Journal of the American Heart Association

ORIGINAL RESEARCH

Sugar-Sweetened Beverage Intake and Cardiovascular Disease Risk in the California Teachers Study

Lorena S. Pacheco, PhD, MPH, RDN, CPH; James V. Lacey, Jr, PhD, MPH; Maria Elena Martinez, PhD, MPH; Hector Lemus, DrPH; Maria Rosario G. Araneta, PhD, MPH; Dorothy D. Sears, PhD; Gregory A. Talavera, MD, MPH; Cheryl A. M. Anderson, PhD, MPH, MS

BACKGROUND: Sugar-sweetened beverage (SSB) consumption has been associated with cardiometabolic risk. However, the association between total and type of SSB intake and incident cardiovascular disease (CVD) end points such as myocardial infarction, stroke, and revascularization is limited.

METHODS AND RESULTS: We examined the prospective association of baseline SSB consumption with incident CVD in 106 178 women free from CVD and diabetes mellitus in the CTS (California Teachers Study), a cohort of female teachers and administrators, followed since 1995. SSBs were defined as caloric soft drinks, sweetened bottled waters or teas, and fruit drinks, and derived from a self-administered food frequency questionnaire. CVD end points were based on annual linkage with statewide inpatient hospitalization records. Cox proportional hazards models were used to assess the association between SSB consumption and incident CVD. A total of 8848 CVD incident cases were documented over 20 years of follow-up. After adjusting for potential confounders, we observed higher hazard ratios (HRs) for CVD (HR, 1.19; 95% CI, 1.06–1.34), revascularization (HR, 1.26; 95% CI, 1.04–1.54]), and stroke (HR, 1.21; 95% CI, 1.04–1.41) in women who consumed ≥1 serving per day of SSBs compared with rare/never consumers. We also observed a higher risk of CVD in women who consumed ≥1 serving per day of fruit drinks (HR, 1.42; 95% CI, 1.00–2.01 [*P* trend=0.021]) and caloric soft drinks (HR, 1.23; 95% CI, 1.05–1.44 [*P* trend=0.0002]), compared with rare/never consumers.

CONCLUSIONS: Consuming ≥1 serving per day of SSB was associated with CVD, revascularization, and stroke. SSB intake might be a modifiable dietary target to reduce risk of CVD among women.

Key Words: cardiovascular disease ■ nutritional epidemiology ■ observational study ■ sugar-sweetened beverages

Sugar-sweetened beverages (SSBs) account for nearly half of the added sugars in the American diet.[1,2] Among US adults, the mean adjusted intake of added sugars is high (308 kcal/d or 17% of total energy),[3] making SSBs a substantial contributor of calories in this population.[1,2] SSBs are manufactured carbonated and noncarbonated beverages containing caloric sweeteners or syrups and include caloric soft drinks (ie, not sugar-free), fruit drinks, sports and energy drinks, sweetened waters, and tea and coffee beverages with added sugars.[1] Reducing intake of added sugars is currently recommended by the World Health Organization,[4] *Dietary Guidelines for Americans*,[1] and the American Heart Association,[5] but intake levels for the majority of Americans exceed recommendations and almost 50% of adults report consuming at least 1 SSB per day.[6]

Consumption of SSBs has been associated with weight gain, visceral adiposity and obesity,[7–13] cardiometabolic risk factors and/or metabolic syndrome and type 2 diabetes mellitus,[9,14–19] hypertension,[20–22] and cardiovascular disease (CVD) events such as

Correspondence to: Cheryl A. M. Anderson, PhD, MPH, MS, 9500 Gilman Drive, MC 0628, La Jolla, CA 92093-0628. E-mail: c1anderson@ucsd.edu

Supplementary materials for this article are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.014883

For Sources of Funding and Disclosures, see page 10.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Prospective studies have addressed the association between sugar-sweetened beverage intake and cardiovascular disease; however, few trials have been adequately statistically powered to examine coronary heart disease or stroke outcomes, with even fewer assessing different types of sugar-sweetened beverages.
- In a large US cohort, intake of sugar-sweetened beverages was positively associated with cardiovascular disease, revascularization, and stroke; and, more specifically, intake of fruit drinks and caloric soft drinks was positively associated with cardiovascular disease.

What Are the Clinical Implications?

- Our findings support clinical and public health efforts to reduce sugar-sweetened beverage intake as a means to promote cardiovascular health.

Nonstandard Abbreviations and Acronyms

BMI	body mass index
CABG	coronary artery bypass grafting
CHD	coronary heart disease
CVD	cardiovascular disease
CTS	California Teachers Study
FFQ	food frequency questionnaire
HR	hazard ratio
MI	myocardial infarction
OSHPD	Office of Statewide Health Planning and Development
PCI	percutaneous coronary intervention
PTCA	percutaneous transluminal coronary angioplasty
RR	relative risk
SSB	sugar-sweetened beverage

coronary heart disease (CHD) and stroke[23–28] among a variety of populations. Several biological mechanisms for this association have been suggested including that sugars augment the levels of glucose and insulin concentrations in the bloodstream, contributing to a high dietary glycemic load.[29] A high glycemic load promotes physiological responses such as appetite stimulation and weight gain/adiposity, inducing insulin resistance and glucose intolerance.[30] Additionally, enhancing levels of oxidative stress and inflammation, altering lipid metabolism including triglyceride synthesis, leading to endothelial dysfunction and beta cell stress.[30–34] These mechanisms influence insulin resistance and risk of type 2 diabetes mellitus,[35] as well as the atherosclerotic process and risk of CVD.[31,32,36]

Although prospective studies have addressed the association between SSB intake and CVD,[23–28] few have been adequately statistically powered to examine CHD[23,24,27] or stroke[25–27] outcomes. This is of particular importance since CHD remains the leading cause of death in the United States, and stroke is fifth.[37] Furthermore, there are a limited number of studies that assess a variety of SSBs with most studies examining one specific SSB. Addressing the impact different SSBs have on CVD risk is necessary and findings can further contribute to the literature on SSBs and inform future recommendations. We aimed to examine the association between SSB consumption and CVD risk, examining incidence of CVD events including myocardial infarction (MI), revascularization, and stroke in a large prospective cohort of adult women over a 20-year period. We hypothesized that higher levels of SSB consumption are associated with incident CVD.

METHODS

All of the data associated with this publication and in the CTS (California Teachers Study) are available for research use. The CTS welcomes all such inquiries and encourages individuals to visit https://www.calteachersstudy.org/for-researchers.

Study Population and Design

The CTS is an ongoing prospective cohort study of 133 477 active and retired female teachers and administrators who completed a mailed questionnaire at study enrollment in 1995–1996 and members of the California State Teachers Retirement System.[38] Annual follow-up, mailings, and participant communication capture change of residence. Linkage with the Office of Statewide Health Planning and Development (OSHPD) identifies inpatient hospitalization and—since 2010—ambulatory, surgery, and emergency department procedures and diagnoses performed in California. Dates and causes of death are determined via linkage with state and national mortality files and the National Death Index.

The CTS has been approved by the institutional review boards at City of Hope, the University of Southern California, the University of California San Francisco, and the University of California at Irvine, and participants provided informed consent. This data analysis was approved by the institutional

review boards of City of Hope and the University of California San Diego.

Dietary Assessment and SSB Intake

Dietary intake during the year preceding baseline was assessed using a validated 103-item self-administered food frequency questionnaire (FFQ), developed from an early version of the Block 95. This FFQ ascertained usual serving size (ie, small, medium, large, or extra-large serving) and frequency of consumption (ie, never or <1 time per month, 1 time per month, 2 or 3 times per month, 1 time per week, 2 times per week, 3or 4 times per week, 5 or 6 times per week, every day, or ≥2 times per day) of 103 food and beverage items. The reproducibility and validity of this instrument in the cohort has been previously published.[39] Estimation of SSB consumption was determined from 3 items on the FFQ, specifically asked as: "First: mark the column to show *How Often*, on the average, you ate the food during the past year; second: mark the column to show *How Much* you usually eat of each food for 'regular soft drinks (not diet soda),' 'Snapple, Calistoga, sweetened bottled waters or iced teas,' and 'Kool-Aid, Hi-C, or other drinks with added Vitamin C.'" The use of brand names was included in the FFQ mailed to participants. These 3 beverage types will be referred to as "caloric soft drinks," "sweetened bottled waters or teas," and "fruit drinks," respectively. Fruit drinks only included sweetened (with added sugar) fruit drinks and excluded fruit juices. From the 9 possible frequency categories, SSB consumption was collapsed into 4 categories: rare or never, >rare/never to <1 serving per week, ≥1 serving per week to <1 serving per day, and ≥1 serving per day. A serving of sweetened bottled waters or teas, and fruit drinks is equivalent to 8 fluid ounces, with an approximate weight of 237 grams. A serving of caloric soft drinks is equivalent to 12 fluid ounces, with an approximate weight of 355 grams.

Ascertainment of CVD Incidence

CVD incidence was defined as first occurrence of fatal or nonfatal MI, revascularization procedure (including coronary artery bypass grafting and percutaneous coronary intervention and/or percutaneous transluminal coronary angioplasty), or fatal or nonfatal stroke. This was ascertained after the return of the baseline questionnaire, with 1995–1996 designated as the study start date. Similarly, incidence of MI, revascularization, and stroke was defined as first occurrence of each event after baseline. Annual linkage with statewide OSHPD hospitalization records, derived medical diagnoses, and in-patient procedures for California residents for incident CVD was completed through December 31, 2015. Participants were followed from study start date until diagnosis with a CVD event, death, moved out of California, or end of follow-up (December 31, 2015), whichever came first. CVD definitions followed the *International Statistical Classification of Diseases, Ninth Revision* (*ICD-9*), and *International Statistical Classification of Diseases, Tenth Revision* (*ICD-10*), coding system.

Assessment of Covariates

Covariates for this analysis included age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, family history of CVD in first-degree relatives, moderate to vigorous physical activity, aspirin use, multivitamin use, menopausal status and menopausal hormone therapy use, oral contraceptive use, history of hypertension, body mass index (BMI), total energy intake, and fruit and vegetable intake. These data were collected at baseline, by self-report, as part of the enrollment questionnaire.

Socioeconomic status was determined by combining three 1990 US block census data variables (occupation, education, and family income), where all block groups in the state were ranked by occupation (percentage of adults employed in managerial/professional occupation), level of education (percentage of adults older than 25 years completing at least a college degree), and median family income, corresponding to quartiles analogous with the statewide adult population. A summary score was developed for socioeconomic status with categories ranging from 1 (lowest) to 4 (highest). Smoking status was derived from 3 questionnaire items addressing cumulative (lifetime) smoking exposure, age when first and last smoked, and average number of cigarettes currently or previously smoked. Alcohol intake was determined from frequency and number of drinks per week of beer, champagne and/or wine, and cocktails and/or liquor. Physical activity, including moderate to vigorous physical activity, was estimated using questionnaire-derived intensity, duration, and frequency of listed activities, on an average day. BMI (kg/m^2) was calculated as weight (kg) divided by height squared (m^2), from self-reported weight and height measurements.

