

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Sensitivity Analyses

We conducted several sensitivity analyses. First, we estimated adjusted hazard ratio of CVD mortality according to usual percentage of calories from added sugar by selected characteristics, including age group (<60 years vs. ≥ 60 years), sex (men vs. women), race/ethnicity (non-Hispanic white, non-Hispanic black, and Mexican American), educational attainment (<12 years vs. ≥ 12 years), physical activity (≥ 5 times/week of moderate-intensity to vigorous activities vs. others), HEI score (top 50% (score ≥ 63.5) vs. other <50%), and BMI (normal vs. overweight/obese) (eTable 1). Second, we compared the baseline characteristics and dietary pattern of participants who consumed <10%, 10% to <25% and $\geq 25\%$ calorie from added sugar (based on first-day 24-hour dietary recall) in NHANES III Linked Mortality File (1988-2006) (eTable 2). Third, we used the percentage of calorie from added sugar derived from the first-day 24-hour dietary recall to examine its association with CVD mortality (eTable 3). Fourth, we used the full sample (including the excluded participants with diabetes, CVD, or cancer at baseline) to estimate the association of percentage of calories from added sugar with CVD mortality (n = 14,338, with 1,701 CVD deaths during 189,699 persons years follow-up) (eTable 4). Fifth, we estimated the association of the percentage of calories from added sugar with total mortality (eTable 5). Sixth, we estimated the association of percentage of calories from added sugar with CVD mortality by adjusting for the components of the Healthy Eating Index score (eTable 6). Seventh, we estimated servings of sugar-sweetened beverages per week from the NHANES III Food Frequency Questionnaires (participants were asked how often in the past month they consumed specific food items, including soda or energy and sports drinks with added sugar). The reported number of servings (360 mL per serving) of sugar-sweetened beverages (per month) was summed, divided by 30, and then multiplied by 7 to estimate consumption per week and examine its association with CVD mortality (eTable 7). Eighth, we estimated adjusted hazard ratio of CVD mortality comparing those who consumed $\geq 10\%$ or $\geq 25\%$ threshold of percentage of calories from added sugar by selected characteristics, including age group (<60 years vs. ≥ 60 years), sex (men vs. women), race/ethnicity (non-Hispanic white, non-Hispanic black, and Mexican American), educational attainment (<12 years vs. ≥ 12 years),

physical activity (≥ 5 times/week of moderate-intensity to vigorous activities vs. others), HEI score (top 50% [score ≥ 63.5] vs. other <50%), and BMI (normal vs. overweight/obese) (eFigure).

eTable 1. Adjusted Hazard Ratio of Cardiovascular Disease Mortality According to Usual Percentage of Calories From Added Sugar by Selected Characteristics Among US Adults Aged ≥ 20 Years—NHANES Linked Mortality Files, 1988-2006

Characteristic		Mid-value of Quintiles of Usual Percentage of Calories from Added Sugar for US Adults					p-value ^a
		Q1 7.4%	Q2 11.4%	Q3 14.8%	Q4 18.7%	Q5 25.2%	
Age <60 years							
CVD deaths /participants/ total person years	144/8,835 /129,914						
Range/Usual percentage (%)	0%-100%	0- <9.6%	9.6- <13.1%	13.1- <16.7%	16.7- <21.3%	$\geq 21.3\%$	
Fully adjusted HR ^b		1.00	1.05 (0.98 - 1.13)	1.12 (0.94 - 1.34)	1.26 (0.89 - 1.77)	1.67 (0.78 - 3.58)	0.184
≥ 60 years							
CVD deaths /participants/ total person years	687/2,898 /33,125						
Fully adjusted HR ^b		1.00	1.06 (1.00 - 1.12)	1.15 (1.00 - 1.31)	1.31 (1.00 - 1.71)	1.83 (1.01 - 3.31)	0.046
Gender - Male							
CVD deaths/participants /total person years	434/5,639/ 78,028						
Fully adjusted HR ^b		1.00	1.03 (0.95 - 1.11)	1.07 (0.89 - 1.29)	1.14 (0.79 - 1.64)	1.34 (0.60 - 3.00)	0.471
Female							
CVD deaths/participants	397/6,094/ 85,011						

