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Sweetened Beverages and Incident All-Cause Dementia Among Older Adults

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IMPORTANCE Intake of sweetened beverages, including sugar-sweetened beverages (SSB) and artificially sweetened beverages (ASB), has been linked to multiple health outcomes, but their associations with dementia risk among older adults are unclear.

OBJECTIVE To assess whether the consumption of SSB and ASB is associated with the risk of all-cause dementia in older adults.

DESIGN, SETTING, AND PARTICIPANTS This multicohort study examined data from US adults aged 65 and older enrolled in the Health and Retirement Study (2013), the Atherosclerosis Risk in Communities study (1987-1995), the Chicago Healthy and Aging Project (1993-2012), the Rush Memory and Aging Project (1997-2005), the Framingham Heart Study original cohort (1986-1994), and its offspring cohort (1991-2001). Data were analyzed from May 27 to September 24, 2024.

EXPOSURES SSB and ASB intake was assessed using validated food frequency questionnaires.

MAIN OUTCOMES AND MEASURES The primary outcome was all-cause dementia ascertained at least 2 years after baseline from active research follow-ups and passive surveillance. Cox proportional hazard regression models were used to assess the associations of SSB and ASB with incident dementia.

RESULTS Of 10 974 participants (60.0% female, mean [SD] age: 73.2 [6.8] years), 2445 developed incident all-cause dementia over 116 067 person-years of follow-up. Consumption of SSB and ASB in older adulthood was not associated with dementia risk in later life. The pooled hazard ratio (HR) per serving per week for SSB was 0.99 (95% CI, 0.98-1.01; $P = .18$; $I^2 = 0\%$) and for ASB was 1.00 (95% CI, 0.99-1.01; $P = .99$; $I^2 = 1\%$). The pooled HRs comparing the highest (≥1 serving per day) with lowest (0 to <1 serving per month) consumption groups were 0.90 (95% CI, 0.78-1.03) for SSB and 1.00 (95% CI, 0.83-1.21) for ASB. These findings were similar across cohorts and subgroups. In contrast, an inverse association was observed for the Mediterranean diet score (HR, 0.92; 95% CI, 0.85-0.99 per 5-unit increment) as a positive control.

CONCLUSIONS AND RELEVANCE In this study, late-life consumption of SSB or ASB was not associated with the risk of dementia. However, given their detrimental effects on metabolic health and related chronic diseases during early life and midlife, the effects of early-life consumption of SSB and ASB on the risk of dementia warrant further investigation.

Supplemental content

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Dementia is a clinical syndrome characterized by cognitive decline severe enough to interfere with daily life and independence, primarily caused by neurodegeneration.[1] It imposes significant burdens on individuals and health care systems.[1,2] This underscores the need for primary prevention strategies and research aimed at identifying risk factors.[1,3] Diet, a modifiable risk factor, has been linked to dementia risk, making it a target for primary prevention strategies.[4,5] Excessive sugar consumption[6] contributes to the burden of metabolic diseases such as obesity and diabetes,[7,8] which are important risk factors for dementia.[9] Sugar-sweetened beverages (SSB) are a major source of sugar intake,[10] and approximately 20% of older adults had daily consumptions of SSB in the US as of 2013.[11] Animal studies have shown that excessive sugar intake, including that from SSB, contributed to Alzheimer disease (AD)-like pathologic features, including upregulation of apolipoprotein E and accelerated aggregation of β-amyloid.[12] Nevertheless, the brain is the most energy-demanding organ and may need sufficient and efficient energy sources; simple sugar serves as one of the main fuels,[13,14] and the complexities of this association necessitate further investigations.

Previous population-based evidence on the association of sweetened beverages with dementia is still scarce and inconclusive.[15-19] In the UK Biobank, higher intake of SSB (>2 units per day vs none) was associated with higher risks of all-cause dementia and AD,[15,20] while another community-based study in the US reported no association.[16] Artificially sweetened beverages (ASB), marketed as a healthier alternative, also raised concerns with respect to their potential neuropsychologic effects, while existing evidence is mixed.[15,16] These inconsistencies may result from the differences in dietary assessment methods, the accuracy of dementia diagnosis, and age range in the population at dietary assessments.[4] As underdiagnosis and misclassification are common concerns in dementia research, active follow-up is essential to minimize potential biases and improve diagnostic accuracy. More importantly, given the long preclinical phase of dementia,[4,21] long-term follow-up is needed, as prediagnosis cognitive decline and mental disorders may affect dietary habits.[21] To address these knowledge gaps, we evaluated whether SSB and ASB consumption was associated with the risk of all-cause dementia in 6 US cohort studies, leveraging validated diet measurement methods and long-term active follow-up for dementia diagnosis.

Key Points

Question Is consumption of sugar-sweetened beverages (SSB) and artificially sweetened beverages (ASB) associated with risk of all-cause dementia in adults aged 65 and older?

