Nutrition Journal

RESEARCH

Open Access

Associations of sugary beverage intake with type 2 diabetes and the role of physical activity: a prospective cohort study

Yihong Ding[1†], Hui Chen[1†], Jie Shen[1], Liyan Huang[1], Yaying Cao[2], Yan Zheng[3,4], Geng Zong[2*] and Changzheng Yuan[1,5*]

Abstract

Background Higher consumption of sugary beverages (SB) has been associated with type 2 diabetes (T2D), but whether these associations are modified by physical activity remains unclear. This study aimed to examine the associations of SB intake, including sugar-sweetened beverages (SSB), artificially sweetened beverages (ASB), and natural juices (NJ) with the risk of incident T2D, and the potential role of physical activity.

Methods We included 153,862 diabetes-free participants in the UK Biobank who completed both the International Physical Activity Questionnaire at recruitment (2006–2010) and at least one 24-h dietary recall questionnaire in 2009–2012. We assessed the associations of each SB with the risk of incident T2D using Cox proportional hazard models, and explored the interactions between each SB and physical activity.

Results During a median follow-up of 11.8 years, 6631 participants developed incident T2D. Participants consuming more SSB and ASB (comparing > 2 to 0 unit/d) had a higher hazard of T2D (hazard ratio [HR]: 1.17, 95% confidence interval [CI]: 1.05–1.31 for SSB; 1.54, 1.37–1.74 for ASB), while medium intake of NJ showed an inverse association ($HR_{>0–1 \text{ vs. } 0 \text{ unit/d}}$: 0.87, 95% CI: 0.82–0.92; $HR_{>1–2 \text{ vs. } 0 \text{ unit/d}}$: 0.88, 95% CI: 0.81–0.97) with incident T2D. No significant interactions between physical activity and SSB/ASB were found (P-interaction=0.204 for SSB, 0.926 for ASB), but the protective association of medium NJ intake with T2D was stronger among participants with higher level of physical activity (*P*-interaction = 0.043).

Conclusions Higher intake of SSB and ASB was related to higher risks of T2D. Medium NJ intake was associated with a lower risk of T2D, particularly among individuals with higher physical activity level. These findings emphasized the importance of healthy beverage intake and adequate physical activity in diabetes prevention.

Keywords Sugary beverages, Physical activity, Type 2 diabetes, Interactions, Cohort study

†Yihong Ding and Hui Chen contributed equally as co-first authors.

*Correspondence:
Geng Zong
zonggeng@sinh.ac.cn
Changzheng Yuan
chy478@zju.edu.cn
Full list of author information is available at the end of the article

Introduction

The global number of prevalent diabetes cases was estimated to be 463 million (9.3% of adults aged 20–79 years), and type 2 diabetes (T2D) accounted for approximately 90% of the total diabetes cases [1]. T2D imposes enormous healthcare costs and individual burdens [2, 3], making its prevention a major public health priority [4]. Previous studies have identified several lifestyle factors related to T2D [5, 6], such as smoking, alcohol intake, physical activity, and dietary factors [7–9]. Physical activity is a critical factor for diabetes and prediabetes [10, 11], potentially through blood glucose control and weight loss [12, 13]. Among dietary factors, the consumption of sugary beverages (SB), including sugar-sweetened beverages (SSB), artificially sweetened beverages (ASB), and natural juices (NJ), has also been associated with incident T2D [14], which has received considerable attention from both scientific and public communities [15–17].

Previous studies have examined the individual associations of physical activity and SB intake with T2D. However, the associations of physical activity and beverage intake with T2D might involve similar pathways and thus constitute interactions [18–20]. For example, physical activity may influence sensory stimuli and taste perceptions [21], which are likely to alter sugar metabolism through nervous signaling. Additionally, physical activity itself constitutes a major component of energy expenditure [22], and excess energy intake from SB could potentially be compensated for by intense physical activity. However, very few studies to date have examined the moderating effects of physical activity on the associations of SB with T2D. Therefore, population-based evidence is needed to explore whether the associations between SB intake and T2D can be modified by physical activity, and whether these two factors are synergistically or additively related to the risk of T2D. As such, we leveraged data from the UK Biobank, a large-scale cohort study in the UK, to evaluate the association between SB intake and T2D and the potential role of physical activity.

Research design and methods

Study population

The study was based on the UK Biobank, a prospective cohort study that recruited ~ 500,000 participants from 2006 to 2010 at 22 centers across the UK [23]. At recruitment, participants aged 37–73 years completed a touchscreen questionnaire [24], which collected extensive information on socioeconomic status, lifestyle, health conditions, etc. Research nurse interviews and physical examinations were also administered at recruitment. The UK Biobank study was approved by the North West Multi-Center Research Ethics Committee, and all participants provided written informed consent. The present study was conducted under application number 55005 of the UK Biobank resource.

From 2009 to 2012, ~ 42% of the UK Biobank participants repeatedly completed 24-h dietary recalls [25]. Among the 210,966 participants who completed at least one 24-h diet recall, we excluded 18,958 participants reporting extremely high total energy intake (> 20 MJ, i.e., 4785 kcal). Among the remaining participants, 158,447 completed the International Physical Activity Questionnaire (IPAQ), and we further excluded 4,585 participants who had diabetes at baseline or who were lost to follow-up with an unknown date of loss. The formal analyses included 153,862 participants (Figure S1).

Intake of SB

In the UK Biobank, SB intake was assessed using the Oxford WebQ, a validated web-based questionnaire for 24-h diet recalls [25–27]. Eligible participants were invited to complete the online questionnaire on five occasions between April 2009 and June 2012, and the average number of repetitions in this study was 1.98. The specific time windows for the five events were April 2009 to September 2010, February 2011 to April 2011, June 2011 to September 2011, October 2011 to December 2011, and April 2012 to June 2012. In the questionnaire, participants were asked how many units (Glass/Carton/250 ml) of each type of beverage they consumed in the past 24 h. The options were 0, 0.5, 1, 2, 3, 4, 5, and 6+. In the current study, we defined SSB as carbonated (fizzy) drinks and commercial fruit drinks (data fields 100,170 and 100,180), ASB as low-calorie drinks (data field 100,160), and NJ as pure orange juices, pure grape juices, and other pure juices (data fields 100,190, 100,200, and 100,210). For participants who completed the WebQ more than once (~ 50%), we took the average intake levels of the beverages. Consumption of SSB, ASB, and NJ was categorized as 0, > 0–1, > 1–2, or > 2 units/d according to a previous study [28].

