Published in final edited form as:

J Food Compost Anal. 2011 December 1; 24(8): 1103–1109. doi:10.1016/j.jfca.2011.04.007.

Flavonoid intakes in the Baltimore Longitudinal Study of Aging

Janice E. Maras, MS^a, Sameera A. Talegawkar, PhD^b, Ning Qiao, MS^c, Barbara Lyle, PhD^d, Luigi Ferrucci, MD^e, and Katherine L. Tucker, PhD^{a,*},¹

^aDepartment of Health Sciences, Northeastern University, Boston, MA, USA.

^bCenter for Human Nutrition, Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA.

^cJean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, MA, USA.

^dKraft Foods, Northfield, IL, USA.

^eThe Baltimore Longitudinal Study of Aging, Baltimore, MD, USA.

Abstract

Major sources of flavonoids were identified, and mean intakes over several decades were reported, among 1638 participants (mean age 62.1 $\pm$ 16.0 y), of the Baltimore Longitudinal Study of Aging (BLSA). Dietary data were collected using 7-day diet records during three time periods (1980s, 1990s and 2000–present), and the USDA flavonoid, proanthocyanidin and isoflavone databases were used to estimate dietary flavonoid intakes. Dietary intake data were divided according to decade of visit. Foods were matched with appropriate foods in the USDA databases. Mixed dishes were disaggregated to individual foods and a similar procedure was followed. Total flavonoids and five sub-classes of flavonoids, including flavonols, flavones, flavanones, flavan-3-ols and anthocyanidins, were computed by summing appropriate compounds. The median intakes of flavonoids and the contributions of various foods to intakes were calculated by decade. Age and sex adjusted mean (SE) daily intakes of flavonoids increased from 250 (7.4) in the 1980s to 280 (9.9) mg in the 2000s. Top contributors of flavonoids were tea, apple/pear (and juices), citrus fruits (and juices), peaches, plums, grapes, nectarines (and juices) and chocolate. The data show an increase in the consumption of flavonoids over the three decades, which appears to be related to intake of fruit.

Keywords

Flavonoids; Antioxidants; Aging; Diet records; Database; Food data management; Food composition

¹**Funding sources:** This research was supported in part by a grant from Kraft Foods, Inc., Northfield, IL US Department of Agriculture, Agricultural Research Service contract 58-1950-7-707; and the National Institutes of Health National Institute of Aging Intramural Research Program.

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*Corresponding author: Department of Health Sciences, 316 Robinson Hall, Northeastern University, 360 Huntington Ave., Boston, MA 02115, Tel: 617-373-3666; fax: 617-373-2968, k.l.tucker@neu.edu (K.L. Tucker).

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Conflicts of interest: B. Lyle is a Program Manager for Kraft Foods, Inc. No other authors report a conflict of interest.

1 Introduction

Several observational studies have demonstrated protective effects of higher fruit and vegetable intake in the prevention of chronic disease (Dauchet et al., 2006; Gandini et al., 2000; He et al., 2006). Flavonoids, the most abundant polyphenol group in the diet, are found in fruit and vegetables and are thought to contribute to the health benefits conferred by the intake of plant foods (Beecher, 2003; Lampe, 1999; Timberlake & Henry, 1986). The best-described property of a majority of the flavonoids is their capacity to act as antioxidants, counteracting the impact of excessive generation of reactive oxygen species (Pietta, 2000; Rice-Evans & Miller, 1996; Rice-Evans et al., 1996). In addition to functioning as antioxidants, *in vitro* studies have also documented anti-inflammatory properties of flavonoids (Jang et al., 2008; Kim et al., 2004; O'Leary et al., 2004; Rein et al., 2006).

