Sugar-Sweetened Beverages, Weight Gain, and Incidence of Type 2 Diabetes in Young and Middle-Aged Women

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Context Sugar-sweetened beverages like soft drinks and fruit punches contain large amounts of readily absorbable sugars and may contribute to weight gain and an increased risk of type 2 diabetes, but these relationships have been minimally addressed in adults.

Objective To examine the association between consumption of sugar-sweetened beverages and weight change and risk of type 2 diabetes in women.

Design, Setting, and Participants Prospective cohort analyses conducted from 1991 to 1999 among women in the Nurses' Health Study II. The diabetes analysis included 91249 women free of diabetes and other major chronic diseases at baseline in 1991. The weight change analysis included 51603 women for whom complete dietary information and body weight were ascertained in 1991, 1995, and 1999. We identified 741 incident cases of confirmed type 2 diabetes during 716300 person-years of follow-up.

Main Outcome Measures Weight gain and incidence of type 2 diabetes.

Results Those with stable consumption patterns had no difference in weight gain, but weight gain over a 4-year period was highest among women who increased their sugar-sweetened soft drink consumption from 1 or fewer drinks per week to 1 or more drinks per day (multivariate-adjusted means, 4.69 kg for 1991 to 1995 and 4.20 kg for 1995 to 1999) and was smallest among women who decreased their intake (1.34 and 0.15 kg for the 2 periods, respectively) after adjusting for lifestyle and dietary confounders. Increased consumption of fruit punch was also associated with greater weight gain compared with decreased consumption. After adjustment for potential confounders, women consuming 1 or more sugar-sweetened soft drinks per day had a relative risk [RR] of type 2 diabetes of 1.83 (95% confidence interval [CI], 1.42-2.36; $P<.001$ for trend) compared with those who consumed less than 1 of these beverages per month. Similarly, consumption of fruit punch was associated with increased diabetes risk (RR for ≥1 drink per day compared with <1 drink per month, 2.00; 95% CI, 1.33-3.03; $P=.001$).

Conclusion Higher consumption of sugar-sweetened beverages is associated with a greater magnitude of weight gain and an increased risk for development of type 2 diabetes in women, possibly by providing excessive calories and large amounts of rapidly absorbable sugars.

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TYPE 2 DIABETES MELLITUS AFfects about 17 million US individuals.[1-3] The prevalence of diabetes has increased rapidly during the last decades[2,4,5] in parallel to the obesity epidemic.[2,5] Coinciding with the increasing prevalence of obesity and type 2 diabetes, soft drink consumption in the United States increased by 61% in adults from 1977 to 1997[6] and more than doubled in children and adolescents from 1977-1978 to 1994-1998.[7] Recent evidence suggests an association between the intake of sugar-sweetened soft drinks and the risk of obesity in children,[8] but data among adults are limited. Besides contributing to obesity, sugar-sweetened soft drinks might increase risk of diabetes because they contain large amounts of high-fructose corn syrup, which raises blood glucose similarly to sucrose.[9] Soft drinks are the leading source of added sugars in the US diet,[10] and each serving represents a considerable amount of glycemic load that may increase risk of diabetes.[11] In addition, cola-based soft

See also p 978 and Patient Page.

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drinks contain caramel coloring, which is rich in advanced glycation end products that might increase insulin resistance[12] and inflammation.[13] However, no study has examined the association between the consumption of soft drinks and other sugar-sweetened beverages and risk of type 2 diabetes. We therefore examined the relationships between sugar-sweetened beverage consumption and weight gain and diabetes risk in a large cohort of young and middle-aged women, controlling for potential confounding factors. Because the majority of sugar-sweetened beverages consumed in this cohort are soft drinks, we particularly emphasized soft drink consumption.

METHODS

Study Population

The Nurses' Health Study II is a prospective cohort study of 116671 female US nurses aged 24 to 44 years at study initiation in 1989. This cohort is followed up using biennial mailed questionnaires, with a follow-up rate exceeding 90% for every 2-year period. For the analyses presented here, women were excluded if they did not complete a dietary questionnaire in 1991 or if more than 9 items on it were left blank; if the reported dietary intake was implausible with regard to total energy intake (ie, <500 kcal/d or >3500 kcal/d); if they had a history of diabetes, cancer (except nonmelanoma skin cancer), or cardiovascular disease at baseline; or if they had not provided data on physical activity in 1991. The final sample for the diabetes analysis consisted of 91249 women. For the analysis on weight change, we also excluded women who did not complete questions on sugar-sweetened soft drink consumption, who had a history of diabetes or cardiovascular disease before 1995 or reported the diagnosis of cancer (except nonmelanoma skin cancer) on any questionnaire, who did not report body weight on any questionnaire, or who had no data on physical activity assessed in 1997. These exclusions left a total of 51603 women for the analyses. The study was approved by the human research committees at the Harvard School of Public Health and Brigham and Women's Hospital, Boston, Mass; completion of the self-administered questionnaire was considered to imply informed consent.

