



# Changes in Consumption of Sugary Beverages and Artificially Sweetened Beverages and Subsequent Risk of Type 2 Diabetes: Results From Three Large Prospective U.S. Cohorts of Women and Men

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## OBJECTIVE

We evaluated the associations of long-term changes in consumption of sugary beverages (including sugar-sweetened beverages and 100% fruit juices) and artificially sweetened beverages (ASBs) with subsequent risk of type 2 diabetes.

## RESEARCH DESIGN AND METHODS

We followed up 76,531 women in the Nurses' Health Study (1986–2012), 81,597 women in the Nurses' Health Study II (1991–2013), and 34,224 men in the Health Professionals' Follow-up Study (1986–2012). Changes in beverage consumption (in 8-ounce serving/day) were calculated from food frequency questionnaires administered every 4 years. Multivariable Cox proportional regression models were used to calculate hazard ratios for diabetes associated with changes in beverage consumption. Results of the three cohorts were pooled using an inverse variance-weighted, fixed-effect meta-analysis.

## RESULTS

During 2,783,210 person-years of follow-up, we documented 11,906 incident cases of type 2 diabetes. After adjustment for BMI and initial and changes in diet and lifestyle covariates, increasing total sugary beverage intake (including both sugar-sweetened beverages and 100% fruit juices) by >0.50 serving/day over a 4-year period was associated with a 16% (95% CI 1%, 34%) higher diabetes risk in the subsequent 4 years. Increasing ASB consumption by >0.50 serving/day was associated with 18% (2–36%) higher diabetes risk. Replacing one daily serving of sugary beverage with water, coffee or tea, but not ASB, was associated with a 2–10% lower diabetes risk.

## CONCLUSIONS

Increasing consumption of sugary beverages or ASBs was associated with a higher risk of type 2 diabetes, albeit the latter may be affected by reverse causation and surveillance bias.

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The relationship between the consumption of sugar-sweetened beverages (SSBs; i.e., soft drinks, punches, fruit drinks, sugared iced tea, and sports drinks) and type 2 diabetes is now supported by substantial epidemiological evidence (1,2). Moreover, several randomized trials have demonstrated deleterious effects of SSB consumption on cardiometabolic risk factors, providing further support for this association (2). Consumption of 100% fruit juices has been considered a healthy alternative to SSBs because of the vitamins and minerals in fruit juices. However, they typically contain similar amounts of sugar and calories as SSBs (3,4). Epidemiologic evidence suggests that 100% fruit juices are also positively associated with risk of diabetes (1), raising concerns for the negative health effects of sugary beverages, regardless of whether the sugar is added or naturally occurring (1,3–5). As noncaloric drinks, artificially sweetened beverages (ASBs) also appear as healthy alternatives to SSBs. Randomized controlled trials demonstrated that replacing SSBs with ASBs has beneficial effects on body weight (6,7), which should translate to a lower diabetes risk in the long term. Still, a recent meta-analysis of 10 prospective cohort studies observed that long-term ASB consumption was associated with a higher diabetes risk (1). While this meta-analysis raises doubts about the healthy halo of these drinks, it needs to be interpreted with caution as the association of ASB consumption with diabetes risk may be affected by the reverse causation bias, i.e., individuals at higher risk of diabetes may switch from sugary beverages to diet drinks (1,2,8,9).

Data from National Health and Nutrition Examination Survey indicated that SSB consumption has been declining in the U.S. over the last decade, along with intakes of fruit juices and ASBs (8,10,11). However, to our knowledge, whether longitudinal changes in the consumption of sugary beverages (which include SSBs and 100% fruit juices) or ASBs are associated with a subsequent risk of type 2 diabetes has never been thoroughly evaluated.

In the current study, we evaluated the associations between changes in consumption of sugary beverages (total, SSBs, or 100% fruit juices) and ASBs with subsequent type 2 diabetes risk. Our analysis is based on the repeated assessments of diet every 4 years over up to 26 years of follow-up in the Nurses' Health Study (NHS), the NHS II, and the Health Professionals' Follow-up

Study (HPFS). We also used these repeated measurements of diet to estimate the effect of replacing sugary beverages with ASBs or other beverages (water, coffee, tea, or milk) on subsequent risk of diabetes.

## RESEARCH DESIGN AND METHODS

### Study Population

The NHS is a prospective cohort study of 121,701 U.S. registered female nurses aged 30–55 years at study inception in 1976 (12). The NHS II is a prospective cohort study that included 116,430 U.S. registered female nurses aged 25–42 years when it was initiated in 1989 (12). The HPFS is a prospective cohort study of 51,529 U.S. male health professionals aged 40–75 years at study inception in 1986 (13). The three studies are ongoing, and ~10% of participants dropped-out or were lost during follow-up.

In the three cohorts, diet was thoroughly assessed every 4 years, and information of lifestyle practices and occurrence of new-onset diseases was collected every 2 years, starting in 1986 in the NHS and the HPFS and in 1991 in the NHS II. Because our primary analysis used the 4-year change in beverage consumption to evaluate the risk of type 2 diabetes in the subsequent 4-year period, the year 1990 in the NHS and HPFS, and 1995 in the NHS II were used as baseline for the current analysis. We excluded participants with diabetes, cancer, cardiovascular disease, or who died prior to baseline. We also excluded participants whose last returned questionnaire was at baseline. Participants in whom change in beverage consumption was impossible to calculate because they did not complete consecutive food frequency questionnaires (FFQs) and participants who reported implausible calorie intake (<500 or >3,500 kcal/day for women or <800 or >4,200 kcal/day for men) were excluded from the intervals with the missing/implausible data and re-entered when those data were available/plausible. After exclusions, the current analysis includes 76,531 women in the NHS, 81,597 women in the NHS II, and 34,224 men in the HPFS (Supplementary Fig. 1).

