Zheng, M., Rangan, A., Olsen, N. J., Andersen, L. B., Wedderkopp, N., Kristensen, P. L. ... Heitmann, B. L. (2014). Sugar-sweetened beverages consumption in relation to changes in body fatness over 6 and 12 years among 9-year-old children: the European Youth Heart Study. *European Journal of Clinical Nutrition, 68,* s. 77-83.

Sugar-sweetened beverages consumption in relation to changes in body fatness over 6 and 12 years among 9-year-old children: the European Youth Heart Study.

Running title: Sugar-sweetened beverages and body fatness

Miaobing Zheng[1], Anna Rangan[1], Nanna Julie Olsen[2], Lars Bo Andersen[3,4], Niels Wedderkopp[3], Peter Kristensen[3], Anders Grøntved[3], Mathias Ried-Larsen[3], Susanne Merethe Lempert[5], Margaret Allman-Farinelli[1], Berit Lilienthal Heitmann[2,5],

[1]School of Molecular Bioscience, the University of Sydney, NSW, Australia (MZ, AR, MAF)
[2]Research Unit for Dietary Studies, Institute of Preventive Medicine, Bispebjerg and Frederiksberg Hospitals - a part of Copenhagen University Hospital, Frederiksberg, Denmark (NJO, BLH)
[3]Research Center of Childhood Health, Department of Exercise Epidemiology, Institute of Sport Sciences and Clinical Biomechanics, Odense, Denmark (LBA, NW, PK, AG, MRL)
[4]Department of Sports Medicine, Norwegian School of Sport Sciences, Oslo, Norway (LBA)
[5]National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark (SML, BLH)

Corresponding author:
Miaobing Zheng
School of Molecular Bioscience, Molecular Bioscience Building (G08), University of Sydney, NSW, 2006, Australia
Email: mzhe4938@uni.sydney.edu.au
Telephone: +61 2 9351 3816
Fax: +61 2 9351 5858

Reprints will not be available from the authors

Word count:
Abstract: 328
Manuscript: 4205

Abstract

Background: Limiting sugar-sweetened beverages (SSB) consumption has been widely acknowledged as a primary strategy for obesity prevention in children and adolescents. In particular, finding suitable alternatives for SSB is an important public health issue.

Objectives: The purpose of this study was to examine the associations between different types of beverage intake and 6 y changes in body fatness, and to evaluate the effects of substituting water, coffee/tea, milk, and 100% fruit juice for SSB.

Design: A cohort of 9-year-old children (n=358) who participated in the Danish part of the European Youth Heart Study was followed for development in fatness over 6-y. Multivariate linear regression was used to examine the association between beverage consumption at baseline and change in body fatness (body mass index (BMI) z-score), waist circumference (WC), and sum of four skinfolds (Σ4SF)) over 6-y with adjustment for potential confounders. Substitution models were used to evaluate the effects of substituting various beverages for SSB, controlling for total beverage intake, energy from non-beverage sources, physical activity, socioeconomic status, and pubertal status.

Results: Intake of SSB at age 9 y, but not other beverages, was directly associated with subsequent 6-y changes in BMI z-score (β=0.05, *P*=0.02) and Σ4SF (β=0.86, *P*=0.02). Substitution of 100g water for 100g SSB was inversely associated with changes in BMI z-score (β= -0.04, *P*=0.02), WC (β= -0.29, P=0.04) and Σ4SF (β= -0.91, P=0.02) over 6-y. Substitution of 100g milk for 100g SSB was also inversely associated with changes in BMI z-score (β= -0.05, *P*=0.02), WC (β= -0.33, P=0.046) and Σ4SF (β= -0.79, P=0.06). An inverse association was also found between change in WC and substitution of 100g coffee/tea for 100g SSB (β= -0.74, *P*=0.03). No effect was observed for substitution of SSB by 100% fruit juice.

Conclusions: Our results suggest SSB intake is associated with long term change in body fatness in children, and replacing SSB with water and milk, but not 100% fruit juice, has a beneficial effect on body fatness development.

Introduction

Increased consumption of beverages, in particular sugar sweetened beverages (SSB) is thought to play a role in the etiology of obesity (1, 2). It is assumed that energy consumed in a liquid form is less saiating than energy consumed in a solid form and may lead to an incomplete compensatory reduction in energy from other sources, resulting in excess energy intake and subsequent weight gain (3). Moreover, shifts in beverage consumption patterns, i.e. increases in SSB consumption and decreases in milk consumption particularly in children and adolescents, and the interrelation of beverage consumption with other unhealthy eating patterns may also contribute to weight gain and obesity (4). The effects of excess energy intake from caloric beverages and the high glycemic effects of SSB are also likely to increase the obesity risk (4).

