Establishing 24-Hour Urinary Sucrose Plus Fructose as a Predictive Biomarker for Total Sugars Intake

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ABSTRACT

Background: Twenty-four–hour urinary sucrose and fructose (24uSF) has been studied as a biomarker of total sugars intake in two feeding studies conducted in the United Kingdom (UK) and Arizona (AZ). We compare the biomarker performance in these populations, testing whether it meets the criteria for a predictive biomarker.

Methods: The UK and AZ feeding studies included 13 and 98 participants, respectively, aged 18 to 70 years, consuming their usual diet under controlled conditions. Linear mixed models relating 24uSF to total sugars and personal characteristics were developed in each study and compared. The AZ calibrated biomarker equation was applied to generate biomarker-estimated total sugars intake in UK participants. Stability of the model across AZ study subpopulations was also examined.

Results: Model coefficients were similar between the two studies [e.g., log(total sugars): UK 0.99, AZ 1.03, $P = 0.67$], as was the ratio of calibrated biomarker person-specific bias to between-person variance (UK 0.32, AZ 0.25, $P = 0.68$). The AZ equation estimated UK log(total sugar intakes) with mean squared prediction error of 0.27, similar to the AZ study estimate (0.28). Within the AZ study, the regression coefficients of log(total sugars) were similar across age, gender, and body mass index subpopulations.

Conclusions: Similar model coefficients in the two studies and good prediction of UK sugar intakes by the AZ equation suggest that 24uSF meets the criteria for a predictive biomarker. Testing the biomarker performance in other populations is advisable.

Impact: Applications of the 24uSF biomarker will enable improved assessment of the role of sugars intake in risk of chronic disease, including cancer.

See related commentary by Prentice, p. 1151

Introduction

Establishing an unbiased biomarker for objective assessment of sugars intake in epidemiologic research would greatly facilitate more reliable evaluation of relationships between sugars intake and health outcomes. There is already good evidence that such relationships cannot be reliably assessed using self-reported sugars intake, due to their inherent measurement error. For example, a positive association between sugars intake and obesity was found when using urinary biomarker levels as a measure of sugars intake (1, 2), but no association (1) or an inverse association (2) when using self-reports. In the Women's Health Initiative, type 2 diabetes risk was negatively associated with self-reported sugars intake, but not with biomarker-calibrated intake estimates (3).

Twenty-four–hour urinary sucrose and fructose (24uSF) was developed as a potential predictive biomarker of total sugars intake based on three UK feeding studies (4, 5). Predictive biomarkers exhibit a strong temporal relationship with true intake, yet are associated with a certain level of person-specific, intake-related and covariate-related bias, and within-subject random error. Under the assumption that their relationship with true intake is stable and their measurement error parameters, estimated from a feeding study against true intake, do not vary across populations (see criteria for predictive biomarkers under statistical analysis), predictive biomarkers can be calibrated for their intake-related and covariate-related biases to provide reference dietary instruments. Similar to recovery biomarkers, predictive biomarkers can then be used for evaluating measurement error structure in dietary self-report and, most importantly, for correcting the biased estimation that is caused by dietary measurement error in diet–disease association studies, including diet–cancer studies. In the Discussion section, we explain how a predictive biomarker can be used to achieve such bias correction.

Tasevska and colleagues (6) proposed 24uSF as a candidate predictive biomarker for usual total sugars intake and developed an equation to calibrate the biomarker based on the estimated relationship between the 24uSF level and daily true sugars intake in a habitual-diet feeding study involving 13 participants in the UK. This calibrated biomarker has since been used as a reference instrument to correct for bias due to measurement error in nutritional epidemiologic studies (3, 6–8), although without having confirmed that it was unbiased for true intake in other than UK populations. Therefore, we conducted a second controlled feeding study, to investigate its performance in US participants (9). In this report, we examine whether 24uSF reasonably meets the criteria of a predictive biomarker by comparing the calibrated biomarker equations developed in the UK and AZ feeding studies, as well as investigating the stability of the biomarker–intake relationship across subgroups in the AZ study.