Assessment of physical activity

Physical activity was assessed using the IPAQ [29], which asked how many minutes the participants spent on each type of physical activity. We calculated the Metabolic Equivalent Task Scores by summing weighted minutes per week for all activities, including walking, and moderate and vigorous activity, with weights of 3.3, 4.0, and 8.0, respectively. According to the strategy of a previous study and following the recommendation of the World Health Organization, we categorized participants into low, moderate, and high physical activity groups [30]. The

corresponding variables were provided as data category 54 in the UK Biobank showcase.

Ascertainment of T2D

The outcome of interest was the incidence of T2D. We incorporated data from self-reported diagnoses and medication and Hospital Episode Statistics (HES) data (ICD-9 250 and ICD-10 E10-E14) to identify prevalent and incident T2D cases, as described elsewhere [31]. Data on the linkage to HES was updated until December, 2022.

Other covariates

We included multiple covariates for confounding adjustments. All covariates, including sociodemographic, lifestyle, and health-related factors, were measured at recruitment. Sociodemographic factors included age, sex, race (White or non-White), education level (high school and below or college and above), and area-based Townsend deprivation index (TDI). Lifestyle factors (other than physical activity and beverage intake) included alternate healthy eating index (calculated according to a previous study [28]), smoking status (current, former, or never smokers), and drinking status (current, former, or never drinkers). Health-related factors included objectively measured body mass index (BMI) categories (calculated as weight in kilograms divided by height in meters squared, categorized into normal weight, overweight, and obesity with cutoffs of 25 and 30 [32]), hypertension, cardiovascular diseases, cancer, and dyslipidemia. History of chronic health conditions was self-reported and identified using linkages to the HES system, similar to T2D. Family history of diabetes was defined as the existence of diabetes among parents or other first-degree relatives.

Statistical analyses

We chose the date of completion of the first valid 24-h dietary recall as the study baseline. We calculated person-time from the study baseline to the date of the first record of incident T2D, date of death, or the end of follow-up (December, 2022), whichever occurred first. Baseline characteristics of participants were described by their physical activity categories. Continuous variables were presented as mean (standard deviation, SD), and categorical variables as number (percentage). We first assessed the independent relationships of intake of SSB, ASB, NJ, and physical activity with incident T2D with Cox proportional hazard models, with sequential adjustments for baseline socioeconomic status, health-related behaviors, and health conditions. Model 1 was adjusted for age, squared age, sex, and race. Model 2 was based on Model 1 and further adjusted for total energy intake, alternate healthy eating index, TDI, education level, physical activity (not when physical activity was the exposure of interest), smoking status, drinking status, and family history of diabetes. Model 3 was based on Model 2 and additionally adjusted for BMI categories.

To examine whether an individual's level of physical activity modifies the effects of SB intake on T2D, we stratified the data according to physical activity level and used the above-mentioned Model 3 to explore whether each SB intake has different effects on T2D in different physical activity level groups. To evaluate the interactions between physical activity and SSB, ASB, and NJ, we performed Wald tests on the multiplicative terms of physical activity and each SB and reported *P*-interactions.

To assess their joint associations with T2D, we combined physical activity with each level of SB intake, respectively, forming three 12-level variables: physical activity × SSB, physical activity × ASB, and physical activity × NJ. With the above-mentioned Model 3, we calculated the hazard ratios (HRs) with 95% confidence intervals (CIs) for the levels of the combined variables. The reference groups were participants with high physical activity and zero intake of the corresponding SB.

We conducted several sensitivity analyses to test the robustness of our primary findings. First, we additionally adjusted the models for hypertension, cardiovascular diseases, cancer, and dyslipidemia to assess whether the observed associations were confounded by these chronic health conditions. Second, we additionally adjusted the models for the indicator of the first dietary assessment (e.g., participants who completed the first dietary assessment from April 2009 to September 2010 coded as 1, February 2011 to April 2011 coded as 2, etc.) to better control for the time lag between covariate set and dietary assessment. Third, we further adjusted the relations for total sugar intake. Fourth, we excluded participants who developed T2D within the first five years to reduce reverse causality and address the possibility that T2D cases may have occurred during the exposure measurements. Fifth, we mutually adjusted for three types of SB in the same model to test their independent associations with T2D. Finally, we evaluated the additive rather than multiplicative interactions using relative excess risk due to interaction (RERI), which reflected biological interactions [33].

Missing values for all continuous covariates were imputed by means, and categorical variables were imputed by the most populated categories. We reported two-sided *P*-values throughout and a *P*-value lower than 0.05 was considered an indicator of statistical significance. Statistical analyses were performed using R 4.1.0 from March to July, 2022.