Findings In this multicohort study including data from 10 974 older adults in the US, consumption of SSB and ASB was not associated with the risk of all-cause dementia during a mean follow-up of 10.7 years. The pooled hazard ratios per serving per week were 0.99 for SSB and 1.00 for ASB.

Meaning In this study, higher late-life consumption of SSB and ASB was not associated with the risk of dementia among older individuals; however, early-life consumption of sugar-sweetened and artificially sweetened beverages and risk of dementia warrant further investigation.

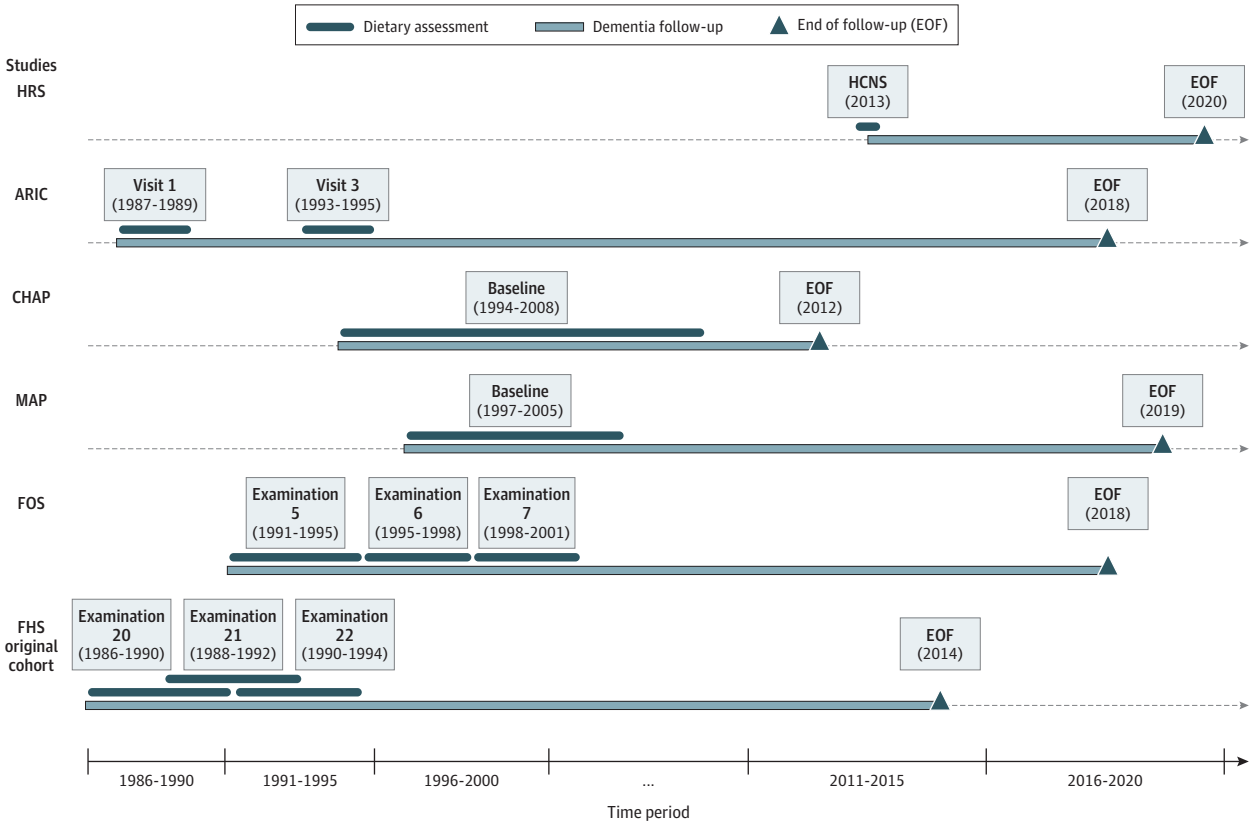
Methods

Study Participants

We harmonized individual-level data from 6 prospective studies: the Health and Retirement Study (HRS [2013]), the Atherosclerosis Risk in Communities (ARIC [1987-1995]) study, the Chicago Healthy and Aging Project (CHAP [1993-2012]), the Rush Memory and Aging Project (MAP [1997-2005]), the Framingham Heart Study (FHS) original cohort (1986-1994), and its offspring cohort (FOS [1991-2001]). Data were analyzed from May 27 to September 24, 2024. The HRS is a large nationally representative survey of community-dwelling adults aged 50 years or older,[22] and dietary assessment was administered in the 2013 Health Care and Nutrition Study (n = 8035). Commenced in 1987-1989, the ARIC recruited 15 792 participants aged 44-66 years from field centers in 4 US communities,[23] with 2 diet assessments at visits 1 (1987-1989) and 3 (1993-1995). The CHAP began in 1993 and has enrolled 10 802 individuals 65 years of age or older in Chicago, Illinois, as of 2012,[24] and participants completed a dietary assessment after recruitment. The MAP (n = 2022) is an ongoing population-based cohort study since 1997 in the Chicago metropolitan area.[25] From 2004, MAP participants were invited to complete dietary assessments at the annual clinical evaluations. The FHS is a community-based cohort study since 1948.[26] Surviving participants of the original cohort aged 67 to 96 years completed the dietary assessments in the 20th, 21st, and 22nd examinations (1986-1994). Children of the original cohort and their spouses formed the FOS cohort in 1971 and completed dietary assessments in examinations 5 (1991-1995), 6 (1995-1998), and 7 (1998-2001).[27] This study followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies. The HRS was approved by the University of Michigan, the ARIC was approved by each participating site, the CHAP and MAP were approved by Rush University Medical Center, and the FHS original cohort and FOS were approved by the Boston University Medical Center. All participants provided written informed consent. This pooling project was approved by School of Public Health, Zhejiang University.

We included participants aged 65 years or older with valid dietary information (total energy intake 500-3500 kcal/d for women, 800-4200 kcal/d for men[28]). We defined baseline as the date of completion of (the latest) food frequency questionnaire (FFQ) and excluded participants without information on dementia diagnosis or with dementia at baseline and those who developed dementia in the first 2 years of follow-up. Therefore, dietary assessments preceded the ascertainment of dementia by at least 2 years. Of the remaining participants, we excluded those with a history of stroke before or at baseline because it may directly and substantially impact cognitive status (eFigure 1 in Supplement 1). The study time-

Figure 1. Graphical Representation of Exposure and Outcome Assessment in the 6 Studies