Analytic Sample

This analysis includes 106 178 female study participants. We excluded participants who specified their data only be used for breast cancer research (n=22); those who resided outside of California at baseline (n=8847); those who returned incomplete or incomprehensible questionnaires (n=4); those who had incomplete FFQ data at baseline including vitamin use (n=2); those who had extreme caloric intake values (<600 [n=10 889] or >5000 [n=558] kcal/d); those who were aged ≥85 years at baseline (n=1611); those with a history of CVD including heart attack, stroke,

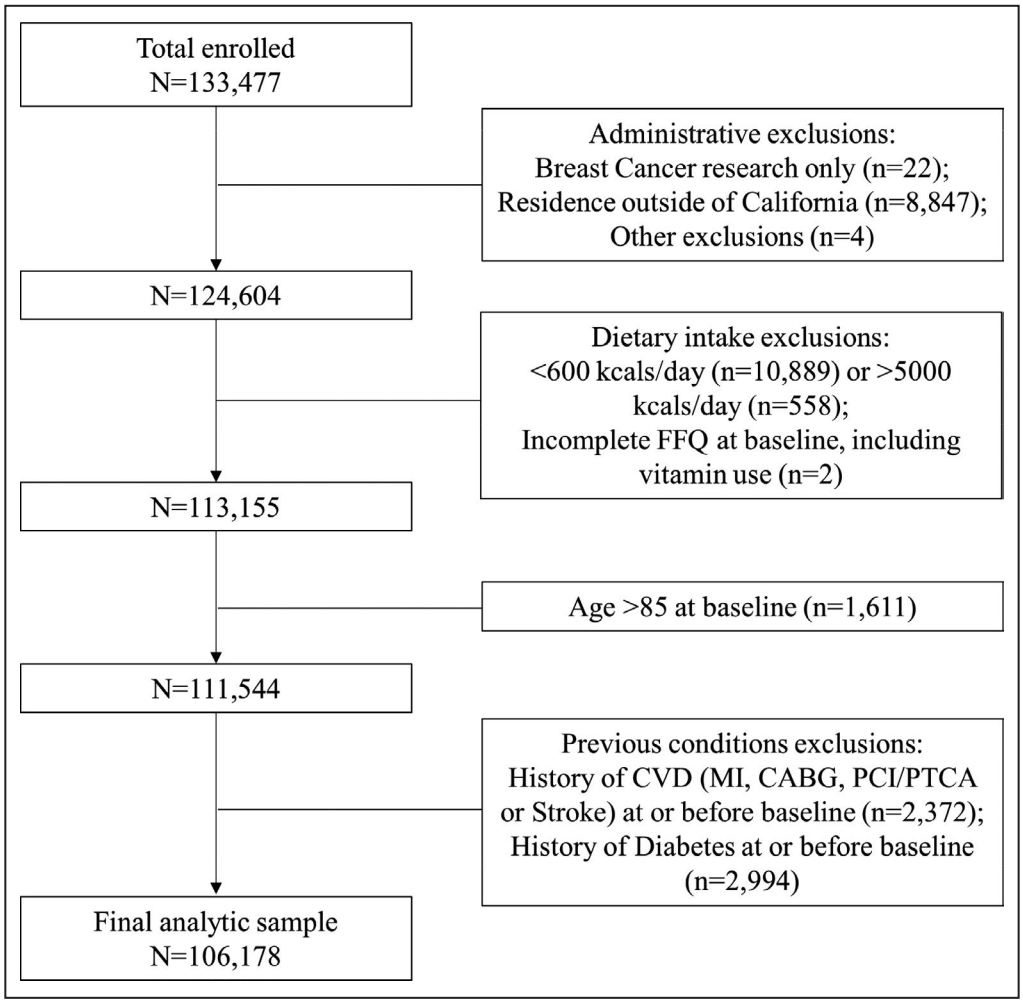

Figure 1. Flowchart showing enrollment, exclusions, and final analytic sample for sugar-sweetened beverage consumption and cardiovascular disease (CVD) risk in the CTS (California Teachers Study). CABG indicates coronary artery bypass grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention; and PTCA, percutaneous transluminal coronary angioplasty.

and revascularization procedures at or before baseline (n=2372); and those with a history of diabetes mellitus at or before baseline (n=2994) (Figure 1).

Statistical Analysis

Mean and SEM or proportion and frequency were calculated for baseline characteristics of study participants in each SSB consumption category. Cox proportional hazard modeling was used to estimate hazard ratios (HRs) and 95% CIs of CVD incidence according to SSB consumption. This approach was also used for first occurrence of MI, revascularization, and stroke, separate from the first CVD event. We also examined the independent association between type of SSB and incident CVD. In our analysis, a median method was used to examine the linear trend across intake categories. The median intake value of SSB in each category was designated to all individuals in that category. The statistical significance of the linear trend was tested by Cox proportional hazard model using the median intake value as a continuous independent variable in the multivariable model. The proportional hazards assumption was tested by inspecting the survival curves according to SSB consumption categories as well as testing time-varying covariates in the model.

In multivariable analysis, we adjusted for the following potential confounders: age; race/ethnicity (white, Asian/Pacific Islander, black, Hispanic, Native American, or mixed/other; further categorized as white versus all other before including it in the model); socioeconomic status (quartiles: first, second, third, fourth, or unknown); smoking status (never, past, current cigarette use [1–12, 13–24, ≥25 per day], or unknown use); alcohol intake (0, <20, or ≥20 g/d); family history of CVD (yes or no), moderate to vigorous physical activity (quintiles minutes per week: 0–30, 30–105, 105–210, 210–360, >360, or unknown); aspirin use (1–3 times per week, 4–6 times per week,

daily, undetermined frequency, or unknown); multivitamin use (never, 1–3 times per week, 4–6 times per week, daily, undetermined frequency); menopausal status and menopausal hormone therapy use (premenopausal or perimenopausal/postmenopausal with never, past, or current hormone therapy use of estrogen, estrogen and progesterone, or other hormone combinations); oral contraceptive use (never, past, or current); and history of hypertension (yes or no). In separate models, we further adjusted for BMI, total energy intake, and fruit and vegetable intake as a measure of diet quality as possible mediators. Fruit and vegetable intake was adjusted for total energy by using the residual method,[40] before including it in the model. Three progressively adjusted multivariable Cox regression models after the age-adjusted model were fitted. Model 1 included all of the above-mentioned covariates except for BMI, total energy intake, and fruit and vegetable intake. Model 2 additionally adjusted for BMI, total energy intake, and fruit and vegetable intake. The final model, model 3, includes covariates that were known and tested (if ≥10% change in HR) confounders in this exposure and outcome association. Variables with a $P<0.05$ remained in model 3. Additionally, the models examining the association between type of SSB and risk of CVD were adjusted for the other beverage types, ie, the sweetened water or tea analysis was adjusted for fruit drink and caloric soft drink, and vice versa.

A sensitivity analysis was conducted to further assess the amount of SSB and determine whether key information about the association was lost with our semiquantitative categorization. For this analysis, we categorized SSB intake in cups per day (1 cup=8 fl oz) as: rarely/never, up to .5 cup per day, up to 1 cup per day, up to 1.5 cups per day, and ≥1.5 cups per day. Another sensitivity analysis was conducted to examine the possibility of reverse causality. We excluded CVD events that occurred within the first 2 and 4 years of follow-up. All *P* values presented are from 2-tailed analyses; $P<0.05$ was considered statistically significant. Analyses were conducted with SAS version 9.4 (SAS Institute Inc).

RESULTS

CTS participants were, on average (mean±SD), aged 52.1±13.4 years, and followed for 1 807 182 person-years to first CVD event. During 20 years of follow-up, we ascertained 8848 incident cases of CVD, 2677 incident cases of MI, 2889 incident cases of revascularization, and 5258 incident cases of stroke. Among all participants, 4.2% were daily consumers of SSBs, whereas 40.9% of participants reported rarely/never consuming SSBs. This included consumption of any type of SSB measured: sweetened bottled waters or teas, fruit drinks, and caloric soft drinks. Regarding consumption by type of SSB among all participants, 4.3% were daily consumers of sweetened bottled waters or teas, 0.4% were daily consumers of fruit drinks, and 3.1% were daily consumers of caloric soft drinks (Table S1). Participants with the highest SSB intake tended to be younger, current smokers (7.6%), and past or current oral contraceptive users (72.6%), and averaged (mean±SEM) 220.1±3.68 minutes per week of moderate to vigorous physical activity (Table 1). With respect to dietary intake and clinical factors, participants with the highest SSB intake had a daily higher intake of total energy and carbohydrate; had a lower intake of protein, fat, and fruit and vegetables; had the highest obesity rates (17.5%); and 15% had hypertension. Comprehensive participant characteristics are reported in Table S2.

After adjusting for CVD risk factors and potential confounders, we observed a positive, significant association between SSB intake and risk of CVD (Table 2). Women who consumed SSBs daily had an 18% higher risk of CVD (HR, 1.18; 95% CI, 1.05–1.32 [*P* trend=0.019]) compared with women who rarely/never consumed SSBs (model 1, Table 2). Further adjustment for BMI, total energy intake, and fruit and vegetable intake (diet quality marker), as potential mediators, attenuated the effect size (HR, 1.16; 95% CI, 1.03–1.31 [*P* trend=0.052]) (model 2, Table 2 and model 4, Table S3), yet the final model showed a 19% higher risk of CVD (HR, 1.19; 95% CI, 1.06–1.34 [*P* trend=0.016]) (model 3), among SSB daily consumers compared with those participants who rarely/never consumed SSBs. Further adjustment for specific dietary intake covariates is provided in Table S3.

The risk of first revascularization event and risk of stroke, was 26% (HR, 1.26; 95% CI, 1.04–1.54 [*P* trend=0.037]) and 21% (HR, 1.21 [95% CI, 1.04–1.41 [*P* trend=0.056]) higher, respectively, in daily versus rare/never consumers of SSBs (model 3, Table 2).