Table 1 Baseline characteristics of the study participants according to physical activity levels

Variables	Overall	Physical activity levels			
		High	Medium	Low	*P*-value
n	153,862	61,606	65,063	27,193	
Female (%)	82,417 (53.6)	32,060 (52.0)	36,276 (55.8)	14,081 (51.8)	< 0.001
White (%)	147,454 (95.8)	59,046 (95.8)	62,485 (96.0)	25,923 (95.3)	< 0.001
Age (mean (SD))	55.9 (8.0)	56.0 (8.1)	56.0 (7.9)	55.4 (7.7)	< 0.001
TEI, kcal (mean (SD))	2107.8 (586.9)	2137.3 (609.8)	2095.7 (569.3)	2069.7 (572.1)	< 0.001
SSB, unit/d (%)					
0	108,527 (70.5)	43,318 (70.3)	46,168 (71.0)	19,041 (70.0)	< 0.001
> 0–1	28,806 (18.7)	11,409 (18.5)	12,250 (18.8)	5147 (18.9)	
> 1–2	10,833 (7.0)	4451 (7.2)	4506 (6.9)	1876 (6.9)	
> 2	5696 (3.7)	2428 (3.9)	2139 (3.3)	1129 (4.2)	
ASB, unit/d (%)					
0	125,216 (81.4)	50,108 (81.3)	53,215 (81.8)	21,893 (80.5)	< 0.001
> 0–1	17,586 (11.4)	6997 (11.4)	7427 (11.4)	3162 (11.6)	
> 1–2	7224 (4.7)	2936 (4.8)	2924 (4.5)	1364 (5.0)	
> 2	3836 (2.5)	1565 (2.5)	1497 (2.3)	774 (2.8)	
Natural juices, unit/d (%)					
0	76,246 (49.6)	30,574 (49.6)	31,547 (48.5)	14,125 (51.9)	< 0.001
> 0–1	58,508 (38.0)	23,169 (37.6)	25,387 (39.0)	9952 (36.6)	
> 1–2	14,937 (9.7)	6059 (9.8)	6433 (9.9)	2445 (9.0)	
> 2	4171 (2.7)	1804 (2.9)	1696 (2.6)	671 (2.5)	
AHEI (mean (SD))	50.8 (11.8)	52.0 (12.0)	50.5 (11.7)	49.1 (11.4)	< 0.001
TDI (%)					
Low	56,019 (36.4)	22,105 (35.9)	23,796 (36.6)	10,118 (37.2)	< 0.001
Moderate	52,736 (34.3)	21,207 (34.4)	22,155 (34.1)	9374 (34.5)	
High	45,107 (29.3)	18,294 (29.7)	19,112 (29.4)	7701 (28.3)	
College and Above (%)	69,524 (45.2)	26,256 (42.6)	31,067 (47.7)	12,201 (44.9)	< 0.001
Smoking status (%)					
Current	11,585 (7.5)	4359 (7.1)	4798 (7.4)	2428 (8.9)	< 0.001
Former	54,361 (35.3)	22,615 (36.7)	22,562 (34.7)	9184 (33.8)	
Never	87,916 (57.1)	34,632 (56.2)	37,703 (57.9)	15,581 (57.3)	
Current drinker (%)	144,795 (94.1)	57,974 (94.1)	61,492 (94.5)	25,329 (93.1)	< 0.001
BMI categories (%)					
Normal and underweight	59,788 (38.9)	26,252 (42.6)	25,196 (38.7)	8340 (30.7)	< 0.001
Overweight	64,668 (42.0)	25,895 (42.0)	27,486 (42.2)	11,287 (41.5)	
Obesity	29,406 (19.1)	9459 (15.4)	12,381 (19.0)	7566 (27.8)	
Hypertension (%)	75,512 (49.1)	29,826 (48.4)	31,826 (48.9)	13,860 (51.0)	< 0.001
Cardiovascular Diseases (%)	26,063 (16.9)	10,128 (16.4)	10,843 (16.7)	5092 (18.7)	< 0.001
Dyslipidemia (%)	65,367 (42.5)	25,403 (41.2)	28,018 (43.1)	11,946 (43.9)	< 0.001
Cancer (%)	8566 (5.6)	3343 (5.4)	3623 (5.6)	1600 (5.9)	0.074
Family history of diabetes (%)	30,680 (19.9)	12,230 (19.9)	12,738 (19.6)	5712 (21.0)	< 0.001

All variables were measured at recruitment (2006–2010) but dietary factors were calculated from the 2009–2012 dietary assessment

TEI Total energy intake, *ASB* Artificially sweetened beverages, *SSB* Sugar-sweetened beverages, *AHEI* Alternate healthy eating index, *TDI* Townsend deprivation index, *BMI* Body mass index. Physical activity levels were defined according to the recommendations from the World Health Organization

Results

Baseline characteristics

Of the 153,862 study participants, the mean (SD) age was 55.9 (8.0) years, and 82,417 (53.6%) were female (Table 1). In total, 61,606 individuals (40.0%) had high physical activity, 65,063 (42.3%) had medium physical activity, and 27,193 (17.7%) had low physical activity. In general, participants with higher physical activity had higher total energy intake and lower prevalence of current smoking, obesity, chronic health conditions, and family history of diabetes ($P < 0.001$).

Table 2 Multivariable adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for type 2 diabetes according to sugary beverages intake and physical activity

Variables	Cases	Person-years	Model 1	Model 2	Model 3
Sugar-sweetened beverages, unit/d					
0	4506	1,235,825.5	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
> 0–1	1271	328,877.0	1.04 (0.98, 1.11)	1.03 (0.96, 1.09)	1.00 (0.94, 1.07)
> 1–2	512	123,979.8	**1.15 (1.05, 1.27)**	**1.12 (1.02, 1.23)**	1.05 (0.96, 1.15)
> 2	342	64,496.5	**1.52 (1.36, 1.70)**	**1.38 (1.24, 1.55)**	**1.17 (1.05, 1.31)**
Per one unit/d			**1.11 (1.08, 1.14)**	**1.08 (1.05, 1.11)**	**1.04 (1.01, 1.06)**
Artificially sweetened beverages, unit/d					
0	4934	1,428,670.6	1.00 (Reference)	1 (Reference)	1.00 (Reference)
> 0–1	950	199,906.8	**1.53 (1.42, 1.64)**	**1.45 (1.36, 1.56)**	**1.22 (1.13, 1.30)**
> 1–2	463	81,593.8	**1.96 (1.78, 2.16)**	**1.83 (1.66, 2.01)**	**1.38 (1.25, 1.52)**
> 2	284	43,007.5	**2.41 (2.13, 2.71)**	**2.15 (1.90, 2.42)**	**1.54 (1.37, 1.74)**
Per one unit/d			**1.31 (1.28, 1.35)**	**1.27 (1.24, 1.31)**	**1.14 (1.11, 1.18)**
Natural juices, unit/d					
0	3610	864,682.1	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
> 0–1	2246	667,947.0	**0.76 (0.73, 0.81)**	**0.82 (0.78, 0.87)**	**0.87 (0.82, 0.92)**
> 1–2	582	172,339.8	**0.77 (0.70, 0.84)**	**0.83 (0.76, 0.91)**	**0.88 (0.81, 0.97)**
> 2	193	48,209.8	0.87 (0.75, 1.01)	0.92 (0.79, 1.06)	0.91 (0.78, 1.05)
Per one unit/d			**0.89 (0.86, 0.92)**	**0.93 (0.90, 0.96)**	**0.94 (0.91, 0.98)**
Physical activity					
High	2276	707,675.1	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Medium	2768	740,896.2	**1.19 (1.12, 1.25)**	**1.22 (1.16, 1.29)**	**1.13 (1.06, 1.19)**
Low	1587	304,607.4	**1.66 (1.56, 1.77)**	**1.67 (1.57, 1.78)**	**1.33 (1.25, 1.42)**