Dietary Assessment

In 1991, the mailed questionnaire included a 133- item semiquantitative food frequency questionnaire. Women were asked how often they had consumed a commonly used unit or portion size of each food on average over the previous year, including 3 items on consumption of sugar-sweetened soft drinks ("Coke, Pepsi, or other cola with sugar," "caffeine-free Coke, Pepsi, or other cola with sugar," and "other carbonated beverages with sugar"), 4 items on fruit juice ("apple juice," "orange juice," "grapefruit juice," and "other juice"), 1 item on fruit punch, and 3 items on diet soft drinks ("low-calorie cola with caffeine," "low-calorie caffeine-free cola," and "other low-calorie beverages"). We summed the intake of single items to create a total of sugar-sweetened soft drink, diet soft drink, and fruit juice consumption. The 9 possible responses, ranging from "never" to "6 or more times per day," were aggregated into 4 categories (<1 drink per month, 1-4 drinks per month, 2-6 drinks per week, and ≥1 drink per day). Similar questionnaires were used to collect dietary information in 1995 and 1999. Nutrient intakes were computed by multiplying the frequency response by the nutrient content of the specified portion sizes. Values for nutrients were derived from the US Department of Agriculture sources[14] and supplemented with information from manufacturers. The validity and reliability of food frequency questionnaires similar to those used in the Nurses' Health Study II have been described elsewhere.[15,16] Briefly, the correlation coefficients between questionnaire and multiple dietary records were 0.84 for cola-type soft drinks (sugar-sweetened and diet combined), 0.36 for other carbonated soft drinks, 0.84 for orange juice, and 0.56 for fruit punch in the Nurses' Health Study I[15] and were 0.84 for sugar-sweetened cola, 0.55 for other sugar-sweetened soft drinks, 0.73 for diet cola, 0.74 for other diet soft drinks, 0.78 for orange juice, 0.77 for apple juice, 0.75 for grapefruit juice, and 0.89 for other fruit juices in the Health Professionals Follow-up Study,[16] 2 similar cohort studies among US health care professionals.

Assessment of Nondietary Exposures

Information on age, weight, smoking status, contraceptive use, postmenopausal hormone therapy, and pregnancies was collected on biennial questionnaires. We calculated body mass index (BMI) as weight in kilograms divided by the square of height in meters; height was assessed at baseline only. Self-reports of body weight were highly correlated with technician-measured weights ($r=0.96$) in the Nurses' Health Study I.[17] Family history of diabetes was reported in 1989 only. In 1991 and 1997, participants were asked how many flights of stairs they climb daily and the amount of time per week they spent on average on each of the following activities: walking or hiking outdoors; jogging; running; bicycling; lap swimming; tennis, squash, or racquetball playing; calisthenics; and other aerobic recreation. From this information, weekly energy expenditure in metabolic equivalent hours was calculated, weighting each activity by its intensity level.[18] Physical activity reported on the questionnaire was highly correlated with activity recorded in diaries or by 24-hour recall (0.79 vs 0.62).[19] Because physical activity was not assessed in 1995 or 1999, for our analysis on weight change, we used the 1997 estimate for both of these time points instead.

Ascertainment of Type 2 Diabetes

Women reporting a new diagnosis of diabetes on any of the biennial questionnaires were sent supplementary questionnaires asking about diagnosis and treatment of their diabetes, as well as history of ketoacidosis to confirm the self-report and to distinguish between type 1 and type 2 diabetes. In accordance with the criteria of the National

Diabetes Data Group,[20] confirmation of diabetes required at least 1 of the following: (1) an elevated plasma glucose concentration (fasting plasma glucose ≥7.8 mmol/L [140 mg/dL], random plasma glucose ≥11.1 mmol/L [200 mg/dL], and/or plasma glucose ≥11.1 mmol/L [200 mg/dL] after ≥2 hours during an oral glucose tolerance test) plus at least 1 classic symptom (excessive thirst, polyuria, weight loss, or hunger); (2) no symptoms but at least 2 elevated plasma glucose concentrations (by the aforementioned criteria) on different occasions; or (3) treatment with hypoglycemic medication (insulin or oral hypoglycemic agent). We used the National Diabetes Data Group criteria to define diabetes because the majority of our cases were diagnosed prior to the release of the American Diabetes Association criteria in 1997.[21] In substudies of the Nurses' Health Study I and the Health Professionals Follow-up Study, 98% and 97% of the self-reported diabetes cases documented by the same supplementary questionnaire were confirmed by medical record review.[22,23]

Statistical Analysis

We calculated the mean weight changes for groups defined by change in soft drink consumption from 1991 to 1995 and from 1995 to 1999, adjusting for age, alcohol intake, physical activity, smoking, BMI, and other lifestyle and dietary confounders at baseline for each period. We also adjusted for food items that have been previously shown to be associated with sugar-sweetened soft drink consumption.[24] We additionally adjusted for changes in these covariates (except BMI) during the period 1991 to 1995 in a separate model for that period.