With regards to type of SSB, a significant positive association was observed for fruit drinks and caloric soft drinks with incident CVD risk. Women who consumed ≥1 serving per day of fruit drinks had greater CVD (HR, 1.42; 95% CI, 1.00–2.01 [*P* trend=0.021]) risk, versus those who were rare/never consumers of fruit drinks (Figure 2). Similarly, compared with the rare/never consumers of caloric soft drinks, women who consumed ≥1 serving per day of caloric soft drinks had a 23% (HR, 1.23; 95% CI, 1.05–1.44 [*P* trend=0.0002]) higher risk of CVD. We observed a nonsignificant, positive association for sweetened bottled water or tea consumption and CVD risk. Details on the progressively adjusted models for these beverage-specific associations

Table 1. Baseline Characteristics of CTS Participants According to SSB Consumption Categories*,†

Characteristic	Total	Rare/Never	>Rare/Never to <1 Serving Per wk	≥1 Serving Per wk to <1 Serving Per d	≥1 Serving Per d
No.	106 178	43 425	35 422	22 825	4506
SSB intake, fl oz/d	2.6±0.0	0±0.0	2.6±0.0	5.5±0.0	13.5±0.1
Dietary intake					
Energy, kcal/d	1902.1±2.1	1753.2±3.2	1949.9±3.6	2042.6±4.5	2248.6±10.1
Carbohydrate, g/d	255.1±0.3	251.4±0.2	253.1±0.2	259.8±0.2	282.3±0.5
Protein, g/d	77.2±0.1	80.1±0.1	76.7±0.1	74.2±0.1	67.7±0.2
Total fat, g/d	59.9±0.1	59.6±0.1	61.4±0.1	59.6±0.1	53.6±0.2
Fruit and vegetable, g/d	321.2±0.6	361.2±0.8	301.4±0.9	286.7±1.2	265.0±2.6
Age, y	52.1±0.0	56.0±0.1	49.5±0.1	49.3±0.1	49.0±0.2
Race/ethnicity					
White	92 654 (87.3)	39 208 (90.3)	29 989 (84.7)	19 500 (85.4)	3957 (87.8)
All other	13 524 (12.7)	4217 (9.7)	5433 (15.3)	3325 (14.6)	549 (12.2)
Education‡					
Academic/professional doctorate	2501 (2.4)	1079 (2.5)	770 (2.2)	522 (2.3)	130 (2.9)
Master's degree	27 802 (26.2)	11 130 (25.6)	9444 (26.7)	6018 (26.4)	1210 (26.9)
Bachelor's degree	23 654 (22.3)	9677 (22.3)	8269 (23.3)	4804 (21.1)	904 (20.1)
Associate's degree or less	416 (0.4)	141 (0.3)	147 (0.4)	106 (0.5)	22 (0.5)
Unknown	51 805 (48.8)	21 398 (49.3)	16 792 (47.4)	11 375 (49.8)	2240 (49.7)
Occupation					
Teacher, any kind	61 940 (58.3)	21 846 (50.3)	22 358 (63.1)	14 708 (64.4)	3028 (67.2)
Pupil services	3235 (3.1)	1213 (2.8)	1155 (3.3)	723 (3.2)	144 (3.2)
Administration	3834 (3.6)	1401 (3.2)	1297 (3.7)	926 (4.1)	210 (4.7)
Any other combination	1751 (1.7)	623 (1.4)	648 (1.8)	402 (1.8)	78 (1.7)
Unknown	35 418 (33.4)	18 342 (42.2)	9964 (28.1)	6066 (26.6)	1046 (23.2)
Socioeconomic status					
First quartile, low	4393 (4.1)	1627 (3.8)	1565 (4.4)	1012 (4.4)	189 (4.2)
Second quartile, low-medium	17 953 (16.9)	7005 (16.1)	6147 (17.4)	4046 (17.7)	755 (16.8)
Third quartile, medium-high	34 326 (32.3)	13 724 (31.6)	11 737 (33.1)	7354 (32.2)	1511 (33.5)
Fourth quartile, high	48 109 (45.3)	20 524 (47.3)	15 479 (43.7)	10 109 (44.3)	1997 (44.3)
Unknown	1397 (1.3)	559 (1.3)	504 (1.4)	309 (1.3)	54 (1.2)
Marital status					
Married	49 355 (46.5)	19 500 (44.9)	17 219 (48.6)	10 581 (46.4)	2055 (45.6)
Separated or divorced	9670 (9.1)	4099 (9.4)	3198 (9.0)	1958 (8.6)	415 (9.2)
Widowed	6758 (6.4)	3694 (8.5)	1742 (4.9)	1123 (4.9)	199 (4.4)
All other	40 395 (38.0)	16 132 (37.2)	13 263 (37.4)	9163 (40.1)	1837 (40.8)
Moderate to vigorous physical activity, min/wk	225.9±0.8	238.3±1.2	214.4±1.3	221.0±1.6	220.1±3.9
Smoking, current	5352 (5.0)	2222 (5.1)	1584 (4.5)	1202 (5.3)	344 (7.6)
Alcohol consumption, ≥20 g/d	9114 (8.6)	4388 (10.1)	2615 (7.4)	1767 (7.7)	344 (7.6)
Obese, BMI ≥30 kg/m^2	13 683 (12.9)	5343 (12.3)	4369 (12.3)	3181 (13.9)	8790 (17.5)
Hypertension	16 196 (15.3)	7849 (18.1)	4545 (12.8)	3130 (13.7)	672 (14.9)
Daily aspirin use	6904 (6.5)	3576 (8.2)	1821 (5.1)	1222 (5.4)	285 (6.3)
Daily antihypertensive medication use	14 432 (13.6)	7183 (16.5)	3915 (11.0)	2730 (12.0)	604 (13.4)
Daily multivitamin use	38 307 (36.1)	17 723 (40.8)	11 485 (32.4)	7515 (32.9)	1584 (35.2)
CVS family history§	50 805 (47.9)	22 417 (51.6)	15 956 (45.1)	10 346 (45.3)	2086 (46.3)
Menopausal status and menopausal HT use					
Premenopausal	43 404 (40.9)	13 143 (30.3)	17 130 (48.4)	10 978 (48.1)	2151 (47.8)
Perimenopausal or postmenopausal, no HT use	12 469 (11.7)	6349 (14.6)	3398 (9.6)	2301 (10.1)	421 (9.3)

(*Continued*)

Table 1. Continued

Characteristic	Total	Rare/Never	>Rare/Never to <1 Serving Per wk	≥1 Serving Per wk to <1 Serving Per d	≥1 Serving Per d
Perimenopausal or postmenopausal, past HT use	7899 (7.4)	4129 (9.5)	2151 (6.1)	1359 (6.0)	260 (5.8)
Perimenopausal or postmenopausal, current HT use, estrogen	13 375 (12.6)	6620 (15.2)	3864 (10.9)	2399 (10.5)	492 (10.9)
Perimenopausal or postmenopausal, current HT use, estrogen, and progesterone	15 063 (14.2)	7203 (16.6)	4503 (12.7)	2832 (12.4)	525 (11.7)
Perimenopausal or postmenopausal, all other HT combinations	13 968 (13.2)	5981 (13.8)	4376 (12.4)	2956 (13.0)	655 (14.5)
Oral contraceptive use, past and current	70 188 (66.1)	25 715 (61.5)	24 968 (70.5)	16 235 (71.1)	3270 (72.6)

BMI indicates body mass index; CTS, California Teachers Study; CVD, cardiovascular disease; HT, hormone therapy; and SSB, sugar-sweetened beverage.
*Values are expressed as mean±SEM or number (percentage).
†1 serving of caloric soft drink is 12 fluid ounces, 1 serving of sweetened bottled water or tea, or fruit drink is 8 fluid ounces.
‡Education was obtained after baseline, during fourth mail-in questionnaire follow-up (2005–2006).
§Cardiovascular disease family history includes first-degree relatives' (parent, sibling, offspring) heart attack/myocardial infarction and stroke.

are provided in Table S4. Beverage-specific associations for MI, revascularization, and stroke are presented in Table S5.

Our sensitivity analysis addressing SSB intake in cups per day showed findings similar to those of the main analysis. The HR of CVD for participants consuming up to 1.5 cups per day was 1.19 (95% CI, 1.07–1.34] and for >1.5 cups per day was 1.22 (95% CI, 1.09–1.37] (*P* trend<0.0001) compared with rare/never consumers of SSBs (model 3, Table S4). The risk of MI and the risk of stroke were 25% (HR, 1.25; 95% CI, 1.02–1.54 [*P* trend=0.063]) and 26% (HR, 1.26; 95% CI, 1.09–1.46 [*P* trend=0.001]) higher, respectively, among women who consumed >1.5 cups per day of SSBs versus rare/never consumers. Revascularization risk was equivalent to the main analysis results (model 3, Table S6). Sensitivity analyses excluding events that occurred during the first 2 and 4 years of follow-up did not alter the association found between SSB consumption and risk of CVD (Tables S7 and S8).

DISCUSSION

We observed a significant positive association between daily consumption of SSBs and risk of CVD event among adult women over a period of 20 years. We also found a higher risk of revascularization and stroke with daily consumption of SSBs. We observed a significant, positive association between caloric soft drink and fruit drink consumption and risk of CVD.

The positive association found between daily SSB intake and risk of CVD is consistent with results from another longitudinal analysis of SSB consumption and CHD in an all-female cohort,[23] where Fung et al[23] observed a 23% higher risk (relative risk [RR], 1.23; 95% CI, 1.06–1.43) in CHD among middle-aged women who consumed 1 or 2 SSB servings per day. We did not observe a statistically significant association between SSB consumption and incident MI when using a semiquantitative exposure categorization, as Fung et al[23] did, but we did see an association when SSBs were classified by cups per day (HR, 1.25; 95% CI, 1.02–1.54) comparing >1.5 cups per day versus rare/never. This SSB intake is equal to consuming >1 can of 12 fluid ounces of caloric soft drink or .75 of a 16 fluid ounce bottle of sweetened water and/or tea or fruit drink per day. Our findings for fruit drinks and soft drinks are also in line with findings from the NHS (Nurses' Health Study), where researchers observed a positive association with a 2-serving increase per day in fruit drinks and cola-type carbonated beverages and incident CHD.[23]

Our documentation of a 26% greater risk (HR, 1.26; 95% CI, 1.04–1.54) of a revascularization procedure in women who consumed ≥1 serving per day of SSB versus those who rarely/never consumed SSBs, with identical risk by cups per day SSB classification, is a novel contribution. Since coronary artery bypass grafting and percutaneous coronary intervention/percutaneous transluminal coronary angioplasty revascularization intervention procedures are representative of a degree of coronary artery disease that leads to MI, we consider them in the context of our MI findings. Our HR findings for revascularization and MI risk with SSB intake as cups per day were nearly identical. Nonetheless, further research on SSB intake and incident revascularization is warranted.

Data on the association between SSB consumption and stroke are rare. The associations we observed in our primary analysis (semiquantitative categorization) and our sensitivity analysis (cups per day) are similar to those of Bernstein et al[25] using data from the NHS. In the NHS, women who consumed ≥1 serving per day of sugar-sweetened soda,

Table 2. CVD* Risk According to SSB Consumption in Semiquantitative Frequency Categories

	SSB Consumption†				
	Rare/Never	>Rare/Never to <1 Serving Per wk	≥1 Serving Per wk to <1 Serving Per d	≥1 Serving Per d	*P* Trend
CVD					
No. of cases	4648	2382	1494	324	
Rate per 10 000 person-y	64.8	38.7	37.8	41.4	
Age-adjusted HR (95% CI)	1.0	0.99 (0.95–1.05)	1.02 (0.96–1.08)	1.26 (1.13–1.42)	0.0006
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.00 (0.95–1.06)	1.01 (0.95–1.07)	1.18 (1.05–1.32)	0.019
Model 2	1.0	1.00 (0.95–1.05)	1.00 (0.94–1.07)	1.16 (1.03–1.31)	0.052
Model 3	1.0	1.01 (0.96–1.07)	1.02 (0.96–1.09)	1.19 (1.06–1.34)	0.016
MI‡					
No. of cases	1441	681	460	95	
Rate per 10 000 person-y	19.6	10.9	11.5	12.0	
Age-adjusted HR (95% CI)	1.0	0.95 (0.87–1.04)	1.06 (0.95–1.18)	1.26 (1.02–1.55)	0.022
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	0.96 (0.87–1.05)	1.05 (0.94–1.16)	1.14 (0.92–1.40)	0.148
Model 2	1.0	0.95 (0.87–1.06)	1.04 (0.93–1.16)	1.15 (0.92–1.43)	0.154
Model 3	1.0	0.98 (0.89–1.07)	1.07 (0.96–1.19)	1.18 (0.95–1.47)	0.060
Revascularization§					
No. of cases	1468	798	505	118	
Rate per 10 000 person-y	20.0	12.8	12.6	14.9	
Age-adjusted HR (95% CI)	1.0	1.01 (0.93–1.10)	1.03 (0.93–1.15)	1.35 (1.12–1.64)	0.006
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.03 (0.94–1.12)	1.03 (0.93–1.15)	1.24 (1.02–1.50)	0.044
Model 2	1.0	1.04 (0.95–1.14)	1.02 (0.92–1.14)	1.23 (1.01–1.50)	0.082
Model 3	1.0	1.05 (0.96–1.15)	1.04 (0.94–1.16)	1.26 (1.04–1.54)	0.037
Stroke‖					
No. of cases	2787	1415	867	189	
Rate per 10 000 person-y	38.2	22.7	21.7	23.9	
Age-adjusted HR (95% CI)	1.0	1.01 (0.94–1.08)	1.01 (0.93–1.09)	1.26 (1.09–1.46)	0.017
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.02 (0.95–1.08)	1.00 (0.93–1.08)	1.19 (1.03–1.39)	0.076
Model 2	1.0	1.00 (0.94–1.07)	0.99 (0.92–1.08)	1.18 (1.01–1.37)	0.146
Model 3	1.0	1.01 (0.95–1.08)	1.01 (0.93–1.09)	1.21 (1.04–1.41)	0.056

Model 1 adjusted for age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, multivitamin use, menopausal status, menopausal hormone therapy use, oral contraceptive use, and history of hypertension. Model 2 adjusted for variables in model 1 and body mass index, total energy intake, and fruit and vegetable intake. Model 3 adjusted for age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease (CVD) family history, physical activity, aspirin use, menopausal status, menopausal hormone therapy use, history of hypertension, body mass index, and total energy intake. HR indicates hazard ratio; and SSB, sugar-sweetened beverage.

