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Cross-Sectional Associations between Sugar-Sweetened Beverage Intake and DEXA-Scan Adiposity among WHI Observational Study Participants

THESIS

submitted in partial satisfaction of the requirements for the degree of

MASTER OF SCIENCE

in Epidemiology

by

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2022

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ABSTRACT OF THE THESIS

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Excess visceral adipose tissue (VAT) is associated with increased risk of metabolic syndrome, diabetes, cardiovascular disease, cancer, and mortality. Excess subcutaneous adipose tissue (SAT) is thought to contribute to development of insulin resistance and type 2 diabetes. The influence of sugar-sweetened beverage (SSB) consumption on VAT, SAT, and VAT:SAT ratio is not yet well established. The associations of FFQ-reported SSBs and adjusted mean DEXA-scan measured adiposity was examined in 5,898 postmenopausal women aged 49-79 from the WHI Observational Study. Consuming ½ - 1 serving/d was associated with lower mean SAT compared to 0 servings/d (352.56cm^2 vs. 364.82cm^2, $p = 0.05$). Consuming more than 1 serving/d was associated with higher VAT (164.21cm^2 vs. 154.32cm^2, $p = 0.01$). Consuming any amount of SSB was associated with significantly higher VAT:SAT ratio. Findings suggest any level of SSB consumption is associated with increased VAT:SAT ratio, increased VAT (when consumption is greater than 1 serving/d), and decreased SAT (when consumption is between ½ - 1 serving/d).

INTRODUCTION

Visceral adipose tissue (VAT) is the fat that surrounds the internal organs of the abdominal cavity. VAT has an imperative role in the protection and insulation of vital organs and produces essential hormones. However, carrying excess VAT is associated with increased risk of metabolic syndrome, diabetes, cardiovascular disease, certain cancers, and mortality.[1, 2] While there is no sufficient evidence for an association between SSBs and overall adiposity (e.g., percent body fat, BMI), recent literature has found a positive association between sugar-sweetened beverage (SSB) consumption and VAT [3-7] and visceral-to-subcutaneous adipose ratio [5, 6] which is a measure of relative adipose distribution that is also correlated with increased cardiometabolic risk independent of VAT[7]. Subcutaneous adipose tissue (SAT) is the fat below the skin responsible for the storage and use of lipid energy.[8] Excess SAT has shown either a negative[6] or null[3] association with SSBs and is thought to contribute to insulin resistance and type 2 diabetes[10]. Upon literature review, study populations from relevant publications were either large or included significant proportions of racial/ethnic minorities, but not both. Of the five studies, three used study populations that were either entirely Non-Hispanic White (NHW) and a sample size of 791, or a vast majority NHW and sample sizes of 1,003 and 2,596. One studied 60 Non-Hispanic Black and Hispanic adolescents aged 14-18, one studied 2,665 Greek children aged 9-13, and one used a longitudinal study design.

This study utilized a larger, more racially diverse dataset from the Women's Health Initiative observational cohort to examine the relation between SSB intake and VAT, SAT, and VAT-to-SAT ratio among 5,898 postmenopausal women.

METHODS

An observational cross-sectional study was conducted using data from the Women's Health Initiative Observational Study to investigate the association between consumption of sugar-sweetened beverages (SSBs) and VAT, SAT, and VAT:SAT ratio which provides information about relative fat distribution, among postmenopausal women aged 49-79 from 2000-2006. Participants were excluded from analysis due to incomplete or missing exposure or outcome data, improbable or missing total energy intake, or missing dietary data. Exclusion criteria yielded a final analytical sample size of 5,898.