The study was approved by the institutional review boards of Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health. Completion of the self-administered questionnaire was considered to imply informed consent.

### Dietary Assessment

In the three cohorts, dietary information was collected and updated every 4 years using a validated FFQ (14). Participants were asked how often, on average, they consumed a standard portion size of each food or beverage, from "never or less than once per month" to "≥6 times per day." Questionnaire items on SSBs included carbonated and noncarbonated beverages with sugar (soft drink, punch, lemonade, fruit drink, or sugared ice tea), with one glass, bottle, or can (12 ounces) as the standard serving size. Consumption of 100% fruit juice was ascertained with apple juice, orange juice, grapefruit juice, and other fruit juices, with one small glass (4–6 ounces) as the reference serving. For the current analysis, daily consumption of SSBs and fruit juices was converted into 8-ounce servings and summed to obtain total daily sugary beverage consumption. Questionnaire items on ASBs included low-calorie beverages with or without caffeine and the standard portion size was one glass, bottle, or can (12 ounces). Daily consumption of ASBs was also converted into 8-ounce servings for analysis. Consumption of water, coffee, tea, reduced-fat milk (0–2% milk-fat), and whole milk was also ascertained in the questionnaire with 8 ounces as the standard serving size. The amount of sugar and dairy added to coffee or tea was not assessed in the FFQ. In the current analysis, for any beverage, one serving equals 8 ounces. The reproducibility and validity of the FFQ were previously described (14,15). For instance, in the NHS, the deattenuated correlation coefficients between the FFQ and multiple dietary records were 0.84 for soft drinks, 0.56 for fruit punch, 0.84 for orange juice, 0.36 for ASBs, 0.81 for reduced-fat milk, 0.78 for coffee, and 0.93 for tea (15). The correlation coefficient for water (0.53) was only available in the validation study in the HPFS (14).

### Assessment of Type 2 Diabetes

The primary outcome of the present analysis was incidence of confirmed type 2 diabetes. Cases were first identified by self-report from participants on the main questionnaire completed every 2 years. Cases were subsequently confirmed by the completion of a validated supplementary questionnaire on the symptoms, diagnostic tests, and

treatment of diabetes. Before 1998, criteria from the National Diabetes Data Group were used (16–19). The report of at least one of the following criteria were used to confirm a case of diabetes: 1)  $\geq 1$  classic symptoms (excessive thirst, polyuria, weight loss, or hunger) and fasting glucose concentrations  $\geq 7.8$  mmol/L or random glucose concentrations  $\geq 11.1$  mmol/L; 2)  $\geq 2$  elevated glucose concentrations on different occasions (fasting concentrations  $\geq 7.8$  mmol/L, random glucose concentrations  $\geq 11.1$  mmol/L, and/or concentrations of  $\geq 11.1$  mmol/L after  $\geq 2$  h shown by oral glucose tolerance testing) in the absence of symptoms; or 3) treatment with hypoglycemic medication (insulin or oral hypoglycemic agent). After 1998, cases were defined using the American Diabetes Association criteria, which lowered the threshold for fasting glucose for the diagnosis of diabetes to 7.0 mmol/L, instead of 7.8 mmol/L (20). The current study only includes confirmed cases.

#### Assessment of Covariates

Using the main questionnaires, we collected and updated information on multiple diabetes risk factors or confounders (age, race, body weight, cigarette smoking, physical activity, family history of diabetes, history of hypercholesterolemia, high blood pressure, and physical examination). In women, we ascertained menopausal status and the use of postmenopausal hormones and oral contraceptives. Information on alcohol intake was collected via the FFQs. We used the 2010 Alternative Healthy Index (AHEI), calculated with FFQ data, as an overall indicator of diet quality (21).

#### Statistical Analysis

We calculated each participant's person-years from the date of return of the baseline questionnaire to the date of diabetes diagnosis, death, or the end of the follow-up (30 June 2012 for the NHS, 30 June 2013 for the NHS II, and 31 January 2012 for the HPFS), whichever came first.

We used changes in beverage consumption updated every 4 years as a time-varying exposure to estimate the risk of diabetes in the subsequent 4-year period. For instance, changes in total sugary beverage consumption between 1986 and 1990 were used to evaluate the risk of diabetes between 1990 and 1994,

and so on. Participants were divided into five categories of change in beverage intakes: no change or relatively stable consumption ( $\pm 0.14$  serving/day, or  $\pm 1.0$  serving/week), increase or decrease in consumption ranging from 1.0 serving/week to 0.50 serving/day, and increase or decrease in consumption by  $> 0.50$  serving/day. To minimize the influence of outliers, changes in beverage consumption  $< 0.5$  and  $> 99.5$  percentiles were recoded into the value of the 0.5 and the 99.5 percentiles, respectively.

We used time-dependent Cox proportional hazards regression models to calculate hazard ratios (HRs) of type 2 diabetes for changes in beverage consumption. Model 1 was stratified by calendar year in 4-year intervals and adjusted for initial age. Model 2 was further adjusted for race; family history of diabetes; physical examination during the 4-year cycle; initial menopausal status and postmenopausal hormone (NHS and NHS II) and oral contraceptive use (NHS II only); simultaneous change in smoking status; initial and change in physical activity level; initial and change in alcohol consumption; initial and change in AHEI score (calculated without the alcohol and sugary beverage components); initial and change in intakes of water, coffee, tea, and milk; initial intakes of sugary beverages and ASBs; change in ASB/sugary beverage intake depending on the main exposure; initial BMI; and initial calorie intake.