*Incident CVD event was defined as the first noted myocardial infarction (MI), revascularization (including coronary artery bypass grafting or percutaneous transluminal coronary angioplasty) or stroke, total person-time 1 807 182 years.

†One serving of caloric soft drink is 12 fluid ounces and 1 serving of sweetened bottled water or tea or fruit drink is 8 fluid ounces.

‡Total person-time 1 843 233 years.

§Revascularization includes coronary artery bypass grafting and percutaneous transluminal coronary angioplasty, total person-time 1 835 429 years.

‖Total person-time 1 831 462 years.

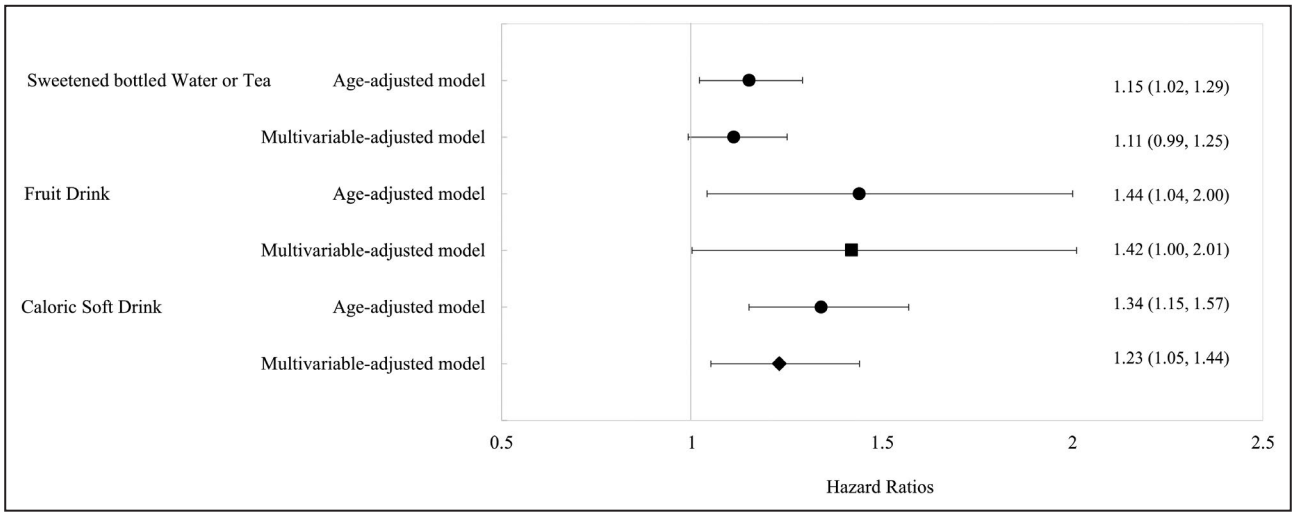

Figure 2. Association of specific sugar-sweetened beverage consumption and incident cardiovascular disease (CVD). Hazard ratios comparing ≥1 sugar-sweetened beverage serving per day vs rare/never (reference) categories. Multivariable-adjusted model adjusted age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, CVD family history, physical activity, aspirin use, menopausal status, menopausal hormone therapy use, history of hypertension, body mass index, total energy intake, and consumption of sugar-sweetened bottled waters or teas, fruit drinks, and caloric soft drinks (other than the main exposure, depending on model). ■*P* for trend statistical significance at $P<0.05$. ♦*P* for trend statistical significance at $P<0.001$.

had a 19% greater risk of total stroke (HR, 1.19; 95% CI, 1.05–1.48) in comparison to women who reported no SSB intake.[25] Additionally, in a Swedish cohort of adult men and women followed for 10.3 years, Larsson et al[26] observed a 19% greater risk of total stroke (RR, 1.19; 95% CI, 1.04–1.36) among adults consuming the highest (>2 servings per day [200 mL per serving)] versus the lowest (0.1 to <0.5 servings per day) intake of SSBs. In contrast to our findings, the association in their female-only model was statistically insignificant (RR, 1.14; 95% CI, 0.92–1.41). The findings from a cohort of Japanese women followed for 18 years comparing almost every day versus rare/never consumers reported an HR of 1.21 (95% CI, 0.88–1.68).[27]

Our results are partially consistent with recently published meta-analyses assessing the relationship between SSB consumption and CVD risk.[22,41] Xi et al[22] pooled data from 4 prospective cohort studies including adult men and women and found a positive association between intake of SSBs and risk of CHD where those in the highest SSB consumption group had a 16% greater risk (RR, 1.16; 95% CI, 1.06–1.27]) of CHD than those in the lowest SSB consumption group.[22] The CHD definition included other end points including MI. The same meta-analysis found a marginal association between the highest SSB intake and risk of total stroke (RR, 1.10; 95% CI, 1.00–1.20) compared with the lowest SSB intake, with no significant association between SSB consumption and the risk of stroke in dose-response analysis (summary RR, 1.06; 95% CI, 0.97–1.15 [*P* trend >0.05]). Narain et al[41] reported that a high SSB intake was associated with a 19% greater risk of MI (RR, 1.19; 95% CI, 1.09–1.31) compared with low SSB intake, yet found no effect on risk of stroke (RR, 1.10; 95% CI, 0.97–1.25).[41] When stratified by sex, SSB consumption was only highly associated with ischemic stroke in women (RR, 1.33; 95% CI, 1.07–1.66).[41]

As previously mentioned, there are several plausible biological mechanisms by which SSBs might impact CVD risk, including an increase in bloodstream concentrations of both glucose and insulin inducing a high glycemic load,[29] appetite stimulation, and weight gain, contributing to impaired glucose tolerance and insulin resistance.[30] Furthermore, this chain of events alters lipid metabolism and promotes synthesis of triglycerides, contributing to endothelial dysfunction and β-cell stress[30–34] and influencing metabolic[35] and CVD risk.[31,32,36] It is also possible that SSB consumption may serve as an indicator of a suboptimal diet and unfavorable lifestyle. Individuals who frequently consume SSBs are more likely to follow suboptimal diets.[42–44] In our sample, we observed unfavorable dietary intake and behaviors among women who frequently consumed SSBs and adjusted for these lifestyle factors.

Study Strengths

Our study has several strengths including a large sample size, extensive follow-up time, and prospective data collection on SSBs, diet, and lifestyle characteristics. Our sensitivity analysis addressed the possibility of reverse causality, and our analyses adjusted for potential confounders. Additional study strengths include our ability to annually link with statewide hospitalization

and procedure records, which allowed for well-defined and characterized end points, minimizing participant burden, and reducing bias caused by loss to follow-up.

Study Limitations

Limitations of this study include being restricted to a single dietary assessment in which SSB consumption was measured, and we recognize the possibility of random measurement error. Additionally, assessment of other beverages, such as artificially sweetened beverages including low-calorie sweet carbonated beverages (diet soft drinks) and other diet carbonated beverages, as well as sweetened hot beverages, were not included in the FFQ version used and could not be evaluated. Although dietary data were collected prospectively, social desirability bias cannot be disregarded, nor the potential for residual and unmeasured confounding. In addition, we cannot rule out change in beverage consumption intake over time, which we could not measure. We also acknowledge that the proportion of daily SSB consumption in our study population is small and relatively sparse when compared with the other SSB categories, leading to possible inflated measures of association as an implication of our findings. SSB consumption trends among US adults has declined in recent years.[45,46] Thus, considering our findings, we would expect an attenuation in the magnitude of the measure of association with current consumption shifts. In addition, our analyses could have benefited from further adjustment of cardiometabolic risk factors such as measured systolic and diastolic blood pressure and blood assay values for total and high-density lipoprotein cholesterol and particularly triglycerides, which are shown to be an independent risk factor for CVD in women.[47,48]

CONCLUSIONS

We found that daily consumption of at least 1 serving of a SSB is associated with a higher risk of CVD, revascularization, and stroke in women after accounting for CVD risk factors, suboptimal lifestyle behaviors, and dietary intake. Daily caloric soft drink consumption was also found to be associated with a higher risk of first CVD event. In sensitivity analysis, a higher risk of MI was observed among women with a daily intake of >1.5 cups of SSBs. Our results expand the literature on unfavorable effects of SSB intake, highlighting the importance of efforts to reduce SSB intake and changes to support healthier beverage consumption.

ARTICLE INFORMATION

Received October 10, 2019; accepted March 2, 2020.

Affiliations

From the Department of Family Medicine and Public Health, School of Medicine, University of California San Diego, La Jolla, CA (L.S.P., M.E.M., M.R.G.A., D.D.S., C.A.M.A.); School of Public Health, San Diego State University, San Diego, CA (L.S.P., H.L., G.A.T.); Division of Health Analytics, Department of Computational and Quantitative Medicine, City of Hope, Duarte, CA (J.V.L.); Moores Cancer Center, University of California San Diego, La Jolla, CA (M.E.M.); College of Health Solutions, Arizona State University, Phoenix, AZ (D.D.S.).

Acknowledgments

The authors would like to thank the participants and staff of the CTS for their continuous involvement and valuable contributions. We also acknowledge the workforce of the California's Office of Statewide Health Planning and Development and California Cancer Registry. The authors would like to thank the CTS Steering Committee that is responsible for the formation and maintenance of the study within which this research was conducted. A full list of CTS team members is available at https://www.calteachersstudy.org/team. The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Cancer Institute or the National Institutes of Health. The opinions, findings, and conclusions expressed herein are those of the author and do not necessarily reflect the official views of the State of California, Department of Public Health, National Cancer Institute, National Institutes of Health, Centers for Disease Control and Prevention or their Contractors and Subcontractors, or the Regents of the University of California or any of its programs.