Given the important role that flavonoid intake may play in health and disease, it is important to accurately estimate intake levels in population-based studies. However, the flavonoid content of foods is not currently available in most nutrient databases, particularly for mixed dishes. Thus, quantities of flavonoids in the diet are difficult to estimate correctly, which can compromise the ability to quantify associations with disease risk. In 2007, the U.S. Departments of Agriculture and Health and Human Services released the *USDA Database for the Flavonoid Content of Selected Foods, Release 2.1* (US Department of Agriculture, 2007). The USDA 2007 release updated flavonoid values with recently published data and new analyses of foods in the USDA's National Food and Nutrient Analysis Program (NFNAP)². The database contains values for 385 food items for five sub-classes of flavonoids, including flavonols, flavones, flavanones, flavan-3-ols and anthocyanidins. The USDA released a Database for the Proanthocyanidin Content of Selected Foods - 2004 which complements the first database (US Department of Agriculture, 2004). The proanthocyanidins database contains 205 foods, which are polymers of flavon-ol-3, and include subclasses: monomers, dimers, trimers, 4–6 mers (tetramers, pentamers and hexamers), 7–10 mers (heptamers, octamers, nonamers and decamers) and polymers (DP>10). Another subclass of flavonoids is isoflavones, known for important estrogen-like components to reduce chronic disease. Isoflavones are found primarily in soybeans, soybean products, and to a lesser extent, in other legumes. In 2008, the USDA released an isoflavone database (US Department of Agriculture, 2008). The database contains three individual isoflavone compounds—genistein, daidzein and glycitein—in nearly 550 foods.

Because nutrient retention information for flavonoids and proanthocyanidins is lacking, their content in many cooked foods may vary from that presented in current databases. The objectives of the present study were to extend existing data to similar foods by imputation, and to mixed dishes by calculation, to estimate flavonoid intakes of men and women participating in the Baltimore Longitudinal Study on Aging (BLSA), using dietary intake data collected using 7day (d)-diet records. These data were then used to identify major dietary sources of flavonoids in the cohort, and to examine the intakes over several decades.

2 Materials and methods

The BLSA, which was initiated in 1958, was designed to observe normal physiologic and cognitive aspects of aging and disease over time (Shock et al., 1984). Initial study participants were non-Hispanic white, male, community-dwelling volunteers, aged 22–88 y and living in the Baltimore area. In 1978 the study protocol expanded to include women and

²National Food and Nutrient Analysis Program (NFNAP); Baltimore Longitudinal Study on Aging (BLSA); non-fat cocoa solid (NFCS); food frequency questionnaire (FFQ)

minorities. Enrollment in the BLSA is open and participants return approximately every 24 months for repeated measurements of height, weight, body composition, diet, and a variety of other physiologic, psychological, and behavioral measures. Given its open design, however, the present analyses are cross-sectional in nature. Institutional Review Boards of the Johns Hopkins Bayview Medical Research Center and the Gerontology Center approved the BLSA protocol, and all subjects gave written informed consent for their participation. The current study includes data from all individuals who participated in the dietary assessment portion of the study since 1980 (n=1638). The BLSA study in the early/mid 2000s stopped collecting dietary data using food records and used food frequency questionnaires. Given the disparate nature of these two assessment methods we were unable to incorporate data collected using the FFQ in these analyses. We also excluded dietary data from the 1960s and 1970s due to limitations in collecting information on non-caloric beverages, such as tea and coffee.

Dietary data were collected using 7-d diet records. Earlier reports of dietary intake in the BLSA population and a full description of the dietary data collection methods are published elsewhere (Hallfrisch et al., 1990; McGandy et al., 1966). In brief, BLSA participants were trained to record their food intake by dietitians during their examination visit, food records were completed at home by the participant and sent back to the study center and ambiguous or incomplete records were clarified by telephone interview. Before 1993, subjects were given food models and a booklet for to help them assess portion size. Since 1993, subjects have been given a portable scale to weight food portions.

Throughout the study, dietary data were coded and analyzed for nutrient content at different locations. Dietary data collected from 1984 to 1991 were coded into a nutrient database maintained by the BLSA. Since 1993, dietary data have been entered into the Minnesota Nutrient Data System (NDS) (Program 2.9, Food Database version 11A, Nutrient Database version 26, University of Minnesota Nutrition Coordinating Center) at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University. Dietary data from previous years were re-coded into NDS, and nutrient intakes from earlier years were back-adjusted to correct for changes in the food supply, specifically changes in the composition of pork, beef, breakfast cereals, and other fortified foods, using data from the USDA for appropriate time intervals (US Department of Agriculture, 1993; Watt, 1963).

