Association of Soft Drink Intake With Cardiovascular Disease Mortality and Morbidity: A Large Prospective Cohort Study

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Original investigation

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Abstract

Background

The associations of SSBs, ASBs and pure fruit/vegetable juices with CVD events have not been thoroughly evaluated. The present study determined the association of soft drinks with CVD and effects of the substitution of alternative beverages for soft drinks and the population-attributable fraction of CVD mortality due to soft drinks.

Methods

A cohort study was performed using data from UK Biobank and 168007 participants (mean (SD) age, 55.6 (7.9) years) without CVD/cancer at baseline were eligible for this analysis. Dietary consumption of SSBs, ASBs and pure fruit/vegetable juices was self-reported via a 24-hour dietary questionnaire between 2009 and 2012 and followed up to 2018.

Results

During a median follow-up of 7.0-year, we recorded 5922 incident CVD cases and 884 CVD deaths. Multivariable adjusted analyses revealed that compared to non-consumers, participants who consumed >2.5 drinks/day had a higher risk of CVD mortality and incidence with HR (95% CI) of 1.63 (1.22–2.17) and 1.23 (1.09–1.39) for SSBs, and 1.77 (1.23–2.56) and 1.20 (1.02–1.42) for ASBs, respectively. Compared to non-consumers, moderate pure fruit/vegetable juice consumers (>0–2.5 drinks/day) have an 8% (2%–13%)–34% (16%–48%) lower risk for CVD incidence and mortality. There was a positive dose-response association of SSBs per 5% energy with CVD mortality and incidence with HR (95% CI) of 1.15 (1.17–1.25) and 1.06 (1.03–1.10), respectively. Substituting one drink/day of pure fruit/vegetable juice, un-sweetened tea/coffee for SSBs and ASBs was associated with 4%–24% lower risks for CVD mortality and incidence. A reduced SSB intake to below 5% energy may prevent 4% (1%–8%) of CVD mortality.

Conclusion

SSBs and ASBs was associated with a higher CVD mortality and morbidity. Pure fruit/vegetable juice and un-sweetened tea/coffee are suitable alternatives to SSBs and ASBs to reduce CVD risk.

Introduction

Substantial observational evidence supports a link between the consumption of sugar-sweetened beverages (SSBs), including carbonated drinks, fruit punches and other non-carbonated fruit drinks, and cardiovascular disease (CVD) events [1–9]. Several randomized controlled trials (RCTs) support this association and have demonstrated deleterious effects of SSB intake on CVD risk factors, such as high blood pressure and dyslipidemia [10]. Positive and null associations have been reported for artificially sweetened beverages (ASBs) and CVD events [3, 11, 12], but a confounding or reverse causality effect of adiposity is possible in this association [8]. Evidence for pure fruit/vegetable juice consumption is more limited and inconsistent, and reverse, positive and null associations have been reported [11, 13–15]. In addition to these uncertainties, little is known about the association of the percent contribution to total energy intake (%TEI) consumed as SSBs with CVD mortality and morbidity. Policies have been implemented to reduce the high level of SSB consumption [16–19], but there is insufficient evidence of what constitutes appropriate replacement beverages to make recommendations.

Therefore, the present study provides detailed data to overcome these limitations and examines three associated objectives: (1) the associations of different types of soft drinks, including SSBs, ASBs and pure fruit/vegetable juices with CVD mortality and morbidity; (2) whether the contribution of SSBs to TEI affects the incidence of CVD; and (3) the potential effects of substituting alternative beverages for soft drinks on the incidence of CVD. The population impact of SSB consumption on lowering the incidence of CVD is also evaluated.

Methods

Study design

The UK Biobank is a large prospective cohort of over half a million participants aged 40–69 years at the time of recruitment between 2006 and 2010. Participants who were registered with the National Health Service and attended 1 of 22 assessment centers across the UK (England, Wales and Scotland) were contacted. They completed a touch-screen questionnaire, face-to-face interviews, and physical measurements and provided biological samples, as described in detail elsewhere [20, 21]. Participants provided informed consent to have their records linked to hospital admissions, cancer registrations and death registries.

Assessment of soft drink intake

Dietary information was collected using a web-based 24-hour dietary recall questionnaire called the Oxford WebQ [22]. Participants were invited to complete the questionnaire on five occasions over one year to account for seasonal variations in dietary intake and provide an average measure as a marker of habitual intake between April 2009 and June 2012. The information provided from Oxford WebQ is comparable to a 24-hour dietary recall assessing the types and quantities of foods, including beverages and daily nutrient intakes, and has been validated in detail elsewhere [22].