In analyses with change in SSBs or fruit juices as the main exposure, initial sugary beverage consumption was replaced with initial intake of SSBs or fruit juices, and changes in SSB or fruit juice consumption were mutually adjusted. We tested for a linear trend across categories of change in beverage consumption by treating the median value of each category of change as a continuous variable in the models.

In sensitivity analyses, we further adjusted model 2 for concurrent 4-year changes in calorie intake and/or change in body weight as these are believed to be in the causal pathway between changes in sugary beverage consumption and diabetes risk (22,23). SAS macro %mediate (publicly available at <http://www.hsph.harvard.edu/donna-spiegelman/software/mediate/>) was then applied, and the formula of  $1 - (\beta_{\text{mediator model}}/\beta_{\text{base model}})*100$

was used to evaluate the mediation effect of the concurrent body weight change on the association between changes in beverage consumption and diabetes risk (24). The percentage derived from the mediation effect reflects the relative contribution of change in body weight in the causal pathway between changes in sugary beverage consumption and diabetes risk. To address the potential reverse causation in the relationship between ASB consumption and diabetes risk (2), we used a 4-year lagged analysis to minimize the impact of recent dietary changes made among higher-risk individuals. We also evaluated the association of 8-year changes in beverage consumption with subsequent 8-year risk of diabetes. To address surveillance bias (i.e., higher risk individuals are likely to be screened for diabetes and diagnosed more rapidly), we evaluated the association of 4-year change in beverage consumption and risk of symptomatic diabetes, ascertained by the report of at least one symptom of diabetes in the supplementary questionnaire. Finally, we conducted stratified analyses according to initial diet quality, initial BMI, and 4-year change in physical activity level. Interactions were tested using likelihood ratio tests by including cross-product terms of each stratum and changes in beverage consumption in the multivariable models.

We estimated the effect on diabetes risk of decreasing the consumption of sugary beverage and simultaneously increasing the consumption of another beverage by one daily serving. To do so, we included in Cox proportional hazards models all beverages simultaneously (initial and change, both continuous, in serving/day of sugary beverage, ASB, water, coffee, tea, and reduced-fat milk), and calculated the HR from the difference in  $\beta$  coefficients of changes in intakes of different beverages and the 95% CI from the corresponding variances and covariance (22).

Analyses were conducted separately in each cohort. Because the three cohorts have similar design, results were pooled using an inverse variance-weighted, fixed-effects meta-analysis. The Q statistic was used to evaluate heterogeneity between the cohorts. Statistical analyses were performed using SAS software version 9.4. Statistical significance was considered at  $P < 0.05$  (two-sided).

## RESULTS

During a total of 2,783,210 person-years of follow-up, we documented 11,906 incident cases of type 2 diabetes (5,993 in the NHS, 3,613 in the NHS II, and 2,300 in the HPFS). Table 1 presents the age-adjusted characteristics of participants according to baseline 4-year changes in total sugary beverage consumption. Individuals who decreased their sugary beverage consumption by  $>0.50$  serving/day were those with the highest initial sugary beverage and energy intakes, and with the lowest initial AHEI score. In the first 4-year period, body weight increased more among those who increased their sugary beverage consumption than among those who maintained a stable consumption or decreased their consumption.

Supplementary Table 1 presents the age-adjusted characteristics of participants according to baseline 4-year changes in ASB consumption. Initial BMI, physical activity level, and AHEI score, as well as the rates of hypertension, high cholesterol, family history of diabetes, and fasting blood glucose screening were higher among individuals who decreased or increased ASB consumption by  $>0.50$  serving/day compared with those who maintained a stable consumption. Individuals who increased their ASB consumption tended to gain less weight than those whose consumption decreased in the first 4 years of follow-up.

Table 2 presents pooled HRs for incidence of type 2 diabetes according to updated 4-year changes in beverage consumption. In the multivariable analysis, individuals who decreased their total sugary beverage consumption by  $>0.50$  serving/day had a similar risk of diabetes in the subsequent 4 years as participants who maintained stable intake. Increasing total sugary beverage intake by  $>0.50$  serving/day was associated with a 16% (95% CI 1%, 34%) higher risk of diabetes compared with maintaining a stable consumption. Increasing consumption of only SSBs or fruit juices by  $>0.50$  serving/day was associated with a 9% (95% CI 3%, 17%) and 15% (95% CI 7%, 23%) higher risk of diabetes, respectively. Decreasing ASB consumption was not associated with diabetes compared with maintaining a stable consumption. Increasing ASB consumption by  $>0.50$  serving/day was

associated with a 18% (95% CI 2%, 36%) higher risk of diabetes in the subsequent 4-year period compared with the reference category. Results were similar across each cohort (Supplementary Table 2).

In sensitivity analyses, the main findings were not materially changed after further adjustment for concurrent change in calorie intake and/or change in body weight (Supplementary Table 3). Weight change statistically explained 27.9% (95% CI 17.5%, 41.3%) of the linear trend between changes in total sugary beverage consumption and diabetes risk, 38.7% (95% CI 16.1%, 67.4%) of the association between changes in SSB consumption and diabetes risk, 22.5% (95% CI 10.4%, 42.0%) of the association between changes in fruit juice consumption and diabetes risk, and 7.1% (95% CI 2.8%, 16.9%) of the linear trend between changes in ASB consumption and diabetes risk. The 4-year lagged analysis, the 8-year change analysis, and the analysis on symptomatic diabetes cases yielded similar results (Supplementary Table 3). In stratified analyses (Supplementary Table 4), no significant interaction was detected for AHEI, BMI, and change in physical activity.