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Materials and Methods

A full description of the designs of the UK and AZ studies may be found in previous publications (5, 9). Here, we give a brief summary.

UK Feeding Study

Thirteen healthy volunteers (7 male, 6 female), aged 23 to 66 years, living in the area of Cambridge, UK, participated in a 30-day in-patient controlled feeding study during 2003 to 2004 (5). After assessing their diet over a month using a food diary, they were provided with their usual diet over a 30-day period while living in a volunteer suite. Food intake was calculated from the food provided minus the uneaten food. Nutrient intake was derived from the UK food composition tables (10). Urine was collected continuously to provide 24-hour urines over all 30 days of study, and completeness of collection was assessed each day by p-aminobenzic acid (PABA) marker. Only four urine collections out of the 390 (13 participants × 30 collections) had to be omitted from the analysis; one because of incompleteness, two because of spillage and one because the participant did not take the PABA tablets. Sucrose and fructose in urine were measured with a kit specific for sucrose, glucose, and fructose (sucrose/D-glucose/D-fructose from Biochemica Mannheim, R-Biopharm, Roche) using Cecil CE 2041 2000 Series spectrophotometer to measure the absorbance. All subjects gave their fully informed written consent, and the study was approved by the Cambridge Local Research Ethics Committee (LREC No. 01/421).

AZ Feeding study

One hundred and thirteen men and women volunteers, aged 18 to 70 years, living in the Phoenix Metropolitan Area participated between March 2016 and June 2019 (9). After assessing their diet using a 7-day food diary applied twice to cover a 2-week period, they were provided with their usual diet over a 15-day period. Food intake was calculated using the same methodology as in the UK study. Nutrient intake was derived from the Nutrition Data System for Research database Version 2016–2018 (Nutrition Coordinating Center, Minneapolis, Minnesota). All participants signed written informed consent and the study was approved by the Institutional Review Board of Arizona State University. Twenty-four–hour urine was collected every other day to provide 8 days of urine over the 15-day study period, and completeness of collection was assessed each day by PABA. One hundred of the participants completed the study protocol and provided 795 24-hour urine collections. In 25% of these samples, the PABA recovery in urine was <77.9% (11) or the participants reported more than one missed void or >0.5 oz missed volume; these urine collections were omitted from statistical analysis. Sucrose and fructose in urine were measured on a Beckman DU 730 Life Science UV/Vis spectrophotometer using the same method as in the UK study (5).

Statistical analysis

The main focus of our analyses was to evaluate whether 24uSF meets the two main criteria that define a predictive biomarker; see the Appendix in Tasevska and colleagues (6). Suppose that the relationship between the biomarker M and true intake T is described by the linear mixed effects model:

$$\log(M_{ij}) = \beta_0 + \beta_T \log T_{ij} + \beta_X^T X_i + u_i + \varepsilon_{ij} \qquad \text{(A)}$$

Where, in our case, M_{ij} is the 24uSF level on the j^{th} day of assessment of participant i, T_{ij} is the total sugars intake of that participant on the same day, X_i is a vector of covariate values for participant i, u_i is the person-specific bias, and ε_{ij} is the random error of the regression equation. As explained in Tasevska and colleagues (6), the first criterion is that the regression coefficients β_0, β_T, and β_X have very similar values across different populations. The second criterion is that the ratio of $\text{var}(u_i)$ to $\beta_T^2\text{var}(\log T_i)$ is stable across different populations, where T_i is the usual total sugars intake of participant i. This is operationalized by calculating the ratio $k = \text{var}(u_i)/[\text{var}(u_i) + \beta_T^2\text{var}(\log T_i)]$ and considering its value for different populations.