2.1 Sources of flavonoid data

Dietary flavonoid intake was estimated from 6 major subclasses and their 29 component flavonoids: flavonols (quercetin, kaempferol, and myricetin), flavones (apigenin and luteolin), flavanones (eriodictyol, hesperetin and naringenin), flavan3ols (epicatechin, epithreagalate, epigallocatechin, epigallocatechin, catechin, galocatechin, catthreagalate, theaflavin, theathreedigalate, theathreepgalate, theathreegalate and thearubigins), anthocyanidin (cyanidin, delphinidin, malvidin, pelargonidin, peonidin, and petunidin) and isoflavanoes (daidzein, genistein, and glycitein) (US Department of Agriculture, 2004, 2007, 2008).

2.2 Estimation of flavonoid content of foods

For this study, all foods containing flavonoids were identified by creating 10 flavonoid food groups, which were then merged to USDA food groups and separated by decade to create three flavonoid reference databases. Each of these foods was then assigned a USDA code from the USDA flavonoid database. For foods that were not an exact match to USDA foods, similar foods were selected for the best possible match from the USDA flavonoid databases, and interpolated values were calculated. In most cases, an exact match for the foods consumed by the study participants was available in the flavonoid database. However, many

of the foods in the BLSA database include recipes or mixed dishes with more than one ingredient, such as fruit pies, cakes and casseroles. To quantify the flavonoid content and the percent contribution to flavonoid intake from these mixed dishes and recipes, the combined flavonoids database (flavonoid, proanthocyanidin and isoflavone databases) was merged with the Continuing Survey of Food Intakes by Individuals 1994–96 recipe database to disaggregate whole foods into ingredients, and to obtain gram weights of individual ingredients. The flavonoid components of the ingredients were first calculated on the basis of 100g of the total recipe and then remerged with the combined flavonoids database to obtain flavonoid servings. For example, in a blueberry muffin with 11 g of blueberries, the blueberry gram weight per 100 g of total cooked muffin was merged with the combined flavonoid database to obtain 13 mg total flavonoids. The amount per serving consumed was then calculated.

Because dietary intake data were collected using open-ended diet records, one challenge faced was estimation of flavonoid content of foods that were not present in the USDA flavonoid database. For example, when there were no data for dried fruit, we needed to assume an increase in concentration by weight from fresh as a substitution. However, data available in the USDA flavonoid database for some dried foods had lower than expected flavonoid values, such as raisins relative to grapes. Personal communication with the USDA laboratory in 2008 suggested that this could be because of the treatment of grapes in conversion to raisins, including heat treatment, enzymatic oxidation and handling of samples (freeze-drying). Also, the USDA laboratory were unable to specify exactly how the raisins in the 2007 release of the USDA flavonoid database were prepared, due to different source samplings having various heat treatment, enzymatic oxidation and sample handling (freeze drying). Different methods for preparing raisins, sun drying and dipping (for example, golden raisins are treated with SO₂ which prevents oxidation), may result in different retention of flavonoids (Vinson et al., 2005). The 2003 release of the USDA flavonoid database identified only one source for raisins, with a value only for catechins. The 2007 release had more data sources for raisins, but with lower catechin values. There is evidence that catechins and their polymers, proanthocyanidins, are heavily degraded during raisin formation (Karadeniz et al., 2000). Flavonols are affected to a lesser degree. These same effects may be true for plums and prunes as well (Del Caro et al., 2004). Therefore, for dried fruit only, we took the fresh weight and assumed 25% retention, based on the recommendation of a food antioxidant expert (Dr. Jeffrey Blumberg, personal communication-2008).