Model 1 was adjusted for age, age-square, sex, and race

Model 2 was based on Model 1 and further adjusted for total energy intake, alternate healthy eating index, Townsend deprivation index, education level, physical activity (not for physical activity as exposure), smoking status, alcohol drinking status, and family history of diabetes

Model 3 was based on Model 2 and further adjusted for body mass index categories

Individual associations of SB intake and physical activity with T2D

During 1.75 million person-years of follow-up, 6,631 participants developed T2D. Consumption of SB and physical activity were both associated with the incidence of T2D (Table 2). Participants with a higher intake of SSB and ASB (> 2 vs. 0 unit/d) were at a higher hazard of T2D (HR: 1.17, 95% CI: 1.05–1.31 for SSB; 1.54, 1.37–1.74 for ASB), while those who had a medium intake of NJ were at a reduced risk ($HR_{>0-1 \text{ vs. } 0 \text{ unit/d}}$: 0.87, 95% CI: 0.82–0.920; $HR_{>1-2 \text{ vs. } 0 \text{ unit/d}}$: 0.88, 95% CI: 0.81–0.97; and $HR_{>2 \text{ vs. } 0 \text{ unit/d}}$: 0.91, 95% CI: 0.78–1.05). The HRs (95% CIs) were 1.04 (1.01–1.06), 1.14 (1.11–1.18), and 0.94 (0.91–0.98) for each unit increment in daily consumption of SSB, ASB, and NJ, respectively. When non-consumers of any SB were set as the reference group, the relations were not substantially altered (Table S1).

In addition, lower physical activity was associated with a higher risk of T2D. Compared to participants with high physical activity, those with low physical activity had a 33% increased risk of T2D (95% CI: 25%–42%), and the HR (95% CI) for those with medium physical activity was 1.13 (1.06–1.19).

The role of physical activity in SB intake and T2D associations

We did not detect significant multiplicative interactions between physical activity and SSB/ASB (P-interactions=0.204 for SSB and 0.926 for ASB, Figure 1 and Table S2). However, the association of NJ intake with T2D was significantly modified by physical activity (P-interaction=0.043). The protective association of moderate NJ intake was stronger among participants with higher physical activity.

Joint associations of SB intake and physical activity with T2D

Jointly (Table 3), participants with low physical activity and high SSB intake (> 2 units/d) were at a 1.47-fold risk of T2D (95% CI: 1.18–1.82) compared to those with

