample[b] and HANDLS Wave 1,[c] men and women, 1 day.

Flavonoid class	Among foods/beverages reported,[d] food groups containing food codes with non-zero values for specified flavonoid class: Food group (number of codes with non-zero values)	Example(s) of codes in food group and value[e]: Code	Description	Value (mg/100g)	Men: WWEIA, NHANES	Men: HANDLS	Women: WWEIA, NHANES	Women: HANDLS
					% contribution to flavonoid class intake			
Total flavonoids	Tea (23)	92305090	Tea, made from powdered instant, presweetened with low calorie sweetener	59	81	79	82	84
		92302300	Tea, leaf, presweetened with low calorie sweetener	122				
Anthocyanidins	Blueberries (3)	63203110	Blueberries, cooked or canned, not specified as to sweetened or unsweetened; sweetened, not specified as to type of sweetener	76	25	3	26	20
		63203010	Blueberries, raw	163				
	Other vegetables[f] (36)	75210010	Cabbage, Chinese, cooked, fat not added in cooking	0.03	14	6	11	6
		75105000	Cabbage, red, raw	210				
	Wine (6)	93401020	Wine, table, white	0.06	11	21	10	23
		93402000	Wine, dessert (includes marsala, port, madeira)	109				
	Grapes (1)	63123000	Grapes, raw, not specified as to type	24	10	17	11	10
	Strawberries (7)	63223120	Strawberries, cooked or canned, unsweetened, water pack	18	7	12	7	4
		63223020	Strawberries, raw	27				
	Noncitrus juices other than apple (10)	64132500	Strawberry juice	0.02	4	10	5	10
		64105400	Cranberry juice, 100 %, not a blend	54				
Flavan-3-ols	Tea (23)	92302600	Tea, leaf, decaffeinated, presweetened with sugar	63	95	95	95	96
		92302000	Tea, leaf, unsweetened	118				
Flavanones	Orange juice (6)	61210010	Orange juice, freshly squeezed	14	60	70	60	62
		61210620	Orange juice, frozen (reconstituted with water)	29				
	Oranges (1)	61119010	Orange, raw	43	20	13	17	15
Flavones	Sweet peppers (13)	75226050	Peppers, red, cooked, fat not added	0.5	12	21	9	8
		75226010	Peppers, green, cooked, fat not added	5.3				
	Tea (23)	92301160	Tea, not specified as to type, decaffeinated, presweetened with sugar	0.04	9	12	13	15
		92302600	Tea, leaf, decaffeinated, presweetened with sugar	0.05				
	Parsley (2)	75221210	Parsley, cooked (assume fat not added in cooking)	184	15	<1	0	0
		75119000	Parsley, raw	217				
	Meat mixed dishes (167)	27214110	Meat loaf made with beef, with tomato-based sauce	0.01	4	9	6	10
		27420470	Sausage and peppers, no sauce (mixture)	1.10				
	Melons (2)	63149010	Watermelon, raw	0.46	3	4	7	10
		63109010	Cantaloupe (muskmelon), raw (includes melon, not further specified)	0.64				
Flavonols	Tea (23)	92305180	Tea, made from powdered instant, decaffeinated, unsweetened	1.4	37	34	44	45
		92302500	Tea, leaf, decaffeinated, unsweetened	4.6				
	Onions (20)	75415022	Onion rings, from frozen, batter-dipped, baked or fried	8	7	13	4	8
		75221100	Onions, dehydrated	195				
Isoflavones	Protein powders (4)	11832000	Meal replacement, protein type, milk- and soy-based, powdered, not reconstituted	83	39	23	30	23
		41430310	Protein diet powder with soy and casein	167				
	Processed soy products (21)	41812400	Vegetarian pot pie	3	6	38	15	19
		41810250	Bacon bits, meatless	118				
	Milk substitutes (5)	11321000	Milk, soy, ready-to-drink, not baby's, chocolate	7.6	17	10	16	31
		11320000	Milk, soy, ready-to-drink, not baby's	7.8				
	Soups (8)	41601040	Lima bean soup	0.01	5	11	1	9
		41601070	Soybean soup, miso broth	5				
	Doughnuts, sweet rolls, pastries (16)	53610170	Coffee cake, crumb or quick-bread type, with fruit	0.01	8	10	5	8
		53520120	Doughnut, chocolate, cake type	6				
	Asian mixed dishes (55)	27415100	Beef and vegetables (including carrots, broccoli, and/or dark-green leafy (no potatoes)), soy-based sauce (mixture)	0.03	1	1	10	2
		41812500	Tofu and vegetables (including carrots, broccoli, and/or dark-green leafy vegetables (no potatoes)), with soy-based sauce (mixture)	9				

[a] To permit extrapolation to the population of interest, sample weights from the respective surveys were applied to all estimates, and the sample designs were accounted for in the calculation of standard errors. Within flavonoid class, each listed food group contributed ≥10 % of total intake of the specified flavonoid class for at least one of the population subgroups.