SSB intake was ascertained via validated food frequency questionnaire (number of 8-ounce servings) and compared to the area of visceral and subcutaneous fat measured from DEXA scans. WHI eligibility criteria for receiving a DEXA scan were unavailable but Brownbill and Ilich cite a typical scanning table weight limitation of 114-159kg depending on the manufacturer which offers some upper bound for participant inclusion.[11] SSBs originally included non-diet soft drinks, punch drinks, orange and grapefruit juice, and other fruit juices. For the purposes of this study, SSBs were reconfigured to include only non-diet soft drinks and punch drinks per WHI protocol[12] with the reasoning that the health behaviors of individuals who opt for beverages with added sugars differ fundamentally from individuals who avoid added sugars and opt for fruit juices or other forms of naturally occurring sugars that include more complex nutritional content. Confounding factors were adjusted using the following variables from WHI questionnaire forms: physical activity (as represented by minutes of moderate-to-strenuous activity per week - F143), inactivity (as represented by hours per day spent sitting or lying - F42), smoking (as represented by categorical pack-years of smoking which takes into account years of smoking and number of cigarettes smoked per day on average - F34), age at screening (F2), education, race (as represented by race categories for NIH reporting - F41), Hispanic/Latino ethnicity (as represented by ethnicity categories for NIH reporting - F41), family income, total energy intake (kcal/day - F60), and overall dietary pattern. To control for overall dietary pattern, an alternative Mediterranean Diet score was calculated from FFQs using the WHI standard aHEI algorithm.[13] Each participant's score for each food category of the modified Mediterranean Diet score was then dichotomized as being either above or below the sample-specific median for that food category. A score of 1 indicates an individual's intake for the food category is above the sample specific median, and a score of 0 indicates it is below the median. Finally, all categories were summed for a final total score (a total of 9 categories for a maximum score of 9) which was used as the overall dietary pattern adjustment factor.

SAS v9.4 was used to obtain adjusted means of each adiposity outcome to assess the association of FFQ-reported SSB intake with DEXA-measured area of VAT (cm^2) and SAT (cm^2), and VAT:SAT ratio adjusted for confounders.

RESULTS

In the final analytical sample of 5,898, the distribution of SSB servings was highly right-skewed with a median of 0 and 75th percentile equal to 0.29 servings. Approximately half of participants reported 0 servings while 27.9% reported less than ½ serving/day, 10.5% reported between ½ - 1 serving/day, and 10.9% reported >1 serving/day. Table 1 shows the distribution of baseline characteristics across exposure groups. Mean age and hours of inactivity were relatively stable across the four exposure groups. Women who reported consuming any SSBs had a lower Mediterranean Diet score, spent less time engaging in moderate to strenuous physical activity, and had a higher total energy intake. Compared to women who reported no SSB consumption, women who reported having consumed any SSBs tended to have less education, have a lower family income, and were less likely to be White. A little over half of the study participants identified as never smokers

Table 1: Baseline characteristics of WHI Observational Study participants in the year 2000, n = 5,898

Covariates	Exposure group - Sugar-sweetened beverage servings			
	0 servings/d (n = 2996)	**< ½ serving/d (n = 1650)**	**½ - 1 serving/d (n = 617)**	**>1 serving/d (n = 641)**
Age *mean(SD)*	64.2 (7.4)	64.0 (7.4)	62.5 (7.5)	61.3 (7.6)
Education *n(%)*				
Did not finish high school	173 (5.8%)	164 (10.0%)	99 (16.2%)	123 (19.4%)
High school diploma or GED	632 (27.2%)	372 (22.7%)	146 (23.8%)	156 (24.6%)
Vocational or some college	1074 (36.2%)	595 (36.3%)	215 (35.1%)	215 (33.9%)
College graduate or some post-graduate or professional	596 (20.1%)	270 (16.5%)	81 (13.2%)	65 (10.3%)
Graduate degree	490 (16.5%)	236 (14.4%)	72 (11.7%)	75 (11.8%)
Race *n(%)*				
White	2652 (88.6%)	1267 (76.9%)	404 (65.5%)	380 (59.3%)
Black	199 (6.7%)	240 (14.6%)	141 (22.9%)	182 (28.4%)
Asian	10 (0.3%)	11 (0.7%)	2 (0.3%)	1 (0.2%)
AI/AN	20 (0.7%)	25 (1.5%)	14 (2.3%)	21 (3.3%)
More than one race	17 (0.6%)	10 (0.6%)	4 (0.7%)	5 (0.8%)
Unknown/not reported	94 (3.1%)	95 (5.8%)	52 (8.4%)	52 (8.1%)
Hispanic/Latino ethnicity (Yes) *n(%)*	153 (5.1%)	148 (9.0%)	77 (12.5%)	71 (2.7%)
Family income *n(%)*				
<$20,000	617 (6.3%)	446 (28.1%)	188 (31.1%)	229 (36.9%)
$20,000 - <$50,000	1287 (44.7%)	714 (45.0%)	250 (41.3%)	226 (36.4%)
≥$50,000	828 (28.7%)	428 (27.0%)	130 (21.5%)	166 (26.7%)
Don't know	149 (5.2%)	56 (3.5%)	37 (6.1%)	38 (6.1%)
Pack years (smoking) *n(%)*				