Sources of Funding

The CTS and the research reported in this article were supported by the National Cancer Institute of the National Institutes of Health under award numbers U01-CA199277, P30-CA033572, P30-CA023100, UM1-CA164917, and R01-CA077398. Additionally, research described in this article was supported by grant CA023100-29 from the University of California San Diego Moores Cancer Center (principal investigator: Maria Elena Martinez), and grant T32 HL079891-11 from the National Heart, Lung, and Blood Institute (principal investigator: Matthew Allison).

Disclosures

None.

Supplementary Materials

Tables S1–S8

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Supplemental Material

Table S1. Specific Sugar-Sweetened Beverage Consumption by Semi-Quantitative Frequency Categories*.

Categories	Sweetened bottled water or tea	Fruit drinks	Caloric soft drinks
Rare/never	61,716 (58.1)	95,794 (90.2)	70,386 (66.3)
>rare/never to <1 serving per week	20,708 (19.5)	6,089 (5.7)	17,017 (16.0)
≥1 serving per week to <1 serving per day	19,143 (18.0)	3,829 (3.6)	15,468 (14.5)
≥1 serving per day	4,611 (4.3)	466 (0.4)	3,307 (3.1)

*N (percentage).

Table S2. Comprehensive Baseline Characteristics of California Teachers Study Participants According to Sugar-Sweetened Beverage Consumption Categories[*] [†]

Characteristic	Total	Rare/never	>rare/never to <1 serving per week	≥1 serving per week to <1 serving per day	≥1 serving per day
N	106,178	43,425	35,422	22,825	4,506
SSB intake, fl oz/day	2.6 ± 0.0	0 ± 0.0	2.6 ± 0.0	5.5 ± 0.0	13.5 ± 0.1
Dietary Intake					
Energy, kcal/day	1902.1 ± 2.1	1,753.2 ± 3.2	1,949.9 ± 3.6	2,042.6 ± 4.5	2,248.6 ± 10.1
Carbohydrate, g/day	255.1 ± 0.3	251.4 ± 0.2	253.1 ± 0.2	259.8 ± 0.2	282.3 ± 0.5
Protein, g/day	77.2 ± 0.1	80.1 ± 0.1	76.7 ± 0.1	74.2 ± 0.1	67.7 ± 0.2
Total Fat, g/day	59.9 ± 0.1	59.6 ± 0.1	61.4 ± 0.1	59.6 ± 0.1	53.6 ± 0.2
Fruit & Vegetables, g/day	321.2 ± 0.6	361.2 ± 0.8	301.4 ± 0.9	286.7 ± 1.2	265.0 ± 2.6
Age, y	52.1 ± 0.0	56.0 ± 0.1	49.5 ± 0.1	49.3 ± 0.1	49.0 ± 0.2
Race/ethnicity, %					
Asian/Pacific Islander	3,707 (3.5)	1,156 (2.7)	1,593 (4.5)	842 (3.7)	116 (2.6)
African-American	2,602 (2.5)	683 (1.6)	1,098 (3.1)	700 (3.1)	121 (2.7)
Hispanic or Latino	4,364 (4.0)	1,293 (3.0)	1,758 (5.0)	1,118 (4.9)	195 (4.3)
Native American	786 (0.7)	337 (0.8)	263 (0.7)	157 (0.7)	29 (0.6)
White	92,654 (87.3)	39,208 (90.3)	29,989 (84.7)	19,500 (85.4)	3,957 (87.8)
Other or Mixed	1,272 (1.2)	423 (1.0)	473 (1.3)	316 (1.4)	60 (1.3)
Unknown	793 (0.8)	325 (0.8)	248 (0.7)	192 (0.8)	28 (0.6)
Education, % ǂ					
Academic doctorate	1,944 (1.8)	854 (2.0)	598 (1.7)	388 (1.7)	104 (2.3)
Professional doctorate	557 (0.5)	225 (0.5)	172 (0.5)	134 (0.6)	26 (0.6)
Master's degree	27,802 (26.2)	11,130 (25.6)	9,444 (26.7)	6,018 (26.7)	1,210 (26.9)
Bachelor's degree	23,654 (22.3)	9,677 (22.3)	8,269 (23.3)	4,804 (21.1)	904 (20.1)
Associate's degree	384 (0.4)	130 (0.3)	138 (0.4)	98 (0.4)	18 (0.4)
Technical school/certificate/High school	31 (0.03)	11 (0.0)	8 (0.0)	8 (0.0)	4 (0.1)
Less than High school	1 (0)	0 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)
Unknown	51,805 (48.8)	21,398 (49.3)	16,792 (47.4)	11,375 (49.8)	2,240 (49.7)
Occupation, %					
Teacher, single grade Pre-K to High school	53,350 (50.3)	18,557 (42.7)	19,426 (54.8)	12,770 (56.0)	2,597 (57.6)
Teacher, other	7,776 (7.3)	3,009 (6.9)	2,635 (7.4)	1,746 (7.7)	386 (8.6)
Multiple	649 (0.6)	208 (0.5)	258 (0.7)	152 (0.7)	31 (0.7)
Pupil Services	3,235 (3.1)	1,213 (2.8)	1,155 (3.3)	723 (3.2)	144 (3.2)
Administration	3,834 (3.6)	1,401 (3.2)	1,297 (3.7)	926 (4.1)	210 (4.7)
Teacher, Pre-K/Elem/Other or JrH/Hi/Other	814 (0.8)	280 (0.6)	297 (0.8)	192 (0.8)	45 (1.0)
Pupil Services/Administration or Pupil Services/Administration/Teacher combination	1,102 (1.0)	415 (1.0)	390 (1.1)	250 (1.1)	47 (1.0)
Unknown	35,418 (33.4)	18,342 (42.2)	9,964 (28.1)	6,066 (26.6)	1,046 (23.2)
Socioeconomic status, %					
1st quartile, low	4,393 (4.1)	1,627 (3.8)	1,565 (4.4)	1,012 (4.4)	189 (4.2)
2nd quartile, low-medium	17,953 (16.9)	7,005 (16.1)	6,147 (17.4)	4,046 (17.7)	755 (16.8)
3rd quartile, medium-high	34,326 (32.3)	13,724 (31.6)	11,737 (33.1)	7,354 (32.2)	1,511 (33.5)
4th quartile, high	48,109 (45.3)	20,524 (47.3)	15,479 (43.7)	10,109 (44.3)	1,997 (44.3)
Unknown	1,397 (1.3)	545 (1.3)	494 (1.4)	304 (1.3)	54 (1.2)
Marital status, %					
Married	49,355 (46.5)	19,500 (44.9)	17,219 (48.6)	10,581 (46.4)	2,055 (45.6)
Divorced	8,856 (8.3)	3,810 (8.8)	2,902 (8.2)	1,764 (7.7)	380 (8.4)
Separated	814 (0.8)	289 (0.7)	296 (0.8)	194 (0.9)	35 (0.8)
Widowed	6,758 (6.4)	3,694 (8.5)	1,742 (4.9)	1,123 (4.9)	199 (4.4)
Never married	5,273 (5.0)	2,069 (4.8)	1,776 (5.0)	1,147 (5.0)	281 (6.2)
Unknown	35,122 (33.1)	14,063 (32.3)	11,487 (32.4)	8,016 (35.1)	1,556 (34.5)
MVPA, minutes/week	225.9 ± 0.8	238.3 ± 1.2	214.4 ± 1.3	221.0 ± 1.6	220.1 ± 3.7
Smoking, %					
Never	70,258 (66.2)	27,137 (62.5)	24,695 (69.7)	15,517 (68.0)	2,909 (64.6)
Former	30,455 (28.7)	14,012 (32.3)	9,114 (25.7)	6,081 (26.6)	1,248 (27.7)
Current	5,352 (5.0)	2,222 (5.1)	1,584 (4.5)	1,202 (5.3)	344 (7.6)
Unknown	113 (0.1)	54 (0.1)	29 (0.1)	25 (0.1)	5 (0.1)
Number of cigarettes per day, §	12.6 ± 0.1	13.3 ± 0.1	11.6 ± 0.1	12.0 ± 0.1	14.4 ± 0.3
Alcohol consumption, g/day, %					
None	34,365 (32.4)	14,196 (32.7)	11,124 (31.4)	7,353 (32.2)	1,692 (37.6)
<20	62,699 (59.1)	24,841 (57.2)	21,683 (61.2)	13,705 (60.0)	2,470 (54.8)
≥20	9,114 (8.6)	4,388 (10.1)	2,615 (7.4)	1,767 (7.7)	344 (7.6)

Table S2. Comprehensive Baseline Characteristics of California Teachers Study Participants According to Sugar-Sweetened Beverage Consumption Categories[*] [†], Continued

Characteristic		Rare/never	>rare/never to <1 serving per week	≥1 serving per week to <1 serving per day	≥1 serving per day
Body mass index, kg/m^2, %					
Underweight (<18.5)	2,718 (2.6)	1,074 (2.7)	948 (2.7)	570 (2.5)	126 (2.8)
Normal (18.5-24.9)	60,687 (57.2)	24,529 (56.5)	20,856 (58.8)	12,943 (56.7)	2,359 (52.4)
Overweight (25-29.9)	25,382 (23.9)	10,656 (24.5)	8,185 (23.1)	5,443 (23.9)	1,098 (24.4)
Obese (≥30)	13,683 (12.9)	5,343 (12.3)	4,369 (12.3)	3,181 (13.9)	8790 (17.5)
Unknown	3,708 (3.5)	1,823 (4.2)	1,064 (3.0)	688 (3.0)	133 (3.0)
Hypertension, %	16,196 (15.3)	7,849 (18.1)	4,545 (12.8)	3,130 (13.7)	672 (14.9)
Aspirin use, %					
Daily	6,904 (6.5)	3,576 (8.2)	1,821 (5.1)	1,222 (5.4)	285 (6.3)
Up to 6 times per week	15,374 (14.5)	6,115 (14.1)	5,163 (14.6)	3,381 (14.8)	715 (15.9)
Regular use, unknown frequency	599 (0.6)	251 (0.6)	181 (0.5)	143 (0.6)	24 (0.5)
Not regularly taken	81,867 (77.0)	32,827 (75.6)	27,824 (78.6)	17,790 (78.6)	3,426 (76.0)
Unknown use	1,434 (1.4)	656 (1.5)	433 (1.2)	289 (1.3)	56 (1.2)
Antihypertensive medication use, at least 1 medication, %					
Daily	14,432 (13.6)	7,183 (16.5)	3,915 (11.0)	2,730 (12.0)	604 (13.4)
Up to 6 times per week	1,425 (1.3)	621 (1.4)	445 (1.3)	286 (1.3)	73 (1.6)
Regular use, unknown frequency	1,112 (1.1)	524 (1.2)	326 (0.9)	219 (1.0)	43 (1.0)
Not regularly taken	87,776 (82.7)	34,441 (79.3)	30,304 (85.6)	19,301 (84.6)	3,730 (82.8)
Unknown use	1,433 (1.4)	656 (1.5)	432 (1.2)	289 (1.3)	56 (1.2)
Multivitamin use, %					
Daily	38,307 (36.1)	17,723 (40.8)	11,485 (32.4)	7,515 (32.9)	1,584 (35.2)
Up to 6 times per week	18,254 (17.2)	6,215 (14.3)	7,126 (20.1)	4,221 (18.5)	692 (15.4)
Never	16,884 (15.9)	6,906 (15.9)	5,606 (15.8)	3,635 (15.9)	737 (16.4)
Regular use, unknown frequency	32,733 (30.8)	12,581 (29.0)	11,205 (31.6)	7,454 (32.7)	1,493 (33.1)
Myocardial infarction family history, %, ‖	38,384 (36.2)	16,909 (38.9)	11,990 (33.9)	7,888 (34.6)	1,597 (35.4)
Stroke family history, %, #	23,774 (22.4)	10,775 (24.8)	7,369 (20.8)	4,680 (20.5)	950 (21.1)
Cardiovascular disease family history, %,[**]	50,805 (47.9)	22,417 (51.6)	15,956 (45.1)	10,346 (45.3)	2,086 (46.3)
Menopausal status and menopausal HT use, %					
Premenopausal	43,404 (40.9)	13,143 (30.3)	17,130 (48.4)	10,978 (48.1)	2,151 (47.8)
Peri- or postmenopausal, no HT use	12,469 (11.7)	6,349 (14.6)	3,398 (9.6)	2,301 (10.1)	421 (9.3)
Peri- or postmenopausal, past HT use	7,899 (7.4)	4,129 (9.5)	2,151 (6.1)	1,359 (6.0)	260 (5.8)
Peri- or postmenopausal, current HT use, Estrogen	13,375 (12.6)	6,620 (15.2)	3,864 (10.9)	2,399 (10.5)	492 (10.9)
Peri- or postmenopausal, current HT, Estrogen & Progesterone	15,063 (14.2)	7,203 (16.6)	4,503 (12.7)	2,832 (12.4)	525 (11.7)
Peri- or postmenopausal, all other HT combinations	13,968 (13.2)	5,981 (13.8)	4,376 (12.4)	2,956 (13.0)	655 (14.5)
Oral contraceptive use, %					
Current	5,910 (5.6)	1,543 (3.7)	2,486 (7.0)	1,556 (6.8)	325 (7.2)
Past	64,278 (60.5)	24,172 (57.8)	22,482 (63.5)	14,679 (64.3)	2,945 (65.4)
Never	32,164 (30.3)	16,043 (38.4)	9,298 (26.3)	5,760 (25.2)	1,063 (24.0)
Unknown if current or past	3,826 (3.6)	1,667 (3.8)	1,156 (3.3)	830 (3.6)	173 (3.8)