To check whether or not 24uSF appears to conform with these criteria, we performed the following analyses. To check on the first criterion, we fit the linear mixed model (A) to the data from the AZ study and the UK study using the same covariates X and compared the estimated regression coefficients obtained from the two studies. The covariates X chosen to enter the model were those participant characteristics with regression coefficients that were found to be statistically significant ($P < 0.05$) in either or both of the studies. These were sex and log(age). (Although fat and protein intake were found to be significant determinants of biomarker level in the AZ study they were not retained in the final model, given their low contribution to the overall R-squared, their marginal statistical significance (9), and because they would not be typically observable in an epidemiologic study.) We then compared the model (A) regression coefficients β_0, β_T, and β_X, estimated from the two studies. We also predicted the biomarker level for a man and a woman with mean ages and mean total sugar intakes across the two studies using the model equations from the UK and the AZ study and estimated the differences between these predictions with their standard errors (SE).

As an extra check of stability of the model across the two studies, we used the calibrated biomarker equation derived from the AZ study (9), namely,

$$\log(\textit{total sugars}) = \frac{\log(24\text{uSF}) + 0.066 - 0.285 \times \text{sex} + 0.347 \times \log(\text{age})}{1.027} \qquad \text{(B)}$$

Where female sex = 1 and male sex = 0, to generate biomarker-based predictions of the 382 daily total sugars intake of participants in the UK study. The overall bias of the biomarker-estimated intake and the mean squared prediction error were estimated, and the latter compared with that obtained from the AZ study intakes.

Finally, as another check of the first criterion, i.e., the stability of the relationship between biomarker and intake across different populations, we also fit to the data from the AZ study the model (A) with an interaction term between log total sugars intake and a binary participant characteristic. The interaction coefficient then indicates the magnitude of the difference in the regression coefficient of log total sugars between the subgroups defined by the binary characteristic. Small interaction coefficients would then indicate stability of model (A) over different subpopulations. The binary characteristics chosen were sex, age (<44 vs. ≥44 years) and body mass index (BMI; <27.5 vs. ≥27.5).

To check on the second criterion, we estimated the variance ratio k from the data in the two studies and compared their values. SEs of k were estimated in the AZ study using the nonparametric bootstrap method, but in the AZ study, because of the small numbers of participants, the delta method was used.

It could be argued that besides these two criteria, a third criterion, requiring a specified minimum correlation between the predictive biomarker and true intake, should be added, as was proposed by Lampe and colleagues (12). Although we do not propose such a minimum correlation in this paper, we do report on the high correlation achieved.

All analyses were conducted using SAS, version 9.4 (SAS Institute, Inc.).

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The data used in this study are not publicly available as no appropriate publicly available database exist, but are available upon reasonable request from the corresponding author for a period of 6 years after publication of the manuscript.

Results

Personal characteristics, sugars intakes and urinary sugar levels of the participants in the UK and AZ studies, as reported previously (5, 9) are summarized in **Table 1**. While the characteristics of the participants in the two studies were distributed similarly, UK participants tended to consume more sugars than AZ participants did [202 (SD = 69) g vs. 109.4 (46.9) g], and their 24uSF levels were correspondingly higher [98.3 (65.8) mg vs. 50.7 (36.1) mg].

The four estimated coefficients of the linear mixed model (A) are shown in **Table 2** for the two studies. No statistically significant differences were found between the respective coefficients of the two studies. In addition, a test of the global hypothesis that all four coefficients were equal was not rejected ($P = 0.75$). The predicted log 24uSF for a 42-year-old man consuming 155 g/d of total sugars was 3.99 for the AZ study and 4.04 for the UK study [difference = –0.05; 95% confidence interval (CI), –1.38 to 1.28], representing a relative difference of only 5% on the original scale. For a woman with the same age and same total sugars consumption, predicted log 24uSF was 4.28 in the AZ study and 4.15 in the UK study (difference = 0.12; 95% CI, –1.23 to 1.47), representing a relative difference of 13% on the original scale. However, note the wide CIs due to the small size of the UK study.

The estimated ratios of person-specific bias variance to between-person variance of the calibrated biomarker were 0.25 for the AZ study and 0.32 for the UK study. The difference was not statistically significant ($P = 0.68$).

