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### Sugar-Sweetened Beverages are Associated with Increased Liver Stiffness and Steatosis Among Apparently Healthy Adults in the United States

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#### Keywords

NHANES; chronic liver disease; transient elastography; FIB-4; liver fibrosis screening

#### Introduction

Lifestyle change is the cornerstone of Nonalcoholic Fatty Liver Disease (NAFLD) management. Sugar-sweetened beverages (SSB) are a promising target. First, SSBs are associated with NAFLD and interventions to reduce SSB consumption reduce the burden of liver fat.<sup>1</sup> Second, formal guidance uniformly recommend against sugar-sweetened beverages (SSB).<sup>2</sup> Herein, we analyze the 2017–2018 wave of NHANES, examining nationally representative sample of persons without comorbidities or known liver disease to examine the associations between SSB consumption and both liver fibrosis and liver fat using Vibration-Controlled Transient Elastography (VCTE).

#### Methods

#### **Study population**

NHANES is a nationally representative cross-sectional study where participants are interviewed for demographic, socioeconomic, and health information. 24-hour dietary recalls, physical examinations and laboratory tests are conducted on subsets. We restricted the study population to the 2,706 adults 20 years old with complete, valid liver stiffness measurement, not pregnant at the time of the survey, with two days of complete

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dietary recall data, and without a prior diagnosis of chronic conditions, including liver disease, diabetes mellitus, congestive heart failure, coronary heart disease, angina pectoris, myocardial infarction, stroke, emphysema, thyroid problems, liver condition, and cancer. Liver stiffness measurements (LSM) and controlled attenuation parameter (CAP) were considered as both continuous or categorical variables (LSM>7 to classify the population who was not low-risk for advanced fibrosis,<sup>3</sup> CAP>248 for hepatosteatosis).<sup>4</sup>

Dietary intake was assessed using two 24-hour dietary recalls conducted by trained interviewers. SSBs were converted to 8-ounce servings and included soft drinks, fruit drinks with added sugar, sweetened coffee and tea drinks, sport drinks, and sweetened bottled water. Intake of 100% fruit juice, unsweetened milk, flavored milk, coffee, and tea were not categorized as SSBs. All models were adjusted for age, sex, race/ethnicity, education, family income to needs ratio, smoking status, vigorous physical activity, moderate physical activity, alcohol intake frequency, and the Healthy Eating Index (HEI)-2015 score, a measure of overall diet quality. Missing data for education, smoking status, vigorous and moderate physical activity, and alcohol intake frequency were handled using the missing indicator method.<sup>5</sup>

#### Statistical analysis

NHANES two-day dietary weights and robust estimates of variance were used for all analyses to account for differential selection probabilities, nonresponse patterns, and to make nationally representative estimates. Multivariable linear regression was used to estimate the associations between SSB intake and continuous LSM and CAP and logistic regression for the associations with LSM and CAP cutoffs, adjusting for all covariates (Supplementary Table 1).

#### Results

The sample was  $37.9\pm0.6$  years old, 47.4% female, and 60% white.(Supplementary Table). While 16.0% were non-drinkers, 29.1% reported drinking alcohol at least once per week. Daily SSB consumption varied evenly with 38.8% consuming none, 20.2% consuming >0-1 servings (>0-8 ounces), 18.7% consuming >1-2 servings (>8-16 ounces), and 22.2% consuming >2 servings (>16 ounces). SSB consumers were more likely to be smokers, less likely to be physically active, and while they were less likely to be non-drinkers, they were less likely to be weekly-or-greater drinkers.

Overall, 305 (11.3%) of the population had LSM >7.0 kPa and 1,254 (46.3%) subjects had CAP > 248 dB/m. Table 1 presents the associations between SSBs and LSM/CAP. SSBs in excess of 2 servings/day was significantly associated with greater LSM after multivariate adjustment, both as a continuous measure and with respect to the 7 kPa cutoff (OR 2.30, 95% CI1.39–3.79). In the multivariate model, consuming >1–2 SSB servings/day was also associated with elevated CAP. In particular, compared to adults without SSB consumption, those who consumed >1–2 servings/day (OR 1.51, 95% CI 1.18, 1.94) were more likely to have CAP>248.