Never smoker	1476 (51.2%)	955 (60.0%)	345 (57.5%)	350 (57.0%)
<5	393 (13.6%)	232 (14.6%)	98 (16.3%)	93 (15.2%)
5 to < 20	410 (14.2%)	189 (11.9%)	71 (11.8%)	69 (11.2%)
20+	603 (20.9%)	215 (13.5%)	86 (14.3%)	102 (16.6%)
Modified aMed* total score ***mean(SD)***	4.4 (1.8)	4.1 (1.8)	3.8 (1.8)	3.7 (1.7)
Total energy intake (kcal/day) ***mean(SD)***	1448.7 (526.14)	1532.3 (600.36)	1635.4 (591.92)	1825.1 (681.03)
Minutes of moderate to strenuous exercise per week ***mean(SD)***	124.2 (167.3)	94.2 (142.6)	79.4 (129.5)	65.3 (119.7)
Hours/day spent sitting or lying ***mean(SD)***	14.6 (4.2)	14.3 (4.4)	13.9 (4.7)	14.0 (4.8)

* alternative Mediterranean Diet

Table 2. Adjusted means of DEXA-scan measured adiposity by FFQ-reported SSB consumption among WHI Observational Study participants, n = 5,898

DEXA Scan Measurement	**Model 1 mean (95% CI) p-value**	**Model 2 mean (95% CI) p-value**	**Model 3 mean (95% CI) p-value**	
VAT cm^2				
			<65 years	65+ years
0 servings/d	150.20 (147.26, 153.14)	154.32 (151.28, 157.36)	152.26 (147.95, 156.58)	156.66 (152.38, 160.93)
< ½ serving/d	**158.57 (154.61, 162.53) p = 0.0009**	156.17 (152.13, 160.22) p = 0.48	154.27 (148.68, 159.85) p = 0.58	158.39 (152.51, 164.27) p = 0.64
½ – 1 serving/d	**171.02 (164.54, 177.50) p < 0.0001**	158.33 (151.66, 165.00) p = 0.29	148.29 (139.38, 157.19) p = 0.44	**170.98 (160.92, 181.03) p = 0.01**