/total person years							
Fully adjusted HR ^b		1.00	1.11 (1.04 - 1.18)	1.28 (1.09 - 1.50)	1.63 (1.19 - 2.22)	2.95 (1.48 - 5.91)	0.003
Non-Hispanic white							
CVD deaths/participants /total person years	494/4,802/ 64,568						
Fully adjusted HR ^b		1.00	1.10 (1.04 - 1.16)	1.25 (1.09 - 1.43)	1.55 (1.19 - 2.02)	2.67 (1.48 - 4.80)	0.002
Non-Hispanic black							
CVD deaths/participants /total person years	187/3,233/ 45,184						
Fully adjusted HR ^b		1.00	0.97 (0.92 - 1.01)	0.93 (0.83 - 1.03)	0.86 (0.69 - 1.06)	0.71 (0.44 - 1.15)	0.160
Mexican-American							
CVD deaths/participants /total person years	134/3,217 /46,594						
Fully adjusted HR ^b		1.00	1.05 (0.93 - 1.19)	1.14 (0.85 - 1.53)	1.29 (0.72 - 2.30)	1.76 (0.49 - 6.39)	0.381
Education <12 years							
CVD deaths/participants /total person years	455/4,318/ 57,787						
Fully adjusted HR ^b		1.00	1.08 (1.04 - 1.12)	1.21 (1.10 - 1.33)	1.45 (1.20 - 1.75)	2.29 (1.49 - 3.50)	<0.001
≥12 years							
CVD	376/7,415/						

deaths/participants /total person years	105,252						
Fully adjusted HR ^b		1.00	1.05 (0.96 - 1.15)	1.12 (0.91 - 1.39)	1.26 (0.83 - 1.90)	1.67 (0.67 - 4.18)	0.265
Healthy Eating Index - ≥top 50% (score ≥ 63.5)							
CVD deaths/participants /total person year	457/5,673 /77,650						
Fully adjusted HR ^b		1.00	1.11 (1.01 - 1.21)	1.28 (1.03 - 1.59)	1.63 (1.07 - 2.49)	2.96 (1.15 - 7.61)	0.025
Other							
CVD deaths/participants /total person years	374/6,060 /85,389						
Fully adjusted HR ^b		1.00	1.06 (1.00 - 1.11)	1.14 (1.01 - 1.29)	1.30 (1.02 - 1.65)	1.80 (1.05 - 3.07)	0.033
Physical activity High^c							
CVD deaths/participants /total person years	287/4,407/ 61,478						
Fully adjusted HR ^b		1.00	1.07 (0.96 - 1.21)	1.19 (0.90 - 1.57)	1.40 (0.81 - 2.42)	2.12 (0.63 - 7.18)	0.220
Low							
CVD deaths/participants /total person years	544/7,326 /101,561						
Fully adjusted HR ^b		1.00	1.04 (0.99 - 1.09)	1.10 (0.98 - 1.24)	1.21 (0.97 - 1.52)	1.54 (0.93 - 2.53)	0.089

Body mass index - Normal weight (BMI<25)							
CVD deaths/participants /total person years	320/4,697 /65,330						
Fully adjusted HR ^b		1.00	1.04 (0.95 - 1.15)	1.11 (0.87 - 1.0)	1.22 (0.77 - 1.93)	1.55 (0.56 - 4.34)	0.392
Overweight/obese (BMI≥25)							
CVD deaths/participants /total person years	511/7,036 /97,709						
Fully adjusted HR ^b		1.00	1.08 (1.03 - 1.13)	1.20 (1.08 - 1.33)	1.43 (1.16 - 1.77)	2.23 (1.40 - 3.55)	0.001

Abbreviations: HR, hazard ratio; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; Q, quintile.