Participants were required to report the amount (drinks) of soft drinks consumed during the previous day. One drink was equal to approximately 250 mL. SSBs included fizzy drinks, fruit punches, and other non-carbonated fruit drinks. ASBs included low-calorie or diet drinks. Pure fruit/vegetable juices...
Outcomes, and adjustment for BMI may result in overadjustment bias [30]. Therefore, we compared the associations estimated from the models with and without occasions to maximize representation of participants’ typical dietary habits. (3) Dietary intake is associated with BMI, which influences health outcomes through 35 years of follow–up to minimize the influence of reverse causation. (2) We excluded participants who reported their previous day’s diet as atypical on any of the five occasions, which may be found on the UK Biobank website (http://www.ukbiobank.ac.uk).

Assessment of outcomes

Mortality data [23] were obtained from death certificates according to the National Health Service (NHS) Information Centre (England and Wales) and the NHS Central Register Scotland (Scotland). The date and cause of hospital admission were identified from record linkage to Health Episode Statistics records (England and Wales) and Scottish Morbidity Records (Scotland). Mortality data were available through February 25, 2018, for England and Wales and through February 28, 2017, for Scotland. We censored participants in the mortality analysis at this date or the date of death, whichever occurred first. Baseline mortality data were available through April 14, 2017, and we censored participants in the CVD event analysis at this date or the date of first disease incidence or death, whichever occurred first. Outcomes were classified using International Classification of Diseases 10th revision (ICD–10). The primary outcomes included CVD mortality and incident CVD. CVD diagnoses, including coronary heart disease (I20–I25), heart failure (I50), atrial fibrillation (I48) and stroke diagnoses (I60–I64). CVD mortality was defined as codes I00–I99.

Assessment of covariates

We used the baseline questionnaire to assess the following multiple possible risk factors or confounders: age, sex, Townsend deprivation index (TDI), education, ethnicity, smoking status, physical activity, body mass index (BMI), diabetes, hypertension, depression, family history of CVD, vitamin and mineral supplement use, and dietary intakes of fresh fruit, vegetable, red meat, processed meat, alcohol, un–sweetened tea, un–sweetened coffee, total energy and total sugar. The TDI was used as an indicator of socioeconomic status. Positive TDI values indicate areas with high material deprivation, and negative TDI values indicate relative affluence. Hypertension was defined as a self–reported history of hypertension, systolic blood pressure of ≥140 mmHg, diastolic blood pressure of ≥90 mmHg, or the use of antihypertensive drugs. Physical activity performed over the previous 24 hours was self–reported using the Oxford WebQ with questions adapted from the validated International Physical Activity Questionnaire (IPAQ) [24]. Based on the data processing rules published by IPAQ [25], the duration of light, moderate and vigorous physical activity was converted into metabolic equivalents (MET–h/week) by applying weights of 2.5, 4 and 8, respectively. The MET–h/week values were summed to determine overall daily energy expenditure. The details of these assessments may be found on the UK Biobank website (http://www.ukbiobank.ac.uk).

Inclusion and exclusion criteria

For this analysis, participants who had completed the online 24–hour recall questionnaire on at least one occasion were eligible for inclusion. In total, 211,020 individuals completed at least one dietary questionnaire. We excluded participants missing any information required to calculate the basal metabolic rate [26] (n=593), those with an implausible energy intake (defined as < 1.1 or > 2.5 basal metabolic rate, n=14,649), and participants with cancer (n=19,598) or CVD (n=8,633) at baseline, leaving 168,007 participants eligible for inclusion in the study (Figure S1).

Statistical analysis

Baseline characteristics are presented as the mean (standard deviation [SD]) for continuous variables and number (percentage [%]) for categorical variables. We coded missing data into a missing indicator category for categorical variables such as smoking status and as mean values for continuous variables. Detailed information on the missing covariates is presented in Table S1. Daily consumption of soft drinks (SSBs, ABSs and pure fruit/vegetable juices) is provided as an average marker of habitual intake if individuals completed more than one 24–hour recall and is categorized into 0, >0–1, >1–2.5 or >2.5 drinks/day, which is equivalent to an average of 0, 1, 2 and 3 drinks/day. Cox proportional hazards regression was used to estimate HRs and 95% CIs for the prospective association of soft drink intake with CVD mortality and morbidity. The proportional hazards assumption was tested using Schoenfeld residuals.