We estimated the relative risk (RR) of diabetes for each category of intake compared with the lowest category using Cox proportional hazards analysis stratified by 5-year age categories and 2-year intervals. Duration of follow-up was calculated as the interval between the return of the 1991 questionnaire and diagnosis of diabetes, death, or June 1, 1999. The 1991 intake was used for the follow-up between 1991 and 1995, and the average of the 1991 and 1995 intakes was used for the follow-up between 1995 and 1999 to reduce within-participant variation and to best represent long-term diet.[25] We used the 1991 but not the 1995 intake data for individuals who reported on the 1993 or 1995 questionnaire a diagnosis of cancer (except nonmelanoma skin cancer) or cardiovascular disease because changes in diet after development of these conditions may confound the relationship between dietary intake and diabetes.[25]

We used information on covariates obtained from the baseline or subsequent questionnaires in multivariate analyses. Because BMI and total energy intake might represent intermediate end points or pathways rather than confounders for sugar-sweetened soft drinks, we adjusted for BMI and total caloric intake in separate models. Nondietary covariates were updated during follow-up using the most recent data for each 2-year follow-up interval. The significance of linear trends across categories of beverage consumption was tested by assigning to each participant the median value for the category and modeling this value as a continuous variable. We evaluated whether the association between sugar-sweetened soft drink consumption and risk of diabetes was modified by BMI, physical activity, and a family history of diabetes using analyses stratified by these variables and by modeling interaction terms.

All *P* values presented are 2-tailed; $P<.05$ was considered statistically significant. All statistical analyses were performed using SAS software, version 8.0 (SAS Institute Inc, Cary, NC).

RESULTS

Sugar-Sweetened Beverages and Weight Change

Women with a higher intake of sugar-sweetened soft drinks tended to be less physically active, to smoke more, and to have higher intake of total energy and lower intake of protein, alcohol, magnesium, and cereal fiber (**TABLE 1**). Intake of total carbohydrates, sucrose, and fructose as well as the overall glycemic index were higher in women with greater sugar-sweetened soft drink consumption, but starch intake was lower.

Women who increased their sugar-sweetened soft drink consumption between 1991 and 1995 from low (≤1/wk) to high (≥1/d) (n=1007) also increased their reported total energy intake by 358 kcal/d on average (**FIGURE 1**). In contrast, women who reduced their sugar-sweetened soft drink consumption between 1991 and 1995 (n=1020) also reduced their total energy consumption by 319 kcal/d on average. Changes in energy intake from food sources other than sugar-sweetened soft drinks accounted for only 27% to 34% of these changes in total energy intake. Similar associations were observed for the period 1995-1999.

For both periods 1991 to 1995 and 1995 to 1999, women who increased their consumption of sugar-sweetened soft drinks from low to high had significantly larger increases in weight (multivariate-adjusted means, 4.69 kg during 1991-1995 and 4.20 kg during 1995-1999) and BMI (multivariate-adjusted means, 1.72 during 1991-1995 and 1.53 during 1995-1999) than women who maintained a low or a high intake or substantially reduced their intake ($P<.001$) (**TABLE 2**). The lowest weight gain and increase in BMI were observed among women who reduced their intake from high to low (multivariate-adjusted mean change in weight, 1.34 kg during 1991-1995 and 0.15 kg during 1995-1999; respective multivariate-adjusted mean change in BMI, 0.49 and 0.05). Because lifestyle and dietary changes might confound these associations, we repeated the analysis for the period 1991 to 1995, additionally controlling for changes in physical activity and other covariates over time, but results remained similar. We repeated our analysis excluding all women who reported a pregnancy in 1991, 1995, or 1999, but this had minimal impact on our observations (data not shown).

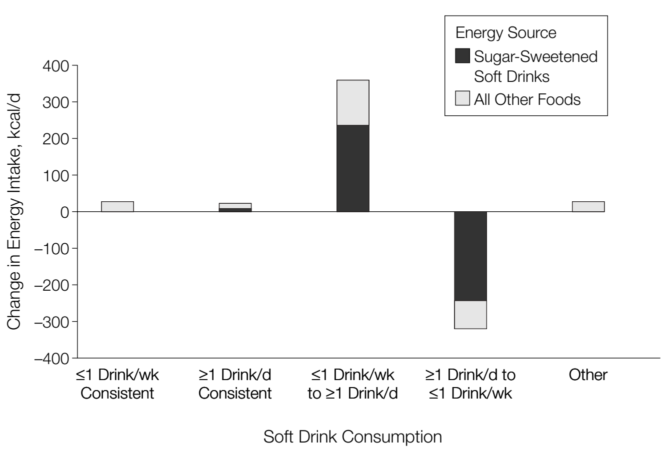
Women who increased consumption of fruit punch from 1 drink or less per week in 1991 to 1 drink or more per day in 1995 gained more weight

Table 1. Age-Standardized Baseline Characteristics According to Frequency of Sugar-Sweetened Soft Drink Consumption in 91 249 Women*