[b] Inclusion criteria for WWEIA, NHANES participants included non-Hispanic origin, Black or White race, age 30–64 years, and household income <$75,000. Women who were pregnant or lactating were excluded.

[c] Data collection for HANDLS Wave 1 took place from August 2004 to March 2009.

[d] Only those codes that were used in coding HANDLS and NHANES dietary recalls were included in this analysis.

[e] Flavonoid values per 100 g are from the Database of Flavonoid Values for USDA Food Codes 2007–2010 (Flavonoid database, 2021).

[f] The group "other vegetables" includes all vegetables and vegetable combinations that were not classified into the other, more specific groups in this analysis – namely, tomatoes, carrots, other red/orange vegetables, lettuce and lettuce-based salads, dark-green vegetables (excluding lettuce), potatoes (three groups: baked/boiled; French fries and other fried; and mashed and mixtures), corn and other starchy vegetables, onions, sweet peppers, hot peppers, celery, and parsley.

illustrate the wide variation in flavonoid content among specific foods within that group.

3.2. Differences between surveys by sex

Results of the flavonoid intake comparisons between HANDLS and WWEIA, NHANES appear in Table 3. To avoid excessive repetition of survey acronyms, all findings are stated in terms of HANDLS relative to WWEIA, NHANES.

Among men overall, intake of total flavonoids and all flavonoid classes differed significantly between surveys ($p < 0.01$). Total flavonoids intake was considerably lower in HANDLS (197.53 mg/d) than in WWEIA, NHANES (303.53 mg/d). For nearly all flavonoid classes, men's intakes were lower in HANDLS. The sole exception was flavanones, with intakes higher in HANDLS.

Among women overall, total flavonoids intake did not differ between surveys, at 250.19 mg/d in HANDLS and 276.08 mg/d in WWEIA, NHANES. Women's intakes of anthocyanidins and flavones were lower in HANDLS, but no differences in total flavonoids or the other flavonoid classes were observed.

3.3. Differences between surveys by age within sex

Consistent with the findings for men overall, men in both the younger (30−49 years) and older (50−64 years) age groups in HANDLS exhibited lower intakes of total flavonoids and four of the six flavonoid classes – anthocyanidins, flavan-3-ols, flavones, and flavonols. However, in contrast to the finding for men overall, only the older group of men in HANDLS had a higher intake of flavanones. Isoflavone intake did not differ between surveys for men when analyzed by age group.

For both age groups of women, intake of anthocyanidins was lower in HANDLS. No differences in women's intakes of total flavonoids or the other flavonoid classes were found for either age group.

3.4. Differences between surveys by poverty status within sex

The pattern of flavonoid intake differences between surveys varied considerably when analyzed among men grouped by poverty status. In the lower poverty status group (<125 % poverty), men in HANDLS had significantly lower intakes of total flavonoids and all flavonoid classes except flavanones and isoflavones. Flavanone intake was higher among men in HANDLS in this poverty status group, but isoflavone intake did not differ. Fewer differences were found between surveys among men in the higher poverty status group (>125 % of poverty), with intakes lower in HANDLS for only two flavonoid classes, anthocyanidins and flavonols.

Among women stratified by income as a percentage of poverty, patterns of differences in flavonoid intake between surveys mirrored those among men for the most part. In the lower poverty status group (<125 % poverty), women in HANDLS had lower intakes of total flavonoids, anthocyanidins, flavan-3-ols, flavones, and flavonols, and a higher intake of flavanones. However, unlike men, HANDLS women in this poverty status group also had a lower intake of isoflavones. As among men, fewer differences between surveys were found among women in the higher poverty status group (>125 % poverty), where only anthocyanidin intake was lower in HANDLS.

4. Discussion

In this study, intakes of total flavonoids and six flavonoid classes were compared between two distinct populations using the same dietary data collection method and flavonoid composition database. Intake differences between surveys were observed in every subgroup analyzed. With few exceptions, intakes were lower in the population represented by HANDLS relative to those of comparable age, race, and income level in the U.S. population represented by WWEIA, NHANES. Some subgroups exhibited a larger number of differences between survey populations than others. This research expands on previously published work that found flavonoid intake differences by race (African American, White) between the two surveys (see table 6 in Fanelli Kuczmarski et al., 2018).