We then used the biomarker calibration equation derived from the larger AZ study to generate biomarker-based estimates for 382 log daily total sugars intake estimates of the participants in the UK study and compared these values with the observed daily intakes. **Figure 1** shows a plot of the biomarker-estimated versus the observed intake values. It can be seen that points fall roughly equally on either side of the line of equality. **Figure 2** shows a Bland–Altman plot of the same data. The mean squared predicted error was 0.27. Notably, this was close to the value of 0.28 reported in **Table 3** of the AZ study report (9). The value of 0.27 indicates that a typical prediction lies within 60% and 168% [$\exp(\pm\sqrt{(0.27)})$] of the true total sugars intake. The mean biomarker-estimated log total sugars intake was 5.20 (181 g/d) versus an observed mean of 5.22 (185 g/d), and the correlation between predicted and observed intake was 0.9 ($P < 0.0001$).

Within the data of the AZ study, we estimated, in extensions of model (A), interactions between the log total sugars intake and gender, age and BMI. The estimated coefficients of log sugars intake were similar within the predefined subgroups as illustrated by the small interaction coefficients, which were not statistically significant (**Table 3**).

Table 1. Characteristics, and sugars intake and urinary sugar levels of participants in the UK and AZ studies[a].

	UK Study ($n = 13$)	AZ Study ($n = 98$)
Male (*n*)	7 (54%)	43 (44%)
Age (years)	43.2 (15.9)	40.8 (13.6)
BMI	25.5 (4.3)	27.2 (4.1)
Total sugars intake (g/d)	202.0 (69.0)	109.4 (46.9)
Sucrose intake (g/d)	82.4 (26.3)	54.4 (27.1)
Fructose intake (g/d)	48.6 (25.4)	19.5 (12.6)
Urinary sucrose (mg/d)	36.5 (16.6)	22.9 (21.6)
Urinary fructose (mg/d)	61.8 (61.3)	21.2 (18.5)
Urinary sucrose & fructose (mg/d)	98.3 (65.8)	50.7 (36.1)

[a]Values are expressed as *n* (%) or mean (SD).

Discussion

In this report, we investigated whether the stability assumptions for predictive biomarkers are met for the 24uSF biomarker for total sugars intake. We compared the relationship between biomarker and observed dietary intake by fitting biomarker model (A) separately to two controlled feeding studies of a similar design conducted in different countries. We found that the estimated regression coefficients and the ratio of variances (k) were similar in the two studies, providing evidence that this relationship was stable across different populations. We also applied the calibrated biomarker equation from the AZ study to 24uSF in the UK study to generate biomarker-estimated intake and obtained estimates that were similar to observed intakes in the UK study population, thereby providing evidence of the transferability of the calibrated biomarker equation generated in the AZ study, and the robustness of the biomarker. The criterion of stability was further confirmed when comparing the biomarker model across different subpopulations in the AZ study defined by sex, age, and BMI.

Despite the difference in level of total sugars intake in the two study samples, the limited range of intake in the US study and the small size of the UK study, the linear mixed models regressing the biomarker on observed 'true' total sugars intake along with age and sex produced similar regression coefficients in the two populations. Most importantly, the coefficient for observed intake, which measures the intake-related bias in the biomarker, was close to 1 in both studies, indicating very little bias.

The importance of establishing the calibrated total sugars biomarker as a predictive biomarker is that it can be used to adjust for the bias in estimated diet–disease association parameters that is caused by dietary measurement error. For example, suppose one wished to conduct a nutritional cohort study of the association between colon cancer and total sugars intake, based on measuring total sugars intake by administering a food frequency questionnaire (FFQ). Having developed the calibrated biomarker equation for total sugars through the feeding studies reported here, the calibrated biomarker could then be included as the reference instrument together with FFQ-reported total sugars intake in an internal validation sub-study of the cohort. This sub-study would allow the development of an FFQ-based calibration equation for total sugars intake, which could then be applied to obtain calibrated FFQ-reported total sugars intake in all cohort participants. The calibrated FFQ-reported total sugars intake could then be used in a regression model of colon cancer risk on total sugars intake, providing an unbiased estimate of their association. This approach is known as regression calibration. It should be noted that when applying regression calibration, the sample size of the internal validation study needs to be increased to overcome the loss of power due to generating biomarker-estimated usual intake through the calibrated biomarker equation rather than measuring it directly using a recovery biomarker (9). In addition, the sample of the cohort study needs to be increased due to use of calibrated FFQ-reported total sugars intake in place of the unknown true usual total sugars intake (13). A second use of the

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Table 2. Coefficients of the linear mixed model estimated from the AZ and the UK study data (SEs in parentheses).