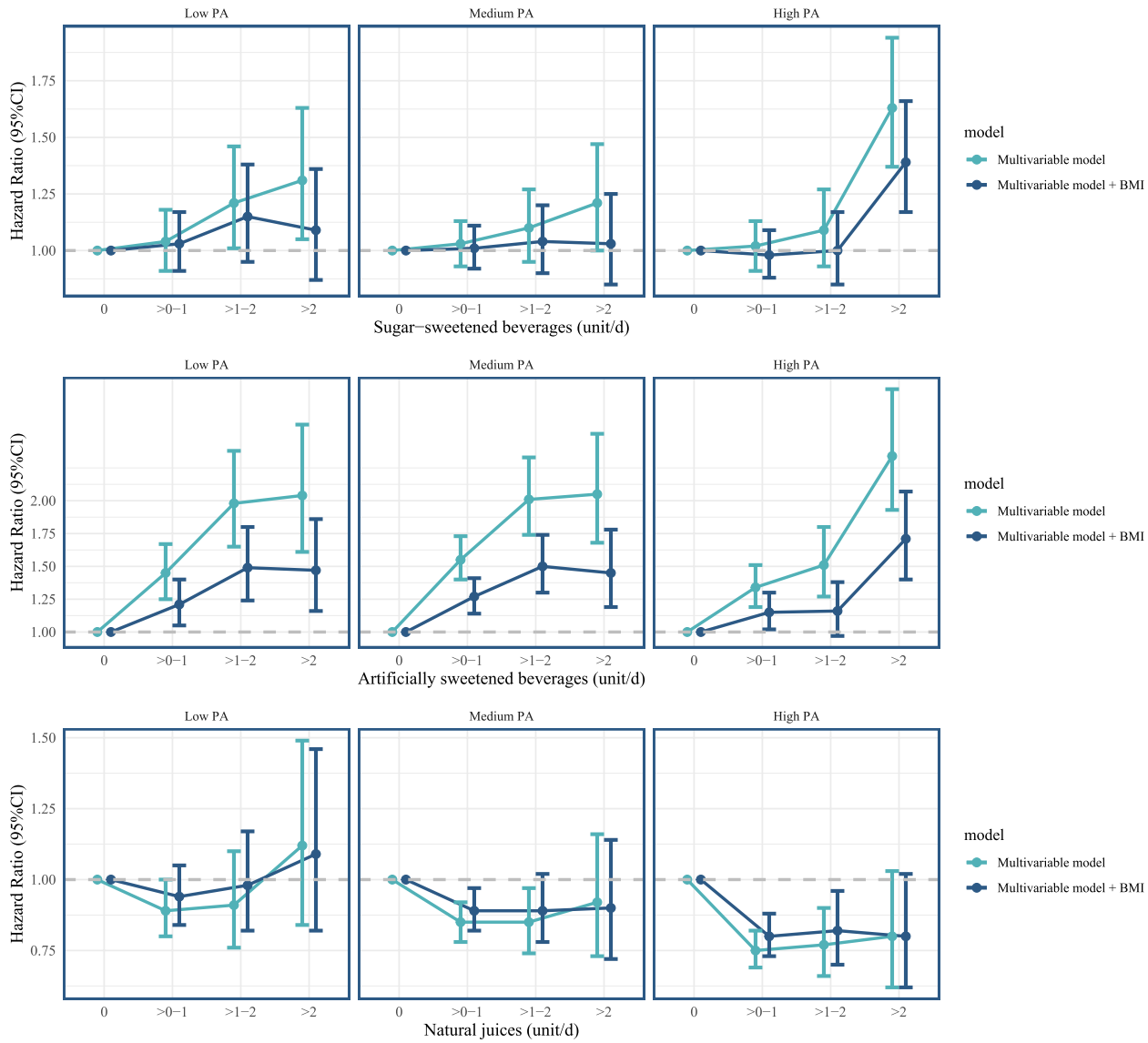

Fig. 1 Multivariable adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for type 2 diabetes according to sugary beverages intake by levels of physical activity. PA: Physical activity; BMI: Body mass index. Multivariable model was adjusted for age, age-square, sex, race, total energy intake, alternate healthy eating index, Townsend deprivation index, education level, physical activity, smoking status, drinking status, and family history of diabetes. *P*-interactions = 0.204 for SSB, 0.926 for ASB, and 0.043 for NJ

high physical activity and zero SSB intake. Similarly, individuals with low physical activity who consumed ASB > 2 units/d were at the highest risk of T2D, with an HR (95% CI) of 1.93 (1.53–2.43). In contrast, T2D risk was lowest in participants with high physical activity and medium NJ intake (0.80, 0.73–0.88 for > 0–1 units/d and 0.82, 0.70–0.95 for > 1–2 units/d, respectively). Individuals with low physical activity and zero or high NJ intake were also at higher risk (1.24, 1.13–1.35 and 1.35, 1.01–1.79, respectively).

Sensitivity analysis

When we further adjusted the models for chronic health conditions, dietary assessment indicator, or total sugar, the individual and joint associations did not substantially change (Tables S3-S6). When we excluded individuals who developed incident T2D within the first five years after baseline, the associations were generally consistent (Tables S3 and S7). When we mutually adjusted for the three SB, the associations remained similar (Table S3). The RERIs for additive interactions are presented in

Table 3 Multivariable adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for type 2 diabetes according to joint categories between sugary beverages intake and physical activity

Sugar-sweetened beverages				Artificially sweetened beverages			Natural juices		
Intake	Cases	Person-years	HR (95% CI)	Cases	Person-years	HR (95% CI)	Cases	Person-years	HR (95% CI)
High physical activity									
0	1539	497,516.7	1.00 (Reference)	1726	575,892.0	1 (Reference)	1290	349,695.8	1.00 (Reference)
> 0–1	424	131,268.5	0.97 (0.87, 1.08)	305	80,414.6	**1.16 (1.03, 1.31)**	729	266,631.2	**0.80 (0.73, 0.88)**
> 1–2	171	51,267.5	0.99 (0.84, 1.16)	136	33,700.3	1.16 (0.98, 1.39)	193	70,329.7	**0.82 (0.70, 0.95)**
> 2	142	27,622.4	**1.37 (1.15, 1.62)**	109	17,668.2	**1.71 (1.41, 2.08)**	64	21,018.5	0.80 (0.62, 1.03)
Medium physical activity									
0	1906	524,964.1	**1.13 (1.06, 1.21)**	2052	606,883.2	**1.10 (1.04, 1.18)**	1456	357,678.0	1.08 (1.00, 1.16)
> 0–1	540	139,908.5	**1.14 (1.04, 1.26)**	417	84,319.5	**1.40 (1.25, 1.56)**	983	289,373.6	0.96 (0.88, 1.04)
> 1–2	209	51,656.7	**1.17 (1.01, 1.35)**	199	32,860.8	**1.65 (1.42, 1.91)**	250	74,265.2	0.96 (0.84, 1.10)
> 2	113	24,366.9	1.17 (0.97, 1.42)	100	16,832.8	**1.59 (1.30, 1.95)**	79	19,579.5	0.97 (0.77, 1.22)
Low physical activity									
0	1061	213,344.6	**1.31 (1.21, 1.42)**	1156	245,895.5	**1.32 (1.22, 1.42)**	864	157,308.3	**1.24 (1.13, 1.35)**
> 0–1	307	57,700.0	**1.37 (1.21, 1.55)**	228	35,172.7	**1.59 (1.38, 1.83)**	534	111,942.2	**1.16 (1.05, 1.28)**
> 1–2	132	21,055.7	**1.54 (1.28, 1.84)**	128	15,032.8	**1.97 (1.65, 2.37)**	139	27,745.0	**1.21 (1.02, 1.44)**
> 2	87	12,507.1	**1.47 (1.18, 1.82)**	75	8506.4	**1.93 (1.53, 2.43)**	50	7611.9	**1.35 (1.01, 1.79)**

HRs were adjusted for age, age-square, sex, race, total energy intake, alternate healthy eating index, Townsend deprivation index, education level, smoking status, drinking status, family history of diabetes, and body mass index categories

Table S8. Compared to participants with low or medium physical activity, the adjusted RERI (95% CI) for > 1–2 units/d of NJ intake was -0.36 (-0.60–-0.12) for individuals with high physical activity.