Figure 1 presents the pooled HRs for diabetes risk according to initial and final consumption of sugary beverages and ASBs during a 4-year period. Compared with participants who consumed  $<1$  serving/week of sugary beverage for 4 years, individuals who increased their consumption from  $<1$  serving/week to  $\geq 1$  serving/day over a 4-year period had a higher risk of diabetes in the subsequent 4 years (HR 1.15, 95% CI 0.98, 1.35). Compared with participants who consumed  $<1$  serving/week of sugary beverages for 4 years, individuals whose consumption decreased from  $\geq 1$  serving/day to  $<1$  serving/week had a 9% (95% CI  $-5\%$ , 25%) diabetes risk, whereas those who consumed  $\geq 1$  serving/day for 4 years had a 23% (95% CI 15%, 33%) higher diabetes risk. For ASB, any increase in consumption was associated with a higher risk of diabetes compared with the reference ASB category ( $<1$  serving/week for 4 years).

Figure 2 presents pooled HRs from substitution models for diabetes associated with decreasing consumption of sugary beverage and concomitantly increasing consumption of another

beverage by one serving/day. We estimated that replacing one daily serving of a sugary beverage with one daily serving of an ASB was not associated with diabetes risk in the subsequent 4 years. However, replacing a sugary beverage with water, coffee, tea, or reduced-fat milk (0–2% fat) was associated with a 2–10% lower diabetes risk.

## CONCLUSIONS

In these three large cohort studies of U.S. women and men, we observed that increasing total consumption of sugary beverages, which include both beverages with added sugar (i.e., SSBs) and 100% fruit juices, or ASBs was associated with a 16–18% higher risk of type 2 diabetes. Further, we estimated that replacing one daily serving of a sugary beverage with water, coffee, or tea, but not with an ASB, was associated with a 2–10% lower risk of diabetes. Overall, our study suggests that increasing consumption of sugary beverages and ASBs is associated with a moderately higher risk of type 2 diabetes. However, the ASB findings may be affected by reverse causation or surveillance bias, as evidenced by higher rates of diabetes risk factors and fasting glucose screening among those who changed their ASB intake patterns over time.

In accordance with previous studies associating SSB consumption with diabetes incidence (1), we observed that long-term changes in SSB consumption were associated with subsequent diabetes risk. The concordance of our observations with previous studies further underscores the importance of limiting SSB consumption and replacing these beverages with healthy alternatives. Although 100% fruit juices have long been considered as a healthy alternative for SSBs, recent meta-analyses of prospective cohort studies reported a modest positive association between fruit juice consumption and diabetes risk (1,25). Our study found that increasing daily fruit juice intake was associated with higher subsequent risk of diabetes. Our study, along with previous ones (1,25), suggests that the relationship between 100% fruit juice consumption and diabetes risk shares more similarities with the association between SSB consumption and diabetes, in contrast to the inverse association between whole fruit consumption and diabetes (25).

**Table 1—Age-adjusted characteristics of participants according to baseline 4-year changes in total sugary beverage consumption**

	Changes in beverage consumption				
	Decrease		No change or relatively stable	Increase	
	>0.50 serving/ day	>0.07–0.50 serving/ day	±0.07 serving/ day	>0.07–0.50 serving/ day	>0.50 serving/ day
<b>NHS</b>					
Participants, <i>n</i>	13,122	18,143	15,812	16,658	12,796
Sugary beverage intake, serving/ day					
Initial	1.93 (1.38)	0.72 (0.59)	0.39 (0.55)	0.53 (0.61)	0.73 (0.77)
Change	−1.21 (0.83)	−0.24 (0.12)	0.00 (0.03)	0.24 (0.12)	1.25 (0.85)
Age, year*	57.7 (8.2)	57.8 (7.9)	58.3 (7.7)	58.4 (7.7)	58.3 (7.9)
Initial BMI, kg/m <sup>2</sup>	25.6 (5.0)	25.4 (4.6)	25.3 (4.6)	25.3 (4.6)	25.4 (4.9)
Weight change, kg	0.7 (5.5)	0.9 (5.1)	1.3 (5.4)	1.6 (5.0)	1.5 (5.4)
Current smoker, %	19.6	17.4	18.7	17.8	19.7
Hypertension, %	34.1	31.0	30.3	31.4	32.7
High cholesterol, %	41.5	40.7	39.9	41.3	41.0
Family history of diabetes, %	27.0	27.3	28.0	27.5	27.6
Fasting blood glucose screening, %†	56.2	56.5	55.6	56.3	56.3
Physical activity, MET-h/week					
Initial	14.9 (21.2)	15.0 (21.6)	14.7 (20.9)	14.5 (20.6)	14.7 (21.0)
Change	1.8 (23.3)	1.8 (22.6)	2.0 (23.2)	1.7 (21.1)	1.8 (22.2)
Total energy intake, kcal/day					
Initial	1,986 (555)	1,766 (505)	1,608 (490)	1,698 (506)	1,770 (527)
Change	−239 (478)	−81 (425)	0 (419)	56 (422)	194 (467)
AHEI score					
Initial	49.0 (10.6)	52.4 (10.5)	55.3 (11.6)	53.8 (11.0)	52.1 (11.2)
Change	4.8 (9.1)	2.8 (8.2)	0.8 (8.1)	−1.2 (7.9)	−3.0 (8.6)
SSB intake, serving/day					
Initial	1.06 (1.35)	0.24 (0.47)	0.11 (0.42)	0.19 (0.47)	0.33 (0.63)
Change	−0.73 (0.94)	−0.07 (0.20)	0.00 (0.12)	0.10 (0.22)	0.85 (0.96)
Fruit juice intake, serving/day					
Initial	0.87 (0.74)	0.48 (0.36)	0.27 (0.33)	0.34 (0.34)	0.40 (0.41)
Change	−0.47 (0.52)	−0.17 (0.21)	0.00 (0.12)	0.14 (0.22)	0.38 (0.49)
ASB intake, serving/day					
Initial	0.68 (1.23)	0.81 (1.29)	0.99 (1.53)	0.77 (1.27)	0.73 (1.26)
Change	0.24 (1.15)	0.08 (1.02)	0.07 (1.12)	0.03 (0.96)	−0.06 (1.04)
<b>NHS II</b>					
Participants, <i>n</i>	17,816	17,734	14,097	16,359	15,591
Sugary beverage intake, serving/ day					
Initial	2.49 (1.85)	0.82 (0.81)	0.41 (0.75)	0.60 (0.81)	0.97 (1.11)
Change	−1.50 (1.11)	−0.25 (0.12)	0.00 (0.04)	0.24 (0.12)	1.45 (1.04)
Age, year*	40.6 (5.6)	41.3 (5.4)	42.0 (5.4)	41.3 (5.3)	40.6 (5.3)
Initial BMI, kg/m <sup>2</sup>	24.5 (5.3)	24.5 (5.1)	24.5 (5.1)	24.6 (5.2)	24.9 (5.6)
Weight change, kg	2.1 (6.4)	2.6 (6.1)	3.2 (6.5)	3.6 (6.4)	3.8 (6.7)
Current smoker, %	12.5	11.5	11.5	10.1	11.3
Hypertension, %	8.8	8.0	8.2	8.7	10.4
High cholesterol, %	20.0	19.3	20.2	20.2	22.0
Family history of diabetes, %	34.6	34.3	34.6	33.9	35.1
Fasting blood glucose screening, %†	46.1	46.8	47.2	47.0	46.3
Physical activity, MET-h/week					
Initial	23.8 (34.5)	24.2 (35.5)	23.6 (32.1)	23.9 (34.4)	23.8 (35.9)
Change	−3.0 (31.8)	−3.2 (32.4)	−2.2 (30.8)	−3.2 (33.2)	−3.4 (34.6)
Total energy intake, kcal/day					
Initial	2,038 (566)	1,769 (510)	1,608 (505)	1,701 (513)	1,772 (537)
Change	−224 (499)	−43 (452)	38 (443)	111 (455)	275 (493)
AHEI score					
Initial	44.9 (10.1)	49.1 (10.5)	53.0 (11.4)	51.2 (11.1)	48.4 (11.1)
Change	5.1 (8.9)	2.9 (8.3)	0.3 (8.4)	−1.4 (8.48)	−3.1 (9.0)
SSB intake, serving/day					
Initial	1.76 (1.84)	0.41 (0.72)	0.21 (0.65)	0.31 (0.70)	0.61 (1.01)