Childhood obesity has become one of the major public health concerns worldwide. Limiting SSB consumption has been acknowledged as one of the primary preventive strategies for combating the childhood obesity epidemic (5, 6). The replacement of SSB for low energy alternatives such as water and diet beverages is likely to promote weight loss and facilitate obesity prevention (7, 8). Previous studies, mostly short term feeding trials and weight loss intervention studies, have documented that the replacement of SSB by water (9, 10) and diet beverages (11, 12) can promote weight loss, reduce fat accumulation and reduce the risk of overweight/obesity. Nutrient dense beverages such as milk and 100% fruit juice, when consumed in recommended amounts are other alternatives for SSB. Indeed, previous intervention trials have revealed a beneficial effect of replacing habitual SSB consumption with regular milk on lean body mass and growth in children (13). However, the effects of replacing SSB with other beverages revealed by these short term experimental studies may not extrapolate to the long term. Only a limited number of studies have examined the long term impact of replacing SSB with other beverages on obesity development (14, 15).

Considering the elevated public health concern on the impact of SSB consumption in childhood obesity and the emerging debate on the effectiveness of limiting SSB consumption on childhood obesity prevention, we aimed to prospectively examine the association between the intake of different beverage types and subsequent 6 y change in body fatness as well as the effect of replacing SSB by water, coffee/tea, milk and 100% fruit juice on subsequent 6 y change in body fatness.

Subjects and methods

Study population

The European Youth Heart Study (EYHS) is an international multicenter study designed to address environmental, personal, lifestyle and physiological factors that may influence the development of cardiovascular risk factors in children. All study protocols complied with the Declaration of Helsinki and were approved by the scientific ethics committee of the local counties of Vejle and Funen, Denmark (VF 20030067). Written explanations of the study aims and possible hazards, discomfort, and inconvenience of test procedures were provided to both parents and children. Data collection was conducted throughout the school year to minimize seasonal effects. Most of the study protocols utilized in the EYHS were standard procedures that are well-validated in children of similar age, otherwise additional validation studies were undertaken (16). Detailed study design and procedures have been described previously (17).

Our current study utilized data of the 9-year-old (3rd grade) children who participated in the Danish part of EYHS in 1997 with a 6-y follow-up in 2003. In 1997, 590 children participated in the baseline interview**.** The dropout rate from baseline to first follow-up interview in 2003 was 34.9% (n=384). The attrition analysis for participant and non-participants were similar in regards to anthropometrics, dietary intake, socioeconomic status, physical activity and pubertal status (18). Twenty-five children who had incomplete dietary information at baseline or incomplete anthropometric data at either time point were excluded from the analysis. Under-reporting of energy intake was assessed by the Goldberg cut-off method by calculating the ratio of reported energy intake (EI) to basal metabolic rate (BMR) (19) which was calculated using the Schofield equation (20). The lower 95th percentile cut-off value of 0.9 was applied to individuals. One female under-reporter was identified and excluded from the analysis resulting in a final sample size of 358 children (201 girls and 157 boys).

Beverage intakes

Dietary intake was assessed by one 24-hr recall face to face interview supplemented with a parent-assisted food record. Different sized drinking glasses, plates, spoons together with food pictures of the most commonly consumed foods and beverages in different portion sizes were used to facilitate the estimation of quantities during the interview. Food records were entered into the software program Dankost 3000 (Danish Catering Centre, Copenhagen, Denmark) for nutrient analysis using the Danish Food Composition Tables 2006 (21). Information on seven types of beverages including plain water (tap or bottled), milk (regular, low fat, skim, plain or flavoured), SSB (regular soft drinks, lemonade or fruit flavoured drinks), 100% pure fruit juice (apple juice, orange juice or other juice), coffee/tea (plain or sweetened), diet soft drinks, and alcoholic drinks were obtained. Diet soft drinks and alcoholic drinks were excluded from the analysis due to the small number of participants who consumed these beverages (<5%). Daily per capita consumption of each beverage type and total beverages in absolute amount in grams (g) were calculated.

Assessment of anthropometry

According to the standardized procedures for anthropometrics measurements, height was measured in bare feet to the nearest 5mm by a stadiometer and body weight was measured in light clothing to the nearest 0.1kg by a beam balance scale. Body mass index (BMI) was calculated as body weight in kilograms divided by square meters of height. Age- and gender- specific BMI z-score was generated using the LMS method (22).Waist circumference (WC) was measured twice with a metal anthropometric tape midway between the lower rib margin and the iliac crest, at the end of gentle expiration. The mean value of the two measurements was used for analysis. Skinfold thickness was measured with Harpenden fat calipers with two measurements taken at each site. The sum of four skinfolds (Σ4SF) was obtained by adding the average skinfolds of the biceps, triceps, subscapular, and suprailiac (16). BMI z-score, WC and Σ4SF are used as indicators for total body fatness, visceral fat and subcutaneous fat, respectively.