*Values are means ± standard error mean or N (percentage). † 1 serving of caloric soft drink is 12 fluid ounces, 1 serving of sweetened bottled water/tea or fruit drink is 8 fluid ounces. ǂ Education was obtained after baseline, during fourth mail-in questionnaire follow-up (2005-2006). § Current and past smokers only. ‖ Myocardial infarction family history includes first-degree relatives' (parent, sibling, offspring) history of heart attack/myocardial infarction. # Stroke family history includes first-degree relatives' (parent, sibling, offspring) history of stroke. ** Cardiovascular disease family history includes first-degree relatives' (parent, sibling, offspring) history of heart attack/myocardial infarction and stroke. Elem indicates Elementary; fl oz, fluid ounces; g/day, grams per day; Hi, High School; HT, hormone therapy; JrH, Junior High School; kcal/day, kilocalories per day; MVPA, moderate-vigorous physical activity; Pre-K, pre-kindergarten; SSB, sugar-sweetened beverage; y, years.

Table S3. Comprehensive Cardiovascular Disease* Risk According to Sugar-Sweetened Beverage Consumption in Semi-Quantitative Frequency Categories.

	Sugar-Sweetened Beverage Consumption †				
	Rare/ never	>rare/never to <1 serving per week	≥1 serving per week to <1 serving per day	≥1 serving per day	P trend
Cardiovascular Disease					
No. of cases	4,648	2,382	1,494	324	
Rate per 10,000 person-year	64.8	38.7	37.8	41.4	
Age-adjusted HR (95% CI)	1.0	0.99 (0.95, 1.05)	1.02 (0.96, 1.08)	1.26 (1.13, 1.42)	0.0006
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.00 (0.95, 1.06)	1.01 (0.95, 1.07)	1.18 (1.05, 1.32)	0.019
Model 2	1.0	1.00 (0.95, 1.05)	1.00 (0.94, 1.07)	1.16 (1.03, 1.31)	0.052
Model 3	1.0	1.01 (0.96, 1.07)	1.02 (0.96, 1.09)	1.19 (1.06, 1.34)	0.016
Model 4	1.0	0.99 (0.94, 1.05)	1.00 (0.94, 1.06)	1.15 (1.03, 1.29)	0.068
Model 5	1.0	0.99 (0.94, 1.04)	1.00 (0.94, 1.07)	1.18 (1.05, 1.33)	0.029
Myocardial infarction ǂ					
No. of cases	1,441	681	460	95	
Rate per 10,000 person-year	19.6	10.9	11.5	12.0	
Age-adjusted HR (95% CI)	1.0	0.95 (0.87, 1.04)	1.06 (0.95, 1.18)	1.26 (1.02, 1.55)	0.022
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	0.96 (0.87, 1.05)	1.05 (0.94, 1.16)	1.14 (0.92, 1.40)	0.148
Model 2	1.0	0.95 (0.87, 1.06)	1.04 (0.93, 1.16)	1.15 (0.92, 1.43)	0.154
Model 3	1.0	0.98 (0.89, 1.07)	1.07 (0.96, 1.19)	1.18 (0.95, 1.47)	0.060
Model 4	1.0	0.94 (0.86, 1.04)	1.02 (0.92, 1.14)	1.10 (0.89, 1.36)	0.297
Model 5	1.0	0.95 (0.86, 1.05)	1.03 (0.92, 1.16)	1.17 (0.94, 1.45)	0.140
Revascularization §					
No. of cases	1,468	798	505	118	
Rate per 10,000 person-year	20.0	12.8	12.6	14.9	
Age-adjusted HR (95% CI)	1.0	1.01 (0.93, 1.10)	1.03 (0.93, 1.15)	1.35 (1.12, 1.64)	0.006
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.03 (0.94, 1.12)	1.03 (0.93, 1.15)	1.24 (1.02, 1.50)	0.044
Model 2	1.0	1.04 (0.95, 1.14)	1.02 (0.92, 1.14)	1.23 (1.01, 1.50)	0.082
Model 3	1.0	1.05 (0.96, 1.15)	1.04 (0.94, 1.16)	1.26 (1.04, 1.54)	0.037
Model 4	1.0	1.02 (0.94, 1.12)	1.02 (0.92, 1.14)	1.23 (1.01, 1.49)	0.069
Model 5	1.0	1.04 (0.95, 1.14)	1.03 (0.92, 1.15)	1.27 (1.04, 1.55)	0.041
Stroke ‖					
No. of cases	2,787	1,415	867	189	
Rate per 10,000 person-year	38.2	22.7	21.7	23.9	
Age-adjusted HR (95% CI)	1.0	1.01 (0.94, 1.08)	1.01 (0.93, 1.09)	1.26 (1.09, 1.46)	0.017
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.02 (0.95, 1.08)	1.00 (0.93, 1.08)	1.19 (1.03, 1.39)	0.076
Model 2	1.0	1.00 (0.94, 1.07)	0.99 (0.92, 1.08)	1.18 (1.01, 1.37)	0.146
Model 3	1.0	1.01 (0.95, 1.08)	1.01 (0.93, 1.09)	1.21 (1.04, 1.41)	0.056
Model 4	1.0	1.00 (0.94, 1.07)	0.99 (0.91, 1.07)	1.16 (1.00, 1.35)	0.217
Model 5	1.0	0.99 (0.92, 1.06)	0.99 (0.91, 1.08)	1.19 (1.02, 1.39)	0.118

*Incident cardiovascular disease event was defined as the first noted myocardial infarction, revascularization (including coronary artery bypass grafting or percutaneous transluminal coronary angioplasty) or stroke, total person-time 1,807,182 years. †1 serving of caloric soft drink is 12 fluid ounces, 1 serving of sweetened bottled water or tea, or fruit drink is 8 fluid ounces. ǂ Total person-time

1,843,233 years. § Revascularization includes coronary artery bypass grafting and percutaneous transluminal coronary angioplasty, total person-time 1,835,429 years.

‖ Total person-time 1,831,462 years. HR indicates hazard ratio; CI, confidence interval.

Model 1 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, multivitamin use, menopausal status, menopausal hormone therapy use, oral contraceptive use, and history of hypertension.

Model 2 adjusted for: variables in Model 1 and body mass index, total energy intake, and fruit and vegetable intake.

Model 3 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, menopausal status, menopausal hormone therapy use, history of hypertension, body mass index, and total energy intake.

Model 4 adjusted for: variables in Model 2 with the exception body mass index. This model assesses the impact of body mass index adjustment.

Model 5 adjusted for: variables in Model 3 and red meat, processed meat, eggs, fish, legumes, and whole wheat bread intakes.

Table S4. Cardiovascular Disease* Risk According to Specific Sugar-Sweetened Beverage Consumption.

Cardiovascular Disease	Sugar-Sweetened Beverage Consumption †				
	Rare/never	>rare/never to <1 serving per week	≥1 serving per week to <1 serving per day	≥1 serving per day	P trend
Sweetened bottled water or tea					
No. of cases	6,224	1,201	1,119	304	
Rate per 10,000 person-years	60.7	33.0	33.3	37.6	
Age-adjusted HR (95% CI)	1.0	0.93 (0.87, 0.99)	0.96 (0.90, 1.03)	1.15 (1.02, 1.29)	0.129
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	0.95 (0.89, 1.01)	0.97 (0.90, 1.03)	1.10 (0.98, 1.23)	0.379
Model 2	1.0	0.95 (0.89, 1.01)	0.96 (0.89, 1.02)	1.10 (0.97, 1.24)	0.456
Model 3	1.0	0.94 (0.88, 1.01)	0.96 (0.89, 1.02)	1.11 (0.99, 1.25)	0.340
Fruit drinks					
No. of cases	8,268	347	197	36	
Rate per 10,000 person-years	50.9	32.4	29.5	44.6	
Age-adjusted HR (95% CI)	1.0	1.13 (1.01, 1.27)	1.05 (0.91, 1.21)	1.44 (1.04, 2.00)	0.015
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.12 (1.01, 1.25)	1.04 (0.90, 1.20)	1.38 (0.99, 1.91)	0.029
Model 2	1.0	1.12 (1.00, 1.26)	1.04 (0.89, 1.20)	1.40 (0.99, 1.98)	0.039
Model 3	1.0	1.14 (1.02, 1.27)	1.05 (0.91, 1.22)	1.42 (1.00, 2.01)	0.021
Caloric soft drinks					
No. of cases	6,428	1,291	960	169	
Rate per 10,000 person-years	54.2	44.1	35.6	29.0	
Age-adjusted HR (95% CI)	1.0	0.98 (0.93, 1.05)	1.09 (1.02, 1.17)	1.34 (1.15, 1.57)	<0.0001
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	0.99 (0.94, 1.06)	1.09 (1.02, 1.17)	1.25 (1.07, 1.45)	0.0004
Model 2	1.0	0.99 (0.93, 1.06)	1.09 (1.01, 1.17)	1.17 (1.00, 1.38)	0.005
Model 3	1.0	1.01 (0.95, 1.08)	1.12 (1.04, 1.20)	1.23 (1.05, 1.44)	0.0002

*Incident cardiovascular disease event was defined as the first noted myocardial infarction, revascularization (including coronary artery bypass grafting or percutaneous transluminal coronary angioplasty) or stroke, total person-time 1,807,182 years. † 1 serving of caloric soft drink is 12 fluid ounces, 1 serving of sweetened bottled water or tea, or fruit drink, is 8 fluid ounces. Models were reciprocally adjusted for the other sugar-sweetened beverage types. HR indicates hazard ratio; CI, confidence interval.