- a. *P*-value for testing significant association between the usual percentage of calories from added sugar and CVD mortality based on Satterthwaite F-test. *P*-value for interactions between percentage of added sugar and age group (<60 years vs. ≥60 years), sex, race/ethnicity, educational attainment (<12 years vs. ≥12 years), Healthy Eating Index score (top 50% (score≥63.5) vs. others), physical activity, and BMI status (<25 vs. ≥25) were 0.204, 0.753, 0.093, 0.089, 0.680, 0.224 and 0.728 respectively; all tests are 2-tailed.
- b. Adjusted for age, sex, race/ethnicity, educational attainment, smoking status, alcohol consumption, physical activity level, antihypertensive medication use, family history of CVD, Healthy Eating Index score, body mass index, systolic blood pressure, total serum cholesterol, and total calorie intake.
- c. High physical activity was defined as ≥5 times per week of moderate intensity to vigorous activities, and rest as low.

eTable 2. Comparison of Baseline Characteristics and Dietary Pattern of Participants by First-Day Percentage of Calories From Added Sugar—NHANES III Linked Mortality File, 1988-2006

Characteristics	Percentage of calorie from added sugar in population ^a			p-value ^b
	<10.0%	10.0 - <25.0%	≥25.0%	
Prevalence, % (se)^c	21.5 (0.02)	68.2 (0.02)	10.3 (0.02)	
Age, years (se)	45.5 (0.55)	42.8 (0.51)	37.2 (0.50)	<0.001
Sex, % (se)				
Male	47.9 (1.33)	50.4 (0.84)	48.7 (1.54)	
Female	52.1 (1.33)	49.6 (0.84)	51.3 (1.54)	0.281
Race/ethnicity, % (se)				
Non-Hispanic white	76.4 (1.72)	76.3 (1.22)	76.4 (1.75)	
Non-Hispanic black	8.2 (0.53)	11.0 (0.66)	14.6 (1.24)	
Mexican American	4.9 (0.43)	5.5 (0.52)	4.4 (0.51)	
Others	10.6 (1.42)	7.2 (0.79)	4.7 (0.90)	<0.001
Years of education, % (se)				
<12 years	22.2 (1.22)	21.3 (1.09)	23.4 (1.42)	
≥12 years	77.8 (1.22)	78.4 (1.09)	76.6 (1.42)	0.251
Smoking status, % (se)				
Never	46.9 (1.08)	47.7 (1.25)	45.7 (2.05)	
Current	25.4 (1.42)	27.7 (1.26)	38.4 (1.44)	
Former	27.7 (0.97)	24.6 (1.06)	15.9 (1.20)	<0.001
High Physical activity, % (se)^d				
High	54.7 (2.37)	41.2 (1.24)	29.3 (2.80)	
Low	45.3 (2.37)	58.8 (1.24)	70.7 (2.80)	<0.001
BMI, mean (se)	26.7 (0.13)	26.3 (0.17)	26.7 (0.22)	0.837
Systolic blood pressure, mean (se)	123.2 (0.42)	121.2 (0.50)	118.1(0.52)	<0.001
Antihypertensive medication use, % (se)				
Yes	11.5 (0.74)	9.3 (0.57)	6.5 (0.70)	
No	88.5 (0.74)	90.7 (0.57)	93.5 (0.70)	<0.001
Total serum cholesterol, mean (se)	205.1 (0.97)	202.3 (1.09)	198.6 (1.51)	<0.001
Family history of CVD, % (se)				
Yes	15.0 (0.75)	16.0 (0.89)	19.4 (1.42)	
No	85.0 (0.75)	84.0 (0.89)	80.6 (1.42)	0.035
Total calorie intake, mean (se)	2143.4 (18.15)	2248.9 (17.55)	2205.9 (21.21)	0.047
Healthy Eating Index	63.8 (0.50)	63.9 (0.35)	61.7 (0.37)	<0.001