We adjusted for baseline age (continuous) and sex (male or female) in model 1 and further adjusted for TDI (continuous), education (degree or not degree), ethnicity (white or other), smoking status (current, former, never or missing), physical activity (continuous), BMI categories [27] (underweight [<18.5], normal [18.5 to <25], overweight [25 to <30], obesity [30 to <35], or obesity class 2 [≥35]), diabetes (yes or no), hypertension (yes or no), depression (yes or no), family history of CVD (yes or no), vitamin and mineral supplement use (yes or no; vitamin A, vitamin B, vitamin C, vitamin D, vitamin E, folic acid, multivitamins/minerals or missing), and intake of fresh fruit, vegetable, red meat, processed meat, alcohol, un–sweetened tea, un–sweetened coffee, total energy and total sugar (total sugar intake was not included in the analysis of SSBs). We mutually adjusted each soft drink because the consumption levels were moderately correlated.

To assess the association of SSB intake and CVD events, intake was expressed as %TEI. A dose–response relationship was examined using a restricted cubic spline with knots at the 25th, 50th and 75th percentiles. We evaluated the association of substituting 1 drink/day of SSBs and ABSs with an equivalent amount of pure fruit/vegetable juices, un–sweetened tea and un–sweetened coffee by including both as continuous variables simultaneously [28]. The impact of reducing SSB intake on CVD events was estimated as the percent population–attributable fraction (PAF) of CVD events attributable to %TEI from SSBs under the assumption of causality [29]. Taking into consideration the distribution of SSBs consumption and achievable levels of consumption, three PAFs with 95% CIs were separately estimated, assuming that participants consumed SSBs at less than 15%, 10% or 5% TEI and treating the %TEI from SSBs as a binary variable.

We performed the following sensitivity analyses to assess the robustness of the results. (1) We excluded participants who developed CVD events within two years of follow–up to minimize the influence of reverse causation. (2) We excluded participants who reported their previous day’s diet as atypical on any of the five occasions to maximize representation of participants’ typical dietary habits. (3) Dietary intake is associated with BMI, which influences health outcomes, and adjustment for BMI may result in overadjustment bias [30]. Therefore, we compared the associations estimated from the models with and without BMI in sensitivity analyses.
without BMI as a covariate. (4) We excluded participants with missing values for covariates, and (5) we excluded participants who lost weight in the year prior to recruitment to exclude individuals with conditions associated with unintentional weight loss.

Analyses were performed using SAS software (version 9.4 for Windows, SAS Institute, Inc., Cary, NC, USA). Statistical tests were two–sided, and $P$ values less than 0.05 were considered statistically significant.

## Results

### Baseline characteristics

Most participants consumed at least one soft drinks (126814, 75.5%). Pure fruit/vegetable juices (54.4%) were the most commonly consumed, and SSBs (37.7%) and ASBs 34 776 (20.7%) were the second most commonly consumed (Table S2). Table 1 shows the baseline characteristics of the study participants according to soft drink consumption. Generally, participants who drank more SSBs and ASBs were more likely to be younger, from a lower social class, obese, current smokers, have reported without family history of CVD, drink un–sweetened tea and coffee. In addition, ASB consumers reported having the lowest energy and sugar intake. Moderate fruit juice consumers (>0–2.5 drinks/day) were of higher social class, less current smoker, less obese, higher reported with family history of CVD.

### Soft drink intake with CVD mortality and incidence

During a median follow–up of 7.0 years (interquartile range [IQR], 6.5–7.8 years for CVD mortality) and 6.1 years (IQR, 5.7–6.9 years for incidence CVD), we recorded 5 922 incident CVD cases and 884 CVD deaths. Multivariable adjusted analyses (Table 2) revealed that compared to non–consumers, participants who consumed >2.5 drinks/day had a higher risk of CVD mortality and incidence with HR (95% CI) of 1.00 (0.90–1.11) and 1.00 (0.90–1.11) for SSBs, and 1.00 (0.87–1.14) and 1.00 (0.85–1.19) for ASBs, respectively. There were no significant interactions with age group, sex, smoking status, BMI, physical activity level, hypertension or family history of CVD were evident (Figure S2–S3). Sensitivity analyses had no substantial impact on the effect estimates (Tables S3–S7), but there was a slight increase in the association when BMI was excluded from the multivariate model (Table S5).

