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Soda and Cell Aging: Associations between Sugar-Sweetened Beverage Consumption and Leukocyte Telomere Length in Healthy Adults from the National Health and Nutrition Examination Surveys

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Abstract

Objectives—We tested whether leukocyte telomere length maintenance, which underlies healthy cellular aging, provides a link between sugar-sweetened beverage (SSB) consumption and risk of cardiometabolic disease. We examined cross-sectional associations between consumption of SSBs, diet soda and fruit juice and telomere length in a nationally representative sample of healthy adults.

Methods—The study population included 5,309 adults, aged 20 to 65 years, with no prior history of diabetes or cardiovascular disease, from the 1999–2002 National Health and Nutrition Examination Surveys. Leukocyte telomere length was assayed from DNA specimens. Diet was assessed using 24-hour dietary recalls. Associations were examined using multivariate linear regression for the outcome of log-transformed telomere length.

Results—After adjustment for sociodemographic and health-related characteristics, sugar-sweetened soda consumption was associated with shorter telomeres (β=−0.010, 95% CI −0.020, −0.001, P=0.04). Consumption of 100% fruit juice was marginally associated with longer telomeres (β= 0.016, 95% CI −0.000, 0.033). No significant associations were observed between consumption of diet sodas or non-carbonated sugar-sweetened beverages and telomere length.

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Conclusions—Regular consumption of sugar-sweetened sodas may influence metabolic disease development through accelerated cell aging.

Sugar-sweetened beverages (SSBs), including soft drinks/sodas, fruit-flavored drinks, sports drinks, and energy drinks, are the largest source of added sugar in the American diet (1, 2). Between 1999 and 2008, it was estimated that adults aged 20–34 years consumed an average of 333–421 calories/day, and adults aged 35 years or older consumed an average of 236–260 calories/day from SSBs (3). Because of these strikingly high levels of consumption, SSBs have emerged as an important target of public health efforts and policies (4, 5).

In parallel to trends in SSB intake, the prevalences of obesity and type 2 diabetes have also increased in recent years (6, 7). Epidemiologic studies have shown that regular consumption of SSBs is associated with increased risks of obesity, metabolic syndrome, type 2 diabetes and cardiovascular disease (8–11). However, the mechanisms for these associations are complex and not yet fully understood. There is evidence to suggest that excess calories (via lowered satiety) and high levels of insulin resistance, oxidative stress, and inflammation, may mediate these associations (9). Given that oxidative stress, inflammation and insulin resistance are also associated with telomere shortening, impaired telomere length maintenance is a potential mechanism that may help to explain the association between SSB consumption and accelerated metabolic disease (12–14).

Telomeres are the DNA-protein caps at the end of chromosomes that promote chromosomal stability and protect the genomic DNA from damage. Telomere length naturally shortens with each cell cycle and, if it falls to a critical short length, the cell is no longer able to divide and often malfunctions (15). In addition to biological age, telomere shortness has been linked to lifestyle behaviors and psychological stress (16–22). In turn, shorter telomeres have been associated with increased risks of chronic diseases, including cardiovascular disease, diabetes and some cancers (17, 23–27). In population studies, evidence exists for a causal role of impaired telomere maintenance in raising risks of pulmonary and cardiovascular disease (28). To date, the associations between dietary intake and telomere length have been examined in only a few studies; results for most food groups and nutrients have been mixed (13, 29, 30).

Given the effects of SSBs on oxidative stress and insulin resistance, the objective of this study was to examine the associations between sugar-sweetened beverage, diet soda, and 100% fruit juice consumption and telomere length in a large, nationally representative sample of healthy adults. We hypothesized that beverages with high sugar content would be the most detrimental to cellular aging, such that sugar-sweetened sodas and non-carbonated SSBs would show the strongest associations with telomere shortness.

METHODS

Study Population

The National Health and Nutrition Examination Survey (NHANES) is an ongoing, multistage cross-sectional survey administered by the National Center for Health Statistics (NCHS). The study population was restricted to 5,309 adults aged 20–65 years, with

complete dietary data and with LTL measured in the 1999–2002 NHANES. Adults with a history of diabetes, coronary heart disease, angina, myocardial infarction, stroke or congestive heart failure were excluded.

