

Sugar-sweetened or artificially-sweetened beverage consumption, physical activity and risk of type 2 diabetes in US adults

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Electronic Supplementary Materials Methods

Study population and design

The Nurses' Health Study (NHS) and NHSII are prospective cohort studies of 121,701 and 116,430 US registered female nurses (aged 30-55 [NHS] and 25-42 [NHSII] years at enrolment) initiated in 1976 and 1989, respectively. The Health Professional's Follow-up Study (HPFS) is a prospective cohort study of 51,529 US male health professionals (aged 40-75 years at enrolment) established in 1986. At enrolment, and biennially, questionnaires were administered to collect and update medical and lifestyle information. The three studies are ongoing, and follow-up rates exceed 90% in each 2-y cycle.

We defined baseline as the first year SSB intake was asked in the food-frequency questionnaire (FFQ): 1980 for the NHS, 1991 for the NHS II, and 1986 for the HPFS (<https://nurseshealthstudy.org/participants/questionnaires>; <https://www.hsph.harvard.edu/hpfs/hpfs-questionnaires/>). We excluded women and men who had diagnoses of type 2 diabetes, cardiovascular disease, or cancer at baseline; those who had missing information on SSBs and physical activity; and those that reported very low or high energy intake ($<2,092$ or $>14,644$ kJ per day in women, and $<3,347$ or $>17,573$ kJ per day in men). We also excluded participants who died before study baseline (enrolled but died before baseline data for the current study was collected) and with missing records. The final analysis included 152,369 women (64,029 in NHS and 88,340 in NHS II) and 39,436 men (**ESM Fig. 1**). The protocol was approved by the institutional review board of Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health.

Dietary assessment and sugar- and artificially-sweetened beverage intake

Dietary intake was measured by FFQs administered every 4-y. The reproducibility and validity of these FFQs have been demonstrated (1–3). Specifically for total sugar, the correlation between FFQ and 7-day dietary records data is 0.75 (4). On each FFQ, participants were asked how often, on average, they consumed a standard portion of foods and beverages (one standard glass, bottle, or can), with possible responses ranging from 'never or less than once per month' to ' ≥ 6 times per day' (never or less than once per month, 1-3 times per month, 1 time per week, 2-4 times per week, 5-6 times per week, 1 time per day, 2-3 times per day, 4-5 times per day, ≥ 6 times per day). Total SSBs were defined as caffeinated colas, caffeine-free colas, other (i.e., noncola) carbonated sugar-sweetened beverages, and noncarbonated sugar-sweetened beverages (fruit punches, lemonades, or other fruit drinks). Fruit juice was not considered an SSB; however, we included a sensitivity analysis combining intake of SSB and fruit juice, as well as a sensitivity analysis on the independent association between fruit juice intake and risk of type 2 diabetes. ASBs were defined as caffeinated, caffeine-free, and noncarbonated low-calorie or diet beverages (i.e., diet sodas [cola and noncola], diet teas, diet lemonade, etc).

Physical activity assessment

Physical activity was assessed biennially, with participants reporting the average time per week spent in various moderate- or vigorous-intensity leisure-time activities in the preceding year, using a validated self-reported questionnaire (5). For each reported activity, the metabolic equivalent of task per hour (MET-h) was calculated based on intensity and duration, and then it was quantified as the weekly sum over all activities (MET-h/week).

Ascertainment of type 2 diabetes

The primary outcome was the incidence of confirmed type 2 diabetes. Cases of type 2 diabetes were identified by biennially mailed questionnaires (<https://nurseshealthstudy.org/participants/questionnaires>; <https://www.hsph.harvard.edu/hpfs/hpfs-questionnaires/>) and confirmed by a validated supplementary questionnaire regarding symptoms, diagnostic laboratory test results, and hypoglycaemic therapy (a copy of the questionnaire is located at the end of the ESM methods section). Before 1998, criteria from the National Diabetes Data Group were used (6–9). The report of at least one of the following criteria was used to confirm a case of diabetes: 1) ≥ 1 classic symptoms (excessive thirst, polyuria, weight loss, or hunger) and fasting glucose concentrations ≥ 7.8 mmol/L or random glucose concentrations ≥ 11.1 mmol/L; 2) ≥ 2 elevated glucose concentrations on different occasions (fasting concentrations ≥ 7.8 mmol/L, random glucose concentrations ≥ 11.1 mmol/L, and/or concentrations of ≥ 11.1 mmol/L after ≥ 2 -h shown by oral glucose tolerance testing) in the absence of symptoms; or 3) treatment with hypoglycaemic medication (insulin or oral hypoglycaemic 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 (10). The current study only includes confirmed cases.

Assessment of covariables

Information on lifestyle factors and medical history including age, sex, body weight, smoking status, medication, supplements, postmenopausal hormone-replacement therapy, and oral contraceptive use, menopausal status; disease diagnoses, and family history of chronic diseases was self-reported and obtained from biennial questionnaires (<https://nurseshealthstudy.org/participants/questionnaires>; <https://www.hsph.harvard.edu/hpfs/hpfs-questionnaires/>). Body mass index (BMI; weight in kilograms divided by height in meters squared) was calculated from body weight reported on each follow-up questionnaire and height reported at study initiation. Height was ascertained at baseline. Information on dietary factors, including alcohol was obtained from updated FFQs. Demographic and ancestry information was also collected. Ancestry information was collected in 1986 in the HPFS, 1992 in NHS, and 1989 for NHSII, and the self-reported categories in the questionnaire included Southern European/Mediterranean, Caucasian/Scandinavian, Other Caucasian, African American, Hispanic, Asian, American Indian, and Other. Since these data were collected more than 30 years ago, the categories may not be consistent with the current classifications. A modified Alternative

Healthy Eating Index (AHEI) score, with SSBs and alcohol removed, was used as an indicator of overall diet quality. A higher score (range 0-90) denotes greater adherence to the AHEI and better diet quality (11).

Statistical analyses

Person-years of follow-up for each participant were calculated from the return of the baseline questionnaire to the date of diagnosis of type 2 diabetes, death, or end of follow-up (June 30, 2016, for NHS; June 30, 2017, for NHS II; and January 31, 2016, for HPFS), whichever came first. Cox proportional-hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of developing type 2 diabetes according to the independent associations of SSB intake, ASB intake, and physical activity, as well as joint associations of SSB or ASB intake and physical activity. Model 1 was adjusted for the following factors: age, race, ancestry, alcohol intake, smoking status and frequency among ever smokers (never, former, current smoker), physical activity metabolic equivalents– h/week), for independent SSB and ASB separate models, in quintiles), family history of diabetes, multivitamin and aspirin use, menopausal status and use of hormone-replacement therapy, in women (premenopausal, postmenopausal [no, past, or current hormone use], women only), total energy intake, and BMI. Model 2 was additionally adjusted for AHEI score (without SSBs and alcohol for the SSB and ASB models only; in quintiles).

To represent the long-term intake of SSBs and ASBs, the primary analysis utilised cumulative averages of the SSB and ASB data created using repeated measures from the FFQs (calculated by taking the mean intake from all FFQs up to the beginning of a follow-up 4-year questionnaire interval). The same approach was used for the time-varying covariables such as alcohol intake, total energy, and dietary factors. Time-varying variables such as smoking status, physical activity, and BMI were included as repeated measurements in the models. Because participants may alter dietary patterns after the diagnosis of major illness, we stopped updating dietary variables when participants reported a diagnosis of coronary artery bypass, angina, or cancer, although follow-up continued until type 2 diabetes endpoint occurrence, death, or the end of the study period (12). If data were missing at a given time point, we used data from the previous cycle.

For the independent association analysis between SSB or ASB intake and risk of type 2 diabetes, frequency of consumption was collapsed into 5 categories: (1) never or less than 1 serving/month (this corresponds to the original possible answer on the FFQ ‘never or less than once per month’; reference), (2) 1-4 servings/month (this merges ‘1-3 times per month’ and ‘1 time per week’ from the original possible answers on the FFQ), (3) 2-6 servings/week (this merges ‘2-4 times per week’ and ‘5-6 times per week’ from the original possible answers on the FFQ), (4) 1-<2 servings/day (this corresponds to the original possible answer on the FFQ ‘1 time per day’ and any intake up to 2 servings/day after cumulative average calculation), and (5) ≥ 2 servings/day (this merges ‘2-3 times per day’, ‘4-5 times per day’, and ‘ ≥ 6 times per day’ from the original possible answers on the FFQ). Linear trends were evaluated using the Wald test on a continuous variable representing the median intake of each

category. The same categorization was applied to SSB and ASB sub-types (i.e., regular and diet carbonated beverages [cola and non-cola], fruit punch). We also evaluated the association for 1 serving increase of SSB or ASB intake/day in the multivariable models. For the independent association between physical activity and type 2 diabetes, physical activity was categorised in quintiles as well as a continuous variable.

We conducted a series of stratified analyses for continuous servings/day of SSBs or ASBs with type 2 diabetes by pre-specified subgroups and calculated p-values for heterogeneity with Wald tests for the multiplication interaction of SSB or ASB exposures (continuous variable) with the effect modifier variables.

For the joint association analyses between SSB or ASB and physical activity and risk of type 2 diabetes, physical activity was dichotomised to <7.5 MET-h/week or ≥ 7.5 MET-h/week, with the cut-point based on the current aerobic physical activity guidelines for US adults (7.5 MET-h/week is equivalent to 150 minutes/week of moderate-intensity physical activity) (13). We further collapsed the last 3 categories of SSB and ASB intake since most participants consumed <2 servings/week, leaving (1) never or less than 1 serving/month (reference), (2) 1-4 servings/month, and (3) ≥ 2 servings/week (this merges '2-6 servings/week', '1- <2 servings/day' and ' ≥ 2 servings/day' categories of the 5-level SSB and ASB independent associations analysis between these beverages and risk of diabetes) as beverage categories, and combined them with the dichotomised physical activity variable. The reference categories were never/rarely consuming SSBs or ASBs and meeting physical activity guidelines. The multivariable models for these analyses were the same as for the independent associations except for physical activity as a covariate. We tested the multiplicative interaction by comparing the -2 log likelihood of the multivariable-adjusted models with and without the cross-product interaction term (14). To assess the additive interaction, we considered SSB or ASB and physical activity as continuous variables and assessed by the derivation of the probability value of the relative excess risk due to interaction as an index of additive interaction (15,16).

We also ran a series of sensitivity analyses to assess the robustness of the results. First, we further examined the joint association between SSB or ASB and physical activity and risk of type 2 diabetes in two subgroups: 1) 'heavy SSB or ASB consumers' (top 25th percentile SSB or ASB consumers vs not) and the dichotomised physical activity variable, and 2) 'heavy SSB or ASB consumers' and 'high physical activity level' (top 25th percentile physical activity vs not). Second, diet was continuously updated until the end of the follow-up. Third, we excluded BMI from the models. Fourth, models were adjusted for median household income and education to test whether the results changed by socioeconomic status. Fifth, instead of adjusting for the AHEI, we adjusted for a set of dietary factors (intake of fruits and vegetables, red and processed meats, whole grains, coffee, tea, milk, water, juice, and mutually adjusted for SSB or ASB where appropriate [in quintiles]; data not shown). Sixth, we ran an independent and joint analysis combining total SSB and fruit juice consumption, as well as the independent association (in quintiles) between fruit juice intake, solely, and incident type 2 diabetes. Lastly,

we conducted a joint association analysis with SSB or ASB and three-levels of physical activity in tertiles. All analyses were performed separately for each cohort and then were pooled with the use of an inverse, variance-weighted meta-analysis with a fixed-effects model. Statistical tests were 2-sided, and *P* values of <0.05 were considered to indicate statistical significance. Data were analysed with the SAS package, version 9.4 (SAS Institute, Cary, NC).

2010 Supplementary Diabetes Questionnaire

Nurses' Health Study I
Health Professionals Follow-Up Study
Harvard Medical School
181 Longwood Avenue
Boston, MA 02115

\$val(id)\$val(cd)
This is your identification number
(Used for maintaining confidentiality)

The following questions pertain to your diagnosis of diabetes. Please answer by checking the appropriate box and providing the requested information where indicated. Please be as specific as possible with your answers. All information supplied will be considered as strictly confidential and used for statistical medical research purposes only.

1. What month and year were you first diagnosed as having diabetes ? _____ month / year
2. Approximate weight at time of diagnosis: _____ pounds
3. At the time you were first diagnosed as having diabetes, was the diagnosis based on routine screening or symptoms? ☐ Screening only ☐ Symptoms
4. At the time you were first diagnosed as having diabetes, were any of the following conditions present?

	NO	YES
Ketoacidosis?	☐	☐
Coma?	☐	☐
Unintended Weight Loss?	☐	☐
Unusual Hunger?	☐	☐
Unusual Thirst?	☐	☐
Unusual Frequency of Urination?	☐	☐
Pruritus of Vulva or Vagina?	☐	☐

The following questions refer to the entire period that you have had diabetes (including first diagnosis and time ever since). Please include home testing.

5. How many **HbA1c** measurements between 5.7% and 6.4% have you ever had?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
6. How many **HbA1c** measurements of 6.5% or higher have you ever had?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
7. How many **fasting blood glucose** measurements between 126 and 139 mg/dl have you ever had?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
8. How many **fasting blood glucose** measurements of 140 mg/dl or higher have you ever had?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
9. How many **non-fasting blood glucose** measurements of 200 mg/dl or higher have you ever had? (Including random and post-meal values but not oral glucose tolerance test)
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
10. How many **abnormal Oral Glucose Tolerance tests** of 200 mg/dl or higher at 2 or 3 hours have you ever had?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested

Please complete the few remaining questions on the reverse side.

11. How many **urine glucose** measurements of **2+ or greater** have you ever had?
☐None ☐Only 1 ☐2 or More ☐Don't know ☐Not tested
12. How many times have you had **ketones** present (**more than trace**) in your urine?
☐None ☐Only 1 ☐2 or More ☐Don't know ☐Not tested
13. Have you ever been hospitalized for **ketoacidosis**? ☐No ☐Yes
If Yes, did it ever occur within the first 2 years of diagnosis? ☐No ☐Yes

(Optional) Please provide year and hospital for most recent admission for ketoacidosis:

14. Have you ever been treated with **insulin** injections? ☐No ☐Yes

If Yes,

- a) When was the insulin started? ☐At time of diagnosis
 ☐After diagnosis but within one year
 ☐More than one year after diagnosis

b) For how long was insulin taken? _____ years

c) What year was insulin started? _____

d) Are you currently receiving insulin daily? ☐No ☐Yes

If Yes, please specify current type and dose _____

e) Have you ever been able to stop your insulin completely for a period of 2 weeks or more? ☐No ☐Yes

15. Have you ever taken **oral medication** for your diabetes?
☐No ☐Yes, currently ☐Yes, past only

If Yes, (either current or past only)

a) please give type of medication and dose _____

b) How long was oral medication taken? _____

c) What year was oral medication started? _____

16. Additional Remarks: _____

THANK YOU!