Interpretation of these differences is complicated by the fact that flavonoid composition varies widely even among foods in the same food group. The between-survey intake differences could potentially stem from differing amounts consumed from flavonoid-containing food/beverage groups, but they could also result from consuming similar amounts of foods from within a given group that differed in their concentration of flavonoids. A detailed investigation of this issue was beyond the scope of this analysis, and further research to clarify this point would be of interest.

There are a few noteworthy patterns among the findings of the present study. First, anthocyanidin intake was lower in HANDLS among both men and women overall and in all age and income subgroups. In addition, intakes of total flavonoids, flavan-3-ols, flavones, and flavonols were also lower in HANDLS among men overall, in both age groups of men, and in the lower poverty status group for both men and women. However, flavanone intakes were higher in HANDLS among men overall and in the older group and among both men and women in the lower poverty status group. Taken together, these findings suggest that, for the most part, individuals in the HANDLS population may experience the health benefits of flavonoids to a lesser degree than individuals in similar demographic groups of the U.S. population.

This analysis was stratified by sex, age, and income, characteristics that themselves predict both dietary intake and health disparities. Since this stratification did not eliminate the intake differences between HANDLS and WWEIA, NHANES, it follows that the factors that explain these between-population differences in flavonoid intake and, by extension, the benefits flavonoids confer, remain to be elucidated. What these factors are deserves further exploration. Inclusion of other variables in the analysis, such as educational level and food security, may be informative. Unfortunately, lack of correspondence between HANDLS and WWEIA, NHANES precludes comparison of some variables of interest, for instance, health knowledge, health literacy, and Supplemental Nutrition Assistance Program (SNAP, formerly known as "Food Stamp") participation.

The lower flavonoid intakes in HANDLS versus WWEIA, NHANES within the lower poverty status stratum may contribute to the prevalence of nutrition-related chronic diseases in HANDLS, which appears

Table 3
Flavonoid intakes (mg/d)[a,b] in WWEIA, NHANES 2007-2010 subsample[c] and HANDLS Wave 1[d], men and women age 30-64 years, by age and poverty status[e], 1 day.

Age or poverty status group and flavonoid class	Men			Women		
	WWEIA, NHANES	HANDLS	Significance	WWEIA, NHANES	HANDLS	Significance
	Mean (SE)			*Mean (SE)*		
All:						
Total flavonoids	304 (26)	198 (10)	****	276 (22)	250 (35)	
Anthocyanidins	9.8 (2.1)	5.8 (1.0)	****	14.0 (2.4)	8.1 (0.5)	****
Flavan-3-ols	258 (25)	157 (12)	****	228 (21)	209 (35)	
Flavanones	10.9 (1.4)	16.0 (2.0)	**	11.0 (1.2)	13.1 (1.5)	
Flavones	0.84 (0.08)	0.57 (0.07)	****	0.84 (0.06)	0.69 (0.04)	**
Flavonols	23.0 (1.2)	16.9 (0.5)	****	21.3 (1.0)	18.3 (1.0)	
Isoflavones	1.11 (0.23)	0.87 (0.20)	**	1.08 (0.26)	1.03 (0.26)	
30–49 y:						
Total flavonoids	293 (21)	221 (13)	***	251 (23)	238 (29)	
Anthocyanidins	8.2 (1.2)	6.6 (1.5)	****	9.3 (2.0)	6.5 (1.3)	****
Flavan-3-ols	247 (20)	177 (15)	****	214 (22)	203 (29)	
Flavanones	12.1 (1.7)	16.4 (1.7)		7.9 (0.8)	10.8 (1.7)	
Flavones	0.93 (0.12)	0.68 (0.10)	****	0.64 (0.05)	0.59 (0.06)	
Flavonols	23.8 (1.3)	19.1 (0.8)	****	18.0 (1.0)	16.3 (0.9)	
Isoflavones	0.89 (0.23)	1.18 (0.29)		1.21 (0.40)	0.62 (0.11)	
50–64 y:						
Total flavonoids	386 (59)	204 (18)	**	254 (29)	232 (22)	
Anthocyanidins	14.0 (4.1)	5.9 (0.8)	****	18.1 (3.5)	9.4 (1.9)	****
Flavan-3-ols	329 (57)	159 (20)	**	201 (27)	190 (21)	
Flavanones	11.8 (1.8)	18.8 (4.2)	****	12.7 (2.4)	13.7 (2.6)	
Flavones	0.95 (0.12)	0.63 (0.07)	****	0.91 (0.08)	0.64 (0.05)	
Flavonols	28.3 (2.5)	18.5 (1.2)	****	20.2 (1.5)	17.0 (1.0)	
Isoflavones	1.61 (0.59)	0.69 (0.25)		0.77 (0.21)	1.44 (0.51)	
<125 % poverty[e]**:**						
Total flavonoids	352 (48)	238 (55)	**	326 (39)	209 (9)	****
Anthocyanidins	9.3 (2.5)	5.4 (2.0)	****	11.0 (2.2)	6.5 (0.7)	****
Flavan-3-ols	304 (47)	200 (56)	****	275 (38)	164 (12)	****
Flavanones	12.3 (2.7)	12.4 (1.3)	***	11.9 (1.6)	18.3 (2.7)	**
Flavones	0.76 (0.12)	0.54 (0.03)	****	0.99 (0.12)	0.68 (0.10)	****
Flavonols	25.5 (1.8)	19.0 (1.6)	****	25.7 (1.8)	18.8 (0.8)	****
Isoflavones	0.63 (0.13)	0.82 (0.27)		1.35 (0.25)	1.01 (0.22)	**
>125 % poverty[e]**:**						
Total flavonoids	251 (27)	224 (34)		253 (21)	239 (24)	
Anthocyanidins	12.9 (4.4)	4.2 (0.8)	****	13.5 (2.3)	8.6 (0.5)	****
Flavan-3-ols	210 (26)	192 (35)		207 (20)	199 (24)	
Flavanones	8.8 (1.0)	8.9 (2.2)		10.6 (1.4)	12.7 (1.4)	
Flavones	0.65 (0.05)	0.47 (0.06)		0.81 (0.06)	0.65 (0.06)	
Flavonols	18.2 (1.1)	17.5 (0.6)	**	19.3 (1.0)	16.3 (0.9)	
Isoflavones	0.61 (0.24)	0.56 (0.18)		1.18 (0.30)	1.04 (0.25)	