Leukocyte Telomere Length (LTL)

DNA samples purified from whole blood were collected from NHANES participants aged 20 years and older in the 1999–2002 waves to establish a national probability sample of genetic material for future research (31). DNA aliquots were processed by the Division of Laboratory Sciences at the National Center for Environmental Health and provided by the Division of Health and Nutrition Examination Surveys, National Center for Health Statistics, Centers for Disease Control and Prevention. The LTL assay was performed in the laboratory of Dr. Elizabeth Blackburn, using the quantitative polymerase chain reaction (PCR) method to measure telomere length relative to standard reference DNA (T/S ratio), as described in detail elsewhere (32, 33). The PCR method was preferred over the Southern blot method because of the smaller amount of DNA required for the assay (34, 35). Each LTL sample was assayed three times on three different days. The samples were assayed on duplicate wells, resulting in six data points. Sample plates were assayed in groups of three plates, and no two plates were grouped together more than once. Each assay plate contained 96 control wells with eight control DNA. Assay runs with eight or more invalid control wells were excluded from further analysis (<1% of runs). Control DNA values were used to normalize between-run variability. Runs with more than 4 control DNAs falling outside 2.5 standard deviations from the mean for all assay runs were excluded from further analysis (<6% of runs). For each sample, any potential outliers were identified and excluded from the calculations (<2% of samples). The mean and standard deviation of T/S ratio were then calculated normally. The inter-assay coefficient of variation was 6.5%. Throughout the paper, we will refer to T/S ratio and relative telomere length as telomere length for brevity.

The conversion from T/S ratio to base pairs was calculated based on comparison of telomeric restriction fragment length from Southern blot analysis and T/S ratios using DNA samples from the human diploid fibroblast cell line IMR90 at different population doublings. The formula used to convert T/S ratio to base pairs was 3,274 + 2,413 * (T/S).

Sugar-sweetened beverage intake

One 24-hour dietary recall was administered to NHANES study participants in the Mobile Examination Center. Beverage variables were derived from the NHANES individual food files. Consumption of sugar-sweetened sodas, non-carbonated SSBs (i.e. fruit drinks, sports drinks, energy drinks, sweetened waters), diet sodas, 100% fruit juice, and all SSBs (including sugar-sweetened sodas and non-carbonated SSBs) were identified using data from the USDA Food and Nutrient Database for Dietary Studies. Serving sizes of 8 ounces (226.8 grams) were applied to all beverages.

We used a statistical method developed by the National Cancer Institute (NCI) to estimate usual dietary intake, because 24-hour dietary recalls may not accurately reflect long-term dietary intake (36). The NCI method requires two or more days of 24-hour dietary recalls on a subset of participants. Because study participants in the 1999–2002 NHANES only

contributed one 24-hour dietary recall, data from 2003–2004 NHANES participants were included to calibrate the distributions of dietary variables. This method, which uses a two-part, nonlinear mixed model for foods consumed episodically (i.e. sugar-sweetened beverages), was applied to participants from 1999–2004 NHANES with sociodemographic and dietary data. Intake distributions were modeled for each beverage, correcting for age, gender, race/ethnicity and weekday/weekend effects. Individual beverage intakes were then estimated for all participants in 1999–2004 NHANES, though only participants in 1999–2002 NHANES were retained in the analytic population. In using this method, we assumed that the distributions of sugar-sweetened beverage intake did not significantly differ between 1999–2002 and 2003–2004. The NCI method's validity in evaluating associations between usual intake of foods and health outcomes has previously been established (37).

Study covariates

Potential confounders included sociodemographic variables, such as participant's age (20–24 y, 25–29 y, 30–34 y, 35–39 y, 40–44 y, 45–49 y, 50–54 y, 55–59 y, 60–65 y), gender, self-reported race/ethnicity (Non-Hispanic White, Black, Hispanic, Other race/multi-racial), highest educational attainment (<12 years, high school diploma or equivalent, some college, college graduate), ratio of household income to federal poverty level (0–100% FPL, 100–200% FPL, 200–300% FPL, 300–400% FPL, >400% FPL), and marital status (married or living with partner, never married, separated/widowed/divorced).