2010 Supplementary Diabetes Questionnaire

Nurses' Health Study II
Channing Laboratory
181 Longwood Avenue
Boston, MA 02115

\$val(id)\$val(cd)
This is your identification number
(Used for maintaining confidentiality)

The following questions pertain to your diagnosis of diabetes. Please answer by checking the appropriate box and providing the requested information where indicated. Please be as specific as possible with your answers. All information supplied will be considered as strictly confidential and used for statistical medical research purposes only.

- 1. What month and year were you first diagnosed as having diabetes ? _____
month / year
- 2. Approximate weight at time of diagnosis: _____ pounds
- 3. At the time you were first diagnosed as having diabetes, was the diagnosis based on routine screening or symptoms? ☐ Screening only ☐ Symptoms
- 4. At the time you were first diagnosed as having diabetes, were any of the following conditions present?

	NO	YES
Ketoacidosis?	☐	☐
Coma?	☐	☐
Unintended Weight Loss?	☐	☐
Unusual Hunger?	☐	☐
Unusual Thirst?	☐	☐
Unusual Frequency of Urination?	☐	☐
Pruritus of Vulva or Vagina?	☐	☐

The following questions refer to the entire period that you have had diabetes (including first diagnosis and time ever since). Please include home testing.

- 5. How many HbA1c measurements between 5.7% and 6.4% have you ever had?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
- 6. How many HbA1c measurements of 6.5% or higher have you ever had?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
- 7. How many **fasting blood glucose** measurements between 126 and 139 mg/dl have you ever had?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
- 8. How many **fasting blood glucose** measurements of 140 mg/dl or higher have you ever had?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
- 9. How many **non-fasting blood glucose** measurements of 200 mg/dl or higher have you ever had? (Including random and post-meal values but not oral glucose tolerance test)
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
- 10. How many **abnormal Oral Glucose Tolerance tests** of 200 mg/dl or higher at 2 or 3 hours have you ever had?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested

Please complete the few remaining questions on the reverse side.

11. How many **urine glucose** measurements of **2+ or greater** have you ever had?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
12. How many times have you had **ketones** present (**more than trace**) in your urine?
☐ None ☐ Only 1 ☐ 2 or More ☐ Don't know ☐ Not tested
13. Have you ever been hospitalized for **ketoacidosis**? ☐ No ☐ Yes
If Yes, did it ever occur within the first 2 years of diagnosis? ☐ No ☐ Yes
 (Optional) Please provide year and hospital for most recent admission for ketoacidosis:
14. Have you ever been treated with **insulin** injections? ☐ No ☐ Yes
If Yes,
 a) When was the insulin started? ☐ At time of diagnosis
☐ After diagnosis but within one year
☐ More than one year after diagnosis
 b) For how long was insulin taken? _____ years
 c) What year was insulin started? _____
 d) Are you currently receiving insulin daily? ☐ No ☐ Yes
If Yes, please specify current type and dose _____
 e) Have you ever been able to stop your insulin completely for a period of 2 weeks or more? ☐ No ☐ Yes
15. Have you ever taken **oral medication** for your diabetes?
☐ No ☐ Yes, currently ☐ Yes, past only
If Yes, (either current or past only)
 a) Please give type of medication and dose _____
 b) How long was oral medication taken? _____
 c) What year was oral medication started? _____
16. Were you ever diagnosed with diabetes during a **pregnancy**? ☐ No ☐ Yes ☐ N/A
If Yes,
 a) Did the diabetes persist for more than 1 month after the pregnancy? ☐ No ☐ Yes
 b) If diabetes did not persist more than 1 month after the end of pregnancy, were you diagnosed at a later date (when not pregnant) to have diabetes? ☐ No ☐ Yes
 Date of later diagnosis: _____ month _____ year
 c) If diabetes persisted more than one month after the end of pregnancy, do you still have diabetes? ☐ No ☐ Yes
17. Additional Remarks:

THANK YOU!

Electronic Supplementary Materials Results

The independent associations between SSB and ASB intakes and physical activity and risk of type 2 diabetes, and the SSB or ASBs and physical activity joint associations findings were slightly weakened when we selectively stopped updating diet (data not shown). When we excluded BMI from the final model, the results for the independent association between SSB and type 2 diabetes were attenuated; however, the independent association between ASB and type 2 diabetes became stronger (**ESM Table 10**). The SSBs and physical activity joint association findings were strengthened in those that did not meet the physical activity recommendations once we removed BMI; whereas the ASBs and physical activity joint association results were strengthened in those that met and did not meet the physical activity recommendations (**ESM Table 10**). Results were consistent when we additionally adjusted for socioeconomic status and when we adjusted for dietary factors instead of AHEI (data not shown). Combined SSB and fruit juice consumption results showed attenuation in the risk of type 2 diabetes when comparing the highest to reference intake categories as well as attenuation in the joint association analysis (**ESM Table 11**). The results for the independent association between intake of fruit juice and risk of type 2 diabetes are shown in **ESM Table 12**. After adjusting for known confounders, the pooled risk of type 2 diabetes in participants in quintile 5 of fruit juice intake was 13% (pooled HR 1.13, 95%CI 1.08, 1.18; p-trend <0.0001) higher, compared to those who were in quintile 1. The supplementary joint association analysis between SSB or ASB and physical activity in tertiles (3-levels) is shown in **ESM Table 13**. Compared to the reference group (those that never or rarely consumed SSBs and were in the top tertile of physical activity), participants who were in the first, second, and third tertile of physical activity and consumed ≥ 2 servings of SSBs/week had a pooled HR of 1.60 (95%CI 1.47, 1.73), 1.37 (95%CI 1.26, 1.49), and 1.23 (95%CI 1.13, 1.34), respectively, for type 2 diabetes.

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ESM Table 1. Baseline^a characteristics of participants according to sugar-sweetened beverage intake and physical activity joint association categories in three large US cohorts.

	Meets the US Physical Activity Guidelines ^b			Does Not Meet the US Physical Activity Guidelines ^b		
	Never or less than 1 SSB serving per month	1-4 SSB servings per month	≥2 SSB servings per week	Never or less than 1 SSB serving per month	1-4 SSB servings per month	≥2 SSB servings per week
Nurses' Health Study						
Participants, n	13,482	7,434	11,779	11,002	7,173	13,159
Age, years	47.3 (7.0)	46.6 (7.1)	44.8 (7.2)	47.4 (6.9)	46.4 (7.0)	44.7 (7.0)
BMI, kg/m ²	23.7 (3.7)	23.6 (3.8)	24.0(4.2)	24.6 (4.5)	24.5 (4.4)	24.9 (4.9)
Physical activity, MET-h/week	26.1 (24.6)	24.2 (24.2)	23.8 (22.4)	2.8 (2.0)	2.8 (2.0)	2.8 (1.9)
Family history of diabetes	28.3	28.0	27.7	30.4	29.4	30.5
Ancestry, white	98.7	97.8	97.4	98.8	98.0	97.0
Current smoker	24.2	22.0	25.7	32.0	28.3	29.7
Hypertension	14.1	12.3	14.1	16.2	14.6	16.5
Hypercholesterolemia	5.0	4.5	4.5	5.6	5.0	4.7
Multivitamin supplement use	37.8	35.8	34.4	33.0	31.8	30.9
Aspirin use	44.2	46.4	49.1	46.3	45.9	49.5
Current menopausal hormone use	7.2	6.8	6.1	7.1	6.7	6.3
Total energy intake, kJ/day	6,042 (1,925)	6,418 (1,966)	7,188 (2,096)	6,046 (1,971)	6,301 (1,979)	7,130 (2,130)
Artificially-sweetened beverages, servings/day	0.6 (1.0)	0.3 (0.7)	0.3 (0.6)	0.6 (1.1)	0.3 (0.7)	0.3 (0.6)
Sugar-sweetened beverages, servings/day	0.0 (0.0)	0.1 (0.0)	0.9 (0.9)	0.0 (0.0)	0.1 (0.0)	1.0 (1.0)
Total beverages, servings/day	5.4 (2.5)	5.2 (2.4)	5.7 (2.6)	5.5 (2.6)	5.3 (2.5)	5.8 (2.6)
Alcohol, g/day	8.0 (11.0)	6.2 (9.6)	5.5 (9.2)	7.9 (12.2)	5.5 (9.9)	5.0 (9.7)
Red and processed meat, servings/day	1.2 (0.8)	1.4 (0.8)	1.5 (0.8)	1.3 (0.8)	1.4 (0.8)	1.6 (0.8)
Nuts, servings/day	0.2 (0.3)	0.2 (0.3)	0.2 (0.3)	0.1 (0.3)	0.1 (0.3)	0.1 (0.3)
Whole grains, servings/day	2.3 (2.0)	2.2 (1.9)	2.0 (1.8)	2.1 (2.0)	2.1 (1.9)	1.9 (1.8)
Fruits and vegetables, servings/day	4.5 (2.2)	4.2 (2.0)	4.1 (2.0)	4.0 (2.1)	3.7 (1.9)	3.6 (1.9)
AHEI ^c	44.6 (9.0)	42.2 (8.5)	40.3 (8.3)	41.2 (8.7)	39.4 (8.2)	37.6 (7.8)
Nurses' Health Study II						
Participants, n	20,698	14,575	23,170	8,907	7,092	13,898
Age, years	36.6 (4.5)	35.8 (4.7)	35.3 (4.7)	37.3 (4.4)	36.5 (4.6)	35.9 (4.7)
BMI, kg/m ²	24.2 (4.7)	24.1 (4.7)	23.9 (4.8)	26.2 (6.1)	25.6 (5.8)	25.1 (6.0)
Physical activity, MET-h/week	31.8 (31.8)	29.3 (28.7)	28.4 (28.3)	3.4 (2.1)	3.5 (2.1)	3.3 (2.1)
Family history of diabetes	29.9	28.2	27.9	31.7	31.0	29.5
Ancestry, white	97.9	97.4	95.7	97.4	96.8	94.0
Current smoker	10.2	10.0	13.0	13.1	12.8	15.2
Hypertension	5.8	5.5	5.7	7.0	6.8	6.7
Hypercholesterolemia	13.8	13.0	14.1	15.7	15.2	15.8
Multivitamin supplement use	44.7	46.3	46.3	39.0	39.5	40.5
Aspirin use	11.5	10.9	11.1	11.6	10.5	10.9
Current menopausal hormone use	2.3	2.4	2.6	2.7	2.4	2.8
Total energy intake, kJ/day	6,820 (2,092)	7,301 (2,130)	8,276 (2,318)	6,615 (2,096)	7,042 (2,088)	7,996 (2,305)
Artificially-sweetened beverages, servings/day	1.4 (1.6)	1.1 (1.4)	0.6 (1.1)	1.6 (1.7)	1.2 (1.4)	0.5 (1.0)
Sugar-sweetened beverages, servings/day	0.0 (0.0)	0.1 (0.0)	1.0 (1.0)	0.0 (0.0)	0.1 (0.0)	1.1 (1.1)
Total beverages, servings/day	8.6 (3.2)	8.3 (3.0)	8.3 (3.1)	8.1 (3.2)	7.7 (2.9)	7.6 (3.0)
Alcohol, g/day	3.6 (6.5)	3.4 (5.9)	3.0 (5.8)	3.0 (6.4)	2.8 (6.0)	2.4 (5.6)
Red and processed meat, servings/day	0.7 (0.6)	0.9 (0.6)	1.1 (0.7)	0.9 (0.6)	1.0 (0.6)	1.2 (0.7)
Nuts, servings/day	0.1 (0.2)	0.1 (0.1)	0.1 (0.1)	0.0 (0.1)	0.1 (0.1)	0.1 (0.1)
Whole grains, servings/day	2.0 (1.6)	1.9 (1.5)	1.8 (1.4)	1.7 (1.4)	1.6 (1.3)	1.5 (1.3)
Fruits and vegetables, servings/day	5.3 (2.9)	5.1 (2.6)	5.1 (2.7)	4.1 (2.4)	4.2 (2.3)	4.1 (2.3)
AHEI ^c	45.1 (9.6)	42.6 (9.1)	39.5 (8.8)	40.0 (9.4)	38.5 (8.7)	36.2 (8.3)

Health Professionals Follow-up Study						
Participants, n	9,067	5,908	10,018	4,522	3,308	6,613
Age, years	54.3 (9.5)	53.4 (9.4)	50.6 (9.1)	55.6 (9.4)	54.3 (9.3)	51.3 (9.1)
BMI, kg/m ²	25.1 (3.1)	25.2 (3.1)	25.2 (3.1)	26.2 (3.7)	25.9 (3.5)	25.9 (3.5)
Physical activity, MET-h/week	32.6 (27.3)	30.4 (25.5)	30.7 (26.0)	3.0 (2.2)	3.1 (2.1)	3.0 (2.1)
Family history of diabetes	20.0	18.4	16.8	20.3	19.2	18.3
Ancestry, white	95.7	96.2	94.1	96.2	95.5	93.9
Current smoker	6.7	7.4	9.1	12.1	11.6	13.6
Hypertension	21.2	19.2	19.6	24.5	22.9	22.5
Hypercholesterolemia	10.9	11.0	9.6	11.4	10.1	9.3
Multivitamin supplement use	46.5	43.7	41.5	41.1	37.4	36.7
Aspirin use	25.6	25.2	27.6	27.1	26.6	27.3
Total energy intake, kJ/day	7,619 (2,335)	8,134 (2,402)	9,284 (2,644)	7,272 (2,284)	7,832 (2,326)	9,050 (2,674)
Artificially-sweetened beverages, servings/day	0.7 (1.1)	0.5 (0.8)	0.3 (0.7)	0.7 (1.2)	0.5 (1.0)	0.3 (0.7)
Sugar-sweetened beverages, servings/day	0.0 (0.0)	0.1 (0.0)	0.7 (0.7)	0.0 (0.0)	0.1 (0.0)	0.8 (0.8)
Total beverages, servings/day	7.2 (3.0)	7.2 (2.8)	7.7 (2.9)	7.2 (3.0)	7.1 (2.9)	7.4 (3.0)
Alcohol, g/day	12.8 (16.2)	11.6 (14.7)	10.8 (14.3)	12.4 (16.9)	11.2 (16.0)	10.0 (15.4)
Red and processed meat, servings/day	0.9 (0.8)	1.0 (0.8)	1.3 (0.8)	1.1 (0.8)	1.2 (0.8)	1.4 (0.9)
Nuts, servings/day	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.2 (0.4)	0.2 (0.4)	0.2 (0.4)
Whole grains, servings/day	1.9 (1.6)	1.8 (1.5)	1.6 (1.4)	1.5 (1.4)	1.5 (1.3)	1.4 (1.2)
Fruits and vegetables, servings/day	5.3 (2.9)	5.2 (2.9)	5.1 (2.7)	4.4 (2.6)	4.3 (2.4)	4.3 (2.4)
AHEI ^c	48.2 (10.2)	45.9 (9.8)	43.1 (9.4)	43.9 (10.1)	41.8 (9.6)	39.6 (9.1)

Values are mean (SDs) for continuous variables and percentages for categorical variables; characteristics are standardised to the age distribution of the study population. Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses' Health Study, n=64,029; Nurses' Health Study II, n=88,340).