The ellipses between 1996-2000 and 2011-2015 indicate a gap in the timeline in which few major study events occurred relevant to this analysis. ARIC indicates Atherosclerosis Risk in Communities; CHAP, Chicago Healthy and Aging Project; FHS, Framingham Heart Study; FOS, Framingham Offspring Study; HCNS, Health Care and Nutrition Study; HRS, Health and Retirement Study; MAP, Rush Memory and Aging Project.

frames and follow-up periods for each cohort are shown in **Figure 1**.

Assessment of Sweetened Beverages Intake

Despite some cohort-specific modifications, intake levels of SSB and ASB in all 6 cohorts were assessed using FFQ[29-33] based on the extensively validated Harvard FFQ.[34] In HRS, CHAP, and MAP, we used the FFQ administered at baseline to collect information on beverage intake. In ARIC, FHS original cohort, and FOS, we calculated average amounts from the repeated assessments. We summed the intake of sugary fruit beverages, sugar-sweetened soft drinks, and carbonated drinks as SSB and low-calorie and diet drinks as ASB. To ensure statistical power, we amalgamated the intake categories into never or less than 1 serving per month (reference), 1 to less than 4 servings per month, 1 to less than 7 servings per week, and 1 or more servings per day based on previous literature[35] and the population distribution.

Ascertainment of Dementia

The outcome in this study was all-cause dementia ascertained at least 2 years after baseline, combining results from active follow-ups and passive collection of diagnosis information in all cohorts. In HRS, dementia was identified according to the Langa-Weir criteria using data from objectively measured cognitive function and proxy interviews.[36] In ARIC, dementia was ascertained from in-person or telephone cognitive assessments, informant interviews, or hospitalization codes or death certificates, and cases were reviewed by a panel of neurologists.[37] In CHAP, MAP, FHS original cohort, and FOS, dementia was ascertained by a team of clinicians led by neurologists and neuropsychologists based on a structured medical history, neurologic examination, and a battery of several cognitive tests.[24,25,38] Details are described in eMethods in Supplement 1.

Covariates

We used questionnaires completed at and before baseline to collect the information on age, sex (male or female), race and ethnicity (American Indian or Alaska Native; Asian; Black or African American; Native Hawaiian or Other Pacific Islander; White; or other [participants describing themselves as race or ethnicity other than the prespecified categories]) (not available in FHS original cohort), educational level (below college or college and above), smoking status (current, former, or never smokers), physical activity, total energy intake, Mediterranean diet score, and body mass index (BMI) categories calculated as weight in kilograms divided by height in meters

squared (<25, ≥25 to <30, or ≥30), depressive symptom, type 2 diabetes (T2D, yes or no), hypertension (yes or no), hypercholesterolemia (yes or no, not available in HRS, CHAP, and MAP), and heart diseases (yes or no). Race and ethnicity was included as a covariate to account for known disparities in dementia risk across these groups. Specifically, the Mediterranean diet score that reflects Mediterranean diet adherence has been extensively studied and found to be associated with better cognition in existing literature.[39] We primarily used covariates collected concurrently with FFQ completion. If such data were missing, the values were carried forward from previous visits, and the remaining missing values were imputed with multiple imputation with chained equations.[40] Details of their measurements were described in eMethods in Supplement 1.