>1 serving/d	**181.28 (174.92 (187.63) p < 0.0001**	**164.21 (157.18, 171.24) p = 0.01**	**165.32 (156.77, 173.87) p = 0.01**	158.83 (146.72, 170.94) p = 0.75
SAT cm²				
0 servings/d	352.58 (347.65, 357.50)	364.82 (359.82, 369.82)	380.02 (372.47, 387.58)	348.38 (341.88, 354.88)
< ½ serving/d	**362.97 (356.34, 369.61) p = 0.01**	358.73 (352.08, 365.37) p = 0.15	374.73 (364.94, 384.51) p = 0.41	340.83 (331.90, 349.76) p = 0.18
½ – 1 serving/d	**382.49 (371.64, 393.34) p < 0.0001**	**352.56 (341.60, 363.51) p = 0.05**	**354.26 (338.65, 369.86) p = 0.004**	353.24 (337.95, 368.52) p = 0.57
>1 serving/d	**416.90 (406.26, 427.55) p < 0.0001**	372.88 (361.33, 384.44) p = 0.22	391.96 (376.97, 406.95) p = 0.18	345.77 (327.36, 364.18) p = 0.80
VAT:SAT Ratio				
0 servings/d	0.409 (0.404, 0.414)	0.408 (0.403, 0.413)	0.383 (0.378, 0.390)	0.434 (0.427, 0.442)
< ½ serving/d	**0.425 (0.418, 0.431) p = 0.0002**	**0.422 (0.415, 0.429) p = 0.001**	**0.398 (0.389, 0.407) p = 0.01**	**0.448 (0.438, 0.458) p = 0.04**
½ – 1 serving/d	**0.436 (0.425, 0.446) p < 0.0001**	**0.432 (0.421, 0.444) p = 0.0001**	**0.403 (0.389, 0.418) p = 0.02**	**0.466 (0.449, 0.483) p = 0.001**
>1 serving/d	**0.430 (0.420, 0.441) p = 0.0003**	**0.429 (0.417, 0.441) p = 0.001**	**0.411 (0.397, 0.425) p = 0.001**	0.445 (0.424, 0.466) p = 0.38

Significant estimates bolded
Model 1: crude
Model 2: adjusted for confounders
Model 3: adjusted model stratified by age (<65 years)
P-values here refer to significance of difference from the mean of the reference group (0 servings/d)

Least squares means plots do not allow for multiple comparisons for this number of categorical exposure levels which can make confidence intervals inconclusive.[14] For this reason, p-values were used to determine statistical significance, not confidence intervals.

In the crude models, any SSB consumption was significantly associated with higher VAT area, SAT area, and VAT:SAT ratio compared to those of the referent group. As seen in model 1, consuming less than ½ serving/d was associated with a mean VAT of 158.57cm^2 ($p = 0.0009$) compared to those who reported 0 servings/d. Consuming ½ - 1 serving/d was associated with a mean VAT of 171.02cm^2 ($p < 0.0001$) and greater than 1 serving/d was associated with a mean VAT of 18.28cm^2 ($p < 0.0001$). The referent group had a mean SAT of 352.58cm^2. Consuming less than ½ serving/d was associated with a mean SAT of 362.97cm^2 ($p = 0.01$). ½ - 1 serving/d was associated with a mean SAT of 382.49cm^2 ($p < 0.0001$) and greater than 1 serving/d was associated with 416.90cm^2 SAT ($p < 0.0001$). Those who reported 0 servings of SSBs per day had a mean VAT:SAT ratio of 0.409. The mean VAT:SAT ratio in participants who reported less than ½ serving/d was 0.425 ($p = 0.0002$) which differed significantly from those who reported 0 servings/d. Consuming ½ - 1 serving/d was associated with a higher mean ratio of 0.436 ($p < 0.0001$). The highest exposure group was associated with a mean VAT:SAT ratio of 0.430 ($p = 0.0003$) and was significantly higher than the referent group.

After adjusting for the aforementioned confounding variables, participants who reported 0 SSB servings/d had the following mean adiposity measures: 154.32cm^2 VAT, 364.82cm^2 SAT, and 0.408 VAT:SAT ratio. The adjusted model (model 2) showed that less than ½ serving of SSB per day was associated with 156.17cm^2 mean VAT ($p = 0.48$). ½ - 1 serving/d was associated with 158.33cm^2 mean VAT ($p = 0.29$), and greater than 1 serving/d was associated with 164.21cm^2 mean VAT ($p = 0.01$). Consuming less than ½ serving/d was associated with a mean SAT of 358.73cm^2 ($p = 0.15$). Consuming ½ - 1 serving/d was associated with a mean SAT of 352.56 ($p = 0.05$) while more than 1 serving/d was associated with 372.88cm^2 ($p = 0.22$). Less than ½ serving/d was associated with a VAT:SAT ratio of 0.422 ($p = 0.001$). ½ - 1 serving/d was associated with a VAT:SAT ratio of 0.432 ($p = 0.0001$) and more than 1 serving/d was associated with a ratio of 0.429 ($p = 0.01$).