Health-related variables included: smoking status (never, former, current), pack-years of smoking (0 pack-years, <30 pack-years, 30–60 pack-years, >60 pack-years), physical activity assessed from questionnaire (some activity, no activity), total energy intake, alcohol intake, and Healthy Eating Index-2005 scores, a dietary pattern developed by the USDA to measure compliance with national dietary guidelines (38). The HEI-2005 is scored out of 100 points and comprised of 12 components: total fruit, whole fruit, total vegetables, dark green and orange vegetables and legumes, total grains, whole grains, milk, meat and beans, oils, saturated fat, sodium, and calories from solid fats, alcoholic beverages and added sugars. HEI-2005 scores were collapsed into gender-specific quartiles: for men, the cut-points were 42.1, 45.9, and 50.5, for women, the cut-points were 44.4, 48.6, and 53.5. Alcohol intake was defined as low (0–0.5 drinks/day for men and women), moderate (0.5–2.0 drinks/day for men; 0.5–1.5 drinks/day for women) and heavy (>2 drinks/day for men, >1.5 drinks/day for women).

Adiposity measures included body mass index (BMI) and waist circumference. BMI was calculated from self-reported height (in m) and weight (in kg), measured by trained personnel using a stadiometer and Toledo weight scale (39). BMI categories were defined as underweight (BMI <18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25.0–29.9), and obese (BMI ≥30). Waist circumference (cm) was measured at the upper lateral border of the right ilium. Elevated waist circumference was defined as ≥102 cm for men and ≥88 cm for women.

Missing indicators were used to account for missing education level (n=6, 0.16% missing), marital status (n=258, 5.5% missing), smoking status (n=8, 0.15% missing), pack-years of

smoking (n=523, 9.1% missing), household income (n=416, 6.9% missing), BMI (n=89, 1.6% missing), and waist circumference (n=126, 2.0% missing).

Statistical analysis

In order to make nationally representative estimates, analyses accounted for the complex NHANES sampling design by incorporating sampling weights for the genetic subsample and strata and PSU indicators. The sampling weights account for different sampling probabilities and potential nonresponse bias of the participants in the NHANES subsample who consented to the use of DNA specimens for future genetic research. First, we examined bivariate associations between LTL and individual-level characteristics. Due to the skewness of LTL, LTL was log-transformed before fitting regression models. Linear regression models were then fit for log-transformed LTL to estimate the difference in LTL for a one-serving increase in beverage intake. The first model adjusted for age categories, gender, and total energy intake. The second model adjusted for all sociodemographic and health-related variables. We also examined heterogeneity in the associations between beverage intake and LTL by gender and race/ethnicity by introducing product terms between beverages and the individual modifiers in the fully adjusted models. Statistical significance of the product terms was determined with the Wald test.

All statistical tests were two-sided and statistical significance considered at $P<0.05$. Statistical analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC) and conducted using ANDRE, the CDC's remote access system for restricted data analysis.

RESULTS

As expected, age was linearly associated with shorter telomeres ($P<0.0001$) (Table 1). Mean telomere length was longest in Blacks and Hispanics, in never smokers, and in normal weight adults, as observed in prior studies (18, 31, 40–43).

Pearson's correlation coefficients for associations among self-reported intakes of different beverages are shown in Table 2. Overall, correlations between beverages were modest. The intakes of sugar-sweetened sodas, non-carbonated SSBs and 100% fruit juice were positively correlated with each other. Diet soda was negatively correlated with SSBs and 100% fruit juice intakes.

Average sugar-sweetened soda consumption was 1.5 servings (12 ounces) per day. Average consumption of diet sodas, non-carbonated SSBs and 100% fruit juice was lower, ranging from 0.3 to 0.5 servings per day. Consumption of all SSBs (including sugar-sweetened soda and non-carbonated SSBs) was averaged at 2.1 servings (16.8 ounces) per day. Associations between SSB intake and telomere length are shown in Table 3. After adjustment for sociodemographic and health-related variables and adiposity, sugar-sweetened soda consumption was inversely associated with telomere length ($\beta= -0.010$, 95% CI −0.020, −0.001). Holding other covariates constant, this difference corresponds to a deficit of 14 base pairs. Given a model-based estimate in this sample of the age-associated rate of telomere shortening of 13.6 base pairs per year, this is equivalent to 1.9 additional years of aging for an 8-ounce serving of sugar-sweetened sodas. For a daily consumption of the

current standard 20-ounce serving size for sugar-sweetened sodas, this corresponds to 4.6 additional years of aging. Approximately 21% of adults in the study population reported daily consumption of ≥20 ounces of sugar-sweetened soda (data not shown).