Statistical Analysis

For descriptive statistics, continuous variables were presented as mean (SD), and categorical variables as number (percentage). The missing rates of covariates were presented in eTable 1 in Supplement 1. Cox proportional hazard regression models were used to examine the associations of SSB and ASB with incident all-cause dementia. Survival time for each observation was calculated from the baseline of each cohort (date of the latest FFQ) to the date of incident dementia, death, loss to follow-up, or the end of follow-up, whichever occurred first. Hazard ratios (HRs) and 95% CIs were estimated with sequential adjustments for covariates, with proportional hazard assumption verified using the Schoenfeld residual method. We analyzed data from each cohort separately and pooled their estimates using random-effects models.[41]

Stratified analyses were performed by age (<75 years or ≥75 years), sex (male or female), BMI category (<30.0 or ≥30.0), and the existence of chronic diseases (T2D, hypertension, hypercholesterolemia, heart disease, yes or no), and interaction terms were tested using likelihood ratio test. We conducted several sensitivity analyses to assess the robustness of the primary findings. First, we mutually adjusted for SSB and ASB to test their independent associations with incident dementia. Second, we further excluded participants who developed dementia in the first 5 years of follow-up because early preclinical changes such as sensory alternations may affect dietary intake behaviors. Moreover, given the long latency of dementia, dietary intake may be less likely to affect risk over a short follow-up period. Third, we restricted our analyses to participants without baseline T2D, because participants with T2D may change their beverage consumption pattern after diagnosis. Fourth, we excluded participants with heart disease at the study baseline. Fifth, considering the competing risk between mortality and incident dementia, we repeated the main analyses using the Fine-Gray competing risk model.[42] As a post hoc positive control analysis to verify that the null associations were not due to dementia misclassification or dietary measurement error, we assessed the association of the Mediterranean diet score with incident dementia.

Statistical analyses were performed using R version 4.3.0 (R Project for Statistical Computing). We reported 2-sided *P* values throughout and $P < .05$ indicated statistical significance.

Results

Baseline Characteristics of Participants

According to inclusion and exclusion criteria, a total of 10 974 participants were included. The mean (SD) age at baseline was 73.2 (6.8) years, and 60.0% participants were female (**Table 1**). Detailed information on the race and ethnicity of study participants is shown in Table 1. The medians (IQRs) of SSB intake ranged from 0.00 (0.00-1.00) servings per week in MAP to 1.25 (0.25-4.00) servings per week in ARIC. ASB intake was lowest in CHAP and MAP (median, 0.00; IQR, 0.00-0.50) and highest in ARIC (median 1.00; IQR, 0.00-4.00) (eTable 2 in Supplement 1).

Association of Sweetened Beverages With Incident Dementia

Over 116 067 person-years, 2445 participants (324 of 18 370 person-years in HRS; 1010 of 48 859 person-years in ARIC; 323 of 11 232 person-years in CHAP; 266 of 15 834 person-years in MAP; 226 of 13 179 person-years in FOS; and 296 of 8593 person-years in FHS original cohort) developed incident all-cause dementia. The incidence rates were 17.6 per 1000-person-years in HRS, 20.7 per 1000-person-years in ARIC, 28.8 per 1000-person-years in CHAP, 16.8 per 1000-person-years in MAP, 17.1 per 1000-person-years in FOS, and 34.4 per 1000-person-years in FHS original cohort (eFigure 2 in Supplement 1).

Consumptions of the 2 types of sweetened beverages were not significantly associated with the risk of incident dementia. In the multivariable-adjusted model, the pooled HRs per serving/week increment were 0.99 (95% CI, 0.98-1.01; P = .18 for trend) for SSB and 1.00 (95% CI, 0.99-1.01; P = .99) for ASB (**Figure 2**). These findings were consistently shown in multiple models with different sets of covariates (eTables 3 and 4 in Supplement 1) and showed minimal heterogeneity across studies (I^2 = 0% for SSB and 4% for ASB). The pooled HRs comparing 1 or more servings per day vs 0 to less than 1 serving per month of intake were 0.90 (95% CI, 0.78-1.03) for SSB intake of SSB and 1.00 (95% CI, 0.84-1.21) for ASB (**Table 2**). One serving per week substitution of SSB with ASB was not associated with the risk of incident all-cause dementia (pooled HR, 1.01; 95% CI, 0.98-1.04) (eFigure 3 in Supplement 1).

Subgroup and Sensitivity Analyses

The findings for SSB and ASB in terms of dementia did not substantially differ across major subgroups of participants defined by age, sex, BMI category, and chronic disease (**Figure 3**; eTables 5 and 6 in Supplement 1). Among individuals aged 75 years or older, the pooled HR for ASB intake (per serving per week) was 1.03 (95% CI, 1.00-1.06).