Scores, mean (se) ^e				
AHA healthy diet score, mean (se)^f	1.3 (0.03)	0.9 (0.03)	0.5 (0.02)	<0.001
Sugar-sweetened beverages (servings/week), mean (se)^g	2.5 (0.11)	5.2 (0.21)	9.6 (0.42)	<0.001
Percentage of calories from major food groups^h				
Milk and milk products	9.4 (0.21)	10.9 (0.27)	9.9 (0.49)	0.367
Meat, poultry, fish, and mixtures	21.5 (0.43)	19.5 (0.41)	17.3 (0.41)	<0.001
Eggs	2.1 (0.14)	1.7 (0.07)	1.2 (0.13)	<0.001
Legumes, nuts, and seeds	3.4 (0.16)	2.6 (0.16)	1.4 (0.13)	<0.001
Grain products	33.9 (0.54)	34.5 (0.45)	29.3 (0.60)	<0.001
Fruits	5.9 (0.20)	4.0 (0.13)	2.6 (0.18)	<0.001
Vegetables	9.5 (0.24)	8.9 (0.20)	7.6 (0.31)	<0.001
Fats, oils, and salad dressings	4.0 (0.18)	3.5 (0.13)	2.4 (0.16)	<0.001
Sugars, sweets, and beverages	10.3 (0.38)	14.4 (0.26)	28.3 (0.41)	<0.001

Abbreviations: NHANES, National Health and Nutrition Examination Survey; BMI, body mass index; AHA, American Heart Association.

- a. We categorized the percentage of calories from added sugar based on first-day 24hrs dietary recalls into three categories which might be subject to the effect of day-to-day variations in intake.
- b. P-values are presented for difference across categories of calories from added sugar. All tests were 2-tailed.
- c. Prevalence of participants who consumed <10%, ≥10% to <25% and ≥25% added sugar was estimated using the NCI method that corrected for the measurement error.
- d. High physical activity was defined as ≥5 times per week of moderate intensity to vigorous activities, and rest as low.
- e. Healthy Eating Index is a score measuring dietary quality that ranges from 0–100 and contains information on the consumption of 10 subcomponents of the diet: grains, fruits, vegetables, dairy, meats, fats, saturated fat, cholesterol, sodium, and dietary variety. A higher Healthy Eating Index score indicates what is thought to be a healthier eating pattern.
- f. AHA's healthy diet score ranges from 0-5 and is calculated by summing the following components, one point each for the consumption of fruits and vegetables (≥4.5 cups/day), fish (≥2 3.5-oz servings/week), fiber-rich whole grains (≥ 3 1-oz-equivalent servings/day), sodium (<1500 mg/d), and sugar-sweetened beverages (≤36-oz/week). We estimated the healthy diet score based on the Food Frequency Questionnaire (FFQ) in NHANES III.

- g. In NHANES III Food Frequency Questionnaire, participants were asked how often in the past month they consumed specific food items including soda, energy and sports drinks with added sugar. Reported number of servings of sugar-sweetened beverage (per month) was summed, divided by 30 and multiple by 7 to estimate the consumption per week.
- h. We calculated the percentage of calories from the USDA nine major food groups by dividing the calories from each food group by the total calories. The calories from each food group included calories from added sugar and other sources.

eTable 3. Adjusted Hazard Ratio of Cardiovascular Disease Mortality According to Percentage of Calories From Added Sugar Based on First-Day 24 Hour Dietary Recall Among US Adults Aged ≥ 20 Years—NHANES Linked Mortality Files, 1988-2006

		Mid-value of Quintiles of Percentage of Calories from Added Sugar for US Adults ^a					
Characteristics		Q1 3.5%	Q2 9.3%	Q3 14.6%	Q4 20.7%	Q5 31.5%	p-value ^b
CVD deaths/participants/ total person years	831/11,733/ 163,039,						
Range/Usual percentage (%)	0%-100%	0- <6.6%	6.6- <11.5%	11.5- <16.6%	16.6- <23.6%	$\geq 23.6\%$	
HR adjusted for age, sex and race/ethnicity only		1.06 (0.95 - 1.20)	1.0	1.00 (0.92 - 1.08)	1.09 (0.96 - 1.23)	1.50 (1.21 - 1.87)	0.006
Fully adjusted HR ^c		1.05 (0.92 - 1.19)	1.0	1.00 (0.92 - 1.10)	1.08 (0.93 - 1.26)	1.43 (1.10 - 1.86)	0.027

Abbreviations: HR, hazard ratio; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; Q, quintile.