Coefficient	AZ study ($n = 98$)	UK study ($n = 13$)	P value for difference[a]
Intercept	0.11 (0.45)	1.46 (1.00)	0.22
log(total sugar intake, g)	1.03 (0.04)	0.99 (0.09)	0.67
log(age, y)	−0.35 (0.11)	−0.64 (0.22)	0.24
Gender	0.28 (0.08)	0.11 (0.17)	0.35

[a]On the basis of a test of z = difference/SE(difference).

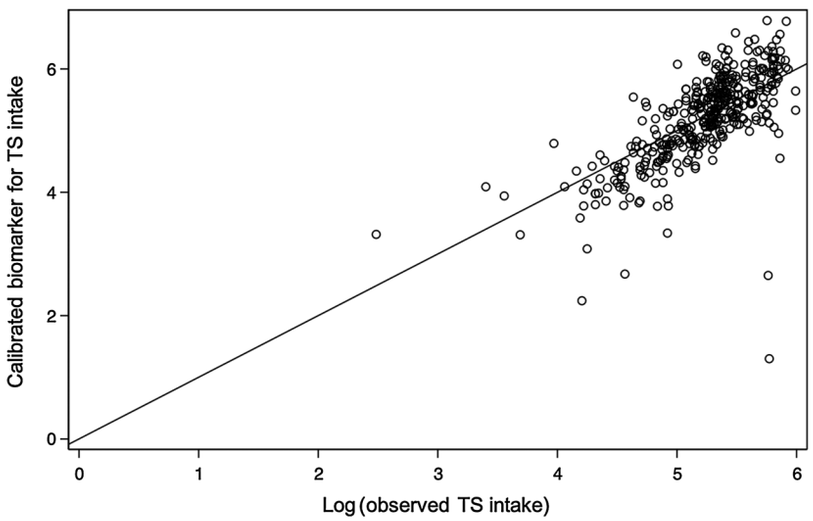

Figure 1.
Plot of 382 daily log biomarker-estimated total sugar intakes (TS) based on the AZ study calibrated biomarker equation versus the observed values intake in the UK study. The line drawn through the points is the line of equality ($r = 0.90$, $P < 0.001$).

predictive biomarker could be as the reference instrument in validation studies that investigate the measurement error properties of dietary self-report instruments.

Several US studies have, so far, used the original calibrated biomarker equation developed in the UK study population (3, 6, 8, 14). Our findings reported here support the previously made assumption of transferability of the biomarker equation across different populations, and validate biomarker applications among US participants.

Applying the calibrated biomarker as a reference dietary instrument in US validation studies (6, 8) revealed considerable intake-related and person-specific bias in total sugars estimates derived from commonly used self-report instruments. Furthermore, the person-specific bias was highly correlated between different types of self-report,