** $p < 0.01$.
*** $p < 0.001$.
**** $p < 0.0001$.
[a] To permit extrapolation to the population of interest, sample weights from the respective surveys were applied to all estimates, and the sample designs were accounted for in the calculation of standard errors.
[b] Flavonoid intake estimates were adjusted for energy and race and, as appropriate, for income and/or age prior to comparisons. Although untransformed estimates are presented, significance results are based on transformed estimates.
[c] Inclusion criteria for WWEIA, NHANES participants included non-Hispanic origin, Black or White race, age 30–64 years, and household income <$75,000. Women who were pregnant or lactating were excluded.
[d] Data collection for HANDLS Wave 1 took place from August 2004 to March 2009.
[e] Poverty status groups are based on the ratio of self-reported household income to the U.S. Department of Health and Human Services 2004 poverty guidelines (2004 HHS Poverty Guidelines, 2004), expressed as a percentage.

high relative to the U.S. population as a whole. Furthermore, these markedly low intakes among HANDLS participants in this income stratum may also be germane to reported disparities within the HANDLS population. Mortality rates in HANDLS between study enrollment and the end of 2013 were significantly higher in the lower poverty status group (<125 % poverty) than in the higher poverty status group (>125 % poverty) among all race-by-sex groups except White men (Zonderman et al., 2016). The most prevalent causes of death were cardiovascular disease (30 %) and cancers (23 %) – diet-related diseases frequently found to be inversely associated with flavonoid intake (Cassidy et al., 2014, 2016; Wang et al., 2014; Woo and Kim, 2013).

Comparing results of the present study to estimates from other studies is problematic, due in part to their use of alternate flavonoid composition databases. Variation in the flavonoid profiles assigned to individual foods in different databases could contribute to the vastly different estimated flavonoid intakes between studies (for example, see table 5 in Sebastian et al., 2015, for flavonoid intake estimates from selected studies). Moreover, when the flavonoid composition databases used in those studies are proprietary, it is impossible to evaluate potential differences. Conversely, comparisons are facilitated when the same flavonoid composition database is used to estimate intakes in different study samples.