No associations were observed between diet soda or non-carbonated SSBs and telomere length. Although a positive association was observed between 100% fruit juice and telomere length in the first model adjusting for age, gender and total energy; this association was attenuated after the inclusion of other potential confounders (P=0.05).

Stratified associations by gender and race/ethnicity are shown in Tables S1–S2. There was no evidence of heterogeneity in the associations by gender or racial/ethnic groups.

DISCUSSION

In this nationally representative sample of healthy adults, the average daily consumption of sugar-sweetened soda was 12 ounces (1.5 servings), a level in excess of the American Heart Association recommended limit for added sugar (5). Consistent with our hypothesis, we found that each daily 8-ounce serving of sugar-sweetened sodas was linearly associated with shorter telomeres, roughly equivalent to 1.9 additional years of aging, independent of sociodemographic and health-related variables. For a daily 20-ounce serving, the current standard serving size, this translates into approximately 4.6 additional years of aging. More than 20% of adults in the study population reported at least 20 ounces of sugar-sweetened soda consumption per day. Although these are modest associations, the magnitude of the association for consuming 20 ounces of sugar-sweetened soda is comparable to observed associations between telomere length and moderate/vigorous levels of physical activity (4.4 years) and smoking (4.6 years, in the opposite direction) (18, 20). To our knowledge, this is the first study to link sugar-sweetened soda consumption with telomere length in a large, nationally representative sample of healthy adults.

Results of telomere length associations with various dietary aspects have not been consistent (13, 29, 30). The Multi-Ethnic Study of Atherosclerosis (MESA) previously examined sugar-sweetened soda consumption in relation to telomere length among adults (30). Their results showed no association after adjustment for sociodemographic characteristics, lifestyle factors and BMI. The fact that MESA had a smaller sample size and an older population, on average, than NHANES may account for why an association was found in the current study but not in MESA.

Our hypothesis that consumption of SSBs would be related to shorter telomeres was derived from the known effects of SSB consumption on impaired fasting glucose and insulin resistance (8–11). SSBs have been known to increase oxidative stress and systemic inflammation, both processes that can influence telomere attrition (13, 14). Telomere shortening in response to, and perhaps contributing to, these disease processes has been reported, reflecting the overall burden of cardiometabolic disease (27, 44, 45). Our results suggest that another link between sugar-sweetened soda consumption and metabolic disease may be through shortened telomere length, a biomarker and mechanism of cellular aging (Figure 1).

We observed no significant associations between consumption of non-carbonated SSBs and telomere length. The lack of association might be attributed to the large degree of heterogeneity in sugar content across beverages (46). In the study population, the average consumption of non-carbonated SSBs (0.3 servings/day) was substantially lower than the average consumption of sugar-sweetened sodas (1.5 servings/day); it may be that sugar consumption in beverages affects telomere length only at higher intake levels. Consumption of non-carbonated SSBs has increased in recent years, while overall intakes of sugar-sweetened sodas have decreased, and an association between consumption of non-carbonated SSBs and telomere length may emerge in future studies (3). Even lacking a significant current association with telomere length, decreasing consumption of SSBs to reduce risks of obesity-related chronic disease seems prudent (8, 10).

A marginally positive association was shown in the current study between 100% fruit juice consumption and telomere length. Previous studies examining fruit juice and health outcomes have yielded mixed findings. Fruit juice has been associated with increased risk of type 2 diabetes in some (47–49), but not all studies (10, 50–52). Consumption of 100% fruit juice has not been shown to have the same effect on cardiometabolic risk factors (53) or markers of insulin resistance, oxidative stress or inflammation as SSB consumption (54–56). Fruit juice consumption may result in different metabolic effects when compared to SSBs, with potentially beneficial effects of phytochemicals and micronutrients balancing out the harmful effect of liquid sugars. Consumption levels of 100% fruit juice are also generally lower than the level of sugar-sweetened soda consumption, as was shown in the current study. Since fruit juice consumption has not been associated with long-term health benefits in epidemiologic studies, limiting its consumption in preference of whole fruit may be advisable.