^a Baseline for Nurses' Health Study is 1980, for Nurses' Health Study II is 1991, and for Health Professionals Follow-up Study is 1986.

^b US physical activity guidelines were met if participant reported ≥150 minutes/week of moderate-vigorous physical activity.

^c AHEI range 0-90, sugar-sweetened beverages and alcohol were removed from the index calculation.

AHEI = alternative healthy index; BMI = body mass index; MET = metabolic equivalent task; MVPA = moderate-vigorous physical activity.

ESM Table 2. Baseline^a characteristics of participants according to artificially-sweetened beverage intake and physical activity joint association categories in three large US cohorts.

Nurses' Health Study	Meets the US Physical Activity Guidelines^b			Does Not Meet the US Physical Activity Guidelines^b		
	Never or less than 1 ASB serving per month	1-4 ASB servings per month	≥2 ASB servings per week	Never or less than 1 ASB serving per month	1-4 ASB per servings per month	≥2 ASB servings per week
Participants, n	15,931	5,350	11,414	16,618	4,762	9,954
Age, years	46.5 (7.3)	46.6 (7.1)	45.7 (7.1)	46.3 (7.1)	46.3 (7.0)	45.7 (7.1)
BMI, kg/m ²	23.0 (3.6)	24.0 (3.7)	24.7 (4.2)	23.7 (4.2)	25.2 (4.5)	26.1 (4.9)
Physical activity, MET-h/week	24.5 (24.2)	24.6 (24.1)	25.4 (23.0)	2.8 (1.9)	2.9 (2.0)	2.8 (2.0)
Family history of diabetes	26.3	29.0	30.0	28.3	30.6	33.2
Ancestry, white	97.8	98.0	98.2	97.7	97.9	98.1
Current smoker	27.3	19.9	22.4	34.3	24.7	26.5
Hypertension	12.1	13.1	16.1	14.3	15.4	19.0
Hypercholesterolemia	4.3	4.7	5.4	4.5	5.5	6.0
Multivitamin supplement use	34.9	37.6	37.3	31.3	32.5	32.4
Aspirin use	43.9	45.6	50.3	45.1	49.0	50.8
Current menopausal hormone use	6.4	6.9	7.1	6.5	6.6	6.9
Total energy intake, kJ/day	6,707 (2,084)	6,385 (2,000)	6,393 (2,038)	6,694 (2,134)	6,351 (2,017)	6,435 (2,071)
Artificially-sweetened beverages, servings/day	0.0 (0.0)	0.1 (0.0)	1.2 (1.0)	0.0 (0.0)	0.1 (0.0)	1.2 (1.1)
Sugar-sweetened beverages, servings/day	0.4 (0.8)	0.3 (0.5)	0.3 (0.7)	0.5 (0.9)	0.4 (0.7)	0.4 (0.8)
Total beverages, servings/day	5.2 (2.4)	5.1 (2.4)	6.0 (2.6)	5.3 (2.5)	5.2 (2.4)	6.1 (2.7)
Alcohol, g/day	6.6 (10.2)	6.3 (9.8)	6.9 (10.2)	6.1 (10.9)	5.7 (10.2)	6.5 (10.9)
Red and processed meat, servings/day	1.4 (0.8)	1.3 (0.8)	1.3 (0.8)	1.5 (0.8)	1.4 (0.8)	1.4 (0.8)
Nuts, servings/day	0.2 (0.3)	0.2 (0.3)	0.2 (0.3)	0.1 (0.3)	0.1 (0.2)	0.1 (0.3)
Whole grains, servings/day	2.2 (1.9)	2.3 (1.9)	2.2 (1.9)	2.0 (1.9)	2.1 (1.9)	2.0 (1.9)
Fruits and vegetables, servings/day	4.2 (2.1)	4.3 (2.0)	4.4 (2.1)	3.6 (2.0)	3.8 (1.9)	4.0 (2.0)
AHEI ^c	41.8 (9.1)	43.1 (8.6)	43.1 (8.6)	38.5 (8.5)	39.8 (8.1)	40.2 (8.2)
Nurses' Health Study II						
Participants, n	16,379	6,058	36,006	9,806	2,924	17,167
Age, years	35.8 (4.6)	36.0 (4.7)	35.9 (4.7)	36.3 (4.6)	36.5 (4.6)	36.6 (4.6)
BMI, kg/m ²	23.0 (4.3)	23.7 (4.5)	24.6 (4.9)	24.0 (5.5)	25.1 (5.8)	26.5 (6.2)
Physical activity, MET-h/week	29.3 (29.1)	29.1 (28.1)	30.2 (30.2)	3.3 (2.1)	3.4 (2.1)	3.4 (2.1)
Family history of diabetes	26.3	27.8	29.8	28.2	30.6	31.8
Ancestry, white	95.3	96.5	97.7	93.4	95.0	97.1
Current smoker	13.6	8.9	10.6	16.6	12.0	12.9
Hypertension	4.6	5.2	6.3	5.1	6.4	7.9
Hypercholesterolemia	12.7	12.7	14.3	14.0	14.1	16.8
Multivitamin supplement use	47.3	49.4	44.5	42.3	42.2	38.2
Aspirin use	10.0	10.6	11.8	10.0	10.8	11.6
Current menopausal hormone use	2.3	2.4	2.5	2.7	2.6	2.7
Total energy intake, kJ/day	7,862 (2,360)	7,389 (2,243)	7,406 (2,251)	7,636 (2,314)	7,230 (2,226)	7,226 (2,251)
Artificially-sweetened beverages, servings/day	0.0 (0.0)	0.1 (0.0)	1.7 (1.5)	0.0 (0.0)	0.1 (0.0)	1.7 (1.5)
Sugar-sweetened beverages, servings/day	0.8 (1.1)	0.4 (0.8)	0.3 (0.6)	1.0 (1.2)	0.5 (0.9)	0.3 (0.6)
Total beverages, servings/day	7.9 (2.9)	7.9 (2.9)	8.7 (3.2)	7.3 (2.9)	7.4 (2.9)	8.1 (3.1)
Alcohol, g/day	2.9 (5.9)	3.1 (5.5)	3.6 (6.3)	2.2 (5.8)	2.5 (5.4)	3.0 (6.1)
Red and processed meat, servings/day	0.9 (0.7)	0.8 (0.6)	0.9 (0.6)	1.1 (0.7)	1.0 (0.6)	1.1 (0.7)
Nuts, servings/day	0.1 (0.2)	0.1 (0.1)	0.1 (0.1)	0.1 (0.2)	0.1 (0.1)	0.1 (0.1)
Whole grains, servings/day	1.8 (1.5)	2.0 (1.5)	1.9 (1.5)	1.5 (1.3)	1.6 (1.3)	1.6 (1.3)
Fruits and vegetables, servings/day	5.2 (2.9)	5.3 (2.7)	5.1 (2.7)	4.1 (2.4)	4.3 (2.4)	4.1 (2.3)
AHEI ^c	41.7 (10.2)	44.0 (9.7)	42.2 (9.1)	37.3 (9.3)	38.9 (8.8)	38.0 (8.6)
Health Professionals Follow-up Study						

Participants, n	10,647	3,141	11,205	6,983	1,822	5,638
Age, years	53.8 (9.8)	53.8 (9.5)	51.2 (8.9)	54.0 (9.6)	54.4 (9.5)	52.2 (9.1)
BMI, kg/m ²	24.5 (3.0)	25.1 (2.7)	25.8 (3.2)	25.2 (3.3)	26.1 (3.4)	26.9 (3.7)
Physical activity, MET-h/week	30.7 (25.8)	30.4 (24.9)	32.1 (27.2)	2.9 (2.1)	3.1 (2.1)	3.0 (2.1)
Family history of diabetes	17.4	19.5	19.0	17.5	20.4	20.8
Ancestry, white	94.7	95.8	95.4	94.4	95.5	95.4
Current smoker	9.5	6.3	6.7	16.2	9.3	10.1
Hypertension	17.0	19.8	23.3	19.9	23.7	26.7
Hypercholesterolemia	8.7	10.5	12.1	8.3	9.1	13.0
Multivitamin supplement use	41.9	44.8	44.9	36.6	38.2	40.0
Aspirin use	23.8	25.9	28.9	25.3	25.5	29.7
Total energy intake, kJ/day	8,657 (2,636)	8,226 (2,523)	8,251 (2,544)	8,435 (2,636)	8,079 (2,536)	8,046 (2,577)
Artificially-sweetened beverages, servings/day	0.0 (0.0)	0.1 (0.0)	1.0 (1.1)	0.0 (0.0)	0.1 (0.0)	1.1 (1.2)
Sugar-sweetened beverages, servings/day	0.4 (0.7)	0.3 (0.5)	0.2 (0.4)	0.5 (0.8)	0.4 (0.6)	0.3 (0.5)
Total beverages, servings/day	7.2 (2.8)	7.1 (2.7)	7.6 (3.0)	7.1 (2.9)	7.0 (2.9)	7.5 (3.1)
Alcohol, g/day	11.7 (15.6)	11.2 (14.0)	12.0 (15.1)	11.4 (16.6)	10.7 (16.0)	10.7 (15.4)
Red and processed meat, servings/day	1.1 (0.9)	1.0 (0.8)	1.1 (0.8)	1.3 (0.9)	1.2 (0.8)	1.2 (0.8)
Nuts, servings/day	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.2 (0.4)	0.2 (0.4)	0.2 (0.4)
Whole grains, servings/day	1.8 (1.6)	1.8 (1.5)	1.6 (1.4)	1.4 (1.3)	1.5 (1.3)	1.4 (1.3))
Fruits and vegetables, servings/day	5.1 (2.9)	5.2 (2.8)	5.2 (2.8)	4.2 (2.4)	4.4 (2.5)	4.5 (2.5)
AHEI ^c	44.8 (10.6)	46.4 (9.9)	46.1 (9.5)	40.2 (9.9)	42.2 (9.5)	42.5 (9.4)

Values are mean (SDs) for continuous variables and percentages for categorical variables; characteristics are standardised to the age distribution of the study population. Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses' Health Study, n=64,029; Nurses' Health Study II, n=88,340).

^a Baseline for Nurses' Health Study is 1980, for Nurses' Health Study II is 1991, and for Health Professionals Follow-up Study is 1986.

^b US physical activity guidelines were met if participant reported ≥150 minutes/week of moderate-vigorous physical activity.

^c AHEI range 0-90, sugar-sweetened beverages and alcohol were removed from the index calculation.

AHEI = alternative healthy index; BMI = body mass index; MET = metabolic equivalent task; MVPA = moderate-vigorous physical activity.

ESM Table 3. Baseline^a characteristics of participants according to categories of sugar- or artificially-sweetened beverage intake and quintiles of physical activity^b in three large US cohorts.