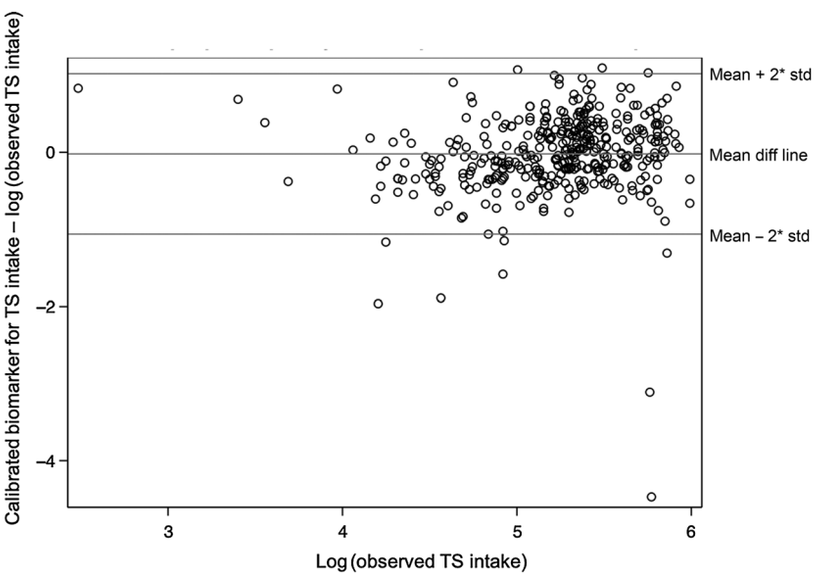

Figure 2.
Bland–Altman plot of biomarker-estimated minus observed values versus observed values for 382 daily log total sugar intakes (TS), where biomarker-estimated values are based on the AZ study calibrated biomarker equation and observed values are those in the UK study. The values of "mean + 2*SD" and "mean − 2*SD" in the graph are 1.02 and −1.06, respectively, and the mean difference is −0.02.

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Table 3. Regression coefficient of the log total daily sugars intake according to subgroups of gender, age and BMI, and interaction coefficients derived from interaction terms in extensions of model (A).

Variable	Subgroup	Regression coefficient for log total sugars intake	Interaction coefficient[a]	$P_{interaction}$[b]
Gender	Male	0.97	0.14	0.07
	Female	1.11		
Age, y	<44	0.99	0.11	0.15
	≥44	1.10		
BMI, kg/m^2	<27.5	1.06	−0.08	0.31
	≥27.5	0.99		

[a]Indicates the magnitude of the difference in the regression coefficient of log total sugar within subgroups.
[b]Wald z-test.

invalidating the use of one self-report instrument for validating other self-report instruments. In a diverse sample of US Hispanics/Latinos, a biomarker-based total sugars intake estimate was almost double the intake measured by multiple 24-hour recalls (167.5 g/d vs. 90.6 g/d), and no correlation between the two was observed ($r = 0.06$), suggesting a high level of misreporting of sugars intake in this population (14). In a prospective investigation of total sugars intake in relation to type 2 diabetes risk in a cohort of postmenopausal women, high intake of uncalibrated sugars was associated with a lower risk of type 2 diabetes (3). This protective association was no longer evident when biomarker-calibrated total sugars intake was instead used to estimate total sugars intake. The calibrated biomarker has also been used in UK studies. In a nationally representative sample of the UK general population, calibrated biomarker as a sole measure of total sugars intake was significantly positively associated with different measures of obesity. Other studies have used the urinary sugars as a biomarker, but without calibrating it (15) or by measuring it in spot or partial urine collections (1, 2, 16, 17), although such applications have not been validated.

A major strength of this report is the use of data from two comparable controlled feeding studies, carefully designed to investigate the characteristics of 24uSF biomarker. Availability of multiple replicate biomarker and dietary measurements ensured reliable assessment of the relationship between biomarker and diet, while the habitual diet design allowed for developing calibrated biomarker equations that are applicable in free-living populations. Nonetheless, while the AZ study was large for a feeding study, the UK study had limited sample size, yielding parameter estimates that were less precise. Thus, although, we found no evidence against the 24uSF being a predictive biomarker that could be used in different populations, further testing using larger comparable feeding studies in other populations is advised. While we have checked the transferability of the calibrated biomarker equation in generally healthy adult populations, the performance of the equation has still not been investigated among children and adolescents, in which age groups only the uncalibrated biomarker has so far been used (18–20). Seventy percent of US children aged 5 to 19 years exceed the Dietary Guidelines for Americans recommendation for added sugars (21), even though added sugars intake has been linked with number of adverse health outcomes (22–25) and nutrient inadequacies (26). Characterizing the application of the sugars biomarker in this at-risk population, and generating strong causal evidence for sugars–disease associations is of high public health relevance. In this report, we have confirmed the stability of the relationship of the 24uSF biomarker with total sugars intake across different populations, giving further support that it complies with the criteria for predictive biomarkers. It, therefore, seems suitable to use as a reference instrument in dietary validation/calibration studies to estimate the measurement error structure in self-reported total sugars intake and to adjust for measurement error estimated relationships between sugars intake and the risk of chronic disease, including cancer.