BLSA diet data included a number of foods that were cooked and processed. However, several of these foods did not have a corresponding value in the USDA flavonoid databases. Several studies have been published examining the impact of cooking and processing on flavonoids for various foods. However, these data are not comprehensive, and those studies that document these changes during cooking vary in the detection methods for flavonoid assessment, number of samples quantified, as well as processing and cooking techniques employed. Given these discrepancies, we did not feel confident in using the values from individual studies. We therefore used the USDA retention data (US Department of Agriculture, Nutrient Data Laboratory, 2007) to account for changes in flavonoid values due to processing and cooking. For example, for vegetables such as watercress and swiss chard, that did not have cooked values, a 95% retention factor was applied to the raw value, based on USDA retention data..

For chocolate containing foods not present in the USDA flavonoid database, we based our calculations on the amount of theobromine present in 100g of the food. Theobromine values were obtained from the original NDS nutrient value output files for the food records. We calculated the non-fat cocoa solid (NFCS) content by assuming that NFCS has 3%

theobromine content (Cooper et al., 2008). For example: chocolate milkshake contains 23 mg theobromine per 100g and therefore would contain 0.7g NFCS. NFCS content was then multiplied by the original flavan-3-ols and re-standardized per 100 g. Herbal teas are not present in the USDA database nor could their values be substituted with green, black or Oolong tea, which contain *Camellia sinensis* leaves fermented to different degrees, and contain considerably more flavonoids than most herbal teas. Herbal teas, if consumed, were therefore assigned a value of zero.

Also, similar to the procedure used by Mink *et al.* (Mink et al., 2007), if a food was included in both the flavonoid and proanthocyanidin databases, and if two monomer values were reported, one in each database, we used the average of both values.

2.3 Statistical analyses

All statistical analyses were performed using the SAS for Windows, version 9.1 (SAS Institute, Cary, NC). Prior to analyses, we excluded subjects who had implausible energy intake (<600 or >4000 kcal/d for women; <800 and >4200 kcal/d for men). All analyses were stratified by decade. Descriptive analyses to assess characteristics of study participants across decades were performed using PROC GLM for continuous variables and chi-square tests for categorical variables. We also assessed the statistical significance (defined as a two-tailed *P* value < 0.05) of differences in reported mean intakes, adjusted for age and sex across decades, across categories of total and sub-groups of flavonoids and isoflavones. Medians (25th and 75th percentiles) for all major flavonoid sub-group intakes were also calculated and food contributors were ranked based on percent contribution to total intake.

3 Results

Mean body mass index, age, waist circumference, and energy intakes as well as percentage of participants taking a multivitamin/mineral supplement and current smokers were significantly different across the decades examined (Table 1). Except for the percentage of current smokers, which was lower in latter decades, other variables tended to increase over time. Total flavonoid intakes increased from the 1980s to the 2000s, but were similar for the last two decades examined.

Age- and sex-adjusted flavonoid intakes for total flavonoids and isoflavones were significantly different across the decades examined, and were higher in the 1990s and 2000s than the 1980s (Table 2). There were significant differences in age- and sex-adjusted intakes across decades for flavonols, flavanones, anthocyanidins, and isoflavones. In general, there was an increase in intake over time, except for flavanones, where intakes appeared to increase from the 1980s to the 1990s, but decreased in the 2000s.

The top contributor to total flavonoid intakes in all three decades examined was brewed tea (hot and cold) (Table 3). Other leading contributors included fruit (non-citrus and citrus) and their juices. The major contributors to flavonol intakes for all three decades were similar and included brewed tea (hot and cold), apple and pear and their juices, and onions. Primary contributors to flavones differed across the decades. In the 1980s citrus fruit and juice, dark and leafy green vegetables, and other vegetables ranked highest. While in the 1990s, dried parsley, citrus fruit and juice and other vegetables were the top sources. In the 2000s, red wine emerged as a leading contributor to flavone intakes. Flavanone sources were similar for the 1980s and 1990s and included citrus fruit and juice, orange vegetables and tomatoes. Citrus fruit and juice, red wine and other fruit (including juice and fruit drinks with juice) were prominent food sources in the 2000s. Brewed teas (hot and cold) and apple and pear (including their juices) were the top two sources of flavan-3-ols. Other leading food sources included chocolate (bar and candy) in the 1980s, cocoa powder in the 1990s and red wine in

the 2000s. Fruit such as berries and cherries, peaches, plums, grapes, nectarines (and their juices and nectarines) were leading sources of anthocyanidins. Legumes were the top contributor of isoflavones.