There was a positive linear association between soft drink intake (%TEI) and CVD incidence and mortality, which was significant at intakes above 10.4% and 10.7% TEI, respectively. Each 5% higher intake was associated with a 6% (3%–10%) higher CVD incidence and a 15% (7%–25%) higher CVD mortality (Figure 1). The PAF of CVD mortality was estimated as 2% (1%–3%) if the participants reduced their SSB intake to below 15% TEI. If intake was reduced to below 10% TEI, the PAF was estimated as 3% (1%–6%), and if intake was reduced to below 5% TEI, the PAF was estimated as 4% (1%–8%). Substituting pure fruit/vegetable juice, un–sweetened tea or coffee for SSBs and ASBs was associated with 4–7% lower risks for incidence CVD, and 12–24% lower risks for CVD mortality when the substitution amount was 1 drink per day (Figure 2).

### Discussion

The current findings of a positive association of SSB and ASB intake with CVD events further support previous studies [8, 16, 31]. The present study also reports several novel findings. This study is the largest report of a U–shaped association of pure fruit/vegetable juice intake with CVD events. We also examined the association between the contribution of %TEI from SSBs and the incidence of CVD and found that each 5% increase in the contribution to TEI was associated with a 6–15% higher CVD morbidity and mortality. The population impact of SSB consumption on CVD events has not been previously evaluated, and we estimated that 2–4% of CVD mortality cases may be prevented if consumers of SSBs reduced their intake to below 5% TEI. We also report that drinking pure fruit/vegetable juices, un–sweetened tea or coffee as alternatives to SSBs and ASBs significantly lowered the CVD morbidity and mortality. These novel findings are of clinical and public health relevance.

Most previous studies on SSBs and CVD events reported a positive association, and the association was independent of BMI [1, 2]. Our categorization of SSBs is largely consistent with the definitions of SSBs in other studies [7, 8], and our findings are consistent with other publications, with an increased risk of CVD events per serving of SSBs, independent of adiposity.

Despite containing few or no calories, some research has suggested the need to discourage the consumption of ASBs as a substitute for SSBs [1–3, 5, 7, 8, 32]. We found significant associations of higher consumption of ASBs with the risk of CVD mortality and morbidity. Possible biological mechanisms were that ASBs may lead to the development of a preference for sweets and may induce insulin resistance [33]. However, previous studies [8, 34] suggested that positive associations were explained by reverse causality because individuals who were unhealthy at baseline (e.g., subjects who were obese or had hypertension) may be likely to switch from drinking SSBs to ASBs to lose weight. Our sensitivity analysis found that the association persisted after the exclusion of CVD events recorded in the first two years of follow–up, when participants with recent weight loss were excluded, and when participants with an atypical diet were excluded. However, the role of BMI in the association between ASB consumption and CVD events is complex, and adiposity likely acts as a mediating and confounding factor. Multivariable model analyses showed that the strengths of the associations were slightly increased in the absence of BMI adjustment, which suggests that adiposity partially mediated some of the effects.

Liquid sugar may be more rapidly absorbed and more likely to induce unhealthy changes than solid sugar [35]. Similarly, fresh fruit has many health benefits, and pure juices may not have the same benefits. However, little is known about pure fruit/vegetable juice consumption and the risk of CVD. In our study, we observed an 8–35% lower risk of the incidence of CVD, CHD, stroke and CVD mortality in the participants with an average consumption of 1–2 drinks/day.
than non–consumers, but this lower risk was not observed in the participants with a higher consumption (> 2.5 drinks/day). These U–shaped effects may be related to beneficial compounds, such as polyphenols and vitamins, that are present in solid fruits and offset the adverse effects of liquid sugar to confer some protection [36–38].

The incidence of CVD events was 6–15% higher per 5% higher TEI from SSBs in the present study. One study in the USA reported an association between the contribution of added sugar above 10% of TEI and higher mortality from CVD events [39]. Non–alcoholic beverages are a major source of sugars worldwide, and our findings support recommendations of restricting the contribution of sugars to energy. Although public health messages recommend limiting sweet beverage consumption [16–19], alternative beverages should be suggested to achieve this goal. However, there is insufficient evidence of appropriate replacement beverages to make recommendations. The current study examined the effects of substituting SSBs and ASBs with un–sweetened tea and coffee or pure juice alternatives. The results of these analyses provide practical suggestions for alternatives to soft drinks and highlight the benefits of substituting soft drinks with un–sweetened tea and coffee or pure juice. To our knowledge, our estimates of the population impact of SSB consumption in reducing CVD events provide the first reported evidence. Our findings are of considerable public health relevance and showed that 2–4% of CVD cases might be prevented under different intake assumptions, as proposed.

