

Associations of Added Sugar from All Sources and Sugar-Sweetened Beverages with Regional Fat Deposition in US Adolescents: NHANES 1999–2006

Catherine E Cioffi,¹ Jean A Welsh,^{1,2,3} Jessica A Alvarez,^{1,4} Terryl J Hartman,^{1,5} KM Venkat Narayan,^{1,6} and Miriam B Vos^{1,2,3}

¹Nutrition and Health Sciences Program, Laney Graduate School, Emory University, Atlanta, GA, USA; ²Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA; ³Department of Gastroenterology, Hepatology, and Nutrition, Children's Healthcare of Atlanta, Atlanta, GA, USA; ⁴Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA; ⁵Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, USA; and ⁶Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA;

ABSTRACT

Background: The relative distribution of upper- versus lower-body fat may be an important determinant of cardiometabolic disease risk in youths. Dietary components associated with adolescent regional body fat distribution require further investigation.

Objective: To evaluate associations of added sugar intake overall and from sugar-sweetened beverages (SSBs) with relative upper-body fat deposition in US adolescents.

Methods: This was a cross-sectional analysis of data from 6585 adolescents (aged 12–19 y) in the NHANES cycles 1999–2006. Trunk, leg, and total fat mass were assessed by DXA. Participants were grouped into categories of total and SSB added sugar intake as a percentage of total energy intake (TEI) in 5% increments. Stepwise multivariable linear regression was used to examine associations of added sugar intake with truncal-to-leg fat ratio (TLR) and truncal-to-total fat ratio (TTR).

Results: There were no associations of total added sugar intake with TLR or TTR. For SSB added sugar, compared with the lowest category of intake (<2% TEI), the highest category (>22% TEI) was associated with higher log-TLR [β (95% CI): >22% TEI versus <2% TEI: 0.05 (0.01, 0.09)] and TTR [1.30 (0.53, 2.07)] in the partially adjusted model with sex, age, race/ethnicity, income, physical activity, and smoking status as covariates (*P*-trend = 0.0001 for both). When BMI *z*-score and TEI were added as covariates, the magnitude of the associations were attenuated, but remained significant [log-TLR β (95% CI): 0.03 (0.005, 0.06), *P*-trend = 0.0018; TTR β (95% CI): 0.75 (0.27, 1.23), *P*-trend = 0.0004]. **Conclusions:** These findings support that added sugar from beverages is associated with higher upper-body adiposity, though the magnitude and clinical significance of the associations may be small, especially when adjusted for BMI and TEI. Additional studies are needed to elucidate the

Keywords: trunk fat, leg fat, soda, cardiometabolic disease, diabetes, body composition

underlying biological mechanisms to explain these findings. Curr Dev Nutr 2019;3:nzz130.

Copyright © The Author(s) 2019. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License

(http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

Manuscript received July 22, 2019. Initial review completed October 24, 2019. Revision accepted November 7, 2019. Published online November 13, 2019.

Supported, in part, by the National Institute of Diabetes, Digestive, and Kidney Disease(NIDDK) grant/award numbers T32DK007734, P30DK111024, and K01DK102851, and the National Heart, Lung, and Blood Institute (NHLBI) grant/award number R01HL125442.

Author disclosures: CEC, JAW, JAA, TJH, KMVN, and MBV, no conflicts of interest.

Supplemental Tables 1–3 and Supplemental Figure 1 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/cdn/.

Address correspondence to CEC (e-mail: Catherine.Cioffi@emory.edu).

Abbreviations used: CMD, cardiometabolic disease; FPED, Food Pyramid Equivalents Database; HFCS, high-fructose corn syrup; MEC, mobile examination center; MPED, MyPyramid Equivalents Database; MVPA, moderate and vigorous physical activity; NCHS, National Center for Health Statistics; PAL, physical activity level; PIR, poverty income ratio; SSB, sugar-sweetened beverage; TEI, total energy intake; TLR, truncal-to-leg fat ratio; TTR, truncal-to-total fat ratio.

Introduction

The prevalence of childhood obesity in the USA is a public health concern, in part due to associations with cardiometabolic disease (CMD) risk factors (1, 2). In particular, higher upper-body adiposity, i.e. truncal or abdominal fat, has been shown to be a strong risk factor for metabolic dysfunction independent of total body fat, whereas higher lower-body adiposity, i.e. leg or hip fat, may be protective (3, 4). Similarly, we recently found in US adolescents that a higher truncal-to-leg fat ratio (TLR) is associated with multiple CMD risk factors, including fasting insulin resistance and dyslipidemia, independent of BMI (5). One hypothesis to explain these findings is that impaired expansion of peripheral subcutaneous fat increases susceptibility to abdominal and ectopic fat deposition, and the subsequent lipotoxic consequences, such as insulin resistance (6, 7).

Understanding if modifiable lifestyle factors influence body fat distribution may be important for reducing future CMD (8). Added sugar intake, especially in the form of sugar-sweetened beverages (SSBs), has been shown to be associated with abdominal visceral fat, but not subcutaneous fat, in observational studies in adults (9, 10) and youth (11, 12). This is also supported by a 6-mo intervention study in adults, which found that daily SSB consumption resulted in greater increases in abdominal visceral fat compared with milk, diet sodas, and water (13). Thus, evidence suggests that added sugar intake contributes to altered lipid partitioning among abdominal fat depots. However, data is lacking on the associations of added sugar with the ratio of upper- versus lower-body fat.

In this study, we aimed to examine associations of added sugar from all sources, and specifically from SSBs, with relative upper-body fat deposition in US adolescents. The primary outcome was truncal-to-leg fat ratio (TLR)measured by dual-energy X-ray absorptiometry (DXA), though we also examined truncal-to-total fat ratio (TTR). Our hypothesis was that higher intakes of added sugar would be associated with higher TLR and TTR, and that this association would be strongest for the intake of added sugars in SSBs.