Model 1 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, multivitamin use, menopausal status, menopausal hormone therapy use, oral contraceptive use, and history of hypertension.

Model 2 adjusted for: variables in Model 1 and body mass index, total energy intake, and fruit and vegetable intake.

Model 3 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, menopausal status, menopausal hormone therapy use, history of hypertension, body mass index, and total energy intake.

Table S5. Myocardial Infarction, Revascularization, and Stroke Risk According to Specific Sugar-Sweetened Beverage Consumption in Semi-Quantitative Frequency Categories.

Cardiovascular disease†	Sugar-Sweetened Beverage Consumption*				
	Rare/ never	>rare/never to <1 serving per week	≥1 serving per week to <1 serving per day	≥1 serving per day	P trend
Myocardial infarction ǂ					
			Sweetened bottled waters/teas		
No. of cases	1946	305	337	89	
Rate per 10,000 person-years	18.5	8.3	9.9	10.9	
Age-adjusted HR (95% CI)	1.0	0.78 (0.69, 0.89)	0.97 (0.86, 1.09)	1.13 (0.91, 1.40)	0.44
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	0.80 (0.71, 0.91)	0.98 (0.86, 1.09)	1.06 (0.86, 1.31)	0.76
Model 2	1.0	0.78 (0.69, 0.89)	0.94 (0.83, 1.07)	1.05 (0.84, 1.30)	0.99
Model 3	1.0	0.78 (0.69, 0.89)	0.95 (0.84, 1.07)	1.06 (0.85, 1.32)	0.88
			Fruit drinks		
No. of cases	2493	120	58	6	
Rate per 10,000 person-year	15.0	11.1	8.6	7.3	
Age-adjusted HR (95% CI)	1.0	1.38 (1.14, 1.66)	1.07 (0.82, 1.39)	0.82 (0.37, 1.83)	0.31
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.34 (1.11, 1.62)	1.04 (0.80, 1.35)	0.80 (0.36, 1.79)	0.47
Model 2	1.0	1.36 (1.12, 1.65)	0.98 (0.74, 1.30)	0.74 (0.31, 1.77)	0.72
Model 3	1.0	1.37 (1.13, 1.66)	0.99 (0.75, 1.31)	0.74 (0.31, 1.78)	0.66
			Caloric soft drinks		
No. of cases	1960	380	289	48	
Rate per 10,000 person-years	16.2	12.8	10.6	8.2	
Age-adjusted HR (95% CI)	1.0	0.97 (0.86, 1.08)	1.11 (0.98, 1.26)	1.36 (1.02, 1.81)	0.013
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	0.97 (0.86, 1.08)	1.09 (0.96, 1.23)	1.21 (0.91, 1.62)	0.08
Model 2	1.0	0.99 (0.88, 1.11)	1.11 (0.97, 1.26)	1.18 (0.88, 1.59)	0.08
Model 3	1.0	1.00 (0.89, 1.12)	1.13 (0.99, 1.28)	1.22 (0.91, 1.64)	0.036
Revascularization §					
			Sweetened bottled waters/teas		
No. of cases	1992	388	396	113	
Rate per 10,000 person-years	19.0	10.5	11.7	13.8	
Age-adjusted HR (95% CI)	1.0	0.88 (0.79, 0.99)	1.00 (0.90, 1.12)	1.25 (1.03, 1.52)	0.040
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	0.89 (0.80, 1.00)	1.00 (0.89, 1.11)	1.18 (0.98, 1.43)	0.13
Model 2	1.0	0.90 (0.80, 1.01)	0.99 (0.88, 1.11)	1.19 (0.97, 1.45)	0.15
Model 3	1.0	0.90 (0.81, 1.01)	0.99 (0.89, 1.11)	1.20 (0.99, 1.47)	0.11
			Fruit drinks		
No. of cases	2688	130	62	9	
Rate per 10,000 person- year	16.3	12.0	9.2	11.0	
Age-adjusted HR (95% CI)	1.0	1.22 (1.02, 1.46)	0.95 (0.74, 1.23)	1.03 (0.54, 1.99)	0.68
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.23 (1.02, 1.47)	0.97 (0.75, 1.25)	1.00 (0.52, 1.92)	0.66
Model 2	1.0	1.20 (1.00, 1.45)	0.92 (0.70, 1.20)	1.09 (0.57, 2.10)	0.80
Model 3	1.0	1.21 (1.00, 1.46)	0.93 (0.71, 1.21)	1.10 (0.57, 2.12)	0.73
			Caloric soft drinks		
No. of cases	2078	433	323	55	
Rate per 10,000 person-years	17.2	14.6	11.9	9.4	
Age-adjusted HR (95% CI)	1.0	1.01 (0.91, 1.12)	1.08 (0.96, 1.21)	1.20 (0.92, 1.57)	0.09
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.04 (0.93, 1.15)	1.10 (0.98, 1.24)	1.13 (0.86, 1.48)	0.10
Model 2	1.0	1.07 (0.96, 1.20)	1.12 (0.99, 1.26)	1.05 (0.79, 1.40)	0.20
Model 3	1.0	1.08 (0.97, 1.20)	1.13 (1.00, 1.28)	1.08 (0.81, 1.43)	0.11
Stroke ‖					
			Sweetened bottled waters/teas		
No. of cases	3712	746	625	175	
Rate per 10,000 person-years	35.6	20.3	18.4	21.4	
Age-adjusted HR (95% CI)	1.0	1.01 (0.93, 1.10)	0.93 (0.85, 1.01)	1.13 (0.97, 1.32)	0.55
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.02 (0.94, 1.10)	0.92 (0.84, 1.01)	1.10 (0.95, 1.28)	0.81
Model 2	1.0	1.02 (0.94, 1.11)	0.92 (0.84, 1.00)	1.08 (0.93, 1.27)	0.98
Model 3	1.0	1.02 (0.94, 1.11)	0.92 (0.84, 1.01)	1.10 (0.94, 1.29)	0.83

Table S5. Myocardial Infarction, Revascularization, and Stroke Risk According to Type of Sugar-Sweetened Beverage Consumption in Semi-Quantitative Frequency Categories, Continued.

	Sugar-Sweetened Beverage Consumption†				
Mortality	Rare or never	>rare/never to <1 serving per week	≥1 serving per week to <1 serving per day	≥1 serving per day	P trend
			Fruit drinks		
No. of cases	4921	181	130	26	
Rate per 10,000 person-year	29.9	16.7	19.3	31.8	
Age-adjusted HR (95% CI)	1.0	0.99 (0.85, 1.15)	1.21 (1.01, 1.44)	1.81 (1.23, 2.66)	0.0008
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	0.98 (0.85, 1.15)	1.19 (1.00, 1.42)	1.76 (1.20, 2.59)	0.002
Model 2	1.0	0.98 (0.84, 1.15)	1.19 (0.99, 1.43)	1.78 (1.18, 2.69)	0.003
Model 3	1.0	0.99 (0.85, 1.16)	1.20 (1.00, 1.44)	1.80 (1.19, 2.71)	0.002
			Caloric soft drinks		
No. of cases	3839	763	553	103	
Rate per 10,000 person-years	31.9	25.8	20.3	17.6	
Age-adjusted HR (95% CI)	1.0	0.98 (0.90, 1.06)	1.08 (0.98, 1.17)	1.46 (1.20, 1.78)	0.0003
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	0.98 (0.91, 1.06)	1.07 (0.98, 1.17)	1.39 (1.14, 1.70)	0.001
Model 2	1.0	0.96 (0.89, 1.05)	1.04 (0.95, 1.15)	1.31 (1.07, 1.61)	0.016
Model 3	1.0	0.97 (0.89, 1.05)	1.06 (0.96, 1.16)	1.34 (1.09, 1.65)	0.006

*1 serving of caloric soft drink is 12 fluid ounces, 1 serving of sweetened bottled water/tea is 8 fluid ounces. † Incident cardiovascular disease event was defined as the first noted myocardial infarction, revascularization (including coronary artery bypass grafting or percutaneous transluminal coronary angioplasty) or stroke. ǂ Total person-time 1,843,233 years. § Revascularization includes coronary artery bypass grafting and percutaneous transluminal coronary angioplasty, total person-time 1,835,429 years. ‖ Total person-time 1,831,462 years. Models were reciprocally adjusted for the other beverage types. HR indicates hazard ratio; CI, confidence interval.

Model 1 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, multivitamin use, menopausal status, menopausal hormone therapy use, oral contraceptive use, and history of hypertension.

Model 2 adjusted for: variables in Model 1 and body mass index, total energy intake, and fruit and vegetable intake.

Model 3 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, menopausal status, menopausal hormone therapy use, history of hypertension, body mass index, and total energy intake.

Table S6. Cardiovascular Disease* Risk According to Sugar-Sweetened Beverage Consumption in Cups per Day.

	Rare/ never	Up to ½ cup/day	Up to 1 cup/day	Up to 1 ½ cups/day	>1 ½ cups/day	P trend
Cardiovascular Disease						
No. of cases	4,648	2,797	690	356	357	
Rate per 10,000 person-years	64.8	41.0	35.0	37.1	31.3	
Age-adjusted HR (95% CI)	1.0	0.98 (0.93, 1.02)	1.03 (0.95, 1.11)	1.22 (1.09, 1.36)	1.29 (1.16, 1.44)	<0.0001
Multivariable-adjusted HR (95% CI)						
Model 1	1.0	0.98 (0.94, 1.03)	1.02 (0.94, 1.10)	1.18 (1.06, 1.31)	1.21 (1.08, 1.35)	<0.0001
Model 2	1.0	0.98 (0.94, 1.03)	1.01 (0.92, 1.09)	1.16 (1.04, 1.30)	1.17 (1.05, 1.32)	0.001
Model 3	1.0	0.99 (0.95, 1.04)	1.03 (0.94, 1.12)	1.19 (1.07, 1.34)	1.22 (1.09, 1.37)	<0.0001
Myocardial infarction†						
No. of cases	1,441	832	206	93	105	
Rate per 10,000 person-years	19.6	12.0	10.3	9.6	9.1	
Age-adjusted HR (95% CI)	1.0	0.97 (0.89, 1.05)	1.04 (0.90, 1.21)	1.09 (0.88, 1.34)	1.33 (1.09, 1.62)	0.007
Multivariable-adjusted HR (95% CI)						
Model 1	1.0	0.98 (0.90, 1.06)	1.02 (0.88, 1.18)	1.03 (0.83, 1.27)	1.19 (0.98, 1.46)	0.127
Model 2	1.0	0.98 (0.90, 1.07)	1.00 (0.86, 1.17)	1.00 (0.80, 1.24)	1.18 (0.96, 1.46)	0.234
Model 3	1.0	1.00 (0.91, 1.09)	1.04 (0.89, 1.21)	1.04 (0.83, 1.29)	1.25 (1.02, 1.54)	0.063
Revascularization‡						
No. of cases	1,468	934	244	113	130	
Rate per 10,000 person-years	20.0	13.5	12.2	11.7	11.3	
Age-adjusted HR (95% CI)	1.0	0.99 (0.92, 1.08)	1.08 (0.95, 1.24)	1.13 (0.93, 1.37)	1.34 (1.11, 1.60)	0.0009
Multivariable-adjusted HR (95% CI)						
Model 1	1.0	1.01 (0.93, 1.10)	1.08 (0.95, 1.24)	1.10 (0.91, 1.33)	1.25 (1.04, 1.50)	0.009
Model 2	1.0	1.02 (0.94, 1.11)	1.07 (0.93, 1.24)	1.10 (0.90, 1.35)	1.22 (1.01, 1.48)	0.029
Model 3	1.0	1.03 (0.95, 1.12)	1.09 (0.95, 1.26)	1.13 (0.92, 1.38)	1.26 (1.04, 1.53)	0.009
Stroke§						
No. of cases	2,787	1,669	379	214	209	
Rate per 10,000 person-years	38.2	24.2	19.0	22.1	18.2	
Age-adjusted HR (95% CI)	1.0	0.99 (0.93, 1.05)	0.97 (0.87, 1.08)	1.26 (1.09, 1.45)	1.32 (1.14, 1.52)	<0.0001
Multivariable-adjusted HR (95% CI)						
Model 1	1.0	1.00 (0.94, 1.06)	0.96 (0.86, 1.07)	1.23 (1.07, 1.41)	1.25 (1.08, 1.44)	0.001
Model 2	1.0	0.99 (0.93, 1.05)	0.96 (0.85, 1.07)	1.19 (1.03, 1.38)	1.21 (1.04, 1.41)	0.008
Model 3	1.0	1.00 (0.93, 1.06)	0.97 (0.87, 1.09)	1.22 (1.06, 1.42)	1.26 (1.09, 1.46)	0.001