Strengths And Limitations

The strengths of this study include its prospective design, large sample size, and wide range of soft drink intake. Detailed data allowed us to include beverages that were not typically examined in soft drink research, including un–sweetened tea and un–sweetened coffee. We acknowledge that our study also has several potential limitations. First, the UK Biobank is not representative of the sampling population, and there is evidence of a “healthy volunteer” selection bias. However, valid assessments of exposure–disease relationships do not require a representative population [40], and our results reflect prior studies in different populations worldwide. Second, although we used the average of five occasions of dietary data collection to represent habitual intake, the baseline exposure might not capture changes in intake over time. Individuals may switch from SSB to ASB consumption. Despite the large size of the cohort, there were relatively few CVD incidences from specific types we were not able to reliably test whether some associations were specific among certain subgroups. However, future analyses of these end points will be possible as the UK Biobank cohort matures.

Conclusions

The consumption of SSBs and ASBs was associated with higher CVD event risk independent of conventional CVD risk factors and other dietary factors in this large prospective study. Our results support current recommendations to limit the consumption of SSBs and ASBs, and to promote the drinking of un–sweetened tea or coffee and pure fruit/vegetable juices as alternatives to improve overall health and longevity.

Abbreviations

SSBs: sugar–sweetened beverages
ASBs: artificially sweetened beverages
CVD: cardiovascular disease
HR: hazard ratio
TEI: total energy intake
TDI: Townsend deprivation index
IPAQ: International Physical Activity Questionnaire
MET: metabolic equivalents
BMI: body mass index

Declarations

Availability of data and materials
The UK Biobank data are available from the UK Biobank upon request (www.ukbiobank.ac.uk/).

Ethics approval and consent to participate
The UK Biobank received ethical approval from the research ethics committee (REC reference for UK Biobank 11/NW/0382) and participants provided written informed consent.

Consent for publication
Not applicable.
Availability of data and materials
Data are available in a public, open access repository. The UK Biobank data are available from the UK Biobank on request (www.ukbiobank.ac.uk/).

Competing interests
The authors declare that they have no competing interests.

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Author contributions
DL performed the statistical analyses and had primary responsibility for writing the manuscript. PDZ, ZHL, DS and XRZ contributed to data cleaning. PLC, WFZ and QMH contributed to the analysis or interpretation of the results. CM designed the survey, directed the study, and was responsible for accuracy of data analysis. All authors read, edited, and approved the final manuscript. DL professionally edited and formatted the final manuscript.

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Table 1. Baseline Characteristics of Study Participants Stratified by Soft Drinks Consumption

| Characteristics                        | Values are mean (SD) unless stated otherwise |
|----------------------------------------|---------------------------------------------|

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| Characteristic                                      | SSBs (drinka)* | ASBs (drinka)* | Pure fruit/vegetable juices (drinka)* |
|----------------------------------------------------|----------------|----------------|--------------------------------------|
| (0/d)                                              |                |                |                                      |
| >0–1/d                                             | 104732 (62.4)  | 38329 (22.8)   | 17489 (10.4)                         |
| >1–2.5/d                                           | 7457 (4.4)     | 133231 (79.3)  | 20840 (12.4)                         |
| >2.5/d                                             | 10073 (6.0)    | 3863 (2.3)     | 76543 (45.6)                         |
| > 0–1/1/d                                          |                |                |                                      |
| >0–1/d                                             | 133231 (79.3)  | 20840 (12.4)   | 10073 (6.0)                         |
| >1–2.5/d                                           | 3863 (2.3)     | 76543 (45.6)   | 22495 (13.4)                         |
| >2.5/d                                             | 5144 (3.1)     |                |                                      |
| Participants, No. (%)                             | 100991 (96.8)  | 36293 (95.1)   | 16397 (94.1)                         |
| Age (years)                                        | 6960 (93.7)    | 127261 (95.9)  | 19908 (95.8)                         |
| BMI, No. (%)                                       | 9754 (97.1)    | 3718 (96.6)    | 72979 (95.7)                         |
| (35.0)                                             |                |                |                                      |
| Physical activity (MET/day), No. (%)               |                |                |                                      |
| <400                                               | 41976 (40.1)   | 133336 (34.8)  | 5377 (30.8)                         |
| ≥400                                               | 62756 (59.9)   | 24993 (65.2)   | 12112 (69.3)                        |
| Smoking status, No. (%)                           |                |                |                                      |
| Never                                              | 59551 (57.0)   | 22553 (59.0)   | 10394 (56.6)                        |
| Former                                             | 36896 (35.3)   | 12878 (33.7)   | 5679 (34.5)                         |
| Current                                            | 8057 (7.7)     | 2797 (7.3)     | 1374 (7.9)                          |
| Physical activity (MET/day), No. (%)               |                |                |                                      |
| <18.5                                              | 647 (0.6)      | 114 (0.5)      | 61 (0.4)                           |
| 18.5 to <25.0                                      | 41616 (39.7)   | 14425 (37.6)   | 6014 (34.4)                         |
| 25.0 to <30.0                                      | 43167 (41.2)   | 16256 (42.4)   | 7465 (42.7)                        |
| 30.0 to <35.0                                      | 14429 (13.8)   | 5613 (14.6)    | 2891 (16.5)                        |
| ≥35.0                                              | 4873 (4.7)     | 1861 (4.9)     | 1058 (6.1)                         |
| BMI, No. (%)                                       |                |                |                                      |
| <18.5                                              | 4382 (4.2)     | 1326 (3.5)     | 672 (3.8)                           |
| 18.5 to <25.0                                      | 58797 (56.1)   | 21790 (56.9)   | 10000 (52.7)                       |
| 25.0 to <30.0                                      | 10567 (10.2)   | 3892 (10.2)    | 1917 (11.0)                        |
| 30.0 to <35.0                                      | 27698 (26.5)   | 9986 (26.1)    | 4383 (25.1)                        |
| ≥35.0                                              | 33478 (32.1)   | 12828 (33.6)   | 5835 (33.5)                        |
| Diabetes, No. (%)                                  |                |                |                                      |
| Hypertension, No. (%)                              | 58797 (56.1)   | 21790 (56.9)   | 10000 (52.7)                       |
| Depression, No. (%)                                | 10567 (10.2)   | 3892 (10.2)    | 1917 (11.0)                        |
| Family history of CVDs, No. (%)                    | 27698 (26.5)   | 9986 (26.1)    | 4383 (25.1)                        |
| Vitamin and mineral supplement use, No. (%)        | 33478 (32.1)   | 12828 (33.6)   | 5835 (33.5)                        |