Sugar-Sweetened Beverages	Nurses' Health Study					Nurses' Health Study II					Health Professionals Follow-Up Study				
	Never or <1 serving per month	1-4 servings per month	2-6 servings per week	1-<2 servings per day	≥2 servings per day	Never or <1 serving per month	1-4 servings per month	2-6 servings per week	1-<2 servings per day	≥2 servings per day	Never or <1 serving per month	1-4 servings per month	2-6 servings per week	1-<2 servings per day	≥2 servings per day
Participants, n	24,484	14,607	12,954	5,134	6,850	29,605	21,667	19,096	6,242	11,730	13,589	9,216	10,861	2,132	3,638
Age, years	47.4 (7.0)	46.5 (7.1)	45.2 (7.1)	45.1 (7.2)	43.7 (7.0)	36.8 (4.5)	36.1 (4.7)	35.7 (4.6)	35.6 (4.8)	35.2 (4.8)	54.7 (9.5)	53.7 (9.4)	51.5 (9.2)	51.1 (9.2)	49.0 (8.4)
BMI, kg/m ²	24.1 (4.1)	24.1 (4.1)	24.2 (4.3)	24.4 (4.6)	24.9 (5.0)	24.8 (5.3)	24.6 (5.2)	24.2 (5.0)	24.3 (5.3)	24.6 (5.8)	25.5 (3.3)	25.4 (3.2)	25.5 (3.3)	25.3 (3.2)	25.6 (3.4)
Physical activity, MET-h/week	15.6 (21.6)	13.7 (20.3)	12.9 (18.3)	13.0 (19.3)	12.2 (18.9)	23.3 (29.7)	20.9 (26.6)	19.2 (24.9)	19.6 (25.6)	18.2 (26.3)	23.0 (26.5)	20.7 (24.4)	20.0 (24.3)	19.3 (24.3)	18.7 (25.0)
Physical activity, ≥150 minutes/week MVPA (meets US guidelines)	55.1	50.9	48.8	48.1	43.8	70.2	67.3	63.9	62.9	59.3	67.3	64.3	61.8	57.9	54.9
Family history of diabetes	29.2	28.7	28.9	29.5	29.7	30.4	29.1	28.1	28.6	29.2	20.1	18.7	17.5	17.0	17.1
Ancestry, white	98.7	97.9	97.5	97.6	96.3	97.7	97.2	95.5	94.9	94.3	95.9	96.0	94.5	93.4	93.0
Current smoker	27.7	25.1	24.6	31.1	31.4	11.1	10.9	11.4	14.2	17.8	8.5	8.9	10.0	11.9	13.0
Hypertension	15.1	13.4	14.3	15.7	17.2	6.2	6.0	5.6	6.1	6.9	22.3	20.5	20.2	21.8	21.9
Hypercholesterolemia	5.3	4.8	4.7	4.5	4.4	14.4	13.7	14.1	14.9	15.7	11.1	10.7	9.5	8.8	10.2
Multivitamin supplement use	35.6	33.9	32.7	33.1	32.0	43.0	44.1	44.9	44.7	42.4	44.7	41.5	40.1	40.1	38.0
Aspirin use	45.1	46.1	48.5	50.1	50.5	11.5	10.8	10.7	11.1	11.4	26.1	25.7	26.9	27.3	28.9
Current menopausal hormone use	7.1	6.7	6.3	6.2	6.0	2.5	2.4	2.5	2.8	2.9	-	-	-	-	-
Total energy intake, kJ/day	6,042 (1,946)	6,360 (1,975)	6,820 (1,983)	7,096 (2,092)	7,870 (2,205)	6,761 (2,092)	7,217 (2,117)	7,757 (2,188)	7,987 (2,276)	9,025 (2,326)	7,502 (2,322)	8,025 (2,381)	8,778 (2,510)	9,234 (2,510)	10,447 (2,791)
Artificially-sweetened beverages, servings/day	0.6 (1.0)	0.3 (0.7)	0.2 (0.5)	0.3 (0.6)	0.4 (0.8)	1.5 (1.6)	1.1 (1.4)	0.7 (1.1)	0.7 (1.2)	0.4 (0.9)	0.7 (1.2)	0.5 (0.9)	0.4 (0.7)	0.3 (0.7)	0.3 (0.8)
Sugar-sweetened beverages, servings/day	0.0 (0.0)	0.1 (0.0)	0.4 (0.1)	0.9 (0.1)	2.1 (1.2)	0.0 (0.0)	0.1 (0.0)	0.4 (0.2)	0.9 (0.1)	2.2 (1.2)	0.0 (0.0)	0.1 (0.0)	0.4 (0.2)	0.9 (0.1)	1.8 (0.9)
Total beverages, servings/day	5.4 (2.6)	5.2 (2.4)	5.3 (2.4)	5.7 (2.5)	6.7 (2.9)	8.4 (3.2)	8.1 (3.0)	7.9 (3.0)	8.0 (3.1)	8.3 (3.3)	7.2 (3.0)	7.2 (2.8)	7.4 (2.9)	7.6 (2.9)	8.1 (3.0)
Alcohol, g/day	8.0 (11.6)	5.9 (9.8)	5.1 (8.9)	5.8 (10.0)	5.0 (10.0)	3.5 (6.5)	3.2 (6.0)	3.0 (5.8)	3.0 (6.0)	2.3 (5.3)	12.7 (16.4)	11.5 (15.2)	10.7 (14.5)	10.6 (15.1)	10.0 (15.6)
Red and processed meat, servings/day	1.2 (0.8)	1.4 (0.8)	1.5 (0.8)	1.6 (0.9)	1.7 (0.9)	0.8 (0.6)	0.9 (0.6)	1.0 (0.6)	1.1 (0.7)	1.2 (0.7)	0.9 (0.8)	1.1 (0.8)	1.3 (0.8)	1.4 (0.9)	1.6 (1.0)
Nuts, servings/day	0.2 (0.3)	0.1 (0.3)	0.1 (0.3)	0.1 (0.3)	0.1 (0.3)	0.1 (0.2)	0.1 (0.1)	0.1 (0.1)	0.1 (0.2)	0.1 (0.2)	0.2 (0.4)	0.2 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)
Whole grains, servings/day	2.2 (2.0)	2.2 (1.9)	2.0 (1.8)	1.9 (1.8)	1.9 (1.9)	1.9 (1.6)	1.8 (1.4)	1.7 (1.4)	1.6 (1.4)	1.5 (1.3)	1.7 (1.6)	1.7 (1.4)	1.6 (1.4)	1.5 (1.4)	1.4 (1.3)
Fruits and vegetables, servings/day	4.2 (2.2)	4.0 (2.0)	3.9 (1.9)	3.9 (2.0)	3.8 (2.0)	4.9 (2.9)	4.8 (2.6)	4.8 (2.5)	4.7 (2.7)	4.5 (2.7)	5.0 (2.8)	4.9 (2.7)	4.8 (2.6)	4.7 (2.5)	4.7 (2.7)
AHEI ^b	43.0 (9.1)	40.8 (8.4)	39.4 (8.1)	39.1 (8.3)	37.8 (8.1)	43.6 (9.8)	41.3 (9.2)	39.6 (8.6)	38.6 (8.8)	36.0 (8.5)	46.8 (10.3)	44.5 (9.9)	42.7 (9.4)	40.6 (9.3)	39.1 (9.1)
Artificially-Sweetened Beverages	Never or <1 serving per month	1-4 servings per month	2-6 servings per week	1-<2 servings per day	≥2 servings per day	Never or <1 serving per month	1-4 servings per month	2-6 servings per week	1-<2 servings per day	≥2 servings per day	Never or <1 serving per month	1-4 servings per month	2-6 servings per week	1-<2 servings per day	≥2 servings per day
Participants, n	32,549	10,112	7,635	9,206	4,527	26,185	8,982	13,807	11,748	27,618	17,630	4,963	8,972	2,362	5,509
Age, years	46.4 (7.2)	46.4 (7.1)	46.4 (7.0)	45.6 (7.0)	44.6 (7.0)	36.0 (4.6)	36.1 (4.7)	36.2 (4.7)	36.4 (4.6)	36.0 (4.7)	53.8 (9.7)	54.0 (9.5)	52.8 (9.2)	51.4 (8.8)	49.6 (8.2)
BMI, kg/m ²	23.4 (4.0)	24.5 (4.2)	25.0 (4.3)	25.3 (4.5)	26.0 (5.0)	23.4 (4.8)	24.2 (5.0)	24.4 (4.9)	24.7 (5.0)	25.8 (5.7)	24.8 (3.1)	25.5 (3.1)	25.7 (3.3)	26.2 (3.7)	26.7 (3.5)
Physical activity, MET-h/week	13.4 (20.1)	14.4 (20.6)	14.9 (20.5)	14.9 (19.7)	14.6 (20.8)	19.6 (26.3)	20.8 (26.1)	21.6 (28.1)	21.6 (28.1)	21.6 (27.7)	19.7 (24.3)	20.4 (23.8)	22.2 (26.1)	21.7 (25.0)	22.9 (26.6)
Physical activity, ≥150 minutes/week MVPA (meets US guidelines)	48.9	52.9	54.1	53.9	51.1	62.5	67.5	68.5	68.6	67.0	60.4	63.5	66.6	66.2	65.7
Family history of diabetes	27.3	29.8	30.4	31.2	33.9	27.1	28.8	29.6	29.8	31.2	17.4	19.8	19.0	20.0	20.6
Ancestry, white	97.8	98.0	98.0	98.4	98.0	94.6	96.0	96.5	97.3	98.1	94.6	95.7	95.0	95.8	95.9
Current smoker	30.8	22.1	22.9	23.5	28.4	14.7	9.9	8.8	10.7	12.8	12.1	7.4	8.3	7.0	7.5
Hypertension	13.2	14.2	16.2	17.6	19.5	4.8	5.5	5.3	5.7	8.0	18.2	21.2	22.8	24.0	27.6
Hypercholesterolemia	4.4	5.1	5.3	5.8	6.0	13.2	13.1	13.6	14.4	16.2	8.5	10.0	11.7	12.8	13.4
Multivitamin supplement use	33.1	35.2	34.1	35.4	35.6	45.4	47.1	45.9	42.5	40.8	39.8	42.4	43.2	42.1	44.6
Aspirin use	44.5	47.2	49.7	50.5	51.9	10.0	10.7	10.5	11.4	12.5	24.4	25.8	28.0	28.9	30.8
Current menopausal hormone use	6.5	6.8	6.8	7.6	6.5	2.5	2.5	2.3	2.6	2.7	-	-	-	-	-
Total energy intake, kJ/day	6,703 (2,109)	6,368 (2,008)	6,406 (2,000)	6,347 (2,042)	6,556 (2,155)	7,778 (2,347)	7,339 (2,238)	7,326 (2,218)	7,201 (2,180)	7,422 (2,297)	8,569 (2,640)	8,171 (2,527)	8,142 (2,515)	7,904 (2,389)	8,389 (2,703)
Artificially-sweetened beverages, servings/day	0.0 (0.0)	0.1 (0.0)	0.4 (0.0)	0.9 (0.1)	3.0 (1.1)	0.0 (0.0)	0.1 (0.0)	0.4 (0.1)	0.9 (0.1)	2.6 (1.5)	0.0 (0.0)	0.1 (0.0)	0.4 (0.2)	0.9 (0.1)	2.2 (1.4)
Sugar-sweetened beverages, servings/day	0.5 (0.9)	0.3 (0.6)	0.4 (0.6)	0.3 (0.6)	0.4 (1.0)	0.9 (1.1)	0.5 (0.8)	0.3 (0.6)	0.3 (0.6)	0.2 (0.5)	0.5 (0.7)	0.3 (0.5)	0.3 (0.5)	0.2 (0.4)	0.2 (0.5)
Total beverages, servings/day	5.3 (2.5)	5.2 (2.4)	5.5 (2.4)	5.8 (2.5)	7.7 (2.9)	7.7 (2.9)	7.8 (2.9)	7.9 (2.9)	7.8 (3.0)	9.1 (3.3)	7.2 (2.9)	7.1 (2.8)	7.1 (2.8)	7.3 (2.8)	8.6 (3.2)
Alcohol, g/day	6.3 (10.6)	6.0 (10.0)	6.5 (10.1)	6.7 (10.2)	7.2 (11.9)	2.6 (5.9)	2.9 (5.5)	3.2 (6.0)	3.3 (6.1)	3.5 (6.4)	11.6 (16.0)	11.0 (14.8)	11.6 (14.9)	12.0 (16.1)	11.2 (15.4)
Red and processed meat, servings/day	1.4 (0.8)	1.4 (0.8)	1.4 (0.8)	1.4 (0.8)	1.4 (0.9)	1.0 (0.7)	0.9 (0.6)	0.9 (0.6)	0.9 (0.6)	1.0 (0.7)	1.2 (0.9)	1.1 (0.8)	1.1 (0.8)	1.1 (0.8)	1.2 (0.8)
Nuts, servings/day	0.2 (0.3)	0.1 (0.3)	0.1 (0.3)	0.1 (0.3)	0.1 (0.3)	0.1 (0.2)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	0.2 (0.4)	0.3 (0.4)	0.2 (0.4)	0.2 (0.4)	0.3 (0.5)
Whole grains, servings/day	2.1 (1.9)	2.2 (1.9)	2.1 (1.9)	2.1 (1.9)	2.0 (2.0)	1.7 (1.5)	1.9 (1.5)	1.8 (1.4)	1.8 (1.4)	1.8 (1.5)	1.6 (1.5)	1.7 (1.5)	1.6 (1.3)	1.5 (1.4)	1.6 (1.4)
Fruits and vegetables, servings/day	3.9 (2.1)	4.0 (2.0)	4.1 (2.0)	4.2 (2.0)	4.2 (2.2)	4.8 (2.8)	5.0 (2.7)	4.9 (2.6)	4.8 (2.6)	4.7 (2.6)	4.8 (2.7)	4.9 (2.7)	4.9 (2.7)	4.8 (2.6)	5.1 (2.9)
AHEI ^b	40.1 (9.0)	41.6 (8.6)	41.7 (8.4)	41.9 (8.5)	41.4 (8.7)	40.1 (10.1)	42.3 (9.7)	42.0 (9.1)	41.3 (9.1)	40.1 (9.2)	43.0 (10.6)	44.9 (10.0)	45.0 (9.5)	44.6 (9.9)	45.0 (9.6)
Physical Activity	Quintile 1 (0 to ≤2.4)	Quintile 2 (>2.4 ≤7.1)	Quintile 3 (>7.1 to ≤14.6)	Quintile 4 (>14.6 to ≤27.2)	Quintile 5 (>27.2)	Quintile 1 (0 to ≤3.6)	Quintile 2 (>3.6 ≤9.6)	Quintile 3 (>9.6 to ≤18.8)	Quintile 4 (>18.8 ≤35.3)	Quintile 5 (>35.3)	Quintile 1 (0 to ≤6.1)	Quintile 2 (>6.1 ≤15.9)	Quintile 3 (>15.9 to ≤29.2)	Quintile 4 (>29.2 ≤51.8)	Quintile 5 (>51.8)
Participants, n	12,920	12,714	12,824	12,754	12,817	17,883	17,389	17,722	17,688	17,658	7,873	7,936	7,776	7,953	7,898
Age, years	46.0 (7.1)	46.3 (7.1)	46.1 (7.2)	46.2 (7.2)	46.2 (7.2)	36.6 (4.6)	36.3 (4.6)	36.2 (4.6)	35.9 (4.7)	35.5 (4.7)	53.2 (9.4)	53.8 (9.5)	52.9 (9.5)	52.3 (9.4)	52.3 (9.4)
BMI, kg/m ²	25.0 (4.9)	24.6 (4.5)	24.2 (4.1)	23.8 (3.9)	23.5 (3.8)	25.8 (6.3)	25.1 (5.5)	24.5 (5.0)	24.0 (4.6)	23.4 (4.2)	26.1 (3.7)	25.9 (3.5)	25.4 (3.3)	25.1 (2.9)	24.8 (3.0)
Physical activity, MET-h/week	0.9 (0.6)	3.3 (0.7)	7.6 (1.7)	15.7 (3.3)	42.7 (29.7)	1.9 (1.2)	6.4 (1.5)	12.7 (2.3)	23.2 (4.2)	60.0 (38.7)	1.3 (0.9)	5.5 (1.6)	12.6 (2.7)	24.6 (4.7)	60.4 (28.6)
Physical activity, ≥150 minutes/week MVPA (meets US guidelines)	0.0	0.0	55.5	100.0	100.0	0.0	30.9	100.0	100.0	100.0	0.0	17.1	100.0	100.0	100.0
Family history of diabetes	30.1	30.2	29.2	28.9	27.2	30.6	30.2	29.4	28.5	27.7	19.4	19.0	18.7	18.5	17.7
Ancestry, white	97.5	98.2	98.1	98.1	97.9	95.2	96.5	97.2	97.1	96.5	94.7	95.1	95.3	95.5	94.8
Current smoker	33.9	28.8	25.6	24.0	24.1	14.4	12.9	11.5	10.6	11.4	14.5	11.2	9.0	7.1	6.7
Hypertension	16.6	16.0	14.5	13.9	12.9	7.1	6.4	6.0	5.4	5.5	23.3	23.0	21.6	19.7	18.3
Hypercholesterolemia	5.4	4.8	5.0	5.0	4.3	16.1	14.9	14.5	13.0	13.1	10.3	10.0	10.9	10.3	10.3
Multivitamin supplement use	30.2	32.0	34.5	36.2	37.4	38.9	41.6	44.7	45.8	48.1	36.8	39.6	42.4	44.3	45.0
Aspirin use	47.5	47.5	47.7	46.6	45.5	11.0	10.9	11.2	11.4	11.1	26.3	27.8	26.4	26.5	25.8
Current menopausal hormone use	6.7	6.7	6.8	6.6	6.7	2.8	2.6	2.4	2.4	2.5	-	-	-	-	-
Total energy intake, kJ/day	6,535 (2,159)	6,565 (2,050)	6,565 (2,063)	6,548 (2,025)	6,540 (2,105)	7,322 (2,301)	7,439 (2,251)	7,498 (2,272)	7,498 (2,255)	7,623 (2,351)	8,130 (2,598)	8,330 (2,594)	8,314 (2,552)	8,330 (2,536)	8,632 (2,669)
Artificially-sweetened beverages, servings/day	0.4 (0.9)	0.4 (0.8)	0.4 (0.8)	0.4 (0.8)	0.4 (0.8)	1.0 (1.5)	1.0 (1.4)	1.0 (1.3)	1.0 (1.4)	1.1 (1.5)	0.5 (1.0)	0.5 (0.9)	0.4 (0.8)	0.5 (0.9)	0.5 (1.0)
Sugar-sweetened beverages, servings/day	0.5 (0.9)	0.4 (0.8)	0.4 (0.8)	0.4 (0.7)	0.3 (0.7)	0.6 (1.0)	0.5 (0.9)	0.5 (0.8)	0.4 (0.8)	0.4 (0.8)	0.4 (0.7)	0.4 (0.6)	0.3 (0.6)	0.3 (0.6)	0.3 (0.5)
Total beverages, servings/day	5.6 (2.6)	5.6 (2.6)	5.5 (2.5)	5.5 (2.5)	5.4 (2.6)	7.6 (3.0)	8.0 (3.1)	8.2 (3.0)	8.4 (3.1)	8.7 (3.2)	7.2 (3.0)	7.3 (2.9)	7.3 (2.9)	7.3 (2.9)	7.5 (2.9)
Alcohol, g/day	6.2 (11.5)	6.0 (10.3)	6.2 (9.9)	6.6 (10.1)	7.1 (10.3)	2.6 (6.1)	2.8 (5.9)	3.0 (5.7)	3.4 (6.1)	3.8					