Our study is strengthened by the use of a large, nationally representative sample of adults. In addition, we used a validated method to estimate usual beverage intake from the extensive NHANES dietary data. Furthermore, the NHANES response rates from 1999–2002 ranged from 76–80%, which are considerably higher than other national health surveys, and helps to improve the generalizability of our findings (57). We have also taken steps to avoid spurious findings, including examining a small number of dietary components for which there are substantially strong a priori hypotheses for associations with oxidative stress and biomarkers of aging.

Our study has limitations to note. First, the cross-sectional nature of the data makes it difficult to infer causation. Longitudinal studies of dietary intake and telomere length are needed to understand how dietary intake can influence telomere length over time and whether the associations are explained by the mechanisms proposed in Figure 1. Collection of biochemical data, such as insulin resistance, oxidative stress and inflammation, would also help to inform the understanding the mechanisms of the association between sugar-sweetened beverage intake and telomeric shortening. LTL was measured from a single DNA specimen, which does not provide information on rates of telomere shortening. Similarly, beverage intake was estimated from a 24-hour dietary recall conducted at the time of the survey, which may not reflect diet or beverage patterns over the life course.

Telomere research in clinical studies is a relatively new field and researchers are still identifying important individual and lifestyle determinants of telomere length. Thus, there is always the possibility of unmeasured confounding. For example, genetic differences may contribute to telomeric shortening; however, the degree of this confounding would be small because it is unlikely that any potential SNPs predictive of telomere length are strongly associated with beverage consumption. Psychosocial stress is another important determinant of telomeric shortening; unfortunately, this construct was not captured within the NHANES questionnaires. Our analyses included all potential sociodemographic and health variables known to be related to telomere length and dietary intake, some of which might act as proxies for psychological stress; the inclusion of these variables did not substantially change the model estimates. Because we examined healthy adults without a history of diabetes or cardiovascular disease, the associations should reflect sugar-sweetened soda consumption independent of cardiometabolic disease.

Understanding the role that nutrition plays in telomere length maintenance is critical in understanding how to improve dietary intake. Independent of adiposity and other individual characteristics, our study results suggest that regular consumption of sugar-sweetened sodas is associated with significantly shorter telomeres. Further epidemiologic studies are needed to confirm this association in longitudinal settings, and experimental research can examine the pathway from soda to cell to better understand the mechanism of this relationship. Still, there is sufficient evidence to limit our consumption of all SSBs to improve cardiometabolic risk factors, reduce chronic disease risk, and improve overall health. This study supports a new link, shortened immune cell telomere length, a biological risk factor for aging, between sugar-sweetened soda consumption and metabolic disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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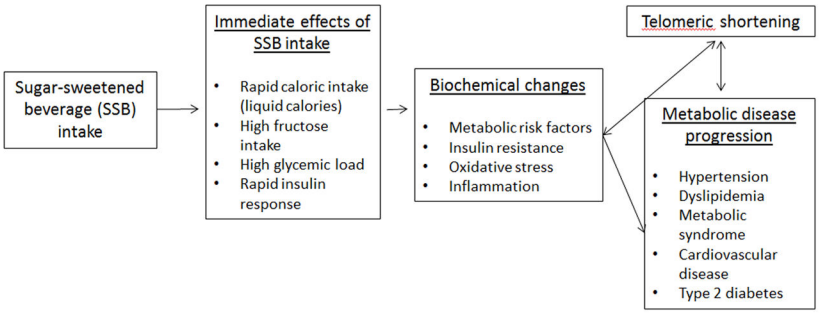

Figure 1.

Conceptual model of the effects of sugar-sweetened beverage intake on telomeric shortening and metabolic disease progression

High sugar-sweetened beverage intake leads to rapid caloric and fructose intake and high glycemic load. This results in an increased risk of metabolic risk factors and a biochemical environment of high insulin resistance, oxidative stress and inflammation. In turn, this can affect telomeric shortening and influence metabolic disease progression, including metabolic syndrome, type 2 diabetes, and cardiovascular disease.