Continued on p. 6

Table 1—Continued

	Changes in beverage consumption				
	Decrease		No change or relatively stable	Increase	
	>0.50 serving/ day	>0.07–0.50 serving/ day	±0.07 serving/ day	>0.07–0.50 serving/ day	>0.50 serving/ day
Change	–1.13 (1.18)	–0.12 (0.24)	0.00 (0.14)	0.12 (0.25)	1.11 (1.14)
Fruit juice intake, serving/day					
Initial	0.73 (0.72)	0.41 (0.36)	0.20 (0.30)	0.28 (0.33)	0.36 (0.40)
Change	–0.35 (0.52)	–0.13 (0.24)	0.00 (0.14)	0.13 (0.24)	0.32 (0.51)
ASB intake, serving/day					
Initial	1.06 (1.82)	1.52 (2.04)	1.97 (2.39)	1.55 (2.07)	1.41 (2.05)
Change	0.16 (1.54)	–0.06 (1.44)	–0.09 (1.63)	–0.16 (1.46)	–0.38 (1.55)
<b>HPFS</b>					
Participants, <i>n</i>	6,820	8,275	6,065	7,316	5,748
Sugary beverage intake, serving/ day					
Initial	2.14 (1.46)	0.87 (0.67)	0.55 (0.70)	0.66 (0.67)	0.89 (0.84)
Change	–1.25 (0.84)	–0.25 (0.12)	0.00 (0.03)	0.25 (0.12)	1.22 (0.81)
Age, year*	56.5 (9.8)	57.6 (9.5)	58.5 (9.5)	57.8 (9.6)	57.1 (9.8)
Initial BMI, kg/m <sup>2</sup>	25.6 (3.2)	25.5 (3.1)	25.3 (3.2)	25.4 (3.1)	25.3 (3.1)
Weight change, kg	0.4 (4.3)	0.6 (4.1)	0.7 (4.4)	0.9 (4.0)	0.8 (3.9)
Current smoker, %	9.2	8.0	8.8	7.6	8.5
Hypertension, %	24.2	23.3	23.0	22.7	23.6
High cholesterol, %	29.0	28.7	28.6	29.3	29.1
Family history of diabetes, %	25.2	26.9	26.4	25.6	25.0
Fasting blood glucose screening, %†	71.3	72.3	72.1	71.9	71.4
Physical activity, MET-h/week					
Initial	20.3 (29.5)	19.7 (24.6)	20.0 (25.9)	19.7 (26.7)	20.0 (25.7)
Change	1.4 (27.5)	1.9 (23.7)	1.4 (24.0)	1.9 (25.3)	2.0 (24.2)
Total energy intake, kcal/day					
Initial	2,252 (653)	1,990 (597)	1,848 (572)	1,917 (591)	2,006 (624)
Change	–313 (532)	–136 (474)	–50 (454)	17 (485)	184 (525)
AHEI score					
Initial	49.9 (11.0)	52.9 (11.1)	55.3 (11.9)	54.5 (11.6)	53.1 (11.6)
Change	4.1 (9.2)	2.4 (8.4)	1.0 (8.3)	–0.8 (8.4)	–2.0 (8.7)
SSB intake, serving/day					
Initial	1.29 (1.39)	0.39 (0.58)	0.23 (0.57)	0.30 (0.55)	0.46 (0.69)
Change	–0.83 (0.91)	–0.12 (0.23)	0.00 (0.14)	0.11 (0.24)	0.79 (0.90)
Fruit juice intake, serving/day					
Initial	0.84 (0.81)	0.48 (0.37)	0.33 (0.37)	0.36 (0.34)	0.43 (0.43)
Change	–0.40 (0.56)	–0.13 (0.23)	0.00 (0.14)	0.13 (0.24)	0.42 (0.56)
ASB intake, serving/day					
Initial	0.63 (1.25)	0.73 (1.29)	0.87 (1.58)	0.70 (1.32)	0.68 (1.33)
Change	0.18 (1.08)	0.05 (0.94)	0.00 (1.00)	0.01 (0.89)	–0.04 (0.98)