In the sensitivity analyses, the findings for sweetened beverages and dementia risk were similar to the primary analysis results. When we mutually adjusted for the 2 sweetened beverages or excluded incident dementia cases that occurred within the first 5 years of follow-up, the findings were unchanged. The findings were also consistent when restricted to

Table 1. Baseline Characteristics of Study Participants

Variable	Cohort, No. (%)						
	Overall (N = 10 974)	HRS (n = 3172)	ARIC (n = 3082)	CHAP (n = 1494)	MAP (n = 1279)	FOS (n = 1103)	FHS original cohort (n = 844)
Age, mean (SD), y	73.2 (6.8)	74.7 (6.8)	67.4 (1.7)	74.9 (5.6)	81.0 (6.8)	70.8 (4.4)	77.5 (4.4)
Sex							
Female	6580 (60.0)	1920 (60.5)	1593 (51.7)	948 (63.5)	969 (75.8)	611 (55.4)	539 (63.9)
Male	4394 (40.0)	1252 (39.5)	1489 (48.3)	546 (36.5)	310 (24.2)	492 (44.6)	305 (36.1)
Race and ethnicity[a]							
American Indian or Alaska Native	NA	NA	0	1 (0.1)	4 (0.3)	NA	NA
Asian	NA	NA	0	0	6 (0.5)	NA	NA
Black or African American	NA	366 (11.5)	551 (17.9)	783 (52.4)	50 (3.9)	NA	NA
Native Hawaiian or Other Pacific Islander	NA	NA	0	2 (0.1)	1 (0.1)	NA	NA
White	NA	2692 (84.9)	2531 (82.1)	708 (47.4)	1212 (94.8)	1093 (99.1)	NA
Other[b]	NA	114 (3.6)	0	0	6 (0.5)	10 (0.9)	NA
Tertiary education	5226 (47.6)	1526 (48.1)	1303 (42.3)	741 (49.7)	742 (58.0)	609 (55.2)	305 (36.1)
Current smoker	1002 (9.1)	214 (6.7)	431 (14.0)	176 (11.8)	27 (2.1)	80 (7.3)	74 (8.8)
Physical exercise							
<1 Time/wk	NA	884 (27.9)	NA	NA	NA	NA	NA
≥1 and <3 Times/wk	NA	1229 (38.7)	NA	NA	NA	NA	NA
≥3 Times/wk	NA	1059 (33.4)	NA	NA	NA	NA	NA
Physical exercise score[c]	NA	NA	2.6 (0.8)	NA	3.6 (3.7)	38.6 (6.3)	33.6 (5.4)
Physical exercise time, mean (SD), min/wk	NA	NA	NA	219.7 (323.2)	NA	NA	NA
BMI							
<25	3386 (31.2)	929 (29.3)	896 (29.1)	465 (33.6)	455 (35.6)	342 (31.0)	299 (35.4)
≥25 and <30	4364 (40.2)	1211 (38.2)	1270 (41.2)	573 (41.3)	484 (37.8)	469 (42.5)	357 (42.3)
≥30	3116 (28.7)	1032 (32.5)	916 (29.7)	348 (25.1)	340 (26.6)	292 (26.5)	188 (22.3)
Energy intake, mean (SD), kcal/d	1704.0 (581.1)	1743.4 (662.2)	1598.2 (516.5)	1723.4 (589.9)	1731.2 (549.8)	1789.0 (502.9)	1755.7 (550.7)
Mediterranean diet score, mean (SD)[d]	28.0 (5.4)	27.9 (5.6)	25.3 (4.0)	28.8 (4.9)	32.3 (5.4)	29.4 (5.0)	29.1 (5.0)
Depressive symptom score, mean (SD)[e]	NA	1.1 (1.7)	29.9 (7.4)	1.3 (1.7)	1.0 (1.5)	14.1 (4.5)	NA
Depressive symptom	NA	NA	NA	NA	NA	NA	23 (2.7)
Type 2 diabetes	1947 (17.7)	782 (24.7)	553 (17.9)	237 (15.9)	143 (11.2)	172 (15.6)	60 (7.1)
Hypertension	6359 (57.9)	2081 (65.6)	1559 (50.6)	697 (46.7)	726 (56.8)	679 (61.6)	617 (73.1)
Hypercholesterolemia	NA	NA	1949 (63.2)	NA	NA	760 (68.9)	186 (22.0)
Heart disease	1940 (17.8)	892 (28.1)	309 (10.0)	173 (11.6)	105 (8.2)	216 (19.6)	245 (29.0)

Abbreviations: ARIC, Atherosclerosis Risk in Communities; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CHAP, Chicago Healthy and Aging Project; FHS, Framingham Heart Study; FOS, Framingham Offspring Study; HCNS, Health Care and Nutrition Study; HRS, Health and Retirement Study; MAP, Rush Memory and Aging Project; NA, not applicable.