	Frequency of Sugar-Sweetened Soft Drink Consumption							
	1991				Change, 1991-1995			
Characteristics	<1/mo	1-4/mo	2-6/wk	≥1/d	Consistent, ≤1/wk	Consistent, ≥1/d	≤1/wk to ≥1/d	≥1/d to ≤1/wk
No. of participants	49 203	23 398	9950	8698	38 737	2366	1007	1020
Age, mean (SD), y	36.4 (4.6)	35.9 (4.7)	35.6 (4.8)	35.6 (4.8)	36.3 (4.6)	35.6 (4.8)	35.6 (4.9)	35.0 (4.9)
BMI, mean (SD)†	24.8 (5.2)	24.2 (5.0)	24.3 (5.5)	24.8 (6.1)	24.3 (4.9)	24.4 (5.9)	25.8 (5.8)	24.9 (5.7)
Physical activity, mean (SD), METs‡	23.2 (29.1)	19.0 (25.0)	17.7 (24.2)	16.4 (23.6)	21.6 (27.0)	15.4 (23.1)	18.1 (23.3)	18.6 (28.4)
Currently smoking	5353 (10.9)	2511 (10.7)	1485 (14.9)	1324 (21.0)	3653 (9.4)	491 (20.8)	128 (12.7)	170 (16.7)
Family history of diabetes§	8419 (17.1)	3608 (15.4)	1491 (15.0)	1409 (16.2)	6275 (16.2)	383 (16.2)	159 (15.8)	169 (16.6)
Currently using oral contraceptives	5550 (11.3)	2342 (10.0)	1003 (10.1)	943 (10.8)	4226 (10.9)	259 (11.0)	99 (9.8)	102 (10.0)
Currently receiving hormone therapy	1220 (2.5)	533 (2.3)	239 (2.4)	253 (2.9)	875 (2.3)	53 (2.3)	22 (2.2)	35 (3.4)
Diet, mean (SD)								
Total energy, kcal/d	1689 (516)	1831 (537)	1914 (553)	2113 (567)	1721 (504)	2087 (539)	1770 (536)	2076 (552)
Energy from nonsoda, kcal/d	1689 (516)	1808 (535)	1821 (551)	1822 (549)	1715 (502)	1774 (520)	1752 (534)	1821 (541)
Alcohol, g/d	3.4 (6.3)	2.9 (5.8)	2.9 (5.9)	2.4 (5.4)	3.3 (6.1)	2.2 (5.1)	2.8 (5.8)	2.7 (5.4)
Total carbohydrates, energy %	48.6 (7.7)	49.8 (6.8)	51.1 (6.5)	55.1 (6.9)	49.1 (7.4)	55.3 (6.8)	48.7 (7.2)	54.8 (6.8)
Starch, energy %	18.2 (4.6)	17.7 (4.2)	16.7 (3.9)	15.1 (3.9)	18.1 (4.4)	14.9 (3.7)	17.6 (4.3)	15.2 (3.9)
Sucrose, energy %	9.9 (3.0)	10.8 (3.0)	11.7 (3.1)	13.0 (3.4)	10.2 (3.0)	13.0 (3.3)	10.8 (3.2)	12.9 (3.4)
Fructose, energy %	4.4 (2.0)	5.0 (1.9)	6.1 (1.8)	9.2 (3.2)	4.6 (1.9)	9.6 (3.4)	4.6 (1.9)	8.8 (3.0)
Protein, energy %	20.2 (3.5)	19.1 (3.0)	18.1 (2.8)	16.2 (3.0)	19.8 (3.3)	16.0 (2.9)	19.4 (3.4)	16.6 (3.0)
Total fat, energy %	31.7 (5.9)	31.9 (5.3)	31.6 (5.1)	29.8 (5.1)	31.6 (5.7)	29.8 (5.0)	32.6 (5.5)	29.5 (5.0)
Saturated fat, energy %	11.2 (2.5)	11.4 (2.3)	11.4 (2.3)	10.7 (2.2)	11.2 (2.4)	10.7 (2.2)	11.6 (2.3)	10.6 (2.2)
Monounsaturated fat, energy %	12.0 (2.6)	12.2 (2.3)	12.1 (2.2)	11.5 (2.2)	12.0 (2.5)	11.5 (2.1)	12.4 (2.4)	11.3 (2.1)
Polyunsaturated fat, energy %	5.8 (1.4)	5.6 (1.3)	5.4 (1.2)	5.0 (1.2)	5.8 (1.4)	5.0 (1.1)	5.8 (1.4)	5.0 (1.2)
Trans-fat, energy %	1.6 (0.6)	1.7 (0.6)	1.7 (0.6)	1.7 (0.6)	1.6 (0.6)	1.7 (0.6)	1.8 (0.6)	1.6 (0.6)
Magnesium, mg/d	333 (75)	314 (66)	289 (61)	251 (60)	328 (73)	243 (59)	308 (68)	266 (63)
Caffeine, mg/d	260 (233)	226 (215)	226 (206)	216 (190)	246 (225)	198 (178)	224 (219)	228 (199)
Cereal fiber, g	6.1 (3.4)	5.6 (2.6)	4.8 (2.2)	4.0 (1.9)	6.0 (3.3)	4.0 (1.8)	5.3 (2.5)	4.3 (2.1)
Glycemic index	53.0 (3.4)	54.1 (3.0)	55.1 (2.7)	56.6 (2.5)	53.3 (3.2)	56.9 (2.4)	54.1 (3.3)	56.1 (2.6)

*Data are expressed as No. (%) unless otherwise indicated.
†Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.
‡Physical activity was computed as metabolic equivalent tasks (METs) per week using the duration per week of various forms of exercise, weighting each activity by its intensity level.
§In a first-degree relative.