Authors' Disclosures

No disclosures were reported.

Authors' Contributions

L.S. Freedman: Conceptualization, formal analysis, methodology, writing–original draft. **V. Kipnis:** Formal analysis, methodology, writing–review and editing. **D. Midthune:** Formal analysis, investigation, methodology, writing–review and editing. **J. Commins:** Formal analysis, writing–review and editing. **B. Barrett:** Formal analysis, writing–review and editing. **V. Sagi-Kiss:** Investigation, writing–review and editing. **S.A. Palma-Duran:** Investigation, writing–review and editing. **C.S. Johnston:** Investigation, writing–review and editing. **D.M. O'Brien:** Investigation, writing–review and editing. **N. Tasevska:** Conceptualization, funding acquisition, investigation, methodology, writing–original draft, writing–review and editing.

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References

1. Bingham S, Luben R, Welch A, Tasevska N, Wareham N, Khaw KT. Epidemiologic assessment of sugars consumption using biomarkers: comparisons of obese and nonobese individuals in the European Prospective Investigation of Cancer Norfolk. Cancer Epidemiol Biomarkers Prev 2007;16:1651–4.
2. Kuhnle GG, Tasevska N, Lentjes MA, Griffin JL, Sims MA, Richardson L, et al. Association between sucrose intake and risk of overweight and obesity in a prospective sub-cohort of the European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk). Public Health Nutr 2015;18:1–10.
3. Tasevska N, Pettinger M, Kipnis V, Midthune D, Tinker LF, Potischman N, et al. Associations of biomarker-calibrated intake of total sugars with the risk of type 2 diabetes and cardiovascular disease in the Women's Health Initiative Observational Study. Am J Epidemiol 2018;187:2126–35.