Data are mean (SD) unless otherwise noted and are standardized to the age distribution of the study population. Sugary beverages include both beverages with added sugar (e.g., SSBs) and 100% fruit juices. SSBs include carbonated and noncarbonated soft drinks, punches, fruit drinks, sugared iced tea and sports drinks. ASBs include low-calorie carbonated and noncarbonated beverages that are artificially sweetened. One beverage serving is 8 ounces. \*Value is not age adjusted. †Values refer to the first assessment of fasting blood glucose examination (1998 for the NHS, 2001 for the NHS II, and 2000 for the HPFS).

Several mechanisms may explain the deleterious effects of sugary beverages on cardiometabolic health (2). Sugar-containing liquids have lower satiety than solid foods containing the same amount of calories and their consumption stimulates appetite, which may lead to excessive calorie intake and increased adiposity and impaired insulin sensitivity in the long term (2). Excess intake of fructose, per se, may promote liver fat

accumulation and induce insulin resistance (2), although this hypothesis remains controversial (26,27). The above mechanisms have been mostly identified from studies on SSBs, but some evidence suggests that excess calorie intake from fruit juices also induces impairments in glucose homeostasis (28). Our study suggests that increasing consumption of sugary beverages, whether they contain added or naturally

occurring sugar, is associated with a higher risk of diabetes.

In our main analysis, decreasing sugary beverage consumption was not differentially associated with diabetes risk relative to the reference category of no change. This analysis may be limited by the moderate amount of sugary beverage reduction over time (10,11). However, the fact that decreasing sugary beverage consumption was not

**Table 2—Pooled HRs (95% CIs) for incident type 2 diabetes according to categories of updated 4-year changes in beverage consumption**

	Changes in beverage consumption					P values for trend
	Decrease		No change or relatively stable	Increase		
	>0.50 serving/day	>0.07–0.50 serving/day	±0.07 serving/day	>0.07–0.50 serving/day	>0.50 serving/day	
<b>Total sugary beverages</b>						
Cases/person-years	2,505/543,788	2,667/653,244	2,265/581,435	2,304/556,698	3,165/448,048	
Model 1	1.07 (0.97, 1.17)	0.95 (0.91, 0.99)	1.00	1.13 (1.04, 1.22)	1.46 (1.28, 1.66)	0.09
Model 2	0.96 (0.87, 1.05)	0.99 (0.95, 1.03)	1.00	1.06 (0.98, 1.16)	1.16 (1.01, 1.34)	<0.0001
<b>SSBs</b>						
Cases/person-years	1,863/379,716	2,291/556,655	4,190/1,043,090	1,954/476,621	1,608/327,128	
Model 1	1.29 (1.22, 1.37)	1.05 (1.00, 1.10)	1.00	1.07 (1.01, 1.12)	1.33 (1.25, 1.41)*	0.86
Model 2	1.01 (0.94, 1.09)	1.02 (0.95, 1.09)	1.00	1.03 (0.97, 1.09)	1.09 (1.03, 1.17)	0.006*
<b>100% fruit juices</b>						
Cases/person-years	1,088/247,199	3,056/721,009	4,081/1,003,887	2,693/605,468	988/205,648	
Model 1	1.06 (1.00, 1.14)	1.06 (1.01, 1.11)	1.00	1.11 (1.05, 1.16)	1.16 (1.08, 1.24)	0.04
Model 2	1.04 (0.96, 1.13)	1.03 (0.97, 1.08)	1.00	1.09 (1.03, 1.14)	1.15 (1.07, 1.23)	0.004
<b>ASBs</b>						
Cases/person-years	2,611/506,409	1,755/422,705	4,136/1,118,683	1,379/336,870	2,025/398,544	
Model 1	1.21 (1.09, 1.34)	0.93 (0.89, 0.97)	1.00	1.23 (1.13, 1.33)	1.87 (1.65, 2.12)	0.60
Model 2	1.05 (0.94, 1.17)	1.00 (0.95, 1.04)	1.00	1.03 (0.95, 1.13)	1.18 (1.02, 1.36)	0.001