*Note: SSBs (drinks) represents sugary soft drinks, ASBs (drinks) represents artificial sweetened beverages, Pure fruit/vegetable juices (drinks) represents pure fruit or vegetable juices.*
| Energy (kcal/d) | 2082.2 (528.3) | 2161.4 (524.7) | 2256.7 (544.2) | 2390.0 (594.8) | 2133.2 (537.7) | 2116.2 (530.7) | 2125.4 (533.9) | 2198.1 (597.6) | 2073.3 (547.1) | 2151.2 (520.6) | 2225.7 (516.3) | 2361.0 (575.7) |
|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Sugar (g/d)    | 112.4 (42.6)   | 127.3 (42.9)   | 142.3 (45.9)   | 166.3 (56.9)   | 121.5 (45.8)   | 119.6 (44.7)   | 120.5 (45.9)   | 125.4 (54.7)   | 110.3 (44.5)   | 124.9 (42.2)   | 139.0 (43.9)   | 163.6 (60.7)   |
| Fruit (servings/d) | 2.3 (1.5)    | 2.2 (1.5)      | 2.2 (1.5)      | 2.2 (1.6)      | 2.2 (1.5)      | 2.3 (1.5)      | 2.3 (1.6)      | 2.3 (1.8)      | 2.2 (1.6)      | 2.3 (1.5)      | 2.4 (1.5)      | 2.5 (1.8)      |
| Vegetables (servings/d) | 5.0 (3.2)    | 4.8 (3.1)      | 4.8 (3.1)      | 4.8 (3.7)      | 4.9 (3.2)      | 4.9 (3.2)      | 5.0 (3.3)      | 5.1 (3.7)      | 5.0 (3.3)      | 4.8 (3.0)      | 5.0 (3.1)      | 5.4 (4.2)      |
| Red meat (servings/d) | 0.5 (0.7)    | 0.6 (0.8)      | 0.7 (0.8)      | 0.7 (0.8)      | 0.6 (0.7)      | 0.7 (0.8)      | 0.7 (0.8)      | 0.6 (0.7)      | 0.6 (0.7)      | 0.7 (0.8)      | 0.7 (0.8)      |                   |
| Processed meat (servings/d) | 0.9 (1.4)    | 1.1 (1.5)      | 1.3 (1.6)      | 1.3 (1.7)      | 0.9 (1.4)      | 1.2 (1.5)      | 1.3 (1.6)      | 1.3 (1.7)      | 0.9 (1.4)      | 1.0 (1.4)      | 1.2 (1.5)      | 1.2 (1.6)      |
| Alcohol (g/d) | 19.4 (21.7)    | 18.8 (20.8)    | 18.4 (21.0)    | 18.7 (22.3)    | 19.1 (21.5)    | 19.1 (21.1)    | 19.2 (21.3)    | 18.2 (22.6)    | 18.3 (22.3)    | 19.7 (21.0)    | 19.9 (20.0)    | 19.3 (20.9)    |
| Unsweetened tea (drinks/d) | 2.5 (2.2)    | 2.3 (2.2)      | 2.0 (2.2)      | 1.7 (2.1)      | 2.5 (2.2)      | 2.2 (2.1)      | 2.2 (2.1)      | 1.9 (2.2)      | 1.5 (2.1)      | 2.3 (2.3)      | 2.4 (2.2)      | 2.3 (2.3)      |
| Unsweetened coffee (drinks/d) | 1.5 (1.8)    | 1.4 (1.8)      | 1.4 (1.8)      | 1.2 (1.8)      | 1.5 (1.7)      | 1.6 (1.9)      | 1.6 (1.9)      | 1.3 (1.9)      | 1.4 (1.8)      | 1.5 (1.7)      | 1.6 (1.8)      | 1.6 (1.9)      |
| SSBs (drinks/d) | 0.0 (0.0)     | 1.0 (0.0)      | 2.0 (0.0)      | 3.0 (0.0)      | 0.5 (0.8)      | 0.7 (0.9)      | 0.9 (1.0)      | 0.9 (1.2)      | 0.5 (0.8)      | 0.6 (0.8)      | 0.7 (0.9)      | 0.8 (1.0)      |
| ASBs (drinks/d) | 0.3 (0.6)     | 0.3 (0.7)      | 0.5 (0.8)      | 0.7 (1.0)      | 0.0 (0.0)      | 1.0 (0.0)      | 2.0 (0.0)      | 3.0 (0.0)      | 0.3 (0.7)      | 0.3 (0.7)      | 0.3 (0.7)      | 0.3 (0.7)      |
| Pure juices (drinks/d) | 0.7 (0.8)     | 0.8 (0.8)      | 0.9 (0.9)      | 0.9 (0.9)      | 0.7 (0.8)      | 0.7 (0.8)      | 0.7 (0.8)      | 0.6 (0.8)      | 0.0 (0.0)      | 1.0 (0.0)      | 2.0 (0.0)      | 3.0 (0.0)      |