Red and processed meat, servings/day	1.5 (0.9)	1.4 (0.8)	1.4 (0.8)	1.4 (0.8)	1.3 (0.8)	1.1 (0.7)	1.0 (0.7)	0.9 (0.6)	0.9 (0.6)	0.8 (0.6)	1.3 (0.9)	1.2 (0.9)	1.2 (0.8)	1.1 (0.8)	1.0 (0.8)
Nuts, servings/day	0.1 (0.3)	0.1 (0.3)	0.1 (0.3)	0.2 (0.3)	0.2 (0.3)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	0.1 (0.2)	0.2 (0.4)	0.2 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)
Whole grains, servings/day	1.9 (1.9)	2.1 (1.9)	2.1 (1.9)	2.2 (1.9)	2.2 (1.9)	1.5 (1.3)	1.7 (1.4)	1.8 (1.4)	1.9 (1.5)	2.0 (1.6)	1.3 (1.3)	1.5 (1.3)	1.6 (1.4)	1.8 (1.5)	1.9 (1.6)
Fruits and vegetables, servings/day	3.6 (2.0)	3.8 (2.0)	4.0 (2.0)	4.2 (2.0)	4.5 (2.2)	4.0 (2.3)	4.4 (2.4)	4.8 (2.5)	5.1 (2.6)	5.8 (3.1)	4.1 (2.4)	4.5 (2.5)	4.9 (2.7)	5.1 (2.7)	5.6 (3.0)
AHEI ^b	38.2 (8.3)	39.6 (8.3)	40.8 (8.6)	42.0 (8.7)	43.8 (9.0)	37.2 (8.8)	39.0 (8.9)	40.7 (9.1)	42.3 (9.3)	44.6 (9.7)	40.6 (9.7)	42.3 (9.7)	44.2 (9.8)	45.9 (9.9)	47.1 (10.2)

Values are mean (SDs) for continuous variables and percentages for categorical variables; characteristics are standardised to the age distribution of the study population. Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses’ Health Study, n=64,029; Nurses’ Health Study II, n=88,340).

^aBaseline for Nurses’ Health Study is 1980, for Nurses’ Health Study II is 1991, and for Health Professionals Follow-up Study is 1986.

^b AHEI range 0-90, sugar-sweetened beverages and alcohol were removed from the index calculation.

AHEI = alternative healthy index; BMI = body mass index; MET = metabolic equivalent task; MVPA = moderate-vigorous physical activity.

ESM Table 4. Associations between frequency of sugar- or artificially-sweetened beverage intake and quintiles of physical activity^a and risk^b of type 2 diabetes in three large US cohorts.

	Never or <1 serving per month	1-4 servings per month	2-6 servings per week	1-<2 servings per day	≥2 servings per day	<i>P</i> for trend	HR (95% CI) for 1 serving increment of SSB or ASB ^c intake per day
Sugar-Sweetened Beverages							
Cases/person-years							
Nurses' Health Study	1,199/372,727	2,868/683,806	3,486/689,360	429/80,772	884/142,937		
Nurses' Health Study II	1,125/424,729	2,164/657,812	2,546/711,664	397/110,590	1,273/274,862		
Health Professionals Follow-Up Study	660/197,008	1,016/282,093	1,361/356,493	173/43,486	359/77,014		
	HR (95% CI)						
Nurses' Health Study	1.00	1.08 (1.01, 1.16)	1.25 (1.17, 1.34)	1.45 (1.30, 1.63)	1.52 (1.38, 1.67)	<0.0001	1.31 (1.24, 1.38)
Nurses' Health Study II	1.00	1.08 (1.00, 1.16)	1.17 (1.09, 1.26)	1.24 (1.10, 1.39)	1.35 (1.23, 1.47)	<0.0001	1.17 (1.12, 1.22)
Health Professionals Follow-Up Study	1.00	1.05 (0.95, 1.17)	1.09 (0.99, 1.20)	1.19 (1.00, 1.41)	1.36 (1.19, 1.56)	<0.0001	1.22 (1.12, 1.33)
Pooled	1.00	1.07 (1.03, 1.12)	1.19 (1.13, 1.24)	1.31 (1.22, 1.41)	1.41 (1.33, 1.50)	<0.0001	1.22 (1.19, 1.26)
Artificially-Sweetened Beverages							
Cases/person-years							
Nurses' Health Study	2,578/740,201	1,377/325,516	2,263/455,921	864/171,779	1,784/276,184		
Nurses' Health Study II	1,149/490,528	779/274,035	1,850/543,125	617/187,754	3,110/684,214		
Health Professionals Follow-Up Study	756/281,614	700/200,278	1,097/280,721	237/52,559	779/140,923		
	HR (95% CI)						
Nurses' Health Study	1.00	0.99 (0.93, 1.06)	1.01 (0.95, 1.07)	1.00 (0.92, 1.08)	1.08 (1.01, 1.15)	0.009	1.04 (1.01, 1.07)
Nurses' Health Study II	1.00	1.00 (0.91, 1.09)	1.03 (0.96, 1.11)	1.03 (0.93, 1.14)	1.08 (1.01, 1.16)	0.01	1.04 (1.01, 1.06)
Health Professionals Follow-Up Study	1.00	1.16 (1.04, 1.29)	1.15 (1.05, 1.27)	1.20 (1.04, 1.40)	1.32 (1.19, 1.47)	<0.001	1.14 (1.08, 1.20)
Pooled	1.00	1.02 (0.98, 1.07)	1.04 (1.00, 1.08)	1.04 (0.98, 1.10)	1.11 (1.07, 1.16)	<0.0001	1.05 (1.03, 1.07)
Physical Activity	Quintile 1 (0 to ≤3.0)	Quintile 2 (>3.0 to ≤8.4)	Quintile 3 (>8.4 to ≤16.5)	Quintile 4 (>16.5 to ≤31.7)	Quintile 5 (>31.7)	<i>P</i> for trend	
Cases/person-years							
Nurses' Health Study	2,562/388,193	1,992/392,157	1,715/396,185	1,469/395,809	1,128/397,257		
Nurses' Health Study II	2,611/433,428	1,781/435,162	1,325/436,679	1,049/437,046	739/437,340		
Health Professionals Follow-Up Study	1,000/186,888	820/190,756	670/192,243	585/192,986	494/193,221		
	HR (95% CI)						
Nurses' Health Study	1.00	0.91 (0.85, 0.96)	0.87 (0.82, 0.93)	0.83 (0.78, 0.88)	0.73 (0.68, 0.78)	<0.0001	
Nurses' Health Study II	1.00	0.91 (0.85, 0.96)	0.83 (0.78, 0.89)	0.81 (0.75, 0.87)	0.73 (0.67, 0.79)	<0.0001	
Health Professionals Follow-Up Study	1.00	0.87 (0.79, 0.95)	0.76 (0.69, 0.84)	0.70 (0.63, 0.78)	0.63 (0.57, 0.71)	<0.0001	
Pooled	1.00	0.90 (0.86, 0.93)	0.83 (0.80, 0.87)	0.80 (0.76, 0.83)	0.71 (0.67, 0.74)	<0.0001	
	HR (95% CI)						
	Per 1 SD or physical activity, as continuous variable, increment						
Nurses' Health Study	0.90 (0.88, 0.93)						
Nurses' Health Study II	0.88 (0.85, 0.91)						
Health Professionals Follow-Up Study	0.86 (0.83, 0.90)						
Pooled	0.89 (0.87, 0.90)						

Total sample size, n=191,805 (HPFS, n=39,436; NHS, n=64,029; NHSII, n=88,340).

^a Physical activity was measured in MET-h/week.

^b Hazard ratios and 95% confidence intervals derived from the age-adjusted model and the multivariable model adjusted for age; race; ancestry; physical activity (excluded in the physical activity as primary exposure models); smoking status; alcohol intake; multivitamin use; in women, postmenopausal status and menopausal hormone use; aspirin use; family history of diabetes; calorie intake; body mass index; and AHEI.

^c 1 serving increment of sugar- or artificially-sweetened beverage intake per day, where appropriate.

AHEI = alternative healthy index; sugar-sweetened beverages and alcohol intake were removed from the index calculation (sugar- and artificially-sweetened models only).

ESM Table 5. Associations between frequency of sugar- or artificially-sweetened beverage subtype intake and risk^a of type 2 diabetes in three large US cohorts.

	Never or <1 servings per month	1-4 servings per month	2-6 servings per week	1-<2 servings per day	≥2 servings per day	<i>P</i> for trend	HR (95% CI) for 1 serving increment of SSB or ASB ^b intake per day
Sugar-sweetened beverages							
Cola carbonated beverages							
Cases/person-years							
Nurses' Health Study	3,241/844,204	3,274/713,087	1,809/325,629	225/43,674	317/43,007		
Nurses' Health Study II	3,513/1,147,356	1,908/578,917	1,427/318,083	218/60,041	439/75,258		
Health Professionals Follow-Up Study	1,229/355,978	1,175/308,493	923/234,926	94/27,480	147/29,200		
	HR (95% CI)						
Nurses' Health Study	1.00	1.10 (1.05, 1.16)	1.27 (1.19, 1.35)	1.55 (1.35, 1.77)	1.61 (1.42, 1.81)	<0.0001	1.34 (1.26, 1.43)
Nurses' Health Study II	1.00	1.04 (0.98, 1.10)	1.20 (1.13, 1.28)	1.24 (1.08, 1.43)	1.27 (1.14, 1.41)	<0.0001	1.16 (1.10, 1.22)
Health Professionals Follow-Up Study	1.00	1.07 (0.98, 1.16)	1.10 (1.01, 1.20)	1.08 (0.88, 1.34)	1.36 (1.14, 1.62)	0.001	1.18 (1.06, 1.30)
Pooled	1.00	1.07 (1.04, 1.11)	1.21 (1.16, 1.26)	1.33 (1.22, 1.45)	1.40 (1.30, 1.50)	<0.0001	1.22 (1.18, 1.27)
Non-cola carbonated beverages							
Cases/person-years							
Nurses' Health Study	5,185/1,202,452	2,708/592,712	619/112,843	284/51,899	70/9,694		
Nurses' Health Study II	3,751/1,178,101	2,429/674,836	1,091/269,800	105/28,216	129/28,704		
Health Professionals Follow-Up Study	1,671/470,775	1,453/388,911	407/88,882	22/4,530	15/2,980		
	HR (95% CI)						
Nurses' Health Study	1.00	1.06 (1.01, 1.11)	1.19 (1.09, 1.29)	1.15 (1.01, 1.29)	1.24 (0.98, 1.57)	0.0003	1.14 (1.06, 1.22)
Nurses' Health Study II	1.00	1.07 (1.02, 1.13)	1.14 (1.07, 1.23)	1.19 (0.98, 1.45)	1.14 (0.96, 1.37)	0.005	1.15 (1.04, 1.27)
Health Professionals Follow-Up Study	1.00	1.01 (0.94, 1.09)	1.22 (1.09, 1.36)	1.44 (0.94, 2.20)	1.32 (0.79, 2.21)	0.0007	1.42 (1.16, 1.75)
Pooled	1.00	1.06 (1.02, 1.09)	1.17 (1.12, 1.23)	1.17 (1.06, 1.29)	1.19 (1.04, 1.36)	<0.0001	1.16 (1.10, 1.23)
Punch							
Cases/person-years							
Nurses' Health Study	4,408/1,079,231	2,921/610,892	1,189/218,878	232/40,661	116/19,939		
Nurses' Health Study II	1,905/651,123	3,163/903,845	1,970/505,840	198/63,051	269/55,796		
Health Professionals Follow-Up Study	1,562/447,434	1,400/373,466	542/121,183	29/7,116	35/6,879		
	HR (95% CI)						
Nurses' Health Study	1.00	1.07 (1.02, 1.12)	1.21 (1.14, 1.30)	1.29 (1.13, 1.47)	1.20 (1.00, 1.45)	<0.0001	1.18 (1.10, 1.26)
Nurses' Health Study II	1.00	1.06 (1.00, 1.12)	1.12 (1.05, 1.19)	1.11 (0.95, 1.28)	1.20 (1.06, 1.37)	0.003	1.12 (1.04, 1.21)
Health Professionals Follow-Up Study	1.00	1.04 (0.97, 1.12)	1.19 (1.08, 1.32)	1.18 (0.82, 1.71)	1.27 (0.91, 1.78)	0.006	1.26 (1.07, 1.49)
Pooled	1.00	1.06 (1.03, 1.10)	1.17 (1.12, 1.22)	1.20 (1.09, 1.32)	1.21 (1.09, 1.34)	<0.0001	1.16 (1.11, 1.22)
Artificially-sweetened beverages							
Diet cola carbonated beverages							
Cases/person-years							
Nurses' Health Study	1,920/618,906	2,063/479,985	3,307/600,452	511/107,882	1,065/162,376		
Nurses' Health Study II	1,676/665,985	1,382/431,899	2,303/569,304	517/173,293	1,627/339,176		
Health Professionals Follow-Up Study	945/338,614	773/216,886	1,060/250,608	201/49,428	589/100,542		
	HR (95% CI)						
Nurses' Health Study	1.00	1.01 (0.94, 1.07)	1.06 (1.00, 1.12)	1.03 (0.93, 1.13)	1.11 (1.03, 1.20)	0.008	1.06 (1.01, 1.10)
Nurses' Health Study II	1.00	1.01 (0.94, 1.08)	1.06 (0.99, 1.13)	0.92 (0.83, 1.02)	1.03 (0.96, 1.10)	0.81	1.00 (0.97, 1.03)
Health Professionals Follow-Up Study	1.00	1.14 (1.03, 1.25)	1.17 (1.07, 1.28)	1.08 (0.93, 1.26)	1.37 (1.23, 1.53)	<0.0001	1.15 (1.09, 1.22)
Pooled	1.00	1.03 (0.99, 1.08)	1.08 (1.04, 1.12)	0.99 (0.93, 1.06)	1.12 (1.06, 1.17)	0.0004	1.04 (1.02, 1.07)