4 Discussion

In the present study, intakes of flavonoids (and their sub-groups) as well as their food sources were estimated in participants of the Baltimore Longitudinal Study of Aging, using 7-d diet records and USDA databases. Median total flavonoid intakes were 199 mg/d in the 1980s, 224 mg/d in the 1990s, and 221 mg/d in the 2000s. Tea, apple/pear (including juices), citrus fruits (and juices), peaches, plums, grapes, nectarines (and their juices), as well as chocolate, were top contributors to flavonoid intakes in this cohort.

Using 24-hour dietary recall data from the NHANES, Chun et al. (Chun et al., 2007) expanded the USDA flavonoid database to estimate flavonoid intakes and their food sources in the U.S population. Mean total flavonoid intakes were 190 mg/d across all the age groups examined and, among adults aged 51–70 and 70+ y, intakes were 215 and 150 mg/d, respectively. Mean sub-group flavonoid intakes for flavonols, flavones, flavanones, flavan-3-ols, anthocyanidins, and isoflavones for 51–70 y old participants were 14.2, 1.4, 15.5, 179, 4.2, and 1.2 respectively; while for the 70 + y participants, they were 10.8, 1.5, 15.0, 119, 2.6, and 0.9 respectively. While sub-group intakes were comparable, intakes of flavan-3-ols were significantly lower (108 to 119 mg/d) in the BLSA as compared to the general U.S. population. A probable reason for this is that, while assigning flavan-3-ol values to teas consumed in the BLSA 1980s and 1990s cohort, no USDA flavonoid values were available to assign to green teas, which may have led to an underestimation of this sub-group.

Top sources of flavonoids in the American diet using the NHANES data were similar to those reported here for the BLSA, including tea, citrus fruit juices and fruit, and wine. Using 24-h diet recall data and flavonoid values from the USDA, flavonoid intakes were calculated for 10,851 subjects aged 19 years and older, in the Australian National Nutrition Survey in 1995. Major food sources of flavonoids included black and green teas as well as onions for flavonols, and black and green teas for flavan-3-ols, with wine, apples, and pears also contributing to these intakes. Top contributors for flavanones included citrus fruits, while parsley, celery, and spinach were the major flavone sources. Wine was a major source of anthocyanidins, followed by cherries and blueberry. Though, the individual contribution of the foods varied, major contributors of flavonoids in the Australian cohort were also, in general, similar to those reported here (Somerset & Johannot, 2008).

Several observational studies have used dietary data from food frequency questionnaires (FFQ) to estimate daily intakes of flavonoids. Flavonoid and lignin intakes of 1500 women living in the Long Island area of New York were estimated with a modified Block FFQ and USDA databases, as well as other published studies. In that cohort of women (mean age 57y, age range: 20–95y), the mean total flavonoid intake was 224 mg/d, slightly lower than reported in the BLSA study (250–280 mg/d). Similar to the BLSA, the leading contributor to intakes in these New York women were the flavan-3-ols (Fink et al., 2006). In the Polyp Prevention Trial, both total and sub-group flavonoid intakes were estimated in 1,905 participants (mean age: 61 y; 64% male) at baseline using a modified Block-NCI FFQ. Overall median total flavonoid intakes were 76.2 mg/1000 kcal (compared to a mean intake value of 140 mg/1000kcal across the three decades in the present study), with tea, citrus fruit juices, other fruit (including grapes, plums, pineapples), and oranges emerging as the top contributors to these phytonutrients (Bobe et al., 2008). Beking and Viera (Beking & Vieira, 2011) estimated total (anthocyanidins, flavonols, flavanols, flavanones, and flavones)

flavonoid intakes in the UK were estimated at 182 mg/day/person, while those for Ireland were 177 mg/day/person, using food consumption values from Food and Agricultural Organization Food Balance Sheets, and flavonoid data from the USDA, supplemented with published studies. For both countries, anthocyanidins and flavanols accounted for about 65% of total consumption (Beking & Vieira). In general, these results generally show lower total intakes than those seen in the present study, which may be due to the more complete database used here. Major sources across studies and countries are generally consistent.