Figure 1. Mean Change in Energy Consumption According to Time Trends in Sugar-Sweetened Soft Drink Consumption Between 1991 and 1995 in 51 603 Women



(3.69 kg) compared with women who decreased consumption (2.43 kg; *P*<.001). Similarly, increased consumption of fruit juice was associated with larger weight gain (4.03 kg) compared with decreased fruit juice consumption (2.32 kg) (*P*<.001). In contrast with sugar-sweetened beverages, weight gain in participants who increased their diet soft drink consumption from 1 drink or less per week in 1991 to 1 drink or more per day in 1995 (1.59 kg) was significantly lower compared with women who decreased their diet soft drink consumption from 1 drink or more per day in 1991 to 1 drink or less per week in 1995 (4.25 kg) (*P*<.001).

Women who increased their soft drink consumption from 1991 to 1995

Table 2. Mean Weight Change According to Time Trends in Sugar-Sweetened Soft Drink Consumption in 51 603 Women

Period	Change in Sugar-Sweetened Soft Drink Consumption* Consistent, ≤1/wk	Consistent, ≥1/d	≤1/wk to ≥1/d	≥1/d to ≤1/wk	Other
1991-1995					
No. of participants	38 737	2366	1007	1020	8473
Weight change, mean (SE), kg					
Model 1†	3.21 (0.03)	3.12 (0.13)	4.69 (0.20)	1.34 (0.20)	3.04 (0.07)
Model 2‡	3.23 (0.03)	3.05 (0.13)	4.85 (0.19)	1.09 (0.19)	2.96 (0.07)
Model 3§	3.23 (0.03)	3.06 (0.13)	4.79 (0.19)	1.17 (0.19)	2.96 (0.07)
Model 4‖	3.22 (0.03)	3.11 (0.13)	4.49 (0.19)	1.56 (0.19)	3.00 (0.07)
BMI change, mean (SE)¶					
Model 1†	1.18 (0.01)	1.15 (0.05)	1.72 (0.07)	0.49 (0.07)	1.12 (0.03)
Model 2‡	1.19 (0.01)	1.13 (0.05)	1.79 (0.07)	0.40 (0.07)	1.09 (0.02)
Model 3§	1.19 (0.01)	1.13 (0.05)	1.76 (0.07)	0.43 (0.07)	1.09 (0.02)
Model 4‖	1.18 (0.01)	1.15 (0.05)	1.65 (0.07)	0.57 (0.07)	1.11 (0.02)
1995-1999					
No. of participants	39 279	2340	765	1107	8112
Weight change, mean (SE), kg†	2.04 (0.03)	2.21 (0.13)	4.20 (0.22)	0.15 (0.18)	2.10 (0.07)
BMI change, mean (SE)¶	0.75 (0.01)	0.81 (0.05)	1.53 (0.08)	0.05 (0.07)	0.77 (0.02)

*Low and high soft drink consumption were defined as 1or fewer drinks per week and 1 or more drinks per day, respectively. Means for low-low, high-high, high-low, and other were all significantly ($P<.001$) different from low-high.
†Adjusted for baseline age (continuous), alcohol intake (0, 0.1-4.9, 5.0-9.9, or ≥10 g/d), physical activity (quintiles of metabolic equivalent task score), smoking (never, past, current, or missing), postmenopausal hormone use (none, current or past, or missing), oral contraceptive use (none, current, or missing), cereal fiber intake (quintiles), total fat intake (quintiles), and body mass index (continuous).
‡Model 1 plus additional adjustment for changes in confounders over time.
§Model 2 plus additional adjustment for baseline energy intake from nonsoda sources and changes over time.
‖Model 3 plus additional adjustment for baseline intake of red meat, french fries, processed meat, sweets, snacks, vegetables, and fruits, and changes over time.
¶Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

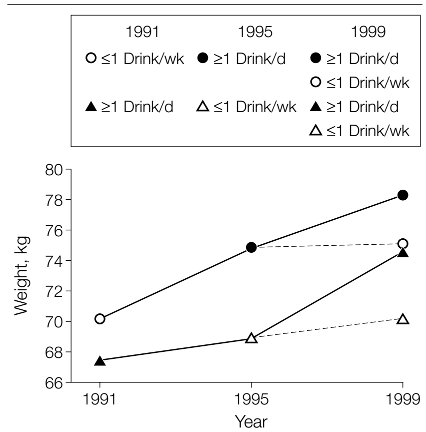
and maintained a high level of intake during 1995-1999 gained, on average, 8.0 kg between 1991 and 1999, whereas women who decreased their consumption between 1991 and 1995 and maintained a low level of intake gained 2.8 kg between 1991 and 1999 on average (FIGURE 2).