- a. Because the relationships between percentage of calories from added sugar derived from first-day 24 hours dietary recall and CVD mortality were not linear (p-value <0.05 for linearity), we used the restricted cubic spline in the multivariable proportional hazards models with three knots (5th, 50th and 95th percentiles of usual percentage) to estimate the adjusted HRs. We used the second quintile as reference (Q5, Q4, Q3, Q1 vs. Q2) because Q2 appeared to be associated with the lower risk for mortality. .
- b. P-value for testing linear of association between percentage of calories from added sugar and CVD mortality; all tests are two-tailed.
- c. Adjusted for age, sex, race/ethnicity, educational attainment, smoking status, alcohol consumption, physical activity level, antihypertensive medication use, family history of CVD, Healthy Eating Index score, body mass index, systolic blood pressure, total serum cholesterol, and total calorie intake.

eTable 4. Adjusted Hazard Ratio of Cardiovascular Disease Mortality by Total Sample According to Usual Percentage of Calories From Added Sugar Among US Adults Aged ≥ 20 Years—NHANES Linked Mortality Files, 1988-2006 (n = 14338)

Characteristics	Mid-value of Quintiles of Usual Percentage of Calories from Added Sugar for US Adults						p-value ^a
		Q1 7.4%	Q2 11.4%	Q3 14.8%	Q4 18.7%	Q5 25.2%	
CVD deaths/participants/total person years	1,582/14,338/ 189,699						
Range/Usual percentage (%)	0%-100%	0- <9.6%	9.6- <13.1%	13.1- <16.7%	16.7- <21.3%	$\geq 21.3\%$	
HR adjusted for age, sex and race/ethnicity only		1.00	1.05 (1.02 - 1.09)	1.13 (1.05 - 1.22)	1.27 (1.10 - 1.48)	1.72 (1.23 - 2.38)	0.002
Fully adjusted HR ^b		1.00	1.04 (1.00 - 1.07)	1.09 (1.01 - 1.17)	1.18 (1.01 - 1.37)	1.44 (1.03 - 2.01)	0.035

Abbreviations: HR, hazard ratio; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; Q, quintile.

- a. *P*-value for testing significant association between the usual percentage of calories from added sugar and CVD mortality based on Satterthwaite F-test; all tests are two-tailed.
- b. Adjusted for age, sex, race/ethnicity, educational attainment, smoking status, alcohol consumption, physical activity level, antihypertensive medication use, family history of CVD, Healthy Eating Index score, body mass index, history of CVD, systolic blood pressure, total serum cholesterol, diabetes, cancer at baseline and total calorie intake.

eTable 5. Adjusted Hazard Ratio of All-Cause Mortality According to Usual Percentage of Calories From Added Sugar Among US Adults Aged ≥ 20 Years—NHANES Linked Mortality Files, 1988-2006

		Mid-value of Quintiles of Usual Percentage of Calories from Added Sugar for US Adults					
Characteristics		Q1 7.4%	Q2 11.4%	Q3 14.8%	Q4 18.7%	Q5 25.2%	p-value ^a
Total deaths/participants/Total person years	2044/11,733/163,039						
Range/Usual percentage (%)	0%-100%	0- <9.6%	9.6- <13.1%	13.1- <16.7%	16.7- <21.3%	$\geq 21.3\%$	
HR adjusted for age, sex and race/ethnicity only		1.00	1.05 (1.03 - 1.08)	1.13 (1.06 - 1.20)	1.27 (1.13 - 1.42)	1.70 (1.31 - 2.19)	<0.001
Fully adjusted HR ^b		1.00	1.02 (0.99 - 1.05)	1.06 (0.99 - 1.14)	1.12 (0.97 - 1.29)	1.28 (0.94 - 1.75)	0.112

Abbreviations: HR, hazard ratio; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; Q, quintile.