Model 2 differed substantially from model 1. After adjusting for confounders, mean SAT differed substantially for participants who reported more than 1 serving/d of SSBs (adhering to the 10% change-in-estimate guideline). After stratifying by age group (<65 years vs. 65+ years), neither stratum differed meaningfully from the overall adjusted model. Therefore, model 2 was selected as the final model.

DISCUSSION

In a large, observational study of 5,898 postmenopausal women aged 49-79 years from the WHI Observational Study, mean VAT was only significantly higher among those who consumed more than 1 serving of SSBs per day and mean SAT was significantly lower among those who consumed between ½ - 1 serving of SSB per day after adjusting for confounders. Consuming any SSB was significantly associated with a higher VAT:SAT ratio which is indicative of increased risk for cardiovascular morbidity and mortality. However, VAT:SAT ratio remained significant for the two groups with at least ½ serving/d after adjustment. These associations were independent of overall dietary pattern, total energy intake, physical activity and inactivity, smoking pack years, race, ethnicity, age, education, and family income. Overall, this study found that consuming more than 1 serving of SSB per day was associated with a greater VAT area, ½ - 1 serving per day was associated with a greater SAT area, and consuming any amount of SSB was associated with greater VAT:SAT ratio. In summary, SSBs increased risk for morbidity and mortality among this population. These findings are in agreement with existing literature in terms of positive association between SSBs and VAT:SAT. A dose-response relationship was not observed between SSBs and VAT or SAT in this study, though certain exposure levels were significantly associated. The small sample sizes of the two highest exposure levels (each group approximately 10% of the total sample) may have been a contributing factor to lack of associations.

Upon reviewing publications of the same topic, ive studies supported a positive relationship between SSBs and VAT, one of which was only significant after adjusting for SAT. Of the two studies examining SAT, one found a negative association[6] and the other showed a null association[3]. Four of the identified studies utilized a cross-sectional design [3-5, 8] and one used a prospective cohort design[6]. These studies had sample sizes ranging from 60-2,665 (compared to >4000 in the current study) and were either overwhelmingly Non-Hispanic white owing to the Framingham offspring or 3rd generation study population used [3, 6], included men [3, 5, 6], included young adults [5], were limited to children [4], or were limited to Non-Hispanic black and Hispanic adolescents [7]. None of the identified studies used DEXA-measured adipose as outcomes, opting for either MRI [5, 8], CT [3, 6], or bioelectrical impedance [4]. One study found DEXA-measured trunk fat (kg) to be moderately correlated with CT-measured visceral fat area ($r = 0.51$ - 0.70, $p < 0.0001$) in premenopausal women with obesity or anorexia nervosa but this correlation broke down in women with obesity.[15] DEXA scans have shown high correlation with MRI measures of visceral adiposity in a study of Kuwaiti adults ($r = 0.94$, $p < 0.0001$ in men and $r = 0.93$, $p < 0.0001$ in women)[16] and in one study of young adults and adolescents in the U.S. ($r = 0.71$, $p < 0.0001$)[17]. Overall, there is some evidence of acceptable levels of correlation between methods of measuring adiposity but only in specific samples with low generalizability. Standardizing adiposity measures and examining a greater number of and/or more representative populations would clarify the answer. The combination of varying sample sizes, study populations, differing confounders, outcome ascertainment, and small sample size for high exposure groups compared to those of this study likely contribute to any discrepant findings.