Abbreviation: TDI, Townsend deprivation index; SSBs, sugar–sweetened beverages; ASBs, artificially sweetened beverages; SD, standard deviation; No., number; MET, metabolic equivalents; BMI, body mass index.

* One drink is equal to approximately 250 mL.
Table 2
Associations Between Soft Drink Consumption and CVD events, HR (95% CI)

| Outcomes                  | Non–consumers | Consumers (drinks/d) | P Value for Trend |
|---------------------------|---------------|----------------------|------------------|
|                           |               | >0–1                 | >1–2.5           | >2.5            |
|                           |               |                      |                  |                 |
| **SSBs**                  |               |                      |                  |                 |
| Incidence CVD             |               |                      |                  |                 |
| Events (%)                | 3648 (3.5)    | 1341 (3.5)           | 628 (3.6)        | 305 (4.1)       |
| Basic model b             | 1 (ref)       | 0.99 (0.93–1.06)     | 1.08 (0.99–1.17) | 1.34 (1.19–1.51) |
| Multivariable model c     | 1 (ref)       | 0.99 (0.93–1.06)     | 1.04 (0.96–1.14) | 1.23 (1.09–1.39) |
| CVD mortality             |               |                      |                  |                 |
| Events (%)                | 536 (0.5)     | 201 (0.5)            | 93 (0.5)         | 54 (0.7)        |
| Basic model b             | 1 (ref)       | 1.02 (0.86–1.19)     | 1.11 (0.89–1.39) | 1.73 (1.31–2.29) |
| Multivariable model c     | 1 (ref)       | 1.05 (0.89–1.23)     | 1.12 (0.90–1.40) | 1.63 (1.22–2.17) |
| **ASBs**                  |               |                      |                  |                 |
| Incidence CVD             |               |                      |                  |                 |
| Events (%)                | 4761 (3.6)    | 665 (3.2)            | 351 (3.5)        | 145 (3.8)       |
| Basic model b             | 1 (ref)       | 1.04 (0.96–1.13)     | 1.24 (1.11–1.38) | 1.43 (1.21–1.68) |
| Multivariable model c     | 1 (ref)       | 0.96 (0.89–1.04)     | 1.08 (0.97–1.21) | 1.20 (1.02–1.42) |
| CVD mortality             |               |                      |                  |                 |
| Events (%)                | 698 (0.5)     | 104 (0.5)            | 51 (0.5)         | 31 (0.8)        |
| Basic model b             | 1 (ref)       | 1.16 (0.94–1.42)     | 1.32 (0.99–1.75) | 2.27 (1.58–3.26) |
| Multivariable model c     | 1 (ref)       | 1.06 (0.86–1.30)     | 1.11 (0.83–1.48) | 1.77 (1.23–2.56) |
| **Pure fruit/vegetable juices** | | | | |
| Incidence CVD             |               |                      |                  |                 |
| Events (%)                | 2769 (3.6)    | 2236 (3.5)           | 744 (3.3)        | 173 (3.4)       |
| Basic model b             | 1 (ref)       | 0.90 (0.85–0.95)     | 0.88 (0.81–0.95) | 0.95 (0.81–1.10) |
| Multivariable model c     | 1 (ref)       | 0.92 (0.87–0.98)     | 0.89 (0.82–0.97) | 0.92 (0.79–1.09) |
| CVD mortality             |               |                      |                  |                 |
| Events (%)                | 451 (0.6)     | 326 (0.5)            | 86 (0.4)         | 21 (0.4)        |
| Basic model b             | 1 (ref)       | 0.80 (0.69–0.92)     | 0.63 (0.50–0.79) | 0.73 (0.47–1.13) |
| Multivariable model c     | 1 (ref)       | 0.85 (0.74–0.98)     | 0.66 (0.52–0.84) | 0.71 (0.45–1.11) |