- P*-value for testing significant association between the usual percentage of calories from added sugar and all-cause mortality based on Satterthwaite F-test; all tests are two-tailed.
- Adjusted for age, sex, race/ethnicity, educational attainment, smoking status, alcohol consumption, physical activity level, antihypertensive medication use, family history of CVD, Healthy Eating Index score, body mass index, systolic blood pressure, total serum cholesterol, and total calorie intake.

eTable 6. Adjusted Hazard Ratio of Cardiovascular Disease Mortality According to Usual Percentage of Calories From Added Sugar Adjusting for Individual Component of Healthy Eating Index Among US Adults Aged ≥ 20 Years—NHANES Linked Mortality Files, 1988-2006

		Mid-value of Quintiles of Usual Percentage of Calories from Added Sugar for US Adults					
Characteristics		Q1 7.4%	Q2 11.4%	Q3 14.8%	Q4 18.7%	Q5 25.2%	p-value ^a
CVD deaths/participants/total person years	831/11,733 /163,039						
Range/Usual percentage (%)	0%-100%	0- <9.6%	9.6- <13.1%	13.1- <16.7%	16.7- <21.3%	$\geq 21.3\%$	
Fully adjusted HR ^b		1.00	1.07 (1.02 - 1.12)	1.18 (1.06 - 1.31)	1.38 (1.11 - 1.70)	2.03 (1.26 - 3.27)	0.004
HR Adjusted for individual component ^c		1.00	1.07 (1.02 - 1.13)	1.18 (1.04 - 1.34)	1.39 (1.08 - 1.78)	2.07 (1.18 - 3.63)	0.012

Abbreviations: HR, hazard ratio; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; Q, quintile.

- P*-value for testing significant association between the usual percentage of calories from added sugar and CVD mortality based on Satterthwaite F-test; all tests are two-tailed.
- Adjusted for age, sex, race/ethnicity, educational attainment, smoking status, alcohol consumption, physical activity level, antihypertensive medication use, family history of CVD, Healthy Eating Index score, body mass index, systolic blood pressure, total serum cholesterol, and total calorie.
- In addition to model b, adjusted for 10 components of Healthy Eating Index instead of Healthy Eating Index, including fruits, vegetables, grains, dairy, meats, fats, saturated fat, cholesterol, sodium, and dietary variety.