The past decade has seen an increase in the number of studies examining the role of polyphenols such as flavonoids in chronic disease prevention. One reason for this may be the disappointing results from large intervention studies, such as those involving carotenoids and chronic disease end-points including cancer and heart disease. Initially thought to be the reason for the protective associations seen by observational studies with increased fruit and vegetable intakes, carefully planned intervention studies with mega-dose beta-carotene supplementation showed either no protection or an unexpected increase in the number of events that they were supposed to prevent. Investigators have attributed these unexpected findings to various causes, including incorrect dosage (Christen et al., 2000; Vainio & Rautalahti, 1998), differential associations among smokers and non-smokers (Albanes et al., 1996; Tornwall et al., 2004), and baseline antioxidant status of the study population (Blot et al., 1993). An alternative hypothesis is the likelihood that other phytonutrients such as flavonoids that are present in fruit and vegetables, contribute to the protective effects erroneously attributed only to carotenoids or tocopherols (Hercberg, 2005).

FFQ are the most commonly used dietary assessment instruments in epidemiological studies. However, computation of dietary and nutrient intake from FFQ depends on the number and type of foods on the food list. Therefore, depending on the match of the food list to the population being studied, estimates from a FFQ can underestimate specific sub-group as well as total flavonoid intakes. A critical shortcoming of the use of a single 24-hour recall in nutrition research is that high within-person variability may lead to misleading estimates of individual estimates. A key strength of the present study is that dietary intakes were assessed using 7-d diet records, which provide detailed data on specific foods over a sufficiently long period of time to avoid many of the limitations inherent in the 24-hour recall, including recall limitations and day-to-day variability.

Another unique strength of this study is the assessment of intakes over several decades. In the BLSA cohort, median total flavonoid intake increased between the 1980s and the 1990s, but was comparable between the 1990s and the 2000s. This increase was due to increases in intakes of flavonols, flavanones, anthocyanidins, and isoflavones across the decades. In general the top contributor to total and sub-group intakes remained the same across decades, the exception being dried parsley in the 1990s versus citrus fruit and juices for flavone intakes. Dried parsley is a rich source of flavones with an estimated 13.5 g per 100g. Although high amounts are rarely consumed, its frequency of consumption and inclusion in recipes led to its rank as a top contributor to flavone intakes.

In general, tea, fruit (including juices), and vegetables were the dominant sources of flavonoids in this cohort. Red wine was a significant contributor for flavonols, flavan-3-ols, flavanones, and anthocyanidins; while white wine was a significant contributor for flavones especially for the 2000s. This may either reflect a change in dietary choices due to a shift in the proportion of women (from 43% in the 1980s to 50% in the 2000s) in the cohort over time, due to an increased awareness of the health benefits of wine consumption, or both (Opie & Lecour, 2007; Zhang et al., 2008). A major contributor to flavan-3-ol intakes in the BLSA cohort was chocolate (both candy and bar form) and cocoa powder. Although this food group did not emerge as a noteworthy contributor to flavonoid intakes in the general

US population (Chun et al., 2007); it was noted as an important contributor in the Iowa Women's Health Study (Mink et al., 2007).

Estimation of flavonoid intakes in this, as in all studies, was limited by the data available for foods (both type and processing method) in the USDA food composition database. Hence, all mixed dishes were disaggregated to individual foods (please see methods for detailed procedure) and USDA retention factors were used for processed foods not present in food composition database.