Methods

NHANES is an ongoing, cross-sectional surveillance survey conducted by the National Center for Health Statistics (NCHS) within the CDC. It uses a multistage, probability sampling design to obtain a nationally representative sample of the US noninstitutionalized population and releases data in 2-y cycles. From 1999-2006 only, whole and regional body fat and lean mass were measured using DXA on NHANES participants aged 8 y or older. Thus, the initial eligible sample for this analysis was 8311 participants aged 12-19 y. Among this sample, participants were excluded for the following consecutive reasons: not having valid scanned or imputed DXA data (n = 261), not having 1 valid dietary recall day (n = 333), implausible total energy intake (TEI) (<500 TEI or > 5000 TEI, n = 293); underweight BMI percentile (n = 181) or missing BMI percentile (n = 29); missing other covariates, i.e. household income status, self-reported physical activity, or self-reported smoking status (n = 629). This resulted in a final sample of 6585 adolescents. A CONSORT diagram is shown in Supplemental Figure 1. It should be noted that from 1999-2006, NHANES oversampled several subgroups, including non-Hispanic blacks, Mexican Americans, lowincome whites, and adolescents aged 12-19 y. NHANES was approved by the NCHS Review Board, and all participants provided written informed consent.

Body composition and anthropometrics

Height in cm and weight in kg were measured using standardized protocols during the mobile examination center (MEC) visit (14). Ageand sex-adjusted BMI percentiles and z-scores were calculated using the 2000 CDC growth charts (15). Subjects were categorized as normal weight (5–84th percentile), overweight (85–94th percentile), or obese (\geq 95th percentile) (16). Body composition was measured by DXA during the MEC visit using a Hologic QDR-4500A fan-beam densitometer (Hologic, Inc.) and Hologic Discovery software version 12.1 (17). Soft tissue measures for fat and lean mass were obtained for the head, arms, legs, and trunk regions. Based on prior analyses showing that DXA overestimated lean mass and underestimated fat mass, values for lean mass were decreased by 5% by the NCHS and an equivalent weight was added to the fat mass (17, 18). Participants were not scanned if pregnant, had amputations other than toes or fingers, weighed >300 lbs, or were taller than 6'5" (195.6 cm). Some DXA scans did not result in 100% valid data; for example, due to nonremovable objects, obesityrelated noise, and arm/leg overlap. This resulted in a decrease in valid DXA data with increasing age and BMI. Multiple imputation was performed by NCHS to account for this nonrandom nature of missing data (17). Among the sample of adolescents in this study, 5856 (88.9%) completed the scan and had 100% valid data, 317 (4.8%) completed the scan but \geq 1 region was invalid and multiply imputed, and 412 (6.3%) did not complete the scan but had valid multiply imputed data. In each dataset, we calculated TLR as (trunk fat mass [g]/[right + left leg fat mass (g)] × 100), consistent with prior reports (5), and TTR as ([trunk fat (g)/total fat mass (g)] \times 100).

Total and SSB added sugar

For 1999-2000 and 2001-2002, dietary intake in NHANES was assessed by 1 24-h dietary recall collected in-person during the household interview. Starting in 2002, an integrated dietary component administered by the USDA in partnership with NCHS, called What We Eat in America, was created and included a second 24-h dietary recall collected by telephone 3–10 d after the MEC visit (19). For consistency across cycles, the first 24-h recall only was used for the primary analysis; although a sensitivity analysis was also performed using 2-d mean intakes from a subset of the sample with a second 24-h recall (n = 3633or 55% of the sample). The USDA's Food and Nutrient Database for Dietary Studies was used to convert dietary recall data into TEI per day. The USDA's MyPyramid Equivalents Database (MPED) versions 1.0 (for 1999-2002) and 2.0 (for 2003-2004), and the Food Pyramid Equivalents Database (FPED) (for 2005-2006) were used to determine added sugar intake. Details on the methodology used by the USDA to calculate the added sugar intake can be found elsewhere (20-22). Briefly, these databases are used to translate dietary intake data from national surveys, including NHANES, into food group equivalents relevant to dietary guidelines (23). This data is released as total intakes per person per day and as intakes per individual food item. The USDA defines added sugars as all caloric sweeteners that are added as ingredients in processed and prepared foods and beverages, including white sugar, brown sugar, raw sugar, corn syrup, corn syrup solids, high-fructose corn syrup (HFCS), malt syrup, maple syrup, pancake syrup, fructose sweetener, liquid fructose, honey, molasses, dextrose, and dextrin. Naturally occurring sugars, such as fructose in fruit or lactose in milk, are not included.

Added sugar from SSBs was calculated using individual food files and by summing per person per day their added sugar intake from sodas, fruit drinks and punches, sports drinks, energy drinks, sweetened tea or coffee drinks, and other SSBs. The food codes used to identify these drinks are summarized in **Supplemental Table 1**. Flavored milk, 100% fruit juice, beverages sweetened by the participant, and alcoholic beverages were not included, consistent with prior

			Total a	dded sugar catego	ry		
	<10% TEI	10-<15% TEI	15-<20% TEI	20- <25% TEI	25<30% TEI	≥30% TEI	P-trend
No. participants	1084 (17)	1151 (17)	1337 (19)	1142 (16)	837 (13)	1034 (18)	_
Median intake, % TEI	6.1%	12.7%	17.5%	22.3%	17.3%	36.0%	
Male sex	569 (50)	609 (55)	745 (56)	626 (59)	479 (53)	599 (60)	0.033
Age, y	15.5 ± 0.1	$15.2~\pm~0.1$	$15.5~\pm~0.1$	15.4 ± 0.1	15.7 ± 0.1	$15.7~\pm~0.1$	0.250
Race/ethnicity							
Non-Hispanic white	297 (62)	277 (60)	329 (59)	306 (63)	240 (66)	319 (68)	0.023
Mexican American	373 (12)	431 (13)	474 (12)	358 (11)	252 (9)	295 (8)	0.001
Non-Hispanic black	309 (11)	258 (14)	426 (16)	394 (16)	279 (14)	338 (13)	0.547
Other/multi-race	105 (15)	85 (13)	108 (13)	84 (11)	66 (11)	82 (12)	0.260
Family income							
PIR <130%	464 (34)	505 (29)	543 (31)	479 (28)	326 (31)	426 (32)	0.823
PIR 130–300%	401 (33)	411 (37)	486 (37)	402 (38)	324 (40)	283 (38)	0.103
PIR >300%	219 (32)	235 (34)	308 (32)	261 (34)	187 (29)	226 (30)	0.312
Current smoker	87 (10)	80 (9)	88 (9)	88 (9)	83 (13)	112 (15)	0.016
Activity, MVPA min/d	$86.1~\pm~5.8$	$77.3~\pm~3.1$	$86.8~\pm~5.5$	$87.3~\pm~5.6$	$75.8~\pm~4.9$	$82.1~\pm~7.0$	0.636
BMI z-score	$0.76~\pm~0.04$	$0.64~\pm~0.05$	$0.51~\pm~0.06$	0.71 ± 0.05	$0.62~\pm~0.07$	$0.70~\pm~0.06$	0.783

TABLE 1 Characteristics of the sample of 6585 adolescents (aged 12–19 y) according to categories of total added sugar intake:NHANES 1999–2006

Results are summarized as means \pm SEs for continuous variables and counts and weighted percentages for categorical variables. *P* values calculated using the median value for each intake category in linear regression for continuous variables and logistic regression for categorical variables. **Bold** indicates significant linear trends at *P* < 0.005. MVPA, moderate and vigorous physical activity; PIR, poverty income ratio; TEI, total energy intake.

reports (24). In the MPED and FPED databases, added sugar is expressed in teaspoon equivalents, and this was converted to grams using the factor of 4.2 g/teaspoon, to kcal using the factor 4 kcal/g, and to a percentage of TEI by dividing by kcal/d. Participants were grouped into 6, approximately equal-sized categories of total added sugar intake, with the lowest level based on the current Dietary Guidelines for Americans recommendation to limit added sugar to <10% TEI: <10%, 10% to <15%, 15% to <20%, 20% to <25%, 25% to <30%, and \geq 30% TEI. For SSB added sugar, participants were grouped into similar 5% incremental categories, but shifted down to mirror an overall shift in the distribution of SSB compared with total added sugar: <2%, 2% to <7%, 7% to <12%, 12% to <17%, 17% to <22%, and >22% TEI.

Covariates

Sociodemographic information was collected during the household interview for sex, racial/ethnic group (non-Hispanic white, Mexican American, non-Hispanic black, or other/mixed race), and age. The selfreported household poverty income ratio (PIR), a ratio of family income to poverty threshold, was used to measure income status and subjects were categorized as low-income (PIR <130%, which was based on the federal threshold for eligibility for Supplemental Nutrition Assistance Program benefits), middle income (PIR 130-350%), and high income (PIR >350%). Physical activity level (PAL) was measured as average minutes of moderate and vigorous physical activity (MVPA) per day, which was calculated based on the self-reported frequency and duration of individual activities per week. For Table 1, participants were categorized relative to the 2018 physical activity guidelines as inactive (<60 min MVPA per day) or active (≥ 60 min MVPA per day) (25), otherwise PAL was analyzed as a continuous covariate in MVPA/d. Smoking status was assessed during the MEC exam by the audio computer-assisted selfinterview. Participants were dichotomized as smokers if they answered "yes" to the question "During the past 5 days, did you use cigarettes?"

Statistical analysis

All analyses were performed in SAS (SAS Institute Inc., version 9.4) and SUDAAN (RTI International; version 9.0.3), unless otherwise noted. Appropriate survey procedures and sample weights were used to adjust for the complex sampling design of NHANES. Analyses involving the multiply-imputed DXA data were performed 5 times in SUDAAN using "Proc Descript" or "Proc Regress", once on each multiply-imputed dataset, and estimates were combined using pooling methods according to NCHS (17). Characteristics of the sample were summarized as means and SEs for continuous variables and counts and weighted frequencies for categorical variables according to category of total or SSB added sugar intake. Linear trends in characteristics across categories of intake were tested by linear regression for continuous variables and logistic regression for dichotomized categorical variables using the median value for each intake category.

Continuous variables were assessed for normality using histograms, and natural log-transformation was performed on TLR to correct for right-skewedness.

Stepwise multivariable-adjusted linear regression was used to estimate associations of total and SSB added sugar intake category with log-TLR and TTR. Covariates were adjusted sequentially as follows to understand their contribution to the model: model 1 was adjusted for age (y), sex, race/ethnicity, PIR, smoking status, and PAL; model 2 was adjusted for BMI *z*-score; and model 3 was adjusted for TEI. In this analysis, we considered the lowest category of intake the reference, and visualized the predicted marginal means and 95% CIs for log-TLR and TTR according to added sugar intake category using the *ggplot2* package in R statistical software (R Foundation for Statistical Computing; version 3.4.2) (26). Linear trends in TLR and TTR across intake category were tested using the median value for each category. Effect modification between added sugar intake and sex, race/ethnicity, and weight status was also tested by product interaction terms in the fully

Results

			Sugar-sweetened	beverage added su	ugar category		
	<2% TEI	2-< 7% TEI	7-<12% TEI	12-<17% TEI	17-<22%	≥22% TEI	P-trend
No. participants	1104 (21)	1108 (14)	1465 (21)	1197 (17)	742 (11)	969 (16)	_
Median intake, %TEI	0%	5.0%	9.4%	14.1%	19.5%	28.2%	_
Male sex	526 (45)	599 (56)	803 (58)	680 (59)	450 (64)	569 (57)	0.002
Age, y	$15.4~\pm~0.1$	15.1 ± 0.1	$15.4~\pm~0.1$	15.5 ± 0.1	15.7 ± 0.1	16.1 ± 0.1	<0.001
Race/ethnicity							
Non-Hispanic white	382 (70)	242 (53)	341 (58)	302 (63)	206 (61)	295 (68)	0.464
Mexican American	311 (9)	362 (13)	532 (13)	405 (11)	247 (11)	326 (9)	0.413
Non-Hispanic black	308 (10)	407 (19)	472 (15)	406 (16)	236 (15)	275 (11)	0.987
Other/multi-race	103 (12)	97 (15)	120 (14)	84 (10)	53 (13)	73 (12)	0.590
Family income							
PIR <130%	207 (27)	516 (37)	610 (28)	496 (32)	293 (29)	421 (35)	0.152
PIR 130–300%	422 (45)	384 (35)	534 (37)	447 (38)	274 (37)	345 (39)	0.145
PIR >300%	275 (38)	208 (28)	321 (35)	254 (29)	175 (34)	203 (26)	0.013
Current smoker	71 (8)	71 (7)	102 (10)	95 (10)	64 (10)	136 (18)	<0.001
Activity, MVPA min/d	$81.9~\pm~4.8$	$81.0~\pm~4.2$	$84.9~\pm~4.2$	$86.5~\pm~4.6$	$79.2~\pm~7.2$	$82.1~\pm~8.0$	0.999
BMI z-score	$0.65~\pm~0.05$	$0.52~\pm~0.05$	$0.56~\pm~0.04$	$0.72~\pm~0.05$	$0.72~\pm~0.06$	$0.80~\pm~0.07$	0.004

TABLE 2 Characteristics of the sample of 6585 adolescents (aged 12–19 y) according to categories of sugar-sweetened beverage added sugar intake: NHANES 1999–2006

Results are summarized as means \pm SEs for continuous variables and counts and weighted percentages for categorical variables. *P* values calculated using the median value for each intake category in linear regression for continuous variables and logistic regression for categorical variables. **Bold** indicates significant linear trends at *P* < 0.005. MVPA, moderate and vigorous physical activity; PIR, poverty income ratio; TEI, total energy intake.

adjusted linear trend models. Lastly, to determine if our results were consistent when 2 dietary recalls were collected, we performed a sensitivity analysis by running the same regression models as above based on 2-d averages for total and SSB added sugar intake in the subsample of participants (n = 3633) who completed a second dietary recall by phone.

When *P* values were reported, a more conservative *P* < 0.005 was considered significant (27); otherwise, point estimates and 95% CIs were used to summarize the results. Additionally, in the linear regression models of added sugar intake with log-TLR and TTR, a Bonferronic correction was applied to correct for multiple testing on 2 adiposity outcomes (i.e., log-TLR and TTR), and *P* < 0.0025 (0.005/2 tests) was considered significant for the evaluation of linear trends and effect modification.

Characteristics of the sample by category of total and SSB added sugar intake are in Table 1 and Table 2, respectively. A higher category of total added sugar intake was associated with a lower proportion of Mexican-American adolescents (*P*-trend <0.005). For SSB added sugar, a higher category of intake was associated with a higher proportion of boys and smokers, and higher mean age and BMI *z*-score (*P*-trend <0.005).

Spearman correlations for the relation between added sugar intake and the adiposity outcomes are detailed in **Table 3**. In multivariableadjusted linear regression models, none of the interaction terms for effect modification by sex, race/ethnicity, or weight status were significant; therefore, overall estimates are presented. There were no significant associations of total added sugar intake with log-TLR or TTR in any of the stepwise models (**Table 4**). However, we did find associations of SSB added sugar with both outcomes (**Table 5**). In model 1, adjusted for age, sex, race/ethnicity, income group, smoking, and PAL, the β (95% CI) comparing the highest category (>22% TEI) to the lowest category of SSB intake (<2% TEI) for log-TLR was 0.05 (0.01, 0.09) and for TTR was 1.30 (0.53, 2.07) (*P*-trend = 0.0001 for both). The predicted marginal means and 95% CIs for TLR and

Overall, the mean \pm SEM for total added sugar intake was 20.3 \pm 0.3% TEI and for SSB added sugar intake was 12.2 \pm 0.3% TEI.

TABLE 3 Spearman correlations among total and sugar-sweetened beverage added sugar variables and adiposity variables in the sample of 6585 adolescents (aged 12–19 y): NHANES 1999–2006

	Total added sugar (% TEI)	SSB added sugar (% TEI)	TLR	TTR	BMI z-score
	(/* 1 = //	(/***=:/			2
Total added sugar, % TEI	1.000	—	—	—	_
SSB added sugar, % TEI	0.636 (P < 0.001)	1.000		_	_
TLR	0.023 (P = 0.060)	0.116 (<i>P</i> < 0.001)	1.000	_	_
TTR	0.021 (P = 0.095)	0.116 (<i>P</i> < 0.001)	0.964 (<i>P</i> < 0.001)	1.000	_
BMI z-score	0.003 (<i>P</i> = 0.834)	- 0.063 (P < 0.001)	-0.464 (P < 0.001)	$-0.574 \ (P < 0.001)$	1.000

All correlation coefficients were calculated using the first multiply-imputed DXA dataset only. SSB, sugar-sweetened beverage; TEI, total energy intake; TLR, truncal-to-leg fat ratio; TTR, truncal-to-total fat ratio.

			Total added sugar	category		
Log-TLR:	10-<15% vs. <10%	15–≤20% vs. ≤10%	20–≤25% vs. ≤10%	25–≤30% vs. ≤10%	≥30% vs. ≤10%	Linear trend
Model: 1	р (73% U) — 0.02 (—0.05, 0.01)	р (10 %су) р — 0.01 (—0.04, 0.02)	р (10 %су) — 0.01 (—0.04, 0.02)	р (уск) р 0.01 (—0.03, 0.04)	р (73% СI) 0.005 (—0.03, 0.04)	r value 0.258
2: + BMI z-score	- 0.004 (-0.03, 0.02)	0.02 (-0.003, 0.04)	0.001 (-0.02, 0.03)	0.03 (0.001, 0.05)	0.01 (-0.01, 0.04)	0.077
3: + TEI, kcal/d	- 0.001 (-0.03, 0.03)	0.02 (-0.001, 0.04)	0.003 (-0.02, 0.03)	0.03 (0.003, 0.06)	0.01 (-0.01, 0.04)	0.099
			Total added sugar	category		
TTR:	10-≤15% vs. ≤10%	15–≤20% vs. ≤10%	20-≤25% vs. ≤10%	25–≤30% vs. ≤10%	≥30% vs. ≤10%	Linear trend
Model: ¹	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	_ β (95% CI)	P value
-	- 0.54 (-1 15, 0.08)	-0.45 (-1.12, 0.22)	-0.17 (-0.84, 0.50)	0.011 (-0.65, 0.88)	0.14 (-0.56, 0.83)	0.194
2: + BMI z-score	- 0.10 (-0.62, 0.43)	0.40 (-0.05, 0.85)	0.05 (-0.43, 0.52)	0.61 (0.12, 1.10)	0.36 (-0.16, 0.88)	0.032
3: + TEI, kcal/d	- 0.02 (-0.55, 0.50)	0.45 (-0.01, 0.90)	0.10 (-0.37, 0.57)	0.66 (0.17, 1.14)	0.33 (-0.18, 0.84)	0.045

TTR across the 6 categories of total and SSB added sugar intake in partially adjusted model 1 are visualized in Figure 1. Note that for log-TLR, we performed back-transformations and geometric means are shown.

With the addition of BMI z-score in model 2, and TEI in model 3, the magnitude of these differences between the highest and lowest categories were attenuated, but the linear trends remained significant (model 3: *P*-trend = 0.0018 for TLR, and *P*-trend = 0.0004 for TTR, Table 5). The means and 95% CIs for TLR and TTR for each category of total and SSB added sugar and for each stepwise model are in Supplemental Table 2.

Results from the sensitivity analyses using mean intakes for total and SSB added sugar among the subsample of participants with 2 dietary recalls (n = 3633) are shown in **Supplemental Table 3**. This revealed that there were minor differences compared with the analyses using 1 dietary recall. First, the CIs were slightly wider in this analysis, which is likely due to the reduction in sample size. In addition, for the models with SSB added sugar intake as the independent variable, most of the linear trends were no longer significant at the Bonferroni-adjusted P < 0.0025, except for model 1 for TTR. Otherwise, the point estimates for the association of the highest compared with lowest categories of SSB added sugar intake with TLR and TTR were similar, if not larger in magnitude in the sensitivity analysis.

Discussion

The etiology of adipose expandability and body fat distribution is multifactorial, and the role of diet remains an active area of investigation. In this study, we examined whether added sugar intake from all sources and from SSBs specifically are determinants of relative upperbody fat deposition in a nationally representative sample of US adolescents. Overall, we observed that higher SSB added sugar intake (>22% TEI) was associated with higher relative trunk fat deposition, assessed as both TLR and TTF ratios. This association was strongest in partially adjusted models with age, sex, race/ethnicity, income, physical activity, and smoking status as covariates. In the additional models holding BMI z-score and TEI constant, the magnitude of the associations were reduced for both outcomes, by approximately half, but remained significant. In contrast, we did not find evidence of an association of added sugar from all sources with any adiposity outcome.

Our results are supported by other pediatric studies showing that liquid sources of added sugars compared with solid sources are more strongly associated with obesity-related outcomes (28, 29). The predominant explanation for this difference is that, compared with solid sources, liquid sources are associated with lower satiety and incomplete compensation at later meals, resulting in excess energy intake and weight gain (30). Because the magnitude of the associations we found were weakened when adjusting for BMI z-score and TEI, this would suggest that the associations we observed of SSB added sugar with trunk fat deposition was at least partially related to this mechanism.

Importantly, however, when we did adjust for body size and TEI, we still observed associations of SSB added sugar with upper-body fat distribution that, although small in magnitude, were partially independent of these covariates. The exact mechanisms for this finding are unclear and warrant further investigation but could relate to the higher

			SSB added sugar	category		
Log-TLR: 2– Model: ¹	-≤7% vs. ≤2% β (95% Cl)	$7-\leq 12\%$ vs. $\leq 2\%$ β (95% Cl)	12-≤17% vs. ≤2% β (95% Cl)	17–≤22% vs. ≤2% β (95% Cl)	<u>≥</u> 22% vs. ≤2% β (95% Cl)	Linear trend P value
1 - 0.	0.03 (-0.07, 0.001)	-0.01 (-0.04, 0.02)	0.02 (-0.01, 0.05)	0.02 (-0.01, 0.06)	0.05 (0.01, 0.09)	0.0001
2: + BMI z-score - 0.	0.02 (-0.05, 0.01)	0.003 (-0.02, 0.03)	0.01 (-0.02, 0.03)	0.02 (-0.01, 0.05)	0.03 (0.01, 0.06)	0.0010
3: + TEI (kcal/d) - 0.	0.01 (-0.04, 0.01)	0.01 (-0.02, 0.03)	0.01 (-0.02, 0.04)	0.02 (-0.01, 0.05)	0.03 (0.005, 0.06)	0.0018
			SSB added sugar	category		
TTR: 2-	-≤7% vs. ≤2%	7–≤12% vs. ≤2%	12–≤17% vs. ≤2%	17–≤22% vs. ≤2%	≥22% vs. ≤2%	Linear trend
Model: ¹	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	$-\beta$ (95% CI)	P value
1 -0.	1.75 (-1.49, 0.01)	-0.32 (-0.94, 0.31)	0.46 (-0.23, 1.15)	0.65 (-0.03, 1.33)	1.30 (0.53, 2.07)	0.0001
2: + BMI z-score – 0	1.35 (-0.88, 0.12)	0.11 (-0.37, 0.60)	0.16 (-0.39, 0.70)	0.51 (-0.07, 1.07)	0.78 (0.30, 1.26)	0.0002
3: + TEI (kcal/d) - 0	1.22 (-0.74, 0.31)	0.22 (—0.36, 0.70)	0.24 (-0.30, 0.70)	0.54 (-0.02, 1.10)	0.75 (0.27, 1.23)	0.0004

ratio.

fat

truncal-to-total

ЩR,

truncal-to-leg fat ratio;

TLR, 1

total energy intake;

Ξ,

beverage;

glycemic index of some SSBs compared with foods with added sugar, which may also contain other nutrients such as fat or fiber that reduce the glycemic index. The higher glycemic index of SSBs may promote trunk fat gain due to the lipogenic effects of an increased insulin response and/or impaired metabolic flexibility (31). This is supported by some adult intervention studies, which suggest that a low-glycemic index diet is associated with a lower insulin secretory response and greater loss in intra-abdominal fat, regardless of weight loss, compared with a high-glycemic index diet (32, 33). SSB intake has also been associated with higher concentrations of proinflammatory markers in observational studies of children (34), and in intervention studies in adults (35). This may be another mechanism to explain associations of SSBs with preferential trunk fat deposition, as low-grade inflammation is hypothesized to be a key determinant of impaired subcutaneous fat expansion and intra-abdominal fat susceptibility (36, 37).

In addition, SSBs are commonly sweetened with HFCS in the US, which consists of approximately equal parts fructose and glucose. Fructose in particular is able to bypass key regulatory steps during liver metabolism, and has been associated with lipogenic gene expression (38, 39), which could promote ectopic and intra-abdominal fat deposition (40, 41). However, because glucose is also present in HFCS, we cannot differentiate whether fructose alone or the combination of fructose and glucose may be responsible for these findings. Further, in this study, the DXA scans did not measure ectopic fat, such as in the liver, nor the specific type of abdominal fat deposition (i.e. visceral versus subcutaneous). More detailed phenotype assessments are needed in future pediatric research examining these diet-body fat distribution associations.

This study has both weaknesses and strengths that should be noted. Due to the cross-sectional nature of this study, we cannot assess directionality. We relied on self-reported dietary intake, which is prone to several biases, such as social desirability bias, especially among overweight and obese adolescents (42, 43). Recall bias may also be more common with foods, especially snacks, compared with beverages, and this might have led to more measurement error in our assessment of total added sugar (44, 45). In addition to not having more detailed body fat deposition assessments, as mentioned above, NHANES also did not assess genotype or pubertal stage, which both may independently influence body fat distribution. Lastly, although we used a more conservative P value to evaluate linear trends, we chose to report point estimates and 95% CIs for all other results; therefore, false positive results are possible and caution should be taken in interpreting the findings.

Strengths of our study included its large, nationally representative sample of adolescents in the USA. The sample was diverse in terms of race/ethnicity and income status, and included children with a range of BMI *z*-scores, which enhances generalizability. NHANES performs a combination of questionnaire-, physical examination-, and laboratorybased measurements, which allowed for the assessment of a comprehensive list of covariates. The availability of 2 dietary recalls among a subsample of participants starting in 2003 enabled us to perform sensitivity analyses to assess whether the results differed in comparison to the original analyses of 1 dietary recall, and this revealed only minor changes that were likely related to the reduction in sample size and subsequently statistical power. Lastly, the NHANES cycles in this study included accurate and reliable measurements of body composition by

TABLE 5 β -coefficients and 95% Cls for the association of sugar-sweetened beverage added sugar intake with log-TLR and TTR in the sample of 6585 adolescents



FIGURE 1 Means and 95% CIs of TLR and TTR according to categories of SSB and total added sugar intake in the sample of 6585 adolescents (aged 12–19 y), NHANES 1999–2006. Estimates are from the partially adjusted models with adjustment for age (y), sex, race/ethnicity, household income group, physical activity (MVPA min/d), and smoking status. (A) TLR and (B) TTR according to category of SSB added sugar intake; (C) TLR and (D) TTR according to category of total added sugar intake. For TLR, geometric means were calculated to account for log-transformation. Abbreviations: MVPA, moderate and vigorous physical activity; SSB, sugar-sweetened beverages; TLR, truncal-to-leg fat ratio; TTR, truncal-to-total fat ratio.

DXA, which is a gold standard for the evaluation of total and regional fat mass.

In conclusion, the findings of this study suggest that SSB added sugar intake is associated with higher relative upper-body fat deposition, expanding on prior studies of adolescents in NHANES that found associations of SSBs with waist circumference, HOMA-IR, and dyslipidemia (46). Together with evidence from adults that the long-term consumption of SSBs is associated with a higher risk of mortality, especially from cardiovascular disease, independent of BMI (47), evidence is mounting that SSBs may have effects on health beyond overall weight gain. How-

ever, it is important to emphasize that the effect sizes we found for the associations of SSB added sugar with TLR and TTR were relatively small, and driven by the highest category of intake; therefore, the clinical significance of our findings may be modest. Additional efforts are needed to understand the potential biological mechanisms that may explain a link between SSBs, body fat distribution, and metabolic dysfunction in youths.

Acknowledgments

The authors' responsibilities were as follows—CEC: designed and conducted the research, and JAW and MBV: provided oversight; CEC: wrote the manuscript, and JAW, JAA, TJH, KMVN, and MBV: reviewed the manuscript and assisted with revisions and interpretation; CEC and MBV: are responsible for the final content; and all authors read and approved the final manuscript.

References

- 1. May AL, Kuklina EV, Yoon PW. Prevalence of cardiovascular disease risk factors among US adolescents, 1999–2008. Pediatrics 2012;129:1035–41.
- Hales CM, Fryar CD, Carroll MD, Freedman DS, Ogden CL. Trends in obesity and severe obesity prevalence in US youth and adults by sex and age, 2007–2008 to 2015–2016. JAMA 2018;319:1723–5.
- Samouda H, Beaufort CD, Stranges S, Hirsch M, Nieuwenhuyse JPV, Dooms G, Gilson G, Keunen O, Leite S, Vaillant M, et al. Cardiometabolic risk: leg fat is protective during childhood. Pediatr Diabetes 2016;17:300–8.
- Staiano AE, Gupta AK, Katzmarzyk PT. Cardiometabolic risk factors and fat distribution in children and adolescents. J Pediatr 2014;164:560–5.
- Cioffi CE, Alvarez JA, Welsh JA, Vos MB. Truncal-to-leg fat ratio and cardiometabolic disease risk factors in US adolescents: NHANES 2003–2006. Pediatr Obes 2019;14:e12509.
- Gray SL, Vidal-Puig AJ. Adipose tissue expandability in the maintenance of metabolic homeostasis. Nutr Rev 2007;65:S7–12.
- Virtue S, Vidal-Puig A. Adipose tissue expandability, lipotoxicity and the metabolic syndrome – an allostatic perspective. Biochim Biophys Acta 2010;1801:338–49.
- Katzmarzyk PT, Shen W, Baxter-Jones A, Bell JD, Butte NF, Demerath EW, Gilsanz V, Goran MI, Hirschler V, Hu HH, et al. Adiposity in children and adolescents: correlates and clinical consequences of fat stored in specific body depots. Pediatr Obes 2012;7:e42–61.
- Ma J, McKeown NM, Hwang SJ, Hoffmann U, Jacques PF, Fox CS. Sugarsweetened beverage consumption is associated with change of visceral adipose tissue over 6 years of follow-up. Circulation 2016;133:370–7.
- Odegaard AO, Choh AC, Czerwinski SA, Towne B, Demerath EW. Sugarsweetened and diet beverages in relation to visceral adipose tissue. Obesity 2012;20:689–91.
- Shearrer GE, Daniels MJ, Toledo-Corral CM, Weigensberg MJ, Spruijt-Metz D, Davis JN. Associations among sugar sweetened beverage intake, visceral fat, and cortisol awakening response in minority youth. Physiol Behav 2016;167:188–93.
- 12. Mollard RC, Senechal M, MacIntosh AC, Hay J, Wicklow BA, Wittmeier KD, Sellers EA, Dean HJ, Ryner L, Berard L, et al. Dietary determinants of hepatic steatosis and visceral adiposity in overweight and obese youth at risk of type 2 diabetes. Am J Clin Nutr 2014;99:804–12.
- Maersk M, Belza A, Stødkilde-Jørgensen H, Ringgaard S, Chabanova E, Thomsen H, Pedersen SB, Astrup A, Richelsen B. Sucrose-sweetened beverages increase fat storage in the liver, muscle, and visceral fat depot: a 6-mo randomized intervention study. Am J Clin Nutr 2012;95: 283–9.
- 14. National Center for Health Statistics. The National Health and Nutrition Examination Survey (NHANES): Anthropometry and Physical Activity

Monitor Procedures Manual. 2005 [cited 2019 Oct 23]; Available from: https://wwwn.cdc.gov/nchs/data/nhanes/2005-2006/manuals/BM.pdf.

- Kuczmarski RJ, Ogden CL, Guo SS, Grummer-Strawn LM, Flegal KM, Mei Z, Wei R, Curtin LR, Roche AF, Johnson CL. 2000 CDC Growth charts for the United States: methods and development. Vital Health Stat 11 2002;246:1– 190.
- Barlow SE. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. Pediatrics 2007;120(Suppl 4):S164–92.
- National Center for Health Statistics. The National Health and Nutrition Examination Survey (NHANES): Technical Documentation for the 1999– 2004 Dual Energy X-Ray Absorptiometry (DXA) Multiple Imputation Data Files. 2008 [cited 2019 Oct 23]; Available from: https://wwwn.cdc.gov/Nchs/ Data/Nhanes/Dxa/dxa_techdoc.pdf.
- Schoeller DA, Tylavsky FA, Baer DJ, Chumlea WC, Earthman CP, Fuerst T, Harris TB, Heymsfield SB, Horlick M, Lohman TG, et al. QDR 4500A dualenergy x-ray absorptiometer underestimates fat mass in comparison with criterion methods in adults. Am J Clin Nutr 2005;81:1018–25.
- Ahluwalia N, Dwyer J, Terry A, Moshfegh A, Johnson C. Update on NHANES dietary data: focus on collection, release, analytical considerations, and uses to inform public policy. Adv Nutr 2016;7:121–34.
- 20. Bowman SA, Clemens JC, Friday JE, Theorig RC, Moshfegh AJ. Food Patterns Equivalent Database 2005–06: Methodology and User Guide. USDA Agricultural Research Service 2014 [cited 2019 Oct 16]; Available from: http s://www.ars.usda.gov/ARSUserFiles/80400530/pdf/fped/FPED_0506.pdf.
- 21. Bowman SA, Friday JE, Moshfegh A. MyPyramid Equivalents Database, 2.0 for USDA Survey Foods, 2003–2004: Documentation and User Guide. USDA Agricultural Research Service 2008 [cited 2019 Oct 16]; Available from: http s://www.ars.usda.gov/ARSUserFiles/80400530/pdf/mped/mped2_doc.pdf.
- 22. Friday JE, Bowman SA. MyPyramid Equivalents Database for USDA Survey Food Codes, 1994–2002. USDA Agricultural Research Service 2006 [cited 2019 Oct 16]; Available from: https://www.ars.usda.gov/ARSUserFiles/8040 0530/pdf/mped/mped1_doc.pdf
- Ahuja JKC, Moshfegh AJ, Holden JM, Harris E. USDA food and nutrient databases provide the infrastructure for food and nutrition research, policy, and practice. J Nutr 2012;143:241S–9S.
- 24. Kit BK, Nielsen SJ, Park S, Fakhouri TH, Ogden CL. Trends in sugarsweetened beverage consumption among youth and adults in the United States: 1999–2010. Am J Clin Nutr 2013;98:180–8.
- Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, George SM, Olson RD. The physical activity guidelines for Americans. JAMA 2018;320:2020–8.
- 26. R Development Core Team. R: a language nnvironment for statistical computing. Vienna (Austria): R Foundation for Statistical Computing.
- Benjamin DJ, Berger JO. Three recommendations for improving the use of P-values. Am Stat 2019;73:186–91.
- 28. Lee AK, Chowdhury R, Welsh JA. Sugars and adiposity: the long-term effects of consuming added and naturally occurring sugars in foods and in beverages. Obes Sci Pract 2015;1:41–9.
- 29. Wang J, Shang L, Light K, O'Loughlin J, Paradis G, Gray-Donald K. Associations between added sugar (solid vs. liquid) intakes, diet quality, and adiposity indicators in Canadian children. Appl Physiol Nutr Metab 2015;40:835–41.
- Pan A, Hu FB. Effects of carbohydrates on satiety: differences between liquid and solid food. Curr Opin Clin Nutr Metab Care 2011;14:385–90.
- 31. Isken F, Klaus S, Petzke KJ, Loddenkemper C, Pfeiffer AF, Weickert MO. Impairment of fat oxidation under high- vs. low-glycemic index diet occurs before the development of an obese phenotype. Am J Physiol Endocrinol Metab 2010;298:E287–95.
- 32. Goss AM, Goree LL, Ellis AC, Chandler-Laney PC, Casazza K, Lockhart ME, Gower BA. Effects of diet macronutrient composition on body composition and fat distribution during weight maintenance and weight loss. Obesity (Silver Spring) 2013;21:1139–42.
- 33. Goree LL, Chandler-Laney P, Ellis AC, Casazza K, Granger WM, Gower BA. Dietary macronutrient composition affects β cell responsiveness but not insulin sensitivity. Am J Clin Nutr 2011;94:120–7.

- 34. Kosova EC, Auinger P, Bremer AA. The relationships between sugarsweetened beverage intake and cardiometabolic markers in young children. J Acad Nutr Diet 2013;113:219–27.
- Sorensen LB, Raben A, Stender S, Astrup A. Effect of sucrose on inflammatory markers in overweight humans. Am J Clin Nutr 2005;82: 421–7.
- 36. Kursawe R, Dixit VD, Scherer PE, Santoro N, Narayan D, Gordillo R, Giannini C, Lopez X, Pierpont B, Nouws J, et al. A role of the inflammasome in the low storage capacity of the abdominal subcutaneous adipose tissue in obese adolescents. Diabetes 2016;65:610–8.
- Caprio S, Perry R, Kursawe R. Adolescent obesity and insulin resistance: roles of ectopic fat accumulation and adipose inflammation. Gastroenterol 2017;152:1638–46.
- 38. White PJ, McGarrah RW, Grimsrud PA, Tso S-C, Yang W-H, Haldeman JM, Grenier-Larouche T, An J, Lapworth AL, Astapova I, et al. The BCKDH kinase and phosphatase integrate BCAA and lipid metabolism via regulation of ATP-citrate lyase. Cell Metab 2018;27:1281–93. e7.
- Kim M-S, Krawczyk SA, Doridot L, Fowler AJ, Wang JX, Trauger SA, Noh H-L, Kang HJ, Meissen JK, Blatnik M, et al. ChREBP regulates fructoseinduced glucose production independently of insulin signaling. J Clin Invest 2016;126:4372–86.
- 40. Bray GA. Energy and fructose from beverages sweetened with sugar or high-fructose corn syrup pose a health risk for some people. Adv Nutr 2013;4: 220–5.

- 41. Stanhope KL, Schwarz JM, Keim NL, Griffen SC, Bremer AA, Graham JL, Hatcher B, Cox CL, Dyachenko A, Zhang W, et al. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. J Clin Invest 2009;119:1322–34.
- 42. Bandini LG, Schoeller DA, Cyr HN, Dietz WH. Validity of reported energy intake in obese and nonobese adolescents. Am J Clin Nutr 1990;52:421–5.
- 43. Walker JL, Ardouin S, Burrows T. The validity of dietary assessment methods to accurately measure energy intake in children and adolescents who are overweight or obese: a systematic review. Eur J Clin Nutr 2018;72:185–97.
- 44. Livingstone MB, Robson PJ, Wallace JM. Issues in dietary intake assessment of children and adolescents. Br J Nutr 2004;92(Suppl 2):S213–22.
- 45. Hewawitharana SC, Thompson FE, Loria CM, Strauss W, Nagaraja J, Ritchie L, Webb KL. Comparison of the NHANES dietary screener questionnaire to the automated self-administered 24-hour recall for children in the healthy communities study. Nutr J 2018;17:111.
- 46. Bremer AA, Auinger P, Byrd RS. Relationship between insulin resistanceassociated metabolic parameters and anthropometric measurements with sugar-sweetened beverage intake and physical activity levels in US adolescents: findings from the 1999–2004 National Health and Nutrition Examination Survey. Arch Pediatr Adolesc Med 2009;163:328–35.
- 47. Malik VS, Li Y, Pan A, Koning LD, Schernhammer E, Willett WC, Hu FB. Long-term consumption of sugar-sweetened and artificially sweetened beverages and risk of mortality in US adults. Circulation 2019;139:2113–25.