Table 1

Mean LTL by sociodemographic characteristics and lifestyle behaviors of 5,309 adults 20–65 years, NHANES 1999–2002

	n	Weighted %[a]	Leukocyte Telomere Length		P[b]
			Mean	SE	
Age (mean ± SE)		39.7 ± 0.3	1.10	0.01	*<0.0001*
Gender					*0.27*
Men	2473	48.2	1.09	0.01	
Women	2836	51.8	1.10	0.02	
Race					*0.009*
Non-Hispanic White	2510	69.2	1.09	0.02	
Black	934	11.0	1.15	0.02	
Hispanic/Latino	1687	15.2	1.11	0.02	
Other race/Multi-race	178	4.6	1.09	0.02	
Education level					*0.25*
<12 years	1554	18.7	1.08	0.02	
High school diploma	1227	25.4	1.09	0.02	
Some college	1429	30.0	1.11	0.02	
College graduate	1093	26.0	1.11	0.02	
Marital status					*<0.0001*
Married or living with partner	3310	65.6	1.07	0.02	
Never married	1021	20.5	1.19	0.02	
Separated, widowed or divorced	720	13.9	1.04	0.02	
Federal poverty level (FPL) (%)					*0.09*
0–100% FPL	887	14.3	1.15	0.03	
100–200% FPL	1111	18.3	1.09	0.02	
200–300% FPL	757	15.1	1.09	0.02	
300–400% FPL	619	13.9	1.10	0.02	
>400% FPL	1519	38.4	1.08	0.02	
Pack-years of smoking					*<0.001*
0 pack-years	2872	57.4	1.11	0.02	
<30 pack-years	1533	34.0	1.09	0.02	

	n	Weighted %[a]	Leukocyte Telomere Length		P[b]
			Mean	SE	
30–60 pack-years	278	6.3	1.00	0.02	
>60 pack-years	103	2.3	0.96	0.02	
Physical activity					*0.03*
Some activity	1974	30.7	1.08	0.02	
No activity	3332	69.3	1.11	0.01	
BMI					*0.004*
Underweight, <18.5 kg/m^2	78	1.8	1.13	0.03	
Normal weight, 18.5–24.9 kg/m^2	1673	35.0	1.13	0.02	
Overweight, 25.0–29.9 kg/m^2	1849	34.4	1.08	0.02	
Obese, ≥30 kg/m^2	1620	28.9	1.07	0.02	
Waist circumference					0.003
Normal, <102 cm for M; <88 cm for W	2693	55.1	1.12	0.02	
Elevated, ≥102 cm for M; ≥88 cm for W	2490	42.9	1.07	0.02	

M, men; W, women

[a] Weighted percentages are representative of the United States civilian, noninstitutionalized population

[b] From chi-squared tests and univariate linear regression

Table 2

Pearson's correlations coefficients for sugar-sweetened beverages: NHANES 1999–2002

	Sugar-sweetened soda	Non-carbonated SSB	Diet soda	100% fruit juice
Sugar-sweetened soda	1.00			
Non-carbonated SSB	0.20	1.00		
Diet soda	−0.23	−0.10	1.00	
100% fruit juice	0.04	0.13	−0.07	1.00

SSB, sugar-sweetened beverages

Table 3

Associations between beverage intake and log-transformed leukocyte telomere length (T/S ratio): NHANES 1999–2002

	Mean LTL by Quartile of Intake				Model 1		Model 2	
	Q1	Q2	Q3	Q4	β	95% CI	β	95% CI
All sugar-sweetened beverages[b]	1.05	1.10	1.11	1.13	−0.01	−0.021, 0.001	−0.008	−0.020, 0.004
Sugar-sweetened soda	1.04	1.13	1.09	1.12	−0.013	−0.023, −0.003	−0.010	−0.020, −0.001
Non-carbonated sugar- sweetened beverages	1.03	1.10	1.12	1.13	0.000	−0.029, 0.029	−0.001	−0.030, 0.028
Diet soda	1.10	1.08	1.09	1.10	−0.003	−0.021, 0.016	−0.000	−0.019, 0.018
100% fruit juice	1.10	1.08	1.08	1.11	0.022	0.003, 0.041	0.016	−0.000, 0.033

Expressed in servings (8 ounces)

[b] Includes sugar-sweetened soda and non-carbonated sugar-sweetened beverages

Model 1 included age, gender, and total energy

Model 2 included age, gender, race/ethnicity, education level, marital status, smoking status, pack-years of smoking, physical activity, poverty level, total energy, alcohol intake, Healthy Eating Index-2005 scores, body mass index categories and waist circumference categories