Currently there are no recommended or available single biomarkers for dietary flavonoid intakes (Linseisen & Rohrmann, 2008). Reasons for this include the wide number of flavonoids in foods, lack of information on the half-life kinetics of flavonoid metabolites in serum, and the lack of sensitivity of flavonoid metabolites in serum or urine as measures of long term dietary exposure (Nielsen et al., 2002). Given these difficulties, estimating long term dietary exposure using dietary assessment methods may currently be the only viable approach to studying flavonoids and their health effects in epidemiological studies.

While more research is clearly needed to better understand the benefits of flavonoids in promoting health and preventing disease and the biological mechanisms involved, the development of research tools, including databases to accurately assess flavonoid intake, is a critical step in completing such research. The creation of a flavonoid databases such as this will increase the ability to precisely measure flavonoid intakes and quantify risk of disease in a research setting.

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Table 1

Sample characteristics of 1638 men and women participating in the Baltimore Longitudinal Study of Aging by decade

Sample characteristics ^{ab}	Decade			P- value for differences across decades
	1980s (n=663)	1990s (n=609)	2000s (n=366)	
Men (%)	57	51	50	0.004
Flavonoids (mg/d)	251 ± 197	281 ± 204	281 ± 214	0.005
Age (y)	62.5 ± 16.5	63.2 ± 15.4	68.9 ± 14.7	<0.001
BMI (kg/m ²)	24.8 ± 3.4	25.7 ± 4.0	26.5 ± 4.0	<0.001
Waist circumference (cm)	85.2 ± 11.9	87.3 ± 12.7	91.3 ± 12.4	<0.001
Average Total Energy (kcal/d)	1905 ± 469	1947 ± 532	1824 ± 469	<0.001
Vitamin Users (%)	21	46	53	<0.001
Current smokers (%)	8	6	3	0.008
Education (%)				0.97
No High School	9	7	7	
High School or vocational degree	11	11	11	
Some college	12	10	9	
College graduate	26	28	31	
Graduate degree	30	34	33	

^a Mean ± SD or %

^b GLM used for continuous and chi-squared test used for categorical data

Table 2

Adjusted mean flavonoid intake (mg/day) and Standard Error (SE) among 1638 men and women participating in the Baltimore Longitudinal Study of Aging by decade ^{a, b, c}

	Decade			<i>P</i> - value for differences across decades
	1980s (n=663)	1990s (n=609)	2000s (n=366)	
Total flavonoids and isoflavones	250 (7.43)	280 (7.02)	280 (9.93)	0.005
Flavonols	12.4 (0.32)	13.5 (0.30)	15.5 (0.43)	<0.001
Flavones	1.38 (0.11)	1.67 (0.19)	1.52 (0.15)	0.192
Flavanones	25.3 (0.90)	27.2 (0.85)	23.2 (1.20)	0.021
Flavan-3-ols	115 (5.71)	119 (5.39)	108 (7.62)	0.510
Anthocyanidins	14.4 (0.93)	17.9 (0.88)	27.0 (1.24)	<0.001
Isoflavones	1.49 (0.58)	4.10 (0.61)	6.4 (0.80)	<0.001

^aLeast Squares Mean (SE)

^bAdjusted for age and sex

^cflavonols (quercetin, kaempferol, and myricetin), flavones (apigenin and luteolin), flavanones (eriodictyol, hesperetin and naringenin), flavan3ols (epicatechin, epithreagalate, epigallocatechin, epigallocatechin, catechin, gallocatechin, catthreagalate, theaflavin, theathreedigalate, theathreepgalate, theathreagalate and thearubigins), anthocyanidin (cyanidin, delphinidin, malvidin, pelargonidin, peonidin, and petunidin) and isoflavones (daidzein, genistein, and glycitein)

Distribution of flavonoid intake (mg/day) and major contributors (%) to flavonoid intakes in among 1638 men and women participating in the Baltimore Longitudinal Study of Aging by decade