[a] Information on race and ethnicity was obtained based on prespecified categories in questionnaires completed at and before baseline.

[b] Participants describing themselves as race or ethnicity other than the prespecified categories (not available in FHS original cohort).

[c] In ARIC, physical activity was measured via the Baecke questionnaire. In MAP, physical activity was measured based on the sum of self-reported minutes spent over the previous 2 weeks on 5 activities. In FOS and FHS original cohort, physical activity was measured using Physical Activity Index based on oxygen consumption or metabolic equivalents.

[d] Mediterranean diet score, range 0-55, where higher scores connote greater accordance. In ARIC, the maximum number of points for the Mediterranean diet score was 50 due to the lack of information on olive oil.

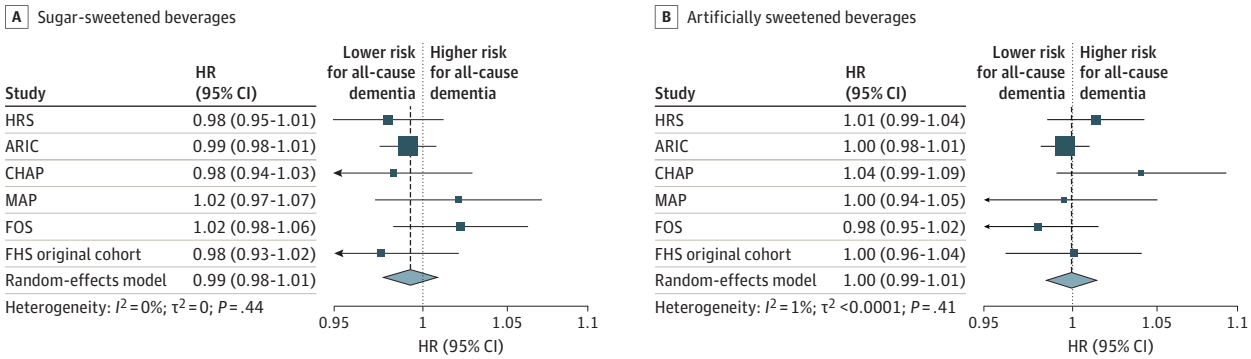
[e] The depressive symptom score was assessed by the validated 8-item Center for Epidemiologic Studies-Depression (CES-D) scale in HRS (scored from 0 to 8), 10-item CES-D scale in CHAP and MAP (scored from 0 to 10), 21-item Vital Exhaustion Questionnaire in ARIC (scored from 0 to 42), and 20-item CES-D scale in FOS (scored from 0 to 40).

participants without T2D or heart disease and competing risk of mortality was accounted for (eTable 7 in Supplement 1). In a post hoc analysis, the pooled HR for every 5-point increment in the Mediterranean diet score increment was 0.92 (95% CI, 0.86-0.99) (eTable 8 in Supplement 1).

Discussion

In 6 prospective cohorts with a total of 10 974 older adults and more than 2000 incident all-cause dementia cases, we did not

Figure 2. Forest Plots for the Associations of Sugar-Sweetened and Artificially Sweetened Beverages With Risk of All-Cause Dementia



We estimated hazard ratios (HRs) and 95% CIs from individual cohorts using Cox proportional hazard regression models adjusted for age, sex, ethnicity (not in Framingham Heart Study [FHS] original cohort), educational level, smoking status (not in Rush Memory and Aging Project [MAP]), physical activity, body mass index, total energy intake, Mediterranean diet score, depressive symptom, diabetes, hypertension, hypercholesterolemia (not in Health and Retirement Study [HRS]), and heart diseases. The pooled estimates were from random-effects models. ARIC indicates Atherosclerosis Risk in Communities; CHAP, Chicago Healthy and Aging Project; FOS, Framingham Offspring Study.

Table 2. Associations of Sugar-Sweetened and Artificially Sweetened Beverages With Risk of All-Cause Dementia

Variable	Sugar-sweetened beverages					Artificially sweetened beverages				
	No. of participants	No. of cases	Person-years	Pooled HR (95% CI)		No. of participants	No. of cases	Person-years	Pooled HR (95% CI)	
				Multivariable model 1[a]	Multivariable model 2[b]				Multivariable model 1[a]	Multivariable model 2[b]
Beverage intake category										
0 To <1 servings/mo	3648	743	36 737.3	1 [Reference]	1 [Reference]	5181	1137	50 728.4	1 [Reference]	1 [Reference]
1 To <4 servings/mo	2354	517	25 179.3	0.99 (0.86-1.13)	1.01 (0.83-1.23)	1746	402	19 346.6	0.96 (0.80-1.15)	0.99 (0.81-1.20)
1 To <7 servings/wk	3800	917	41 953.0	1.11 (0.92-1.34)	1.02 (0.88-1.18)	2875	676	33 238.0	1.02 (0.86-1.22)	1.06 (0.86-1.32)
≥1 Servings/d	1169	268	12 180.1	1.07 (0.88-1.30)	0.90 (0.78-1.03)	1153	228	12 631.5	1.04 (0.82-1.31)	1.01 (0.84-1.21)
Per serving/wk increment	NA	NA	NA	1.01 (0.99-1.03)	0.99 (0.98-1.01)	NA	NA	NA	1.00 (0.99-1.02)	1.00 (0.99-1.01)
P value for trend	NA	NA	NA	.23	.18	NA	NA	NA	.63	.99