Other diet carbonated beverages							
Cases/person-years							
Nurses' Health Study	3,011/807,591	1,649/373,478	2,390/479,351	849/158,045	967/151,136		
Nurses' Health Study II	1,787/713,027	1,722/532,909	2,320/575,430	477/117,964	1,199/240,326		
Health Professionals Follow-Up Study	1,286/428,420	1,232/313,739	873/184,804	76/15,125	101/13,990		
	HR (95% CI)						
Nurses' Health Study	1.00	1.01 (0.95, 1.07)	1.10 (1.04, 1.16)	1.10 (1.01, 1.18)	1.18 (1.10, 1.27)	<0.0001	1.09 (1.05, 1.12)
Nurses' Health Study II	1.00	1.01 (0.95, 1.08)	1.07 (1.00, 1.14)	1.15 (1.03, 1.27)	1.14 (1.06, 1.23)	0.0001	1.08 (1.04, 1.12)
Health Professionals Follow-Up Study	1.00	1.12 (1.03, 1.21)	1.21 (1.11, 1.33)	1.31 (1.03, 1.65)	1.46 (1.19, 1.80)	<0.0001	1.30 (1.16, 1.45)
Pooled	1.00	1.03 (0.99, 1.08)	1.11 (1.06, 1.15)	1.13 (1.06, 1.19)	1.18 (1.12, 1.24)	<0.0001	1.09 (1.07, 1.12)
Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses' Health Study, n=64,029; Nurses' Health Study II, n=88,340).							
^a Hazard ratios and 95% confidence intervals derived from the multivariable model adjusted for age; race; ancestry; physical activity; smoking status; alcohol intake; multivitamin use; in women, postmenopausal status and menopausal hormone use; aspirin use; family history of diabetes; calorie intake; body mass index; and AHEI.							
^b 1 serving increment of sugar- or artificially-sweetened beverage intake per day, where appropriate.							
AHEI = alternative healthy index, sugar-sweetened beverages and alcohol intake were removed from the index calculation.							

ESM Table 6. Pooled and cohort-specific subgroup analyses for the risk^a of type 2 diabetes according to a 1 serving increment of sugar- or artificially-sweetened beverage intake per day^b in three large US cohorts .

	Sugar-sweetened beverages		Artificially-sweetened beverages	
	Adjusted HR (95% CI)	<i>P</i> for interaction	Adjusted HR (95% CI)	<i>P</i> for interaction
Nurses' Health Study				
Age, years				
<65	1.36 (1.27, 1.45)	0.002	1.04 (1.00, 1.09)	0.02
≥65	1.23 (1.12, 1.34)		1.04 (0.99, 1.08)	
Body mass index, kg/m ²				
<25	1.48 (1.29, 1.71)	0.69	1.09 (1.00, 1.20)	0.29
≥25	1.30 (1.23, 1.38)		1.13 (1.09, 1.16)	
Physical activity, meet US guidelines				
No (<150 min/week MVPA)	1.29 (1.21, 1.39)	0.55	1.06 (1.01, 1.10)	0.23
Yes (≥150 min/week MVPA)	1.34 (1.23, 1.45)		1.02 (0.98, 1.07)	
Television watching, hour/week				
<8	1.29 (1.15, 1.44)	0.75	1.03 (0.97, 1.10)	0.73
8 to 15.5	1.32 (1.18, 1.49)		1.07 (1.01, 1.14)	
≥15.5	1.31 (1.22, 1.41)		1.03 (0.99, 1.07)	
Smoking status				
Never	1.29 (1.20, 1.39)	0.34	1.05 (1.00, 1.09)	0.77
Former/current	1.35 (1.26, 1.45)		1.03 (0.99, 1.07)	
Family history of diabetes				
No	1.34 (1.25, 1.44)	0.49	1.01 (0.97, 1.06)	0.31
Yes	1.28 (1.19, 1.38)		1.07 (1.03, 1.12)	
Energy intake per day, kJ				
<median	1.33 (1.22, 1.45)	0.88	1.06 (1.01, 1.10)	0.72
≥median	1.32 (1.24, 1.41)		1.03 (0.99, 1.07)	
AHEI				
<median	1.31 (1.22, 1.40)	0.26	1.03 (0.99, 1.08)	0.78
≥median	1.35 (1.24, 1.46)		1.04 (1.00, 1.09)	
Nurses' Health Study II				
Age, years				
<55	1.16 (1.10, 1.22)	0.97	1.04 (1.01, 1.08)	0.13
≥55	1.19 (1.10, 1.29)		1.03 (0.98, 1.08)	
Body mass index, kg/m ²				
<25	1.21 (1.02, 1.42)	0.96	1.24 (1.12, 1.38)	0.21
≥25	1.13 (1.08, 1.18)		1.12 (1.08, 1.15)	
Physical activity, meet US guidelines				
No (<150 min/week MVPA)	1.16 (1.09, 1.23)	0.34	1.02 (0.98, 1.06)	0.27
Yes (≥150 min/week MVPA)	1.18 (1.11, 1.26)		1.05 (1.01, 1.09)	
Television watching, hour/week				
<8	1.22 (1.13, 1.32)	0.99	1.01 (0.97, 1.06)	0.63
8 to 15.5	1.08 (0.99, 1.18)		1.07 (1.01, 1.12)	
≥15.5	1.19 (1.11, 1.28)		1.03 (0.99, 1.08)	
Smoking status				
Never	1.13 (1.07, 1.19)	0.05	1.02 (0.99, 1.06)	0.11
Former/current	1.26 (1.17, 1.35)		1.06 (1.02, 1.11)	

Family history of diabetes				
No	1.21 (1.13, 1.28)	0.14	1.04 (1.00, 1.08)	0.31
Yes	1.13 (1.07, 1.21)		1.03 (1.00, 1.07)	
Energy intake per day, kJ				
<median	1.21 (1.13, 1.30)	0.20	1.04 (1.00, 1.09)	0.82
≥median	1.17 (1.11, 1.24)		1.03 (0.99, 1.07)	
AHEI				
<median	1.16 (1.11, 1.23)	0.19	1.01 (0.98, 1.05)	0.15
≥median	1.20 (1.10, 1.29)		1.07 (1.03, 1.12)	
Health Professionals Follow-Up Study				
Age, years				
<65	1.28 (1.14, 1.43)	0.18	1.12 (1.04, 1.21)	0.30
≥65	1.14 (1.00, 1.30)		1.15 (1.06, 1.25)	
Body mass index, kg/m²				
<25	1.17 (1.00, 1.36)	0.61	1.62 (1.47, 1.79)	<0.0001
≥25	1.18 (1.07, 1.31)		1.21 (1.13, 1.29)	
Physical activity, meet US guidelines				
No (<150 min/week MVPA)	1.29 (1.12, 1.49)	0.10	1.15 (1.04, 1.27)	0.30
Yes (≥150 min/week MVPA)	1.19 (1.07, 1.32)		1.13 (1.05, 1.20)	
Television watching, hour/week				
<8	1.31 (1.14, 1.50)	0.23	1.19 (1.09, 1.30)	0.27
8 to 15.5	1.16 (0.95, 1.42)		1.11 (0.97, 1.26)	
≥15.5	1.17 (1.02, 1.34)		1.11 (1.02, 1.22)	
Smoking status				
Never	1.21 (1.07, 1.36)	0.59	1.28 (1.18, 1.38)	<0.0001
Former/current	1.24 (1.10, 1.40)		1.01 (0.94, 1.10)	
Family history of diabetes				
No	1.21 (1.09, 1.34)	0.82	1.14 (1.06, 1.22)	0.27
Yes	1.22 (1.05, 1.42)		1.13 (1.02, 1.24)	
Energy intake per day, kJ				
<median	1.28 (1.11, 1.47)	0.12	1.15 (1.06, 1.25)	0.79
≥median	1.14 (1.02, 1.26)		1.13 (1.05, 1.22)	
AHEI				
<median	1.27 (1.15, 1.41)	0.25	1.09 (1.01, 1.17)	0.03
≥median	1.14 (0.97, 1.34)		1.20 (1.10, 1.31)	
Pooled				
Age, years				
<55 or 65 years	1.24 (1.19, 1.28)	0.02	1.05 (1.02, 1.08)	0.004
≥55 or 65 years	1.20 (1.13, 1.26)		1.05 (1.02, 1.08)	
Body mass index, kg/m²				
<25	1.29 (1.18, 1.41)	0.58	1.29 (1.22, 1.37)	0.03
≥25	1.19 (1.15, 1.23)		1.13 (1.11, 1.15)	
Physical activity, meet US guidelines				
No (<150 min/week MVPA)	1.22 (1.17, 1.27)	0.65	1.05 (1.02, 1.07)	0.75
Yes (≥150 min/week MVPA)	1.23 (1.18, 1.29)		1.05 (1.02, 1.08)	
Television watching, hour/week				
<8	1.25 (1.18, 1.33)	0.79	1.04 (1.01, 1.08)	0.88
8 to 15.5	1.16 (1.09, 1.24)		1.07 (1.03, 1.11)	
≥15.5	1.24 (1.18, 1.30)		1.04 (1.01, 1.07)	
Smoking status				
Never	1.19 (1.14, 1.24)	0.03	1.05 (1.03, 1.08)	0.55
Former/current	1.29 (1.23, 1.36)		1.04 (1.01, 1.07)	
Family history of diabetes				
No	1.25 (1.20, 1.31)	0.16	1.04 (1.02, 1.07)	0.67
Yes	1.19 (1.14, 1.25)		1.06 (1.03, 1.08)	

Energy intake per day, kJ				
<median	1.26 (1.20, 1.32)	0.12	1.06 (1.03, 1.09)	0.64
≥median	1.22 (1.17, 1.27)		1.04 (1.01, 1.07)	
AHEI				
<median	1.22 (1.18, 1.27)	0.23	1.03 (1.00, 1.05)	0.11
≥median	1.25 (1.19, 1.32)		1.07 (1.04, 1.10)	

Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses' Health Study, n=64,029; Nurses' Health Study II, n=88,340).

^a Hazard ratios and 95% confidence intervals derived from the multivariable model adjusted for the following: age; race; ancestry; smoking status; alcohol intake; multivitamin use; in women, postmenopausal status and menopausal hormone use; aspirin use; family history of diabetes; calorie intake; body mass index; and AHEI.

^b 1 serving of sugar- or artificially-sweetened beverage. HRs for 1 serving increment of sugar- or artificially-sweetened beverage intake per day in each subgroup category.

AHEI = alternative healthy index, sugar-sweetened beverages and alcohol were removed from the index calculation; MVPA = moderate-vigorous physical activity.

ESM Table 7. Multiplicative^a and additive^b interaction probability values for the sugar- or artificially-sweetened beverage intake and physical activity and risk of type 2 diabetes in three large US cohorts.

Beverage type	Multiplicative interaction	Additive interaction
Sugar-sweetened beverages		
Nurses’ Health Study	0.21	0.43
Nurses’ Health Study II	0.81	0.41
Health Professionals Follow-Up Study	0.18	0.61
Pooled	0.40	0.20
Artificially-sweetened beverages		
Nurses’ Health Study	0.79	0.13
Nurses’ Health Study II	0.92	0.19
Health Professionals Follow-Up Study	0.59	0.51
Pooled	0.28	0.002

Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses’ Health Study, n=64,029; Nurses’ Health Study II, n=88,340).

^a Derived by comparing the -2 log likelihood of the multivariable-adjusted models with and without the cross-product interaction term. The model was adjusted for age; race; ancestry; smoking status; alcohol intake; multivitamin use; in women, postmenopausal status and menopausal hormone use; aspirin use; family history of diabetes; calorie intake; body mass index; and AHEI.

^b Assessed by the derivation of the probability value of the relative excess risk due to interaction (RERI) as an index of additive interaction ^{15,16}.

AHEI = alternative healthy index, sugar-sweetened beverages and alcohol were removed from the index calculation.

ESM Table 8. Pooled joint associations between frequency of sugar- or artificially-sweetened beverage subtype intake and physical activity^a and risk^b of type 2 diabetes in three large US cohorts.