Sugar-Sweetened Beverages and Risk of Diabetes

During 716 300 person-years of follow-up, we documented 741 new cases of type 2 diabetes. Greater sugar-sweetened soft drink consumption was strongly associated with progressively higher risk of type 2 diabetes (TABLE 3). The age-adjusted RR was 1.98 (95% confidence interval [CI], 1.60-2.44) for women consuming 1 or more sugar-sweetened soft drinks per day compared with those consuming less than 1 sugar-sweetened soft drink per month. This association was slightly attenuated after adjustment for lifestyle and dietary confounders (RR for extreme categories, 1.83; 95% CI, 1.42-2.36; $P<.001$ for trend). The RR for extreme categories further controlling for BMI was 1.39 (95% CI, 1.07-1.76; $P=.01$ for trend). This finding suggests that BMI accounted for about half of the excess risk. Adjustment for caloric intake in addition to BMI further attenuated the association, but sugar-sweetened soft drinks remained significantly associated with an increased risk of diabetes (RR for extreme categories, 1.32; 95% CI, 1.01-1.73; $P=.04$ for trend). The results for sugar-sweetened cola alone were similar to those for all sugar-sweetened soft drinks (Table 3). Similar to sugar-sweetened soft drinks, fruit punch consumption was significantly associated with diabetes risk. The multivariate RR for fruit punch consumption of 1 drink or more per day compared with less than 1 drink per month was 2.00 (95% CI, 1.33-3.03; $P=.001$ for trend).

Additional adjustment for the waist-hip ratio among women reporting waist and hip circumferences in 1993 (n=43 756) did not change our results for sugar-sweetened soft drinks. Results were also similar adjusting for intake of caffeine, red meat, french fries, processed meat, sweets, snacks, vegetables, and fruit. Associations did not differ substantially by obesity status, family history of diabetes, physical ac-

Figure 2. Mean Weight in 1991, 1995, and 1999 According to Trends in Sugar-Sweetened Soft Drink Consumption in 1969 Women Who Changed Consumption From 1991 to 1995 and Either Changed or Maintained Level of Consumption Until 1999



Low and high intakes were defined as 1 drink or less per week and 1 drink or more per day, respectively. The number of participants were: low-high-high, 323; low-high-low, 461; high-low-high, 110; and high-low-low, 746. Groups with similar intake in 1991 and 1995 were combined for estimates for these time points. Means were adjusted for age, alcohol intake, physical activity, smoking, postmenopausal hormone use, oral contraceptive use, cereal fiber intake, and total fat intake at each time point. $P=.02$ for difference between low-high-high intake and low-high-low intake and for difference between high-low-high intake and high-low-low intake.

tivity level, cereal fiber intake, *trans*-fat intake, or ratio of polyunsaturated to saturated fat (TABLE 4).

Diet soft drink consumption was associated with a slight, nonsignificant increased diabetes risk after additional adjustment for baseline BMI. The RR for diet soft drink consumption of 1 or more drinks per day compared with less

Table 3. Relative Risk of Type 2 Diabetes According to Frequencies of Sugar-Sweetened Beverage Consumption in 91 249 Women

	Sugar-Sweetened Soft Drink Intake				*P* Value for Trend
	<1/mo	1-4/mo	2-6/wk	≥1/d	
All sugar-sweetened soft drinks					
Cases	368	163	95	115	
Person-years	381 275	188 501	80 086	66 438	
Age-adjusted RR (95% CI)	1.00	0.93 (0.78-1.12)	1.32 (1.06-1.66)	1.98 (1.60-2.44)	<.001
Multivariate-adjusted RR (95% CI)*	1.00	1.06 (0.87-1.28)	1.49 (1.16-1.91)	1.83 (1.42-2.36)	<.001
Sugar-sweetened cola					
Cases	403	142	96	100	
Person-years	420 598	166 656	75 778	53 267	
Age-adjusted RR (95% CI)	1.00	0.92 (0.76-1.12)	1.44 (1.16-1.81)	2.14 (1.72-2.67)	<.001
Multivariate-adjusted RR (95% CI)*	1.00	0.99 (0.80-1.23)	1.56 (1.21-2.02)	1.87 (1.43-2.45)	<.001
Fruit punch					
Cases	589	85	38	29	
Person-years	525 780	124 932	45 958	19 630	
Age-adjusted RR (95% CI)	1.00	0.95 (0.73-1.24)	1.24 (0.86-1.77)	2.31 (1.55-3.45)	<.001
Multivariate-adjusted RR (95% CI)*	1.00	0.90 (0.68-1.18)	1.15 (0.79-1.66)	2.00 (1.33-3.03)	.001

Abbreviations: CI, confidence interval; RR, relative risk.
*Relative risks are adjusted for age; alcohol intake (0, 0.1-4.9, 5.0-9.9, or ≥10 g/d); physical activity (quintiles); family history of diabetes; smoking (never, past, or current); postmenopausal hormone use (never or ever); oral contraceptive use (never, past, or current); intake (quintiles) of cereal fiber, magnesium, *trans*-fat, and ratio of polyunsaturated to saturated fat; and consumption of sugar-sweetened soft drinks, diet soft drinks, fruit juice, and fruit punch (other than the main exposure, depending on model).