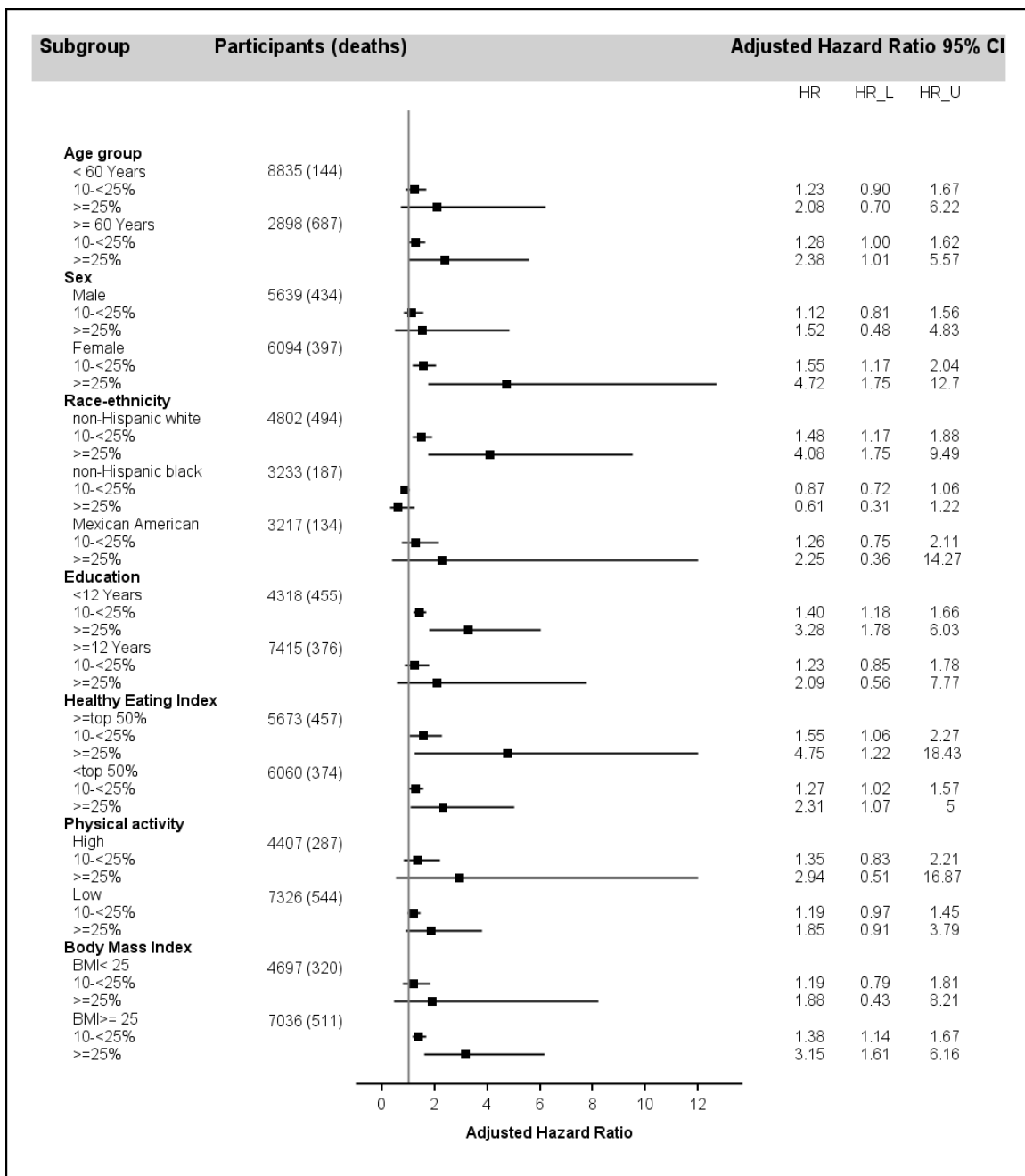
eTable 7. Adjusted Hazard Ratio of Cardiovascular Disease Mortality According to Categories of Sugar Sweetened Beverage Consumption Among US Adults Aged ≥ 20 Years—NHANES Linked Mortality Files, 1988-2006

Characteristics		Servings of Sugar Sweetened Beverage Consumption per week ^a			
		<1	1 to <3	3 to <7	≥ 7
CVD deaths/participants	831/11,733	468/4,348	97/1,288	83/1,829	183/4,268
Total person years	163,039	58,219	17,925	26,199	60,696
HR adjusted for age, sex and race/ethnicity only		1.00	1.01 (0.72 - 1.41)	1.00 (0.72 - 1.35)	1.38 (1.10 - 1.72)
Fully adjusted HR ^b		1.00	1.03 (0.73 - 1.44)	1.04 (0.75 - 1.45)	1.29 (1.04 - 1.60)

Abbreviations: CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey.

- a. Participants were asked how often in the past month they consumed specific food items including soda, energy and sports drinks with added sugar. Reported number of servings of sugar sweetened beverage (per month) was summed, divided by 30 and multiple by 7 to estimate the consumption per week.
- b. Adjusted for age, sex, race/ethnicity, educational attainment, smoking status, alcohol consumption, physical activity level, antihypertensive medication use, family history of CVD, Healthy Eating Index score, body mass index, systolic blood pressure, total serum cholesterol, and total calorie intake.

eFigure. Adjusted Hazard Ratio of Cardiovascular Disease Mortality Comparing $\geq 10\%$ or $\geq 25\%$ to $< 10\%$ of Calories From Added Sugar by Selected Characteristics Among US Adults Aged ≥ 20 Years—NHANES Linked Mortality Files, 1988-2006



Healthy Eating Index score \geq top 50% included the participants with a score ≥ 63.5 ; high physical activity included the participants who had 5 or more times per week of moderate-intensity to vigorous activities.