Abbreviations: TDI, Townsend deprivation index; SSBs, sugar–sweetened beverages; ASBs, artificially sweetened beverages; HR, hazard ratio; CVD, cardiovascular diseases; CHD, coronary heart disease.

a One drink is equal to approximately 250 mL.

b Basic Cox regression model adjusted for age (continuous) and sex.

c Multivariable Cox regression model additional adjusted for TDI (continuous), education (degree or not degree), ethnicity (white or other), smoking status (current, former, never or missing), physical activity (continuous), BMI categories (underweight [<18.5], normal [18.5 to <25], overweight [25 to <30], obesity [30 to <35], or obesity class 2 [≥35]), diabetes (yes or no), hypertension (yes or no), depression (yes or no), family history of CVD (yes or no), vitamin and mineral supplement use (yes or no; vitamin A, vitamin B, vitamin C, vitamin D, vitamin E, folic acid, multivitamins/minerals or missing), and intake of fresh fruit, vegetable, red meat, processed meat, alcohol, un–sweetened tea, un–sweetened coffee, total energy and total sugar (total sugar intake was not included in the analysis of SSBs). Each soft drink was mutually adjusted.

Figures
Figure 1

The association of SSB consumption (% of total energy intake, %TEI) with CVD mortality and morbidity. %TEI was truncated at 25%. The spline-regression model adjusted for age (continuous), sex, TDI (continuous), education (degree or not degree), ethnicity (white or other), smoking status (current, former, never or missing), physical activity (continuous), BMI categories (underweight [<18.5], normal [18.5 to <25], overweight [25 to <30], obesity [30 to <35], or obesity class 2 [≥35]), diabetes (yes or no), hypertension (yes or no), depression (yes or no), family history of CVD (yes or no), vitamin and mineral supplement use (yes or no; vitamin A, vitamin B, vitamin C, vitamin D, vitamin E, folic acid, multivitamins/minerals or missing), and intake of fresh fruit, vegetable, red meat, processed meat, alcohol, un-sweetened tea, un-sweetened coffee and total energy.
### Figure 2

The estimated effect of substituting one drink of alternative beverage for one soft drink on CVD events, HR (95% CI). Estimates for the effect of substitution were calculated as the difference in regression coefficients between the two beverages (continuous). Adjusted for age (continuous), sex, TDI (continuous), education (degree or not degree), ethnicity (white or other), smoking status (current, former, never or missing), physical activity (continuous), BMI categories (underweight [≤18.5], normal [18.5 to <25], overweight [25 to <30], obesity [30 to <35], or obesity class 2 [≥35]), diabetes (yes or no), hypertension (yes or no), depression (yes or no), family history of CVD (yes or no), vitamin and mineral supplement use (yes or no; vitamin A, vitamin B, vitamin C, vitamin D, vitamin E, folic acid, multivitamins/minerals or missing), and intake of fresh fruit, vegetable, red meat, processed meat, alcohol, un–sweetened tea, un–sweetened coffee, total energy and total sugar. Each soft drink was mutually adjusted.

### Supplementary Files

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- [3.supplementarytablesandfigures.docx](3.supplementarytablesandfigures.docx)