	Meet US Physical Activity Guidelines			Does not meet US Physical Activity Guidelines		
	Never or less than 1 serving per month	1-4 servings per month	≥2 servings per week	Never or less than 1 serving per month	1-4 servings per month	≥2 servings per week
Sugar-sweetened beverages						
Cola beverages						
Cases/person-years						
Nurses’ Health Study	1,670/525,930	1,641/425,078	1,051/218,773	1,571/318,273	1,633/288,009	1,300/193,537
Nurses’ Health Study II	1,846/808,048	933/388,560	965/267,710	1,667/339,308	975/190,358	1,119/185,672
Health Professionals Follow-Up Study	840/277,928	865/243,121	782/221,851	389/78,050	310/65,372	382/69,755
	HR (95% CI)					
Pooled risk	1.00	1.08 (1.04, 1.14)	1.29 (1.23, 1.35)	1.23 (1.18, 1.29)	1.31 (1.24, 1.37)	1.49 (1.41, 1.57)
Non-cola carbonated beverages						
Cases/person-years						
Nurses’ Health Study	2,585/725,412	1,340/347,587	437/96,782	2,600/477,040	1,368/245,126	536/77,655
Nurses’ Health Study II	1,940/815,945	1,205/450,650	599/197,723	1,811/362,156	1,224/224,185	726/128,997
Health Professionals Follow-Up Study	1,170/362,687	1,025/306,972	292/73,241	501/108,088	428/81,939	152/23,150
	HR (95% CI)					
Pooled risk	1.00	1.05 (1.00, 1.09)	1.15 (1.08, 1.22)	1.19 (1.14, 1.24)	1.27 (1.22, 1.33)	1.43 (1.35, 1.52)
Artificially-sweetened beverages						
Diet cola						
Cases/person-years						
Nurses’ Health Study	893/345,660	1,091/298,134	2,378/525,986	1,027/273,246	972/181,851	2,505/344,723
Nurses’ Health Study II	817/433,856	703/301,571	2,224/728,892	859/232,129	679/130,328	2,223/352,881
Health Professionals Follow-Up Study	621/252,092	584/173,052	1,282/317,757	324/86,522	189/43,834	568/82,821
	HR (95% CI)					
Pooled risk	1.00	1.05 (1.00, 1.12)	1.08 (1.03, 1.13)	1.21 (1.14, 1.29)	1.21 (1.13, 1.28)	1.32 (1.25, 1.39)
Other diet carbonated beverages						
Cases/person-years						
Nurses’ Health Study	1,433/468,859	830/227,501	2,099/473,421	1,578/338,732	819/145,977	2,107/315,111
Nurses’ Health Study II	858/461,438	871/367/412	2,015/635,469	929/251,589	851/165,497	1,981/298,252
Health Professionals Follow-Up Study	855/321,675	885/251,456	747/169,770	431/106,744	347/62,283	303/44,149
	HR (95% CI)					
Pooled risk	1.00	1.04 (0.98, 1.09)	1.14 (1.09, 1.20)	1.22 (1.16, 1.28)	1.26 (1.19, 1.34)	1.35 (1.28, 1.42)

Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses’ Health Study, n=64,029; Nurses’ Health Study II, n=88,340).

^aPhysical activity was dichotomised to meet or do not meet the US Physical activity guidelines of ≥150 minutes/week of moderate-vigorous physical activity recommendations (corresponds to ≥7.5 MET h/week or <7.5 MET h/week, respectively).

^bHazard ratios and 95% confidence intervals derived from the multivariable model adjusted for age; race; ancestry; physical activity; smoking status; alcohol intake; multivitamin use; in women, postmenopausal status and menopausal hormone use; aspirin use; family history of diabetes; calorie intake; body mass index; and AHEI.

AHEI = alternative healthy eating index, sugar-sweetened beverages and alcohol intake were removed from the index calculation; MET = metabolic equivalent task.

ESM Table 9. Joint associations between top 25% sugar- or artificially-sweetened beverage intake and top 25% physical activity^a and risk^b of type 2 diabetes in three large US cohorts.

Sugar-sweetened beverages	Physical Activity Top 25%		Physical Activity <Top 25%	
	SSB <Top 25%	SSB Top 25%	SSB <Top 25%	SSB Top 25%
Cases/person-years				
Nurses’ Health Study	1,137/390,870	419/105,963	4,962/1,083,085	2,348/389,682
Nurses’ Health Study II	1,180/579,331	1,310/514,448	2,109/503,210	2,906/582,668
Health Professionals Follow-Up Study	672/234,927	775/248,719	958/224,682	1,163/247,749
	HR (95% CI)			
Nurses’ Health Study	1.00	1.27 (1.13, 1.42)	1.21 (1.13, 1.29)	1.55 (1.44, 1.67)
Nurses’ Health Study II	1.00	1.14 (1.05, 1.23)	1.18 (1.09, 1.27)	1.37 (1.28, 1.48)
Health Professionals Follow-Up Study	1.00	1.04 (0.94, 1.16)	1.28 (1.16, 1.42)	1.40 (1.27, 1.55)
Pooled	1.00	1.14 (1.08, 1.20)	1.21 (1.16, 1.26)	1.45 (1.38, 1.51)
Artificially-sweetened beverages	ASB <Top 25%		ASB <Top 25%	
	ASB <Top 25%	ASB Top 25%	ASB <Top 25%	ASB Top 25%
Cases/person-years				
Nurses’ Health Study	1,067/367,808	489/129,025	4,893/1,109,459	2,417/363,309
Nurses’ Health Study II	1,015/551,021	1,475/542,757	1,963/539,351	3,052/546,526
Health Professionals Follow-Up Study	551/229,561	896/254,085	866/240,107	1,255/232,325
	HR (95% CI)			
Nurses’ Health Study	1.00	0.99 (0.89, 1.10)	1.19 (1.11, 1.27)	1.27 (1.18, 1.37)
Nurses’ Health Study II	1.00	1.05 (0.97, 1.14)	1.18 (1.09, 1.28)	1.27 (1.18, 1.37)
Health Professionals Follow-Up Study	1.00	1.14 (1.02, 1.27)	1.34 (1.20, 1.50)	1.49 (1.34, 1.65)
Pooled	1.00	1.06 (1.00, 1.12)	1.21 (1.16, 1.27)	1.31 (1.25, 1.38)

Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses’ Health Study, n=64,029; Nurses’ Health Study II, n=88,340).

^aPhysical activity was dichotomised to top 25% of Physical Activity expenditure yes/no.

^bHazard ratios and 95% CI derived from the multivariable model adjusted for age; race; ancestry; smoking status; alcohol intake; multivitamin use; in women, postmenopausal status and menopausal hormone use; aspirin use; family history of diabetes; calorie intake; body mass index; and AHEI.

AHEI = alternative healthy index, sugar-sweetened beverages and alcohol intake were removed from the index calculation; ASB = artificially-sweetened beverage; MET = metabolic equivalent task; SSB = sugar-sweetened beverage.

ESM Table 10. Independent and joint associations between frequency of sugar- or artificially-sweetened beverage intake and physical activity^a and risk^b of type 2 diabetes without adjusting for BMI in three large US cohorts.

Independent Associations							HR (95% CI) for 1 serving increment of SSB or ASB ^c intake per day
	Never or <1 serving per month	1-4 servings per month	2-6 servings per week	1-<2 servings per day	≥2 servings per day	P for trend	
Sugar-sweetened beverages							
Cases/person-years							
Nurses' Health Study	1,199/372,727	2,868/683,806	3,486/689,360	429/80,772	884/142,937		
Nurses' Health Study II	1,125/424,729	2,164/657,812	2,546/711,664	397/110,590	1,273/274,862		
Health Professional's Follow-up Study	660/197,008	1,016/282,093	1,361/356,493	173/43,486	359/77,014		
	HR (95% CI)						
Nurses' Health Study	1.00	1.04 (0.97, 1.11)	1.18 (1.10, 1.26)	1.36 (1.22, 1.53)	1.47 (1.34, 1.61)	<0.0001	1.30 (1.23, 1.37)
Nurses' Health Study II	1.00	1.03 (0.96, 1.11)	1.01 (0.94, 1.09)	1.02 (0.91, 1.14)	1.11 (1.01, 1.21)	0.02	1.05 (1.01, 1.10)
Health Professional's Follow-up Study	1.00	0.99 (0.90, 1.10)	1.02 (0.92, 1.13)	1.06 (0.90, 1.26)	1.23 (1.07, 1.41)	0.001	1.15 (1.06, 1.26)
Pooled	1.00	1.03 (0.98, 1.07)	1.08 (1.03, 1.13)	1.16 (1.08, 1.25)	1.26 (1.19, 1.33)	<0.0001	1.15 (1.11, 1.19)
Artificially-sweetened beverages							
Cases/person-years							
Nurses' Health Study	2,578/740,201	1,377/325,516	2,263/455,921	864/171,779	1,784/276,184		
Nurses' Health Study II	1,149/490,528	779/274,035	1,850/543,125	617/187,754	3,110/684,214		
Health Professional's Follow-up Study	756/281,614	700/200,278	1,097/280,721	237/52,559	779/140,923		
	HR (95% CI)						
Nurses' Health Study	1.00	1.22 (1.14, 1.30)	1.41 (1.33, 1.49)	1.53 (1.42, 1.66)	1.76 (1.66, 1.87)	<0.0001	1.30 (1.26, 1.33)
Nurses' Health Study II	1.00	1.20 (1.09, 1.31)	1.43 (1.33, 1.54)	1.56 (1.42, 1.73)	1.87 (1.75, 2.00)	<0.0001	1.28 (1.25, 1.32)
Health Professional's Follow-up Study	1.00	1.26 (1.13, 1.40)	1.44 (1.31, 1.58)	1.65 (1.42, 1.91)	2.00 (1.80, 2.22)	<0.0001	1.43 (1.36, 1.51)
Pooled	1.00	1.22 (1.16, 1.28)	1.42 (1.36, 1.48)	1.56 (1.47, 1.65)	1.84 (1.76, 1.92)	<0.0001	1.30 (1.28, 1.33)
Physical activity	Quintile 1 (0 to ≤3.0)	Quintile 2 (>3.0 to ≤8.4)	Quintile 3 (>8.4 to ≤16.5)	Quintile 4 (>16.5 to ≤31.7)	Quintile 5 (>31.7)	P for trend	
Cases/person-years							
Nurses' Health Study	2,562/388,193	1,992/392,157	1,715/396,185	1,469/395,809	1,128/397,257		
Nurses' Health Study II	2,611/433,428	1,781/435,162	1,325/436,679	1,049/437,046	739/437,340		
Health Professional's Follow-up Study	1,000/186,888	820/190,756	670/192,243	585/192,986	494/193,221		
	HR (95% CI)						
Nurses' Health Study	1.00	0.77 (0.73, 0.82)	0.67 (0.63, 0.72)	0.58 (0.55, 0.62)	0.45 (0.42, 0.48)	<0.0001	
Nurses' Health Study II	1.00	0.74 (0.70, 0.79)	0.59 (0.55, 0.63)	0.50 (0.46, 0.53)	0.37 (0.34, 0.41)	<0.0001	
Health Professional's Follow-up Study	1.00	0.79 (0.72, 0.86)	0.64 (0.58, 0.71)	0.57 (0.51, 0.63)	0.49 (0.44, 0.55)	<0.0001	
Pooled	1.00	0.76 (0.73, 0.79)	0.64 (0.61, 0.66)	0.55 (0.52, 0.57)	0.43 (0.41, 0.45)	<0.0001	
Joint Associations							
	Meet US Physical Activity Guidelines			Does not meet US Physical Activity Guidelines			
	Never or less than 1 serving per month	1-4 servings per month	≥2 servings per week	Never or less than 1 serving per month	1-4 servings per month	≥2 servings per week	
Sugar-sweetened beverages							
Cases/person-years							
Nurses' Health Study	581/227,480	1,521/424,906	2,260/517,395	618/145,247	1,347/258,900	2,539/395,673	

Nurses' Health Study II	595/296,950	1,136/462,074	2,013/705,294	530/127,779	1,028/195,738	2,203/391,821
Health Professional's Follow-up Study	451/150,121	737/222,686	1,299/370,093	209/46,887	278/59,390	594/106,900
HR (95 CI)						
Nurses' Health Study	1.00	1.11 (1.01, 1.23)	1.31 (1.19, 1.44)	1.73 (1.54, 1.94)	1.67 (1.52, 1.85)	2.01 (1.83, 2.21)
Nurses' Health Study II	1.00	1.01 (0.91, 1.11)	1.05 (0.96, 1.16)	1.72 (1.53, 1.93)	1.83 (1.65, 2.02)	1.77 (1.61, 1.94)
Health Professional's Follow-up Study	1.00	0.99 (0.88, 1.12)	1.02 (0.91, 1.14)	1.49 (1.26, 1.76)	1.46 (1.25, 1.70)	1.68 (1.48, 1.91)
Pooled	1.00	1.04 (0.98, 1.11)	1.13 (1.07, 1.20)	1.67 (1.56, 1.80)	1.69 (1.58, 1.80)	1.84 (1.74, 1.95)
Artificially-sweetened beverages						
Cases/person-years						
Nurses' Health Study	1,229/423,774	703/197,000	2,430/549,007	1,349/316,427	674/128,516	2,481/354,877
Nurses' Health Study II	541/314,917	406/190,736	2,797/958,664	608/175,611	373/83,299	2,780/456,428
Health Professional's Follow-up Study	500/208,270	512/159,179	1,475/375,453	256/73,344	188/41,099	637/98,734
HR (95% CI)						
Nurses' Health Study	1.00	1.24 (1.13, 1.36)	1.57 (1.46, 1.68)	1.54 (1.42, 1.66)	1.91 (1.74, 2.10)	2.50 (2.33, 2.67)
Nurses' Health Study II	1.00	1.22 (1.07, 1.39)	1.74 (1.58, 1.91)	1.74 (1.55, 1.96)	2.17 (1.90, 2.48)	3.04 (2.77, 3.33)
Health Professional's Follow-up Study	1.00	1.26 (1.11, 1.43)	1.57 (1.42, 1.74)	1.48 (1.27, 1.73)	1.83 (1.55, 2.17)	2.59 (2.30, 2.91)
Pooled	1.00	1.24 (1.16, 1.33)	1.61 (1.54, 1.69)	1.58 (1.49, 1.68)	1.96 (1.83, 2.11)	2.66 (2.53, 2.80)

Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses' Health Study, n=64,029; Nurses' Health Study II, n=88,340).

^a Physical activity was measured in MET-h/week and categorised in quintiles for the independent associations For the joint associations, physical activity was dichotomised to meet or do not meet the US Physical activity guidelines of ≥150 minutes/week of moderate-vigorous physical activity recommendations (corresponds to ≥7.5 MET h/week or <7.5 MET h/week, respectively).