Discussion

In this large-scale prospective study in the UK, higher SSB and ASB intake was related to higher risks of T2D, while medium NJ intake showed an inverse association with T2D. There was no evidence of interaction between SSB or ASB and physical activity in the incidence of T2D. However, we observed both significant multiplicative and additive interactions between NJ intake and physical activity, and the prospective association between medium NJ intake and T2D was more pronounced in participants with higher physical activity level. Jointly, participants with high SSB or ASB intake (> 2 units/d) combined with low physical activity were at the highest T2D risk, while those who consumed medium level of NJ (approximately 1 unit/d) and had high physical activity were at the lowest risk. Our findings on the interaction between NJ intake and physical activity implied potential synergetic roles of healthy beverage intake and physical activity in the prevention of T2D, and the independent associations for SSB, ASB, and physical activity further underscored the importance of overall healthy lifestyles in T2D prevention.

In general, our study aligned with previous evidence on the relationships of SB and physical activity with T2D. According to a recent meta-analysis of cohort studies [34], each unit/d increase in SSB consumption was related to an 11% increased risk of T2D (95% CI, 5%–17%), and the increased risk was 15% (5%–26%) for each unit/d of ASB consumption, when taking publication bias into account. Our study confirmed these associations, with corresponding HRs (95% CIs) of 1.04 (1.01–1.06) for SSB and 1.14 (1.11–1.18) for ASB. For juices, a meta-analysis showed a detrimental association with T2D (1.07, 1.01–1.14) [14], but our study showed an overall protective association (0.94, 0.91–0.98 for each unit/d) for NJ. The differences might stem from different definitions of natural juices. For example, previous studies might have included sweetened juices and commercial juice beverages in this category, thus blurring the potential associations. In the current study, we observed an inverse association for medium NJ intake (around 1 unit/d), which does not challenge the guideline's recommendation of low intake (e.g., up to 1 unit/d) of NJ [35]. In terms of physical activity, a previous meta-analysis reported that adequate physical activity was related to a 26% lower risk of T2D (16%–29%) [11], which was echoed by our findings.

To the best of our knowledge, few studies have explored the role of physical activity in the associations between SB intake and T2D and their joint associations. Interestingly, we observed no significant interactions between SSB or ASB and physical activity in the study population. Contrarily, the protective association for

moderate NJ consumption appeared stronger in those with higher physical activity level, and both multiplicative and additive interactions were significant. We observed a potentially protective effect of high NJ intake on the development of T2D in individuals with moderate or high physical activity levels, but not in those with low physical activity level. This might reflect the synergy of NJ consumption and physical activity in the prevention of T2D and warrants future investigations. Compared with participants with high physical activity and low SSB or ASB intake, those who had low physical activity and high SSB or ASB intake were at a much higher risk of T2D. On the other hand, compared with those who had a high activity but low NJ consumption, participants with moderate NJ consumption and high physical activity were at lower risk of T2D. Nevertheless, participants with a low physical activity were at a higher risk, and associations was not fully countered by NJ consumption.

As mentioned above, the shared underlying pathways of NJ and physical activity might include glycemic load and energy regulation [18]. The protective association of moderate NJ intake may be attributed to the vitamins and bioactive phytochemicals present within these beverages [36], such as hesperidin, narirutin, carotenoids, hydroxycinnamic acids, and anthocyanins [37–39]. On the other hand, since NJ also contain free sugars (primarily fructose) [40], excessive consumption may result in relatively high glycemic load values, which are related to an increased risk of T2D. This risk may be mitigated by sufficient physical activity through energy expenditure and enhanced insulin sensitivity [41, 42]. Nevertheless, the interaction was only observed for NJ rather than SSB or ASB, potentially because higher physical activity level could alter the individuals' antioxidant status [43], in harmony with the bioactive compounds with antioxidant activity contained in NJ. [44, 45]. As such, the benefits of moderate NJ intake could be further augmented in individuals with higher physical activity level. Therefore, our study provides a foundation for future studies to systematically explore the biological nature of T2D to better understand the roles of a healthy diet and adequate physical activity in T2D prevention.

Public policies for promoting healthy lifestyles are critical for T2D prevention, and our findings thus provided important information for public health practice. A high intake of SSB and ASB combined with low physical activity was related to the highest risk of T2D, which emphasized the importance of healthy beverage intake and adequate physical activity in diabetes prevention. Our findings that high physical activity tended to augment the potential protective effects of medium NJ intake and attenuate the harmful effects of SSB and ASB on the development of T2D further highlight the potential benefits of combining healthy lifestyles. In a previous meta-analysis of 14 studies, adults with the healthiest lifestyle (the most combinative healthy lifestyle factors) had a 75% (95% CI: 65%–82%) lower risk of incident diabetes [6], underscoring the role of tackling multiple risk factors simultaneously in reducing the burden of T2D. Future studies are needed to assess the joint associations and potential interactions for other lifestyle factors, such as drinking and smoking, for the development of practical strategies for diabetes prevention.

The strengths of the current study include the comprehensive investigation of the associations between SB intake and incident T2D, and considering their interaction on both multiplicative and additive scales. Other merits of this study include the large study sample size, the prospective design, long-term follow-up, and low rate of loss to follow-up. However, our study has several limitations that should be considered for when interpreting our findings. First, our findings are based on an observational cohort, which does not necessarily imply causality between the exposures and T2D. Although we adjusted the models for multiple demographic, lifestyle, and health-related confounding factors, residual confounding might still exist because both physical activity and SB intake could be associated with other underlying contributors to T2D. Furthermore, all the covariates in this study were measured earlier than the measurement of SB; therefore, some of them could change between the baseline assessment and the date when the web-based 24-h diet recalls were measured. Additionally, even though the exclusion of T2D cases in the first five years did not substantially change our findings, reverse causation is still possible because participants who had underlying health conditions might be inclined to behavioral changes. Second, data on both physical activity and beverage intake were collected using self-administer questionnaires, so measurement errors could not be eliminated. Similarly, we relied on HES for T2D ascertainment, which might introduce ascertainment bias since underdiagnosis and misclassification are possible. However, these errors are more likely to bias the associations toward null. Third, the generalizability of our findings should be further tested, because our study mostly consisted of White individuals. Finally, we could not take temporal changes in physical activity and SB intake into account because physical activity was measured only at recruitment and SB intake was measured during the introductory phase. Future studies could examine temporal relations to provide further evidence for the establishment of causal relations.