Abbreviations: HR, hazard ratio; NA, not applicable.

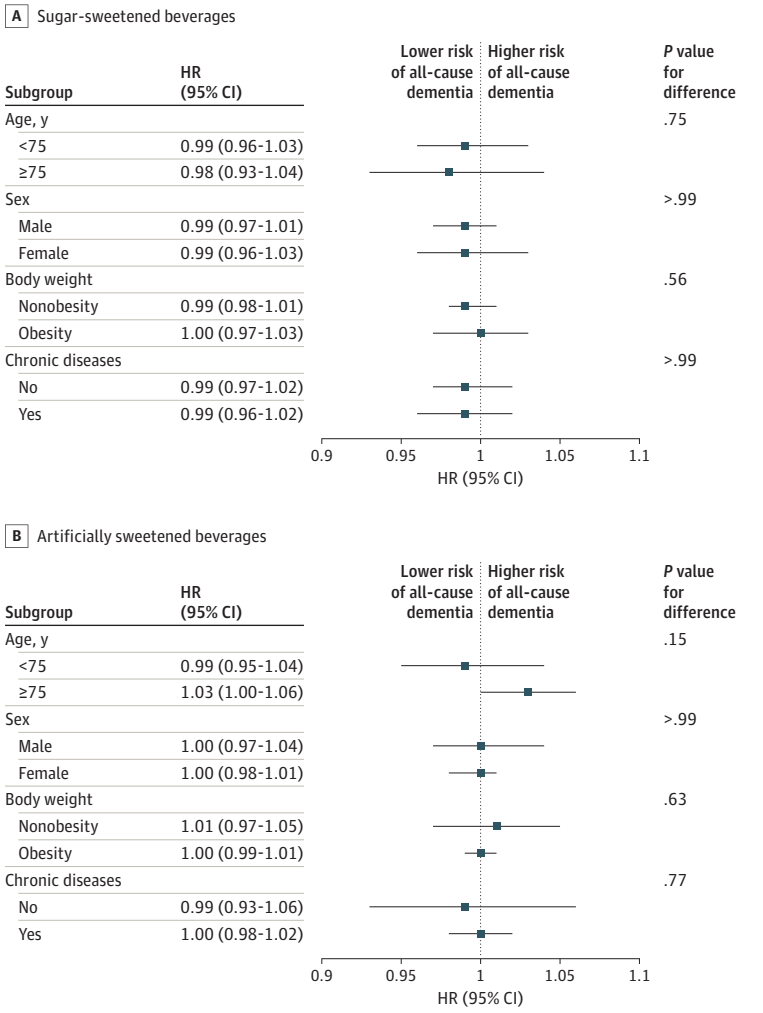
[a] Multivariable model 1 was adjusted for age and sex.

[b] Multivariable model 2 was adjusted for age, sex, ethnicity (not in Framingham Heart Study original cohort), educational level, smoking status (not in Rush Memory and Aging Project), physical activity, body mass index, total energy intake, Mediterranean diet score, depressive symptom, diabetes, hypertension, hypercholesterolemia (not in Health and Retirement Study), and heart diseases.

observe association of consumption of SSB or ASB with the risk of dementia. The findings were consistent across major study subgroups. The multiple sensitivity analysis and positive control of the Mediterranean diet suggested the robustness of methodologic approaches.

Only a few cohort studies have examined the associations of sweetened beverage intake with incident dementia in older adults, and the findings have been inconsistent. In the UK Biobank (median follow-up, 9.5 years; mean age, 56.4 years), higher intake of SSB and ASB (>2 units per day vs nonconsumers) were each associated with a higher risk of dementia[15]; while another cohort study of 2888 participants aged over 60 years found no significant association.[16] Pooling findings from 6 well-characterized cohort studies, we observed null associations of late-life consumptions of SSB and ASB with all-cause dementia, with narrow CIs indicating relatively high precision. This suggests that the lack of associations is less likely due to inadequate statistical power and more reflective of an absence of association between SSB, ASB, and dementia risk. The difference may stem from the dietary measurement approaches and population characteristics. For instance, the UK Biobank consisted mostly of middle-aged participants at baseline and used 24-hour diet recalls that may not well represent long-term dietary habits. In the UK Biobank study, the association for SSB was only found at a very high consumption level (>2 units/d),[15] but few participants in the 6 US cohorts reached such level. In contrast, the FFQ could better capture long-term dietary intake, and the exposure levels were generally stable in repeated measurements. Differences in approaches to energy intake adjustment may further contribute to inconsistencies in previous studies. Some studies adjust for total energy intake, assuming that the source of energy (beverages vs other foods) is critical, while others do not. These differing approaches may partially explain heteroge-