Table 4. Relative Risk of Type 2 Diabetes According to Frequencies of Sugar-Sweetened Soft Drink Consumption by Obesity Status, Physical Activity Level, Family History of Diabetes, and Intake Levels of Cereal Fiber, *Trans*-Fat, and P:S Ratio in 91 249 Women*

	No. of Cases	Sugar-Sweetened Soft Drink Intake, RR (95% CI)				*P* Value for Trend
		<1/mo	1-4/mo	2-6/wk	≥1/d	
Nonobese (BMI <30)†	143	1.00	1.14 (0.74-1.76)	1.60 (0.91-2.79)	1.78 (0.97-3.26)	.06
Obese (BMI ≥30)	579	1.00	1.08 (0.87-1.35)	1.31 (0.98-1.74)	1.35 (1.01-1.80)	.04
P value for interaction						.47
High physical activity‡	308	1.00	0.96 (0.71-1.30)	1.46 (0.99-2.15)	1.54 (1.01-2.33)	.02
Low physical activity‡	433	1.00	1.08 (0.84-1.38)	1.39 (1.01-1.91)	1.68 (1.21-2.32)	.001
P value for interaction						.83
Without family history	459	1.00	1.14 (0.89-1.45)	1.49 (1.09-2.04)	1.86 (1.34-2.56)	<.001
With family history	282	1.00	0.86 (0.62-1.20)	1.32 (0.89-1.96)	1.30 (0.85-1.99)	.12
P value for interaction						.52
High cereal fiber intake§	319	1.00	0.94 (0.71-1.26)	1.33 (0.89-1.98)	1.44 (0.86-2.42)	.08
Low cereal fiber intake	422	1.00	1.15 (0.88-1.50)	1.52 (1.10-2.08)	1.79 (1.31-2.43)	<.001
P value for interaction						.58
High P:S ratio§	356	1.00	1.02 (0.77-1.35)	1.65 (1.16-2.36)	1.64 (1.11-2.43)	.005
Low P:S ratio	385	1.00	1.04 (0.80-1.37)	1.22 (0.87-1.72)	1.53 (1.09-2.15)	.01
P value for interaction						.44
Low *trans*-fat intake§	280	1.00	1.07 (0.78-1.48)	1.69 (1.14-2.50)	1.59 (1.03-2.44)	.02
High *trans*-fat intake	461	1.00	1.00 (0.79-1.28)	1.26 (0.92-1.72)	1.66 (1.21-2.27)	.001
P value for interaction						.87

Abbreviations: BMI, body mass index, calculated as weight in kilograms divided by the square of height in meters; CI, confidence interval; P:S ratio, ratio of polyunsaturated to saturated fat; RR, relative risk.
*Relative risks are adjusted for age; alcohol intake (0, 0.1-4.9, 5.0-9.9, or ≥10 g/d); physical activity (quintiles); family history of diabetes; smoking (never, past, or current); postmenopausal hormone use (never or ever); oral contraceptive use (never, past, or current); intake (quintiles) of cereal fiber, magnesium, *trans*-fat, and P:S ratio; and diet soft drink consumption.
†Denominator is 88 710 participants because of missing values.
‡Low activity: lowest 2 quintiles of metabolic equivalent task (MET) score; high activity: highest 3 quintiles of MET score.
§Strata based on baseline medians (cereal fiber, 5.0 g/d; P:S ratio, 0.50; *trans*-fat, 1.5% of total energy intake).

than 1 drink per month was 1.21 (95% CI, 0.97-1.50; $P=.12$ for trend). Relative risk remained unchanged after additional adjustment for caloric intake.

Fruit juice consumption was not associated with diabetes risk. The multivariate-adjusted RR of diabetes comparing women who consumed more than 1 drink per day of fruit juices with women who consumed less than 1 drink per month of fruit juices was 0.97 (95% CI, 0.64-1.47; $P=.84$ for trend).

COMMENT

In this 8-year follow-up study of women, we found positive associations between sugar-sweetened beverage consumption and both greater weight gain and risk of type 2 diabetes, independent of known risk factors.