Conclusions

In conclusion, high intake of SSB and ASB was associated with higher risks of T2D, while moderate NJ intake was linked to a lower risk of T2D. We did not detect a significant interaction between physical activity and SSB/ASB intake, but the protective association of moderate NJ intake with T2D was stronger among participants with higher levels of physical activity. These findings emphasize the importance of healthy beverage choices and maintaining adequate physical activity for diabetes prevention.

Abbreviations

ASB	Artificially sweetened beverages
BMI	Body mass index
CI	Confidence interval
HES	Hospital Episode Statistics
HR	Hazard ratio
ICD	International Classification of Diseases
IPAQ	International Physical Activity Questionnaire
NJ	Natural juices
RERI	Relative excess risk due to interaction
SB	Sugary beverages
SD	Standard deviation
SSB	Sugar-sweetened beverages
T2D	Type 2 diabetes
TDI	Townsend deprivation index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12937-024-01006-3.

Supplementary Material 1.

Acknowledgements

We thank all of the participating individuals and staff of the UK Biobank who made the study possible.

Authors' contributions

Y.D., H.C. and C.Y. designed and conceptualized the study, interpreted the findings, and drafted and revised the manuscript. Y.D. and H.C. performed data analysis. J.S., L.H., and Y.Z. revised the manuscript. G.Z. provided the computing resources. Y.C. assisted data analysis. All co-authors have critically reviewed this manuscript and approved the final version of the manuscript. C.Y. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Funding

This work was supported by the Zhejiang University Global Partnership Fund (granted to CY), the National Key R&D Program of China (2023YFF1104301), the National Natural Science Foundation of China (82373576; 81922060) (granted to GZ). The funding agencies had no role in study design, data collection, analysis, decision to publish, or manuscript preparation.

Data availability

The UK Biobank data can be accessed by external researchers upon application (https://www.ukbiobank.ac.uk/enable-your-research/apply-for-access).

Declarations

Ethics approval and consent to participate

This research was conducted using the UK Biobank resource under application number 55005. The UK Biobank study was approved by the North West Multi-Center Research Ethics Committee, and all participants provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]School of Public Health, the Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China. [2]CAS Key Laboratory of Nutrition, Metabolism and Food Safety, Shanghai Institute of Nutrition and Health, University of Chinese Academy of Sciences, Chinese Academy of Sciences, Shanghai, China. [3]State Key Laboratory of Genetic Engineering, School of Life Sciences, Fudan University, Shanghai, China. [4]Ministry of Education Key Laboratory of Public Health Safety, School of Public Health, Fudan University, Shanghai, China. [5]Department of Nutrition, Harvard T. H. Chan School of Public Health, Boston, MA, USA.

Received: 18 July 2024 Accepted: 21 August 2024
Published online: 07 November 2024

References

1. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2019;157:107843.
2. IDF Diabetes Atlas 10th Edition. https://diabetesatlas.org/data/. Accessed 10 Aug 2022.
3. Williams R, Karuranga S, Malanda B, Saeedi P, Basit A, Besançon S, et al. Global and regional estimates and projections of diabetes-related health expenditure: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2020;162:108072.
4. Zimmet PZ, Magliano DJ, Herman WH, Shaw JE. Diabetes: a 21st century challenge. Lancet Diabetes Endocrinol. 2014;2:56–64.
5. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018;14:88–98.
6. Zhang Y, Pan X-F, Chen J, Xia L, Cao A, Zhang Y, et al. Combined lifestyle factors and risk of incident type 2 diabetes and prognosis among individuals with type 2 diabetes: a systematic review and meta-analysis of prospective cohort studies. Diabetologia. 2020;63:21–33.
7. Bellou V, Belbasis L, Tzoulaki I, Evangelou E. Risk factors for type 2 diabetes mellitus: an exposure-wide umbrella review of meta-analyses. PLoS ONE. 2018;13: e0194127.
8. Wild SH, Byrne CD. Risk factors for diabetes and coronary heart disease. BMJ. 2006;333:1009–11.
9. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393–403.
10. Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, et al. Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association. Diabetes Care. 2016;39:2065–79.
11. Wahid A, Manek N, Nichols M, Kelly P, Foster C, Webster P, et al. Quantifying the association between physical activity and cardiovascular disease and diabetes: a systematic review and meta-analysis. J Am Heart Assoc. 2016;5:e002495.
12. Catenacci VA, Wyatt HR. The role of physical activity in producing and maintaining weight loss. Nat Rev Endocrinol. 2007;3:518–29.
13. Onaade O, Maples JM, Rand B, Fortner KB, Zite NB, Ehrlich SF. Physical activity for blood glucose control in gestational diabetes mellitus: rationale and recommendations for translational behavioral interventions. Clin Diabetes Endocrinol. 2021;7:7.
14. Imamura F, O'Connor L, Ye Z, Mursu J, Hayashino Y, Bhupathiraju SN, et al. Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: systematic review, meta-analysis, and estimation of population attributable fraction. BMJ. 2015;351:h3576.
15. Deshpande G, Mapanga RF, Essop MF. Frequent sugar-sweetened beverage consumption and the onset of cardiometabolic diseases: cause for concern? J Endocr Soc. 2017;1:1372–85.