Figure 3. Associations of Sugar-Sweetened and Artificially Sweetened Beverages With Risk of All-Cause Dementia in Study Subgroups



We estimated hazard ratios (HRs) and 95% CIs from individual cohorts using Cox proportional hazard regression models adjusted for age, sex, ethnicity (not in FHS original cohort), educational level, smoking status (not in MAP), physical activity, body mass index, total energy intake, Mediterranean diet score, depressive symptom, diabetes, hypertension, hypercholesterolemia (not in HRS), and heart diseases. The subgroup variables were excluded from the covariate set for the corresponding subgroup analysis. The estimates were then meta-analyzed with random-effects models.

neity in effect estimates across studies.[43] There are also debates on whether diabetes, which could be both a confounder and a mediator for the association, should be adjusted for.[16] Nevertheless, our findings did not show substantial changes when these factors were taken into account.

Our study of 6 US-based prospective cohorts provided valuable information with rigorous study designs and relatively long-term follow-up and should be interpreted within the context of several methodological challenges in dietary assessment and dementia diagnosis.[4] The primary strengths of the 6 studies include long-term follow-up with validated approaches to assess dietary intake and active ascertainment to reduce misclassification of dementia. The rigorous follow-up procedures implemented in the 6 cohorts likely minimized the underdiagnosis of dementia, which showed a comparable incidence rate with a previous study involving US older adults.[44] Considering the long preclinical period of dementia, prediagnosis cognitive decline and mental health may well affect the dietary habits of individuals (such as altered taste)[21] and necessitates a sufficiently long-term follow-up. The average follow-up time of the 6 cohorts (10.7 years) in our study was longer than that of most existing studies. We only included incident dementia cases diagnosed 2 or more years after baseline, and the small number of excluded cases did not introduce major selection bias.[45] In addition, our study focused on an older population, which allowed us to exclude early-onset dementia, which differed in pathological features from late-onset dementia. The large number of incident cases (>2000) allowed us to estimate the associations with a high level of precision. Also, our sensitivity analysis on the Mediterranean diet as a positive control further suggests that dietary measurement errors and dementia misclassification may have less bearing on our findings.

Existing literature has pointed out that liquid sources of carbohydrates provide less satiety compared with solid sources and lead to excessive energy intake. In addition, excessive sugar intake might induce a rapid increase in blood glucose,[46] which may elevate dementia risk.[47] However, our findings do not support this hypothesis and reflected the complex associations between SSB intake and brain health, particularly considering that

sugar serves as one of the primary fuel sources supporting brain function.[13,14] The associations between ASB and health outcomes also have been controversial, and the evidence for dementia is still scarce. A meta-analysis showed that ASB might be a risk factor for T2D,[48] while another cohort study over 20.9 years[49] found no association for liver diseases. Our findings, based on 6 well-established cohorts, also found no association between late-life ASB consumption and dementia, which affirms the complexity between artificial sweeteners and cognitive health.

Limitations

However, our findings should be interpreted with caution. First, because we focused our analysis on the older population, most of them surviving to the baseline may be healthier than the general population and less susceptible to the harm of unhealthy dietary intake. Second, unmeasured and residual confounding could still exist. Third, the study population had a lower prevalence of daily SSB and ASB consumption (approximately 10%) compared with the general US older population, where approximately 20% of individuals aged 55 years or older reported daily consumption in 2013.[11] Therefore, the representativeness and generalizability of our findings to broader populations warrant further investigation. Given the association between sweetened beverages and other diseases, especially metabolic diseases, our study does not challenge the existing dietary guidelines for the older population with respect to SSB or ASB. Recognizing the adverse effects of sweetened beverages in several chronic diseases, especially cardiometabolic diseases in midlife, the role of early-life consumption of SSB and ASB in the risk of dementia remains to be investigated. In addition, there are many other sources of sugar (such as sweets and flavored yogurts), so the potential harm of excessive sugar intake should still be monitored.[50]

Conclusions

In this multicohort study using data from 6 studies, consumption of SSB and ASB in older adulthood was not associated with the risk of later-life dementia. Given their detrimental effects in metabolic health and related chronic diseases during midlife, early-life consumption of SSB and ASB and the risk of dementia remain to be investigated.

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