Potential Mechanisms

Some research like that of Stanhope and colleagues posits that the metabolism of fructose induces de novo lipogenesis which causes postprandial hypertriglyceridemia, increasing fat deposition in visceral adipose.[9, 18] Metabolism of fructose is not limited by energy status and fat deposition will continue as long as fructose intake is occurring.[10] Accumulation of SAT occurs through an entirely different pathway - increased sensitivity to lipoprotein lipase activated by insulin which is secreted in response to raised glucose levels. [5, 10] Stanhope et al. assert that the metabolic pathway of glucose may be less impacted by SSB intake which they claim contains more fructose than glucose, driving the differential between VAT and SAT development.[10] However, SSBs can include a variety of sugars that may or may not contain fructose. Other research has essentially shown that SSBs are too broad of a category to accurately assess the association with visceral and subcutaneous fat without some bias. [19, 20] The true nature of this relationship could be better understood by disaggregating SSBs in future studies.

Strengths & Limitations

This study was limited by a sample that was predominantly white and so is less transportable to non-white individuals. Although race was adjusted for statistically, some of the minority race categories simply may have been too sparse to adequately power detection of an effect within members of minority racial groups, especially for women who identified as Asian, American Indian/Alaska Native, or more than one race as well as individuals who identify as having Latino/Hispanic ethnicity. The cross-sectional design of the study also precludes establishment of a temporal relationship between SSBs and adiposity.

The study is strengthened by its large sample size (n = 5,898) and use of reproducible methodology (scoring algorithms, validated questionnaires) for recording exposure, outcome, and confounding variables which can be found in publicly available WHI documentation. The WHI dataset is restricted by sex, age, and menonpausal status which is an inherent form of adjustment that eliminates bias on those characteristics.

The results of this study demonstrate a positive association between any consumption of SSBs and VAT:SAT ratio. Consumption of greater than 1 serving/d of SSBs was associated with greater VAT area, and ½ - 1 serving/d of SSBs was associated with greater SAT area. Other levels of SSB consumption were not associated with visceral or subcutaneous adiposity. In the context of the existing literature, a sample that is more representative of sex, age, and race among U.S. residents would provide a broader perspective to this question, and is both a pertinent and valuable next step for the research. Oversampling or otherwise ensuring equal proportions of high exposure groups to detect differences among individuals who consume higher amounts of SSBs is another important area of research to be improved. Additionally, there is merit for further study of SSBs via more uniform adiposity measurement and disaggregated by sugar source (fructose, glucose, etc.) which could be better achieved with a dietary recall or food log approach to understand specifically which SSBs influence visceral and subcutaneous fat.

References

1. Britton, KA, Massaro, JM, Murabito, JM, Kreger, BE, Hoffman, U & Fox, CS. Body Fat Distribution, Incident Cardiovascular Disease, Cancer, and All-Cause Mortality. *Journal of the American College of Cardiology.* 2013;62(10): 921-925. https://doi.org/10.1016/j.jacc.2013.06.027
2. Shuster, A, Patlas, M, Pinthus, JH & Mourtzakis, M. The clinical importance of visceral adiposity: a critical review of methods for visceral adipose tissue analysis. *The British Journal of Radiology*. 2012;85(1009): 1-10. doi: 10.1259/bjr/38447238
3. Ma, J, McKeown, NM, Hwang, S, Hoffman, U, Jacques, PF & Fox, CS. Sugar-Sweetened Beverage Consumption is Associated with Change of Visceral Adipose Tissue Over 6 Years of Follow-Up. *Circulation: An American Heart Association Journal.* 2017;133(4): 370-377. doi: 10.1161/CIRCULATIONAHA.115.018704
4. Gallagher, C, Moschonis, G, Lambert, KA. et al. Sugar-sweetened beverage consumption is associated with visceral fat in children. *British Journal of Nutrition.* 2020;*125(7)*: 819-827. doi:10.1017/S0007114520003256
5. Odegaard, AO, Choh, AC, Czerwinski, SA, Towne, B & Demerath, EW. Sugar-Sweetened and Diet Beverages in Relation to Visceral Adipose Tissue. *Obesity.* 2012;20(3): 689-691. https://doi.org/10.1038/oby.2011.277
6. Ma, J, Sloan, M, Fox, CS, Hoffman, U, et al. Sugar-Sweetened Beverage Consumption Is Associated with Abdominal Fat Partitioning in Healthy Adults. *The Journal of Nutrition.* 2014;*144(8): 1283-1290. doi: 10.3945/jn.113.188599*
7. Kaess, BM, Pedlely, A, Massaro, JM, Murabito, J, Hoffman, U, Fox, CS. (2012). The ratio of visceral to subcutaneous fat, a metric of body fat distribution, is a unique correlate of cardiometabolic risk. *Diabetologia.* 2012;55(10): 2622-2630. doi: https://doi.org/10.1007%2Fs00125-012-2639-5