^b Hazard ratios and 95% confidence intervals derived from the multivariable model adjusted for age; race; ancestry; physical activity (excluded in the physical activity as primary exposure models) smoking status; alcohol intake; multivitamin use; in women, postmenopausal status and menopausal hormone use; aspirin use; family history of diabetes; calorie intake; and AHEI.

^c 1 serving increment of sugar- or artificially-sweetened beverage intake per day, where appropriate.

AHEI = alternative healthy eating index, sugar-sweetened beverages and alcohol were removed from the index calculation (only for the sugar- or artificially-sweetened beverage models); BMI = body mass index; MET = metabolic equivalent task.

ESM Table 11. Independent and joint associations between frequency of sugar-sweetened beverage and fruit juice intake combined and risk^a of type 2 diabetes in three large US cohorts.

Independent Associations							
	Never or <1 serving per month	1-4 servings per month	2-6 servings per week	1-<2 servings per day	≥2 servings per day	<i>P</i> for trend	HR (95% CI) for 1 serving increment of combined SSB and fruit juice intake ^b per day
Cases/person-years							
Nurses' Health Study	99/36,165	425/134,752	2,964/667,617	1,216/276,197	4,162/854,870		
Nurses' Health Study II	118/52,647	699/220,146	2,862/810,612	676/209,886	3,150/886,365		
Health Professionals Follow-Up Study	75/23,360	230/63,366	1,097/296,931	414/106,605	1,753/465,833		
	HR (95% CI)						
Nurses' Health Study	1.00	0.85 (0.68, 1.06)	1.08 (0.88, 1.32)	1.21 (0.98, 1.49)	1.32 (1.08, 1.61)	<0.0001	1.27 (1.21, 1.33)
Nurses' Health Study II	1.00	1.03 (0.85, 1.25)	1.13 (0.94, 1.36)	1.10 (0.90, 1.34)	1.30 (1.08, 1.56)	<0.0001	1.14 (1.09, 1.18)
Health Professionals Follow-Up Study	1.00	1.00 (0.77, 1.30)	1.02 (0.81, 1.29)	1.11 (0.87, 1.42)	1.14 (0.91, 1.45)	0.002	1.12 (1.04, 1.19)
Pooled	1.00	0.96 (0.85, 1.09)	1.09 (0.96, 1.22)	1.14 (1.01, 1.29)	1.26 (1.12, 1.42)	<0.0001	1.18 (1.15, 1.21)
Joint Associations							
	Meet US Physical Activity Guidelines ^c			Does not meet US Physical Activity Guidelines ^c			
	Never or less than 1 serving per month	1-4 servings per month	≥2 servings per week	Never or less than 1 serving per month	1-4 servings per month	≥2 servings per week	
Cases/person-years							
Nurses' Health Study	40/19,516	184/76,280	4,138/1,073,985	59/16,650	241/58,472	4,204/724,699	
Nurses' Health Study II	58/35,891	319/146,075	3,367/1,282,352	60/16,756	380/74,071	3,321/624,510	
Health Professionals Follow-Up Study	49/16,426	142/46,007	2,296/680,468	26/6,934	88/17,360	967/188,883	
	HR (95% CI)						
Nurses' Health Study	1.00	0.84 (0.59, 1.18)	1.25 (0.92, 1.71)	1.27 (0.85, 1.90)	1.12 (0.80, 1.56)	1.47 (1.07, 2.01)	
Nurses' Health Study II	1.00	0.97 (0.73, 1.28)	1.17 (0.90, 1.51)	1.14 (0.79, 1.64)	1.25 (0.95, 1.65)	1.39 (1.07, 1.80)	
Health Professionals Follow-Up Study	1.00	0.90 (0.65, 1.24)	1.01 (0.76, 1.34)	1.06 (0.66, 1.71)	1.30 (0.91, 1.84)	1.32 (0.99, 1.77)	
Pooled	1.00	0.91 (0.76, 1.09)	1.13 (0.96, 1.33)	1.16 (0.92, 1.47)	1.22 (1.02, 1.47)	1.39 (1.18, 1.64)	

Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses' Health Study, n=64,029; Nurses' Health Study II, n=88,340).

^a Hazard ratios and 95% confidence intervals derived from the age-adjusted model and the multivariable model adjusted for age; race; ancestry; physical activity; smoking status; alcohol intake; multivitamin use; in women, postmenopausal status and menopausal hormone use; aspirin use; family history of diabetes; calorie intake; body mass index; and AHEI.

^b 1 serving increment of sugar-sweetened beverage and fruit juice intake per day.

^c Physical activity was measured in MET-h/week and dichotomised to meet or do not meet the US Physical activity guidelines of ≥150 minutes/week of moderate-vigorous physical activity recommendations corresponds to ≥7.5 MET h/week or <7.5 MET h/week, respectively).

AHEI = alternative healthy index; sugar-sweetened beverages and alcohol intake were removed from the index calculation.

ESM Table 12. Associations between quintiles of fruit juice intake and risk^a of type 2 diabetes in three large US cohorts.

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	<i>P</i> for trend
Cases/person-years						
Nurses' Health Study	1,704/405,144	1,732/362,814	2,004/420,472	1,807/427,288	1,619/353,883	
Nurses' Health Study II	1,581/430,478	1,560/447,425	1,572/432,559	1,464/433,269	1,328/435,925	
Health Professionals Follow-Up Study	717/190,367	730/192,974	758/188,246	710/191,894	653/192,596	
Pooled risk	HR (95% CI)					
Nurses' Health Study	1.00	1.06 (0.99, 1.14)	1.19 (1.12, 1.27)	1.14 (1.06, 1.22)	1.21 (1.13, 1.30)	<0.0001
Nurses' Health Study II	1.00	0.99 (0.92, 1.06)	1.04 (0.96, 1.11)	1.04 (0.97, 1.12)	1.09 (1.01, 1.18)	0.007
Health Professionals Follow-Up Study	1.00	1.01 (0.91, 1.12)	1.08 (0.97, 1.20)	1.03 (0.92, 1.14)	1.02 (0.91, 1.14)	0.68
Pooled	1.00	1.02 (0.98, 1.07)	1.11 (1.06, 1.16)	1.08 (1.03, 1.13)	1.13 (1.08, 1.18)	<0.0001

Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses' Health Study, n=64,029; Nurses' Health Study II, n=88,340).
^a Hazard ratios and 95% confidence intervals derived from the age-adjusted model and the multivariable model adjusted for age; race; ancestry; physical activity; smoking status; alcohol intake; multivitamin use; in women, postmenopausal status and menopausal hormone use; aspirin use; family history of diabetes; calorie intake; body mass index; and AHEI.
AHEI = alternative healthy index; sugar-sweetened beverages and alcohol intake were removed from the index calculation.

ESM Table 13. Joint associations between frequency of sugar- or artificially-sweetened beverage intake and physical activity^a and risk^b of type 2 diabetes in three large US cohorts.

	Physical Activity Tertile 1			Physical Activity Tertile 2			Physical Activity Tertile 3		
	Never or less than 1 serving per month	1-4 servings per month	≥2 servings per week	Never or less than 1 serving per month	1-4 serving per month	≥2 servings per week	Never or less than 1 serving per month	1-4 servings per month	≥2 servings per week
Sugar-sweetened beverages									
Cases/person-years									
Nurses’ Health Study	516/111,581	1,201/213,155	2,244/325,188	385/119,956	920/229,962	1,520/308,519	298/141,190	747/240,690	1,035/279,362
Nurses’ Health Study II	532/127,125	1,046/200,005	2,240/396,431	337/136,825	708/223,170	1,231/367,420	256/160,779	410/234,637	745/333,264
Health Professionals Follow-Up Study	296/65,171	423/89,686	830/159,027	199/64,597	336/95,265	597/160,516	165/67,240	256/97,126	466/157,450
	HR (95% CI)								
Nurses’ Health Study	1.38 (1.19, 1.59)	1.43 (1.26, 1.63)	1.75 (1.55, 1.98)	1.20 (1.03, 1.40)	1.27 (1.11, 1.44)	1.55 (1.37, 1.76)	1.00	1.19 (1.04, 1.36)	1.38 (1.21, 1.57)
Nurses’ Health Study II	1.17 (1.01, 1.36)	1.29 (1.12, 1.48)	1.46 (1.28, 1.67)	1.04 (0.88, 1.22)	1.17 (1.01, 1.35)	1.25 (1.09, 1.44)	1.00	0.95 (0.81, 1.11)	1.16 (1.00, 1.34)
Health Professionals Follow-Up Study	1.36 (1.12, 1.65)	1.41 (1.17, 1.69)	1.56 (1.31, 1.85)	1.08 (0.88, 1.33)	1.21 (1.00, 1.46)	1.24 (1.04, 1.49)	1.00	0.99 (0.81, 1.20)	1.09 (0.91, 1.31)
Pooled	1.29 (1.18, 1.42)	1.37 (1.26, 1.49)	1.60 (1.47, 1.73)	1.11 (1.01, 1.23)	1.22 (1.12, 1.33)	1.37 (1.26, 1.49)	1.00	1.06 (0.97, 1.16)	1.23 (1.13, 1.34)
Artificially-sweetened beverages									
Cases/person-years									
Nurses’ Health Study	1,175/255,645	580/103,710	2,206/290,569	813/245,932	462/111,421	1,550/301,083	590/238,625	335/110,385	1,155/312,232
Nurses’ Health Study II	611/175,809	384/85,225	2,823/462,527	328/160,148	233/93,269	1,715/473,997	210/154,571	162/95,541	1,039/478,568
Health Professionals Follow-Up Study	352/101,448	285/64,022	912/148,414	238/90,925	222/68,328	672/161,125	166/89,240	193/67,927	528/164,648
	HR (95% CI)								
Nurses’ Health Study	1.26 (1.14, 1.39)	1.22 (1.08, 1.37)	1.32 (1.20, 1.45)	1.12 (1.01, 1.25)	1.13 (1.00, 1.28)	1.13 (1.03, 1.25)	1.00	1.00 (0.88, 1.15)	1.02 (0.92, 1.13)
Nurses’ Health Study II	1.30 (1.11, 1.52)	1.27 (1.08, 1.51)	1.35 (1.17, 1.56)	1.11 (0.93, 1.32)	1.07 (0.88, 1.28)	1.20 (1.04, 1.39)	1.00	1.09 (0.89, 1.34)	1.05 (0.90, 1.21)
Health Professionals Follow-Up Study	1.50 (1.25, 1.81)	1.68 (1.39, 2.04)	1.82 (1.54, 2.16)	1.26 (1.03, 1.53)	1.38 (1.13, 1.69)	1.47 (1.23, 1.74)	1.00	1.31 (1.06, 1.62)	1.26 (1.06, 1.51)
Pooled	1.31 (1.21, 1.41)	1.31 (1.20, 1.43)	1.41 (1.31, 1.51)	1.14 (1.05, 1.24)	1.16 (1.06, 1.27)	1.20 (1.12, 1.29)	1.00	1.09 (0.98, 1.20)	1.07 (0.99, 1.15)

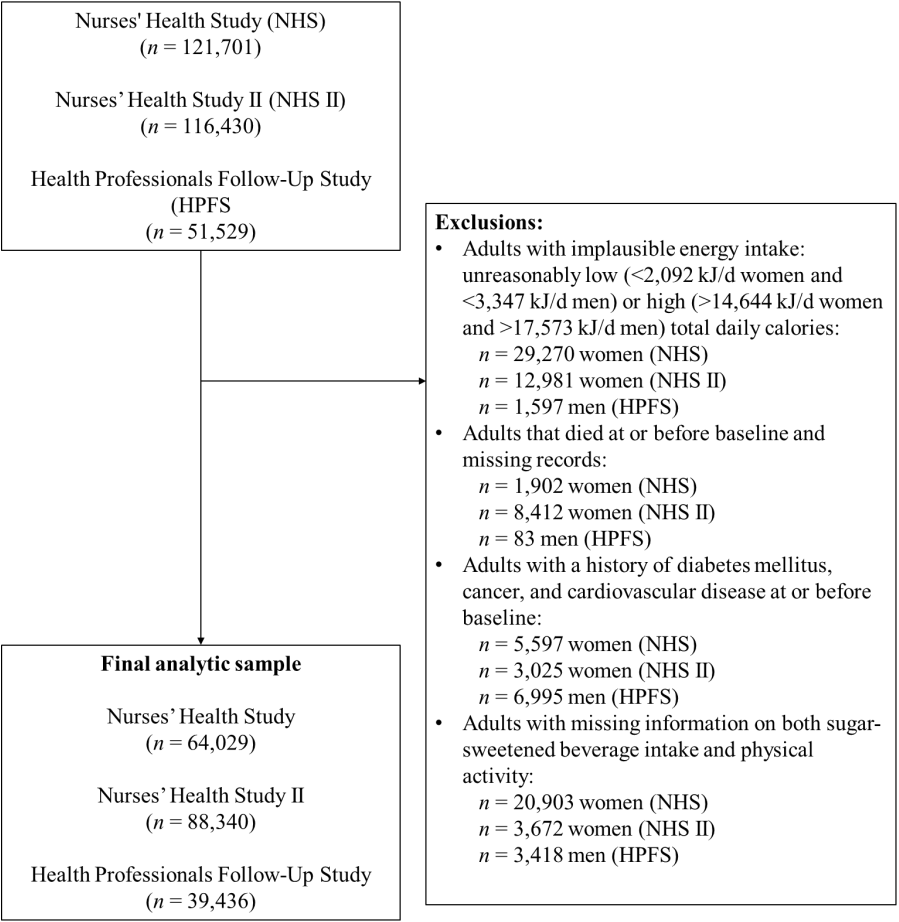
Total sample size, n=191,805 (Health Professionals Follow-up Study, n=39,436; Nurses’ Health Study, n=64,029; Nurses’ Health Study II, n=88,340).

^a Physical activity was measured in MET-h/week and dichotomised to meet or do not meet the US Physical activity guidelines of ≥150 minutes/week of moderate-vigorous physical activity recommendations (corresponds to ≥7.5 MET h/week or <7.5 MET h/week, respectively).

^b Hazard ratios and 95% confidence intervals derived from the age-adjusted model and the multivariable model adjusted for age; race; ancestry; physical activity; smoking status; alcohol intake; multivitamin use; in women, postmenopausal status and menopausal hormone use; aspirin use; family history of diabetes; calorie intake; body mass index; and AHEI.

AHEI = alternative healthy index; sugar-sweetened beverages and alcohol intake were removed from the index calculation.

Electronic Supplementary Figures



ESM Fig. 1. Participant flowchart.