Assessment of covariates

Physical activity level was measured by both a validated accelerometer (Actigraph model 7164, Manufacturing Technology Inc, Fort Walton Beach, FL, USA)(23) and a computer-based questionnaire. Since a large number of participants failed to complete the accelerometer measurements, the questionnaire measurement was chosen to represent the physical activity of the study population to maximize sample size. Subjects were classified as either physically inactive (reported no or sometimes exercise) or physically active (reported regular exercise). The accelerometer measurements were used in a sensitivity analysis that found good agreement with the questionnaire method (24). A computer-based questionnaire was completed by parents to obtain demographic and socioeconomic data. Maternal education, shown to be the best indicator of socioeconomic status for children, was used to represent the socioeconomic status of the current study population (25). The socioeconomic status was categorized as low (elementary, high school and vocational education) or high (short, medium or long term tertiary education). Pubertal status was assessed by trained personnel according to Tanner's stages using a 5-point scale of pictures (26).

Statistical method

Descriptive analysis was performed for all variables at baseline and follow-up. Sample mean ± standard deviation was calculated for continuous variables and percentage of participants was calculated for categorical variables. Paired t-test was used to examine the differences between anthropometric data at baseline and follow-up. Multivariate linear regression analysis was used to test the association between baseline beverage intake and subsequent change in body fatness. Pearson correlation was conducted to assess multicollinearity among individual beverage intake prior to regression analysis. Since correlation coefficients were small (r <0.2), individual beverage intakes (per 100 grams) were included in the same model to account for mutual confounding. Thus, the independent effect of each beverage type on changes in body fatness could be examined. Changes in BMI z-score, WC and Σ4SF calculated by subtracting baseline data from follow-up data, were evaluated separately in three multivariate models. Potential confounders were identified as variables that associated with outcome variables at a P-value <0.25 and those that are predictors of obesity and may be related to beverage consumption(27). All models were controlled for the following potential confounders: age, gender, baseline BMI z-score/WC/Σ4SF, physical activity, socioeconomic status, and pubertal status. The potential effect modification by gender in these models was tested by using interaction terms. No significant interaction with gender was found for most variables in the model, except for socioeconomic status ($P<0.05$). Therefore, boys and girls were analysed together with inclusion of an interaction term between gender and socioeconomic status as a confounder in all models,

Because beverage intake correlates strongly with total energy intake, two analytical approaches were used to adjust for the confounding effects of total energy intake, the "standard multivariate model" and the "energy partition model" (28). Analyses of the standard multivariate model included individual beverage intakes and total energy intake, and the regression coefficients of the individual beverage intakes can be interpreted as the generic non-energy effect of each beverage type on the changes in body fatness. In the energy partition model, total energy is partitioned into energy contributed by energy containing beverages and energy contributed by other sources (non-beverage food sources). Water was excluded from the energy partition model as it contains no energy. Analyses of the energy partition model included individual energy containing beverages and energy from non-beverages sources (29). The regression coefficient of individual energy containing beverages in the energy partition model can be interpreted as both specific energy and non-energy effects of adding respective beverages into the diet, while keeping other sources of energy (i.e. food energy) constant (30).

Water, coffee/tea, milk, fruit juice, and SSB are subcomponents of total beverage intake consumed by this population, and substitution or replacement models can be used to examine effects of beverage types on body fatness (28). To evaluate the relative effects of replacing SSB with water, coffee/tea, milk, or 100% fruit juice on changes in body fatness, the models included total beverage intake along with the type of beverage consumed (water, coffee/tea, milk, and 100% fruit juice), but excluding SSB intake (the reference category) from the model. By keeping the intakes of total beverage and milk, fruit juice and coffee/tea constant, an increase in water by definition results in a corresponding decrease in SSB. Thus, the regression coefficient of water assumes a substitution interpretation, that is, the amount of water that is "substituted" for the same amount of SSB. Similarly, an increase in milk or fruit juice or coffee/tea also implies a decrease in SSB, and these effects were also evaluated. This approach is similar to the substitution models used by Stookey et al (31). For a discussion on how to model substitution effects among subcomponents of food or nutrient intakes in a multivariate model refer to Willett 2013 (28). The substitution models were adjusted for age, gender, baseline BMI/WC/Σ4SF, pubertal status, socioeconomic status, physical activity, energy from food intake (non-beverage sources) and interaction between gender and socioeconomic status. Additional adjustment for energy intake from beverages was performed to assess if energy from beverages may explain