Table 3

	Decade					
	1980s (n=663)	Rank	1990s (n=609)	Rank	2000s (n=366)	Rank
Total flavonoids and isoflavones						
Brewed Tea (hot and cold)	199 ^a (116, 329)	1	224 ^a (140, 371)	1	221 ^a (124, 382)	1
Apple & pear (and juices)	45.0	2	40.2	2	35.8	5
Citrus (and juices)	13.6	3	12.1	3	7.3	4
Peaches, Plums, Grapes, Nectarines (and juices), Nectars	10.2	4	9.7	5	9.1	3
Berries and cherries (and juices)	8.4	5	8.7	4	12.2	2
	8.3		9.6		12.5	
Flavonols	10.7 ^a (7.0, 15.9)		11.6 ^a (7.4, 11.7)		13.3 ^a (8.8, 19.4)	
Brewed Tea (hot and cold)	32.0	1	29.3	1	25.6	1
Apple & pear (and juices)	13.4	2	12.0	2	6.1	2
Onion	13.0	3	13.0	3	13.7	3
Dark & leafy green	11.2	4	11.5	4	15.3	4
Other Vegetables	7.8	5	7.9	5	9.7	5
Flavones	22.8 ^a (9.9, 35.1)		21.9 ^a (8.4, 39.3)		13.6 ^a (3.3, 30.5)	
Citrus (and juices)	24.2	1	21.9	2	24.4	1
Dark & leafy green	20.2	2	14.1	4	12.6	4
Other vegetables	18.7	3	15.1	3	17.5	2
Parsley, dried	18.6	4	29.0	1	-	-
Melons	7.9	5	5.9	5	9.3	5
Red Wine	-	-	-	-	13.8	3
Flavanones	0.7 ^a (0.3, 1.3)		0.9 ^a (0.4, 1.7)		1.1 ^a (0.4, 1.9)	
Citrus (and juices)	99.3	1	99.0	1	96.1	1
Orange vegetables and tomatoes	0.6	2	0.5	2	1.0	4
Red Wine	-	-	-	-	1.5	2
Other fruit (and juices, and fruit drinks with juice)	-	-	-	-	1.0	3
White Wine	-	-	-	-	1.0	5

	Decade					
	1980s (n=663)	Rank	1990s (n=609)	Rank	2000s (n=366)	Rank
Flavan-3-ols	49.0 ^a (10.9,165)		48.0 ^a (12.9, 184)		37.4 ^a (11.7, 154)	
Brewed Tea (hot and cold)	91.2	1	88.7	1	86.8	1
Apple & pear (and juices)	2.8	2	2.6	2	2.3	2
Chocolate solid (bar and candy bar)	1.0	3	1.0	-	-	-
Other fruit (and juices, and fruit drinks with juice)	1.0	4	1.2	4	-	-
Peaches, Plums, Grapes, Nectarines (and juices), Nectars	1.0	5	-	-	-	-
Cocoa, dry powder only	-	-	1.2	3	1.6	5
Red Wine	-	-	-	-	2.0	3
Berries and cherries (and juices)	-	-	1.0	5	1.6	4
Anthocyanidins	7.9 ^a (3.5, 15.9)		10.9 ^a (5.6, 23.0)		15.1 ^a (5.9, 30.1)	
Berries and cherries	41.4	1	41.8	1	45.0	1
Peaches, Plums, Grapes, Nectarines (and juices), Nectars	24.3	2	25.3	2	25.7	2
Other fruit (and juices, and fruit drinks with juices)	19.3	3	19.5	3	15.7	3
Apple & pear (and juices)	10.3	4	7.7	4	-	-
Fruit Pies	2.3	5	-	-	-	-
Red Wine	-	-	1.7	5	6.4	4
Other Vegetables	-	-	-	-	2.0	5
Isoflavones	0.0 ^a (0.0, 0.1)		0.1 ^a (0.0, 0.3)		0.2 ^a (0.1, 1.4)	
Legumes	97.5	1	96.3	1	94.2	1
Peanuts	1.3	2	1.0	3	1.3	3
Other Vegetables	-	-	2.0	2	2.3	2
Brewed Tea (hot and cold)	-	-	1.0	4	1.1	4
Tree Nuts	-	-	-	-	1.0	5

^aMedian (25th, 75th percentile) intakes