8. 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. *Physiology & Behavior*. 2016;167: 188-193, https://doi.org/10.1016/j.physbeh.2016.09.020
9. Frayn, KN & Karpe, F. Regulation of human subcutaneous adipose tissue blood flow. *International Journal of Obesity*. 2013;38: 1019-1026. https://doi.org/10.1038/ijo.2013.200
10. Stanhope, KL, Schwarz, JM, Keim, N.L, et al. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *The Journal of clinical investigation*. 2009;119(5): 1322–1334. https://doi.org/10.1172/JCI37385
11. Brownbill, RA, & Ilich, JZ. (2005). Measuring body composition in overweight individuals by dual energy x-ray absorptiometry. *BMC medical imaging*. 2005;*5*(1): 1. https://doi.org/10.1186/1471-2342-5-1
12. ReadMe for WHI's Alternative Healthy Eating Index (AHEI)-2010 component and total scores computed from the food-frequency questionnaire (FFQ). Women's Health Initiative. Accessed May 26, 2022. https://www.whi.org/doc/f60_ahei_2010_ReadMe_inv.pdf
13. ReadMe for WHI's Alternate Mediterranean Diet (aMed) component and total scores computed from the food-frequency questionnaire (FFQ). Women's Health Initiative. Accessed May 26, 2022. https://www-whi-org.s3.us-west-2.amazonaws.com/wp-content/uploads/f60_aMed_ReadMe_inv.pdf
14. High R. Interpreting the Differences Among LSMEANS in Generalized Linear Models. University of Nebraska Medical Center. September 2011. Accessed June 2, 2022. https://www.mwsug.org/proceedings/2011/dataviz/MWSUG-2011-DG08.pdf

15. Bredella, MA, Ghomi, RH, Thomas, BJ, et al. Comparison of DXA and CT in the assessment of body composition in premenopausal women with obesity and anorexia nervosa. *Obesity.* 2010;*18*(11): 2227–2233. https://doi.org/10.1038/oby.2010.5

16. Mohammad, A, De Lucia Rolfe, E, Sleigh, A, et al. Validity of visceral adiposity estimates from DXA against MRI in Kuwaiti men and women. *Nutr & Diabetes.* 2017;7(e238). https://doi.org/10.1038/nutd.2016.38

17. Laddu, DR, Lee, VR, Blew, RM, Sato, T, Lohman, TG, & Going, SB. Predicting visceral adipose tissue by MRI using DXA and anthropometry in adolescents and young adults. *International journal of body composition research*. 2012;*10*(4): 93–100.

18. Hallfrisch J. Metabolic effects of dietary fructose. *The FASEB Journal*. 1990 Jun;4(9):2652-60. doi: 10.1096/fasebj.4.9.2189777

19. van Buul, VJ, Tappy, L, & Brouns, FJ. Misconceptions about fructose-containing sugars and their role in the obesity epidemic. *Nutrition research reviews*, 2014;*27*(1): 119–130. https://doi.org/10.1017/S0954422414000067

20. Choo VL, Viguiliouk E, Blanco Mejia S, et al. Food sources of fructose-containing sugars and glycaemic control: systematic review and meta-analysis of controlled intervention studies. *British Medical Journal.* 2018;363:k4644. doi:10.1136/bmj.k4644