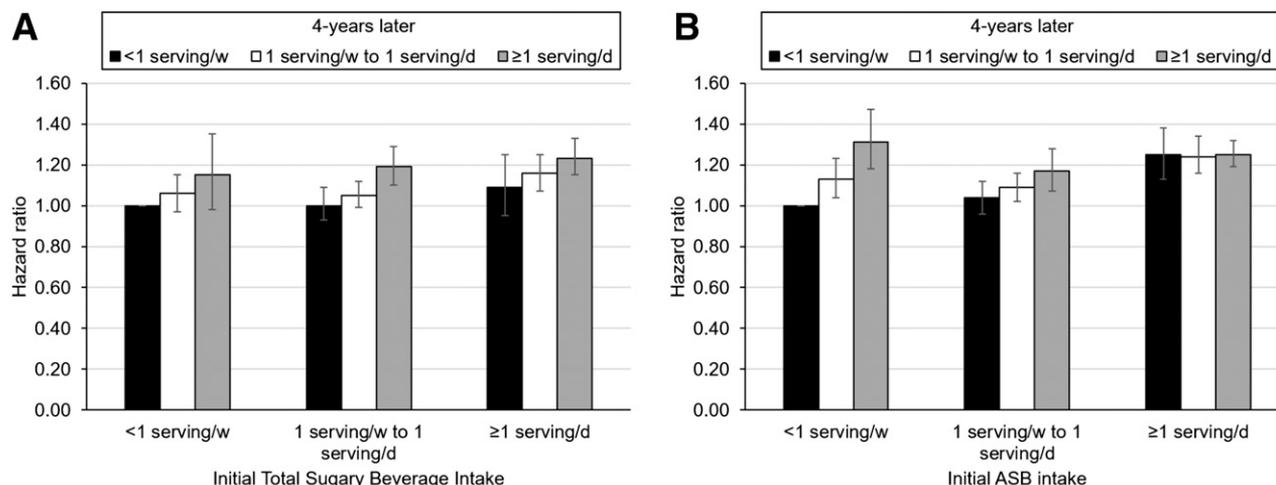
One beverage serving is 8 ounces. Results of the three cohorts were pooled using an inverse variance-weighted, fixed-effect meta-analysis. Models were adjusted as follows. Model 1: adjusted for age and stratified by calendar year in 4-years intervals. Model 2: Model 1 + race (white or nonwhite); family history of diabetes (yes/no); physical examination during the 4-year cycle (yes/no); menopausal status and postmenopausal hormone use (premenopausal, postmenopausal + current use, postmenopausal + past use, postmenopausal + never use, or missing indicator) and oral contraceptive use (never, current, past, or missing indicator); smoking status (never to never, never to current, past to past, past to current, current to past, current to current, or missing indicator); initial and change in physical activity level (MET-h/week, quintiles); initial and change in alcohol consumption (g/day, quintiles); initial BMI (<21.0, 21.0–24.9, 25.0–29.9, 30.0–31.9, ≥32.0 kg/m<sup>2</sup>); initial calorie intake (quintiles); initial and change in AHEI score (calculated without the alcohol and sugary beverage components, quintiles); initial and change in intakes of water, coffee, tea, and milk (serving/day, quintiles or tertiles); initial intakes of sugary beverages, or SSBs and fruit juices, and ASBs (serving/day; depending on the model, quintiles or tertiles); and changes in ASBs, fruit juices, SSBs, or sugary beverages (serving/day; depending on the model, quintiles). \*P heterogeneity < 0.05.

associated with a higher risk of diabetes compared with the reference category suggests that the deleterious effects associated with high initial intakes were mitigated by the reduction in consumption. The latter was further evidenced in our joint analysis in which individuals who decreased their total sugary beverage consumption to <1 serving/week over a 4-year period did not have a higher risk of diabetes compared with individuals who consumed <1 serving/week for 4 years. Thus, our results suggest that maintaining low intakes or decreasing consumption of sugary beverages to low levels is associated with a lower diabetes risk.

Like fruit juices, ASBs are often considered a healthier alternative to SSBs. We observed that increasing ASB consumption was associated with a higher risk of diabetes, but these findings need to be interpreted with caution.

First, changes in ASB consumption were inversely correlated with concurrent weight gain. While this observation is consistent with previous studies suggesting that replacing SSBs with ASBs may be beneficial for weight management (22,29,30), it indicates a discrepancy between potential intermediate biological mechanisms linking ASB consumption to insulin resistance and diabetes onset (31). Second, relative to individuals who maintained a stable ASB consumption, individuals who increased their intake appeared to be at higher risk of diabetes and had a greater prevalence of fasting glucose screening. These observations are consistent with the possibility of reverse causation, i.e., individuals at higher risk are likely to switch from SSBs to ASBs as a strategy to control weight, and surveillance bias, i.e., individuals at higher risk are likely to be

screened more frequently for diabetes (1,2,9). The presence of this confounding may overestimate the strength of the relationship between ASB consumption and type 2 diabetes risk. However, plausible mechanisms supporting associations between ASB consumption with cardiometabolic intermediates have been proposed. Some artificial sweeteners may alter gut microbiota, which could predispose ASB consumers to weight gain and insulin resistance (32,33). Also, the intense sweetness of artificial sweeteners has also been hypothesized to stimulate appetite and lead to increased calorie intake (32). Still, these mechanisms are not consistent with the modest inverse association between change in ASB consumption and weight gain observed in our cohorts (22). Notwithstanding the above, our results do not suggest that consuming ASBs in