16. Gill JM, Sattar N. Fruit juice: just another sugary drink? Lancet Diabetes Endocrinol. 2014;2:444–6.
17. WHO guideline : sugar consumption recommendation. https://www.who.int/news/item/04-03-2015-who-calls-on-countries-to-reduce-sugars-intake-among-adults-and-children. Accessed 14 Oct 2021.
18. Vuori IM. Health benefits of physical activity with special reference to interaction with diet. Public Health Nutr. 2001;4:517–28.
19. Critchley CR, Hardie EA, Moore SM. Examining the psychological pathways to behavior change in a group-based lifestyle program to prevent type 2 diabetes. Diabetes Care. 2012;35:699–705.
20. Hernández-Alvarez MI, Thabit H, Burns N, Shah S, Brema I, Hatunic M, et al. Subjects with early-onset type 2 diabetes show defective activation of the skeletal muscle PGC-1α/Mitofusin-2 regulatory pathway in response to physical activity. Diabetes Care. 2009;33:645–51.
21. Gauthier AC, de Guimarães RF, Namiranian K, Drapeau V, Mathieu ME. Effect of physical exercise on taste perceptions: a systematic review. Nutrients. 2020;12:2741.
22. Cordain L, Gotshall RW, Eaton SB. Physical activity, energy expenditure and fitness: an evolutionary perspective. Int J Sports Med. 1998;19:328–35.
23. Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, et al. UK Biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old Age. PLoS Med. 2015;12:e1001779.
24. Bycroft C, Freeman C, Petkova D, Band G, Elliott LT, Sharp K, et al. The UK Biobank resource with deep phenotyping and genomic data. Nature. 2018;562:203–9.
25. Galante J, Adamska L, Young A, Young H, Littlejohns TJ, Gallacher J, et al. The acceptability of repeat Internet-based hybrid diet assessment of previous 24-h dietary intake: administration of the Oxford WebQ in UK Biobank. Br J Nutr. 2016;115:681–6.
26. Liu B, Young H, Crowe FL, Benson VS, Spencer EA, Key TJ, et al. Development and evaluation of the Oxford WebQ, a low-cost, web-based method for assessment of previous 24 h dietary intakes in large-scale prospective studies. Public Health Nutr. 2011;14:1998–2005.
27. Greenwood DC, Hardie LJ, Frost GS, Alwan NA, Bradbury KE, Carter M, et al. Validation of the Oxford WebQ Online 24-Hour dietary questionnaire using biomarkers. Am J Epidemiol. 2019;188:1858–67.
28. Anderson JJ, Gray SR, Welsh P, Mackay DF, Celis-Morales CA, Lyall DM, et al. The associations of sugar-sweetened, artificially sweetened and naturally sweet juices with all-cause mortality in 198,285 UK Biobank participants: a prospective cohort study. BMC Med. 2020;18:97.
29. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003;35:1381–95.
30. Cassidy S, Chau JY, Catt M, Bauman A, Trenell MI. Cross-sectional study of diet, physical activity, television viewing and sleep duration in 233 110 adults from the UK Biobank; the behavioural phenotype of cardiovascular disease and type 2 diabetes. BMJ Open. 2016;6:e010038.
31. Said MA, Verweij N, van der Harst P. Associations of Combined Genetic and Lifestyle Risks With Incident Cardiovascular Disease and Diabetes in the UK Biobank Study. JAMA Cardiology. 2018;3:693–702.
32. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894:i-xii–1-253.
33. Andersson T, Alfredsson L, Källberg H, Zdravkovic S, Ahlbom A. Calculating measures of biological interaction. Eur J Epidemiol. 2005;20:575–9.
34. Qin P, Li Q, Zhao Y, Chen Q, Sun X, Liu Y, et al. Sugar and artificially sweetened beverages and risk of obesity, type 2 diabetes mellitus, hypertension, and all-cause mortality: a dose-response meta-analysis of prospective cohort studies. Eur J Epidemiol. 2020;35:655–71.
35. Mozaffarian D. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: a comprehensive review. Circulation. 2016;133:187–225.
36. Clemens R, Drewnowski A, Ferruzzi MG, Toner CD, Welland D. Squeezing fact from fiction about 100% fruit juice. Adv Nutr. 2015;6:236S-243S.
37. Bestwick C, Scobbie L, Milne L, Duncan G, Cantlay L, Russell W. Fruit-based beverages contain a wide range of phytochemicals and intervention targets should account for the individual compounds present and their availability. Foods. 2020;9:891.
38. Grosso G, Galvano F, Mistretta A, Marventano S, Nolfo F, Calabrese G, et al. Red orange: experimental models and epidemiological evidence of its benefits on human health. Oxid Med Cell Longev. 2013;2013:157240.
39. Aschoff JK, Rolke CL, Breusing N, Bosy-Westphal A, Högel J, Carle R, et al. Bioavailability of β-cryptoxanthin is greater from pasteurized orange juice than from fresh oranges - a randomized cross-over study. Mol Nutr Food Res. 2015;59:1896–904.
40. Pepin A, Stanhope KL, Imbeault P. Are Fruit Juices Healthier Than Sugar-Sweetened Beverages? A review. Nutrients. 2019;11:1006.
41. van der Velde JHPM, Boone SC, Winters-van Eekelen E, Hesselink MKC, Schrauwen-Hinderling VB, Schrauwen P, et al. Timing of physical activity in relation to liver fat content and insulin resistance. Diabetologia. 2023;66:461–71.
42. Zinman B, Ruderman N, Campaigne BN, Devlin JT, Schneider SH. American Diabetes Association. Physical activity/exercise and diabetes mellitus. Diabetes Care. 2003;26 Suppl 1:S73-77.
43. Rousseau A-S, Margaritis I, Arnaud J, Faure H, Roussel A-M. Physical activity alters antioxidant status in exercising elderly subjects. J Nutr Biochem. 2006;17:463–70.
44. El Assar M, Álvarez-Bustos A, Sosa P, Angulo J, Rodríguez-Mañas L. Effect of physical activity/exercise on oxidative stress and inflammation in muscle and vascular aging. Int J Mol Sci. 2022;23:8713.
45. Crowe-White K, Parrott JS, Stote KS, Gutschall M, Benson-Davies S, Droke E, et al. Metabolic impact of 100% fruit juice consumption on antioxidant/oxidant status and lipid profiles of adults: an Evidence-Based review. Crit Rev Food Sci Nutr. 2017;57:152–62.

Publisher's Note