Sugar-sweetened soft drinks may contribute to weight gain because of the low satiety of liquid foods. Energy provided by sugar-sweetened beverages does not affect subsequent food and energy intake in short-term human studies.[26-28] Similarly, in experimental animals, intake of sugar-sweetened beverages is not fully compensated by reductions in intake of solid foods, resulting in a positive caloric balance and development of obesity.[29] Consequently, consumption of sugar-sweetened soft drinks significantly increased caloric intake and body weight over a 3-week period in normal-weight adults,[30] and supplementing sucrose, mainly in the form of sugar-sweetened soft drinks, over a 10-week period to ad libitum diets in overweight men and women resulted in an increase in energy intake and body weight (by 1.6 kg) compared with decreases with artificially sweetened supplements (by 0.3 kg).[31] Consumption of sugar-sweetened soft drinks has also been associated with greater risk of obesity in children,[8] while consumption of diet soft drinks has not. Interestingly, in our study, women who increased their sugar-sweetened soft drink consumption also increased energy intake from other foods, indicating that these beverages may even induce hunger and food intake. However, experimental data on soft drink consumption and food intake have not provided support for this hypothesis.[32,33] Our observation may, therefore, rather reflect dietary and lifestyle changes accompanying changes in soft drink consumption.

We observed no difference in weight change between women with consistently low or high sugar-sweetened soft drink consumption. The lower weight gain associated with reduction of sugar-sweetened soft drink consumption compared with stable intake suggests that women do benefit from decreasing consumption but that weight trajectories do not continue to diverge with time. Long-term effects of sugar-sweetened beverages on body weight have not been studied in experimental settings so far, and further research is warranted.

Besides their potential contribution to weight gain, sugar-sweetened soft drinks might also increase risk of type 2 diabetes because of their high amount of rapidly absorbable carbohydrates. They contain large amounts of high-fructose corn syrup, which has similar effects on blood glucose as sucrose,[9] and consumption of sugar-sweetened soft drinks induces a fast and dramatic increase in both glucose and insulin concentrations.[34] Sugar-sweetened soft drinks therefore contribute to a high glycemic index of the overall diet, a risk factor for diabetes in this study population[35] and other cohort studies.[11] In addition, cola-type soft drinks contain caramel coloring, which is rich in advanced glycation end products, which may increase insulin resistance[12] and inflammation.[13] However, diet cola was generally not associated with diabetes risk after adjustment for BMI. Advanced glycation end products therefore appear unlikely to account for the association between sugar-sweetened soft drinks and diabetes. In addition, soft drinks often contain caffeine, which might reduce diabetes risk.[36,37] However, the caffeine content of soft drinks (10-16 mg per 100 g) is considerably less than in coffee (35-75 mg per 100 g) or black tea (about 22 mg per 100 g) and soft drinks might therefore contribute moderately to variation in total caffeine consumption in the adult US population. In our study population, adjustment for caffeine did not alter the association for soft drinks.

Fruit juice consumption was not associated with diabetes risk in our study, which suggests that naturally occurring sugars in beverages may have different metabolic effects than added sugars. Fruit juices generally have a lower glycemic index than sugar-sweetened soft drinks and fruit punches.[38] In addition, vitamins, minerals, soluble fiber, and phytochemicals in fruit juices may have beneficial effects counterbalancing potential adverse effects of sugars. In contrast, fruit punches contain only a small proportion of fruit juice but large amounts of added high-fructose corn syrup and, therefore, provide little nutritional value compared with pure fruit juices. Our finding that fruit punch consumption was associated with increased diabetes risk suggests that its physiological consequences may be similar to sugar-sweetened soft drinks.

Imprecise dietary measurement could potentially have influenced our observed associations. However, random errors in dietary assessment measures might have accounted for a lack of association but not the reverse.[25] The repeated dietary measurements made in this study were an advantage because they reduce measurement errors and account for changes in eating patterns over time.[25] Because of the observational nature of the study, we cannot prove that the observed associations are causal because residual confounding could theoretically affect the observed associations. However, we controlled for potential confounding by most known risk factors that are plausibly associated with soft drink consumption and changes in these variables over time. Consistent with our observation, supplementation of sucrose, mainly in the form of soft drinks, resulted in increased energy consumption in an experimental study, with the increase largely attributable to the increased sucrose intake.[31] A further limitation of our study is the reliance on self-reported body weight. It is possible that underreporting of body weight, particularly among heavier women, may have led to an underestimation of weight gain. However, correlation between self-reported and technician-measured body weight was found to be high in a similar cohort of older female nurses,[17] and underreporting may be less prevalent among relatively young women.[39] Also, we used the National Diabetes Data Group criteria to define diabetes,[20] but the diagnostic criteria were changed in 1997[21] such that lower fasting glucose levels would be considered diagnostic. The majority of our cases were diagnosed prior to the release of the revised criteria in 1997; the incidence of diabetes in our cohort is therefore likely an underestimation.

In conclusion, our findings suggest that frequent consumption of sugar-sweetened beverages may be associated with larger weight gain and increased risk of type 2 diabetes, possibly by providing excessive calories and large amounts of rapidly absorbable sugars. Public health strategies to prevent obesity and type 2 diabetes should focus on reducing sugar-sweetened beverage consumption.

Author Contributions: Dr Schulze had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Analysis and interpretation of data: Schulze, Manson, Ludwig, Colditz, Stampfer, Willett, Hu.
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