The following example illustrates how the use of alternate flavonoid databases can lead to different intake estimates and thus complicate flavonoid-related research. Using a database they developed, Chun et al. estimated total flavonoid intakes of adults age ≥ 19 years in NHANES 1999–2002 to be 192.7 mg/d for men and 186.9 mg/d for women (Chun et al., 2007). Those estimates appear lower than this study's estimates of 303.53 mg/d for men and 276.08 mg/d for women in the WWEIA, NHANES subsample, which were calculated using the Flavonoid Database. The direction of the difference between studies is surprising, because Chun et al. (2007) found older age and higher income to be associated with higher flavonoid intake, and their analysis included older adults (≥65 y) and those with higher (>$75,000/y) incomes, population groups that were excluded from the present study. However, because of the proprietary nature of the database used by Chun et al. (2007), it is impossible to evaluate the role it may have played in the intake differences between the studies. Similarly, seminal works that form the basis for attributing specific health benefits to flavonoids reported intakes that were derived using flavonoid composition databases that are not publicly available (Cassidy et al., 2011; Knekt et al., 2002; McCullough et al., 2012; Mink et al., 2007; Nöthlings et al., 2007).

One study whose findings can be appropriately compared with those reported in this study was a secondary analysis of 2003–2007 data from the REasons for Geographic And Racial Differences in Stroke (REGARDS) study, a large sample of Black and White adults in a geographic region of the U.S. sometimes called the "Stroke Belt" (Goetz et al., 2016b). That study applied an earlier but very similar version of the Flavonoid Database (Sebastian et al., 2014) and reported total flavonoid intakes of 227 mg/day for men and 234 mg/day for women, seemingly similar to those found for the HANDLS population in the present study (197.53 mg/d for men and 250.19 mg/d for women).

This study has a number of strengths. It is the first comparison by sex, age, and poverty status of flavonoid intakes between the at-risk population of HANDLS and a subsample of adults with similarly defined demographic characteristics from the nationally representative WWEIA, NHANES. The two surveys employed congruent methodologies, including the application of the same flavonoid composition database to assess intakes. The transformation of flavonoid intake estimates to allow parametric testing increased validity of the statistical results and facilitated their subsequent interpretation. Strengths of the Flavonoid Database itself include its comprehensiveness in regard to the U.S. food supply (7273 food codes with corresponding profiles for 29 individual flavonoids in six classes) and its accounting for flavonoid-containing ingredients in multi-ingredient foods (Sebastian et al., 2016). In addition, unlike many databases used in flavonoid research, it is publicly available.

This study has a few limitations. First, though the two survey samples were harmonized with respect to some characteristics related to dietary intake (age, race, and income), others could not be accommodated. HANDLS encompassed an exclusively urban population, whereas WWEIA, NHANES included both metropolitan and non-metropolitan populations. Second, flavonoid intake estimates in both surveys do not include supplements. Whether prevalence of consuming flavonoid-containing supplements differed between HANDLS and WWEIA, NHANES was not investigated since data on supplement use were not collected during Wave 1 of the HANDLS study. Third, the timeframe for data collection in HANDLS and WWEIA, NHANES was not identical, with HANDLS commencing earlier and spanning more years (2003–2009) than the WWEIA, NHANES subsample (2007–2010). However, there is no existing evidence that flavonoid intake varied substantially during this period. Finally, foods in the Flavonoid Database are reflective of U.S. dietary patterns, a feature that does not affect the current analysis but could be relevant to its application in international research.

5. Conclusions

Flavonoid intakes among adults in HANDLS and WWEIA, NHANES were estimated using the publicly available Database of Flavonoid Values for USDA Food Codes 2007–2010, and intakes of one or more flavonoid classes differed between surveys among all the population subgroups studied. Most of the differences were in the direction of lower intakes in HANDLS. In view of the well-documented health benefits attributable to flavonoid intake, it is possible that these intake differences may contribute to understanding some of the apparent health disparities between the HANDLS population and similar demographic groups in the U.S. population.

The Flavonoid Database is freely available and may be applied in any study through the use of USDA's food codes, thus expanding opportunities to broaden the knowledge base concerning relationships between flavonoids and human health.

Author contributions

Rhonda S. Sebastian: Conceptualization, Methodology, Writing - original draft, Writing - review and editing. **Marie Fanelli Kuczmarski:** Conceptualization, Writing - review and editing. **Cecilia Wilkinson Enns:** Writing - original draft preparation, Writing - review and editing, Visualization. **Joseph D. Goldman:** Formal analysis. **Theophile Murayi:** Formal analysis. **Lois Steinfeldt:** Conceptualization. **Alanna J. Moshfegh:** Supervision. **Alan B. Zonderman:** Funding acquisition. **Michele K. Evans:** Funding acquisition.

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Declaration of Competing Interest

The authors report no declarations of interest.

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