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4. Joosen AM, Kuhnle GG, Runswick SA, Bingham SA. Urinary sucrose and fructose as biomarkers of sugar consumption: comparison of normal weight and obese volunteers. Int J Obes 2008;32:1736–40.
5. Tasevska N, Runswick SA, McTaggart A, Bingham SA. Urinary sucrose and fructose as biomarkers for sugar consumption. Cancer Epidemiol Biomarkers Prev 2005;14:1287–94.
6. Tasevska N, Midthune D, Potischman N, Subar AF, Cross AJ, Bingham SA, et al. Use of the predictive sugars biomarker to evaluate self-reported total sugars intake in the Observing Protein and Energy Nutrition (OPEN) study. Cancer Epidemiol Biomarkers Prev 2011;20:490–500.
7. Beasley JM, Lacroix AZ, Larson JC, Huang Y, Neuhouser ML, Tinker LF, et al. Biomarker-calibrated protein intake and bone health in the Women's Health Initiative clinical trials and observational study. Am J Clin Nutr 2014;99:934–40.
8. Tasevska N, Midthune D, Tinker LF, Potischman N, Lampe JW, Neuhouser ML, et al. Use of a urinary sugars biomarker to assess measurement error in self-reported sugars intake in the Nutrition and Physical Activity Assessment Study (NPAAS). Cancer Epidemiol Biomarkers Prev 2014;23:2874–83.
9. Tasevska N, Sagi-Kiss V, Palma-Duran SA, Barrett B, Chaloux M, Commins J, et al. Investigating the performance of 24-h urinary sucrose and fructose as a biomarker of total sugars intake in US participants: a controlled feeding study. Am J Clin Nutr 2021;114:721–30.
10. Food Standards Agency, Institute of Food Research. McCance and Widdowson's The Composition of Foods Sixth Summary Edition. Cambridge, United Kingdom: Royal Society of Chemistry; 2002.
11. Jakobsen J, Ovesen L, Fagt S, Pedersen AN. Para-aminobenzoic acid used as a marker for completeness of 24-hour urine: assessment of control limits for a specific HPLC method. Eur J Clin Nutr 1997;51:514–9.
12. Lampe JW, Huang Y, Neuhouser ML, Tinker LF, Song X, Schoeller DA, et al. Dietary biomarker evaluation in a controlled feeding study in women from the Women's Health Initiative cohort. Am J Clin Nutr 2017;105:466–75.
13. Keogh RH, Shaw PA, Gustafson P, Carroll RJ, Deffner V, Dodd KW, et al. STRATOS guidance document on measurement error and misclassification of variables in observational epidemiology: Part 1-Basic theory and simple methods of adjustment. Stat Med 2020;39:2197–231.
14. Beasley JM, Jung M, Tasevska N, Wong WW, Siega-Riz AM, Sotres-Alvarez D, et al. Biomarker-predicted sugars intake compared with self-reported measures in US Hispanics/Latinos: results from the HCHS/SOL SOLNAS study. Public Health Nutr 2016;19:3256–64.
15. Abreu TC, Hulshof PJM, Boshuizen HC, Trijsburg L, Gray N, de Vries JHM. Validity coefficient of repeated measurements of urinary marker of sugar intake is comparable to urinary nitrogen as marker of protein intake in free-living subjects. Cancer Epidemiol Biomarkers Prev 2021;30:193–202.
16. Ramne S, Gray N, Hellstrand S, Brunkwall L, Enhörning S, Nilsson PM, et al. Comparing self-reported sugar intake with the sucrose and fructose biomarker from overnight urine samples in relation to cardiometabolic risk factors. Front Nutr 2020;7:62.
17. Ramne S, Brunkwall L, Ericson U, Gray N, Kuhnle GGC, Nilsson PM, et al. Gut microbiota composition in relation to intake of added sugar, sugar-sweetened beverages, and artificially sweetened beverages in the Malmö Offspring Study. Eur J Nutr 2021;60:2087–97.
18. Perrar I, Gray N, Kuhnle GG, Remer T, Buyken AE, Alexy U. Sugar intake among German adolescents: trends from 1990 to 2016 based on biomarker excretion in 24-h urine samples. Br J Nutr 2020:1–9.
19. Johner SA, Libuda L, Shi L, Retzlaff A, Joslowski G, Remer T. Urinary fructose: a potential biomarker for dietary fructose intake in children. Eur J Clin Nutr 2010; 64:1365–70.
20. Della Corte KA, Penczynski K, Kuhnle G, Perrar I, Herder C, Roden M, et al. The prospective association of dietary sugar intake in adolescence with risk markers of type 2 diabetes in young adulthood. Front Nutr 2020;7:615684.
21. U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020 –2025. 9th Edition. December 2020. Available from: DietaryGuidelines.gov.
22. Keller A, Bucher Della Torre S. Sugar-sweetened beverages and obesity among children and adolescents: a review of systematic literature reviews. Child Obes 2015;11:338–46.
23. Vos MB, Kaar JL, Welsh JA, Van Horn LV, Feig DI, Anderson CAM, et al. Added sugars and cardiovascular disease risk in children: a scientific statement from the American Heart Association. Circulation 2017;135:e1017–e34.
24. Chi DL, Scott JM. Added sugar and dental caries in children: a scientific update and future steps. Dent Clin North Am 2019;63:17–33.
25. DiStefano JK, Shaibi GQ. The relationship between excessive dietary fructose consumption and paediatric fatty liver disease. Pediatr Obes 2021;16:e12759.
26. González-Padilla E, A Dias J, Ramne S, Olsson K, Nälsén C, Sonestedt E. Association between added sugar intake and micronutrient dilution: a cross-sectional study in two adult Swedish populations. Nutr Metab 2020;17:15.

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