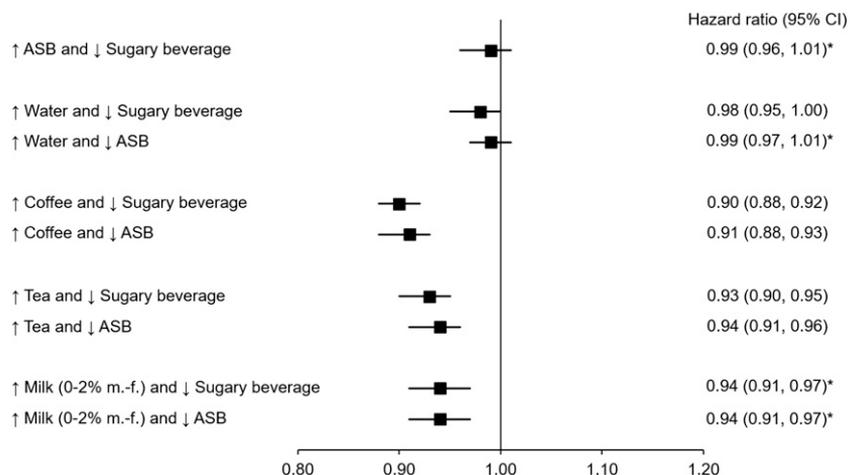


**Figure 1**—Pooled HRs (95% CIs) for type 2 diabetes according to updated 4-year changes in intakes of sugary beverages (A) and ASBs (B). The vertical bars represent consumption 4 years later: black bars, <1 serving/week; white bars, ≥1 serving/week to <1 serving/day; and gray bars, ≥1 serving/day. One beverage serving is 8 ounces. Cox proportional hazards models stratified by calendar year and adjusted for age, race (white or nonwhite), family history of diabetes (yes/no), physical examination during the 4-year cycle (yes/no), menopausal status and postmenopausal hormone use (premenopausal, postmenopausal + current use, postmenopausal + past use, postmenopausal + never use, or missing indicator), oral contraceptive use (never, current, past, or missing indicator), smoking status (never to never, never to current, past to past, past to current, current to past, current to current, or missing indicator), initial and change in physical activity level (MET-h/week, quintiles), initial and change in alcohol consumption (g/day, quintiles), initial and change in AHEI score (calculated without the alcohol and sugary beverage components, quintiles), initial and change in intakes of coffee, tea, milk and water (quintiles or tertiles), initial and change in intakes of ASBs (for A) or sugary beverages (for B), initial BMI (<21.0, 21.0–24.9, 25.0–29.9, 30.0–31.9, ≥32.0 kg/m<sup>2</sup>), and initial calorie intake (quintiles). Results of the three cohorts were pooled using an inverse variance-weighted, fixed-effect meta-analysis.

place of sugary beverages is associated with substantial benefits with regard to diabetes risk. However, we observed

that replacing sugary beverages with water, coffee, or tea was associated with a lower risk of diabetes, which is

consistent with the relationship between these replacement beverages and diabetes risk, as previously reported (34–36).



**Figure 2**—Pooled HRs (95% CIs) for type 2 diabetes associated with increasing consumption of a beverage and concomitantly decreasing consumption of sugary beverages or ASB by one serving (8 ounces) per day. Cox proportional hazards models including all beverages simultaneously (initial and change, both continuous, in servings/day), adjusted for race (white or nonwhite), family history of diabetes (yes/no), physical examination during the 4-year cycle (yes/no), menopausal status and postmenopausal hormone use (premenopausal, postmenopausal + current use, postmenopausal + past use, postmenopausal + never use, or missing indicator), oral contraceptive use (never, current, past, or missing indicator), smoking status (never to never, never to current, past to past, past to current, current to past, current to current, or missing indicator), initial and change in physical activity level (MET-h/week, quintiles), alcohol consumption (g/day, quintiles), and AHEI score (calculated without the alcohol and sugary beverage components, quintiles), initial calorie intake (quintiles), and initial BMI (<21.0, 21.0–24.9, 25.0–29.9, 30.0–31.9, >32.0 kg/m<sup>2</sup>). Results of the three cohorts were pooled using an inverse variance-weighted, fixed-effect meta-analysis. \*P for heterogeneity <0.05. m.-f., milk-fat.

The design of our study is a major strength. Indeed, the NHS, the NHS II, and the HPFS are among the few studies with long-term repeated assessments of diet, which allowed us to calculate changes in beverage consumption (37,38). This element increases the generalizability of our findings because changes in beverage consumption were made in a real-world setting. The large sample size and the high follow-up rate in the three cohorts contribute to our ability to detect moderate associations. On the other hand, the study population is mainly composed of Caucasian, educated, health professionals, which may limit the generalizability of our results to other groups. Also, we did not directly assess decisions leading to changes in beverage consumption, and therefore, underlying reasons to switch from SSB to ASB, for example, are unknown. Measurement errors in consumption of sugary beverages and ASBs as well as other dietary items are inevitable, and confounding due to unmeasured dietary items (e.g., amount of sugar or dairy added to coffee and tea) and random error in the setting of a prospective cohort study

may have led to an underestimation of the relationship between beverage intakes with diabetes risk. Finally, we cannot exclude the presence of residual confounding, reverse causation, or surveillance bias, particularly with respect to intentional switching between types of beverages.

In conclusion, our study suggests that increasing consumption of sugary beverages including fruit juices is associated with risk of type 2 diabetes among U.S. women and men. Decreasing sugary beverage consumption and replacing these drinks with noncaloric beverage free of artificial sweeteners like water, coffee, or tea was associated with a lower risk of diabetes. Increasing ASB consumption is also associated with higher diabetes risk, although reverse causation or surveillance bias may in part explain this association.

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**Author Contributions.** J.-P.D.-C. contributed to the development of the hypotheses, conducted the analyses, interpreted the data, and drafted, reviewed, and edited the manuscript. Y.Z. developed the hypotheses and reviewed and edited the manuscript. Y.L. contributed to the analyses and reviewed and edited the manuscript. V.M. contributed to the development of the hypotheses and reviewed and edited the manuscript. A.P., S.N.B., D.K.T., J.E.M., and W.C.W. reviewed and edited the manuscript. F.B.H. developed the hypotheses, interpreted the data, and reviewed and edited the manuscript. F.B.H. is the guarantor of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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