*Incident cardiovascular disease event was defined as the first noted myocardial infarction, revascularization (including coronary artery bypass grafting or percutaneous transluminal coronary angioplasty) or stroke, total person-time 1,807,182 years. †Total person-time 1,843,233 years. ‡ Revascularization includes coronary artery bypass grafting and percutaneous transluminal coronary angioplasty, total person-time 1,835,429 years. § Total person-time 1,831,462 years. HR indicates hazard ratio; CI, confidence interval.

Model 1 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, multivitamin use, menopausal status, menopausal hormone therapy use, oral contraceptive use, and history of hypertension.

Model 2 adjusted for: variables in Model 1 and body mass index, total energy intake, and fruit and vegetable intake.

Model 3 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, menopausal status, menopausal hormone therapy use, history of hypertension, body mass index, and total energy intake.

Table S7. Cardiovascular Disease* Risk According to Sugar-Sweetened Beverage Consumption after removal of events that occurred at 2 years follow-up (n=103,518).

	Sugar-Sweetened Beverage Consumption †				
	Rare/ never	>rare/never to <1 serving per week	≥1 serving per week to <1 serving per day	≥1 serving per day	P trend
Cardiovascular Disease					
No. of cases	4,353	2,262	1,400	307	
Rate per 10,000 person-years	60.8	36.8	35.5	39.3	
Age-adjusted HR (95% CI)	1.0	1.00 (0.95, 1.05)	1.01 (0.95, 1.08)	1.27 (1.13, 1.42)	0.001
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.01 (0.96, 1.06)	1.01 (0.96, 1.07)	1.18 (1.05, 1.33)	0.028
Model 2	1.0	1.01 (0.95, 1.06)	1.00 (0.93, 1.06)	1.17 (1.03, 1.32)	0.072
Model 3	1.0	1.02 (0.96, 1.07)	1.01 (0.95, 1.08)	1.20 (1.06, 1.35)	0.019
Myocardial infarction ǂ					
No. of cases	1,365	652	436	92	
Rate per 10,000 person-years	18.6	10.4	10.9	11.6	
Age-adjusted HR (95% CI)	1.0	0.96 (0.87, 1.05)	1.06 (0.95, 1.18)	1.28 (1.04, 1.59)	0.019
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	0.96 (0.88, 1.06)	1.05 (0.94, 1.17)	1.16 (0.94, 1.43)	0.124
Model 2	1.0	0.97 (0.88, 1.07)	1.04 (0.93, 1.17)	1.18 (0.94, 1.47)	0.118
Model 3	1.0	0.99 (0.90, 1.09)	1.07 (0.95, 1.20)	1.21 (0.97, 1.51)	0.048
Revascularization §					
No. of cases	1,368	757	474	108	
Rate per 10,000 person-years	18.7	12.2	11.9	13.7	
Age-adjusted HR (95% CI)	1.0	1.02 (0.93, 1.11)	1.03 (0.93, 1.14)	1.31 (1.08, 1.60)	0.020
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.03 (0.94, 1.13)	1.03 (0.92, 1.14)	1.20 (0.99, 1.46)	0.102
Model 2	1.0	1.05 (0.95, 1.15)	1.01 (0.90, 1.13)	1.19 (0.97, 1.46)	0.206
Model 3	1.0	1.06 (0.97, 1.16)	1.03 (0.92, 1.15)	1.22 (0.99, 1.50)	0.107
Stroke ‖					
No. of cases	2,634	1,352	817	182	
Rate per 10,000 person-years	36.2	21.7	20.5	23.0	
Age-adjusted HR (95% CI)	1.0	1.01 (0.95, 1.08)	1.00 (0.92, 1.08)	1.27 (1.10, 1.48)	0.021
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.02 (0.96, 1.09)	1.00 (0.92, 1.08)	1.21 (1.04, 1.41)	0.080
Model 2	1.0	1.01 (0.94, 1.08)	0.99 (0.91, 1.07)	1.19 (1.02, 1.40)	0.148
Model3	1.0	1.02 (0.95, 1.09)	1.00 (0.92, 1.09)	1.22 (1.04, 1.43)	0.069

*Incident cardiovascular disease event was defined as the first noted myocardial infarction, revascularization (including coronary artery bypass grafting or percutaneous transluminal coronary angioplasty) or stroke, total person-time 1,804,121 years. †1 serving of caloric soft drink is 12 fluid ounces, 1 serving of sweetened bottled water or tea, or fruit drink, is 8 fluid ounces. ǂ Total person-time 1,840,533 years. § Revascularization includes coronary artery bypass grafting and percutaneous transluminal coronary angioplasty, total person-time 1,832,659 years. ‖ Total person-time 1,828,654 years. HR indicates hazard ratio; CI, confidence interval. Model 1 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, multivitamin use, menopausal status, menopausal hormone therapy use, oral contraceptive use, and history of hypertension. Model 2 adjusted for: variables in Model 1 and body mass index, total energy intake, and fruit and vegetable intake. Model 3 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, menopausal status, menopausal hormone therapy use, history of hypertension, body mass index, and total energy intake.

Table S8. Cardiovascular Disease* Risk According to Sugar-Sweetened Beverage Consumption after removal of events that occurred at 4 years follow-up (n=100,739).

	Sugar-Sweetened Beverage Consumption †				
	Rare/never	>rare/never to <1 serving per week	≥1 serving per week to <1 serving per day	≥1 serving per day	P trend
Cardiovascular Disease					
No. of cases	3,993	2,094	1,304	286	
Rate per 10,000 person-years	56.1	34.2	33.2	36.8	
Age-adjusted HR (95% CI)	1.0	1.00 (0.94, 1.05)	1.02 (0.95, 1.08)	1.27 (1.12, 1.43)	0.002
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.01 (0.95, 1.06)	1.01 (0.95, 1.08)	1.18 (1.05, 1.33)	0.030
Model 2	1.0	1.00 (0.95, 1.06)	1.00 (0.94, 1.07)	1.16 (1.02, 1.32)	0.077
Model 3	1.0	1.01 (0.96, 1.07)	1.02 (0.96, 1.09)	1.19 (1.05, 1.35)	0.023
Myocardial infarction ǂ					
No. of cases	1,272	617	400	86	
Rate per 10,000 person-years	17.4	9.9	10.0	10.9	
Age-adjusted HR (95% CI)	1.0	0.97 (0.88, 1.07)	1.03 (0.92, 1.16)	1.28 (1.03, 1.60)	0.042
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	0.97 (0.88, 1.07)	1.02 (0.91, 1.15)	1.16 (0.93, 1.44)	0.218
Model 2	1.0	0.97 (0.88, 1.08)	1.02 (0.91, 1.15)	1.17 (0.93, 1.47)	0.207
Model 3	1.0	0.99 (0.90, 1.10)	1.05 (0.93, 1.18)	1.20 (0.96, 1.51)	0.098
Revascularization §					
No. of cases	1,224	699	436	99	
Rate per 10,000 person-years	16.8	11.3	11.0	12.6	
Age-adjusted HR (95% CI)	1.0	1.03 (0.94, 1.13)	1.04 (0.93, 1.16)	1.31 (1.07, 1.62)	0.019
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.05 (0.95, 1.15)	1.04 (0.93, 1.16)	1.20 (0.98, 1.48)	0.098
Model 2	1.0	1.06 (0.96, 1.17)	1.03 (0.91, 1.15)	1.21 (0.97, 1.49)	0.155
Model 3	1.0	1.08 (0.98, 1.19)	1.04 (0.93, 1.17)	1.23 (1.00, 1.53)	0.083
Stroke ‖					
No. of cases	2,447	1,252	775	172	
Rate per 10,000 person-years	33.8	20.2	19.5	21.8	
Age-adjusted HR (95% CI)	1.0	1.00 (0.93, 1.07)	1.01 (0.93, 1.09)	1.28 (1.09, 1.49)	0.015
Multivariable-adjusted HR (95% CI)					
Model 1	1.0	1.01 (0.94, 1.08)	1.00 (0.93, 1.09)	1.21 (1.04, 1.42)	0.061
Model 2	1.0	0.99 (0.92, 1.07)	1.00 (0.91, 1.09)	1.18 (1.00, 1.39)	0.138
Model 3	1.0	1.00 (0.93, 1.07)	1.01 (0.93, 1.10)	1.21 (1.03, 1.42)	0.066

*Incident cardiovascular disease event was defined as the first noted myocardial infarction, revascularization (including coronary artery bypass grafting or percutaneous transluminal coronary angioplasty) or stroke, total person-time 1,795,512 years. † 1 serving of caloric soft drink is 12 fluid ounces, 1 serving of sweetened bottled water or tea, or fruit drink, is 8 fluid ounces. ǂ Total person-time 1,833,047 years. § Revascularization includes coronary artery bypass grafting and percutaneous transluminal coronary angioplasty, total person-time 1,824,901 years. ‖ Total person-time 1,820,872 years. HR indicates hazard ratio; CI, confidence interval. Model 1 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, multivitamin use, menopausal status, menopausal hormone therapy use, oral contraceptive use, and history of hypertension. Model 2 adjusted for: variables in Model 1 and body mass index, total energy intake, and fruit and vegetable intake. Model 3 adjusted for: age, race/ethnicity, socioeconomic status, smoking status, alcohol intake, cardiovascular disease family history, physical activity, aspirin use, menopausal status, menopausal hormone therapy use, history of hypertension, body mass index, and total energy intake.