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#### Discussion

In this nationally representative study from NHANES 2017–2018, we show that SSB consumption is associated with liver fibrosis and liver fat in healthy adults, independent of sociodemographic characteristics and other health behaviors, such as overall diet quality, physical activity, and alcohol intake.

#### SSB are a prime target to curb NAFLD

The risk associated with SSB consumption can be used both for counseling and to support future policies. These findings amplify data from trials where reduced SSB consumption reduced liver fat.1 Further, given that the United Kingdom's 2016 tax on SSBs led to a 50% reduction in SSB sales,6 our data highlight the potential benefits of such policies.

#### Limitations

Fist, our data are cross-sectional and causality between SSB and liver outcomes cannot be inferred. Second, those with failed VCTE exams (including high IQR/m) were not captured in the study and could represent a significant at-risk group. Third, we examined liver but not trunk or appendicular fat. However, as shown by Unalp-Arida and Ruhl, liver fat and fibrosis are strongly associated with fat elsewhere.<sup>7</sup>

#### Conclusion

SSB consumption is associated with increased liver stiffness and steatosis in a nationally representative population of healthy adults.

#### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Tapper is the guarantor of this article

#### Conflicts of interest:

Elliot Tapper has served as a consultant to Norvartis, Axcella, and Allergan, has served on advisory boards for Mallinckrodt, Bausch Health, Kaleido, Novo Nordisk, and has received unrestricted research grants from Gilead and Valeant. No other author has a conflict of interest.

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# Table 1:

Associations between sugar-sweetened beverage consumption (SSB) and liver stiffness among 2,706 healthy adults from 2017–18 NHANES

	Ē	Liver stiffness median (continuous)	dian (con	tinuous)		Liver stiffn	ess med	Liver stiffness median >7 kPa	
Sugar-sweetened beverage consumption	Age- an	d sex adjusted	Multiva	Age- and sex adjusted Multivariate-adjusted Age- and sex adjusted	Age- and	l sex adjusted	M	Multivariate-adjusted	ldjusted
	ھ	95% CI	в	95% CI	OR	95% CI	OR	95%	95% CI
0 servings	Ref.		Ref.		Ref.		Ref.		
>0-1 serving	0.64	-0.07, 1.34	0.61	-0.03, 1.24	1.80	0.96, 3.38	1.77	1.04	1.04, 3.04
>1-2 servings	0.88	-0.54, 2.31	0.81	-0.55, 2.18	1.93	1.26, 2.96	2.05	1.20	1.20, 3.52
>2 servings	0.58	0.14, 1.02	0.48	0.03, 0.93	2.18	1.35, 3.54	2.30	1.39	1.39, 3.79
P-trend		0.05		0.08		0.001		0.001	
		CAP (continuous)	ntinuous)			CAP	CAP >248 dB/m	B/m	
Sugar-sweetened beverage consumption	Age- an	Age- and sex adjusted Multivariate-adjusted	Multiva	riate-adjusted	Age-	Age- and sex adjusted	pa	Multivaria	Multivariate-adjusted
	<u>م</u>	95% CI	٩	95% CI	OR	95% CI		OR	95% CI
0 servings	Ref.		Ref.		Ref.			Ref.	
>0-1 serving	60.9	-4.31, 16.50	3.82	-5.09, 12.73	1.19	0.80, 1.77	2	1.11	0.79, 1.56
>1-2 servings	16.43	6.41, 26.44	12.86	3.30, 22.43	1.68	1.22, 2.30	•	1.51	1.18, 1.94
>2 servings	15.48	3.52, 27.43	10.31	-0.97, 21.59	1.73	1.19, 2.52	•	1.48	1.02, 2.14
P-trend		0.005		0.03		0.001		9	0.006

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and waist circumference are mediators CAF = Controlled alternation parameter, return an involution the causal pathway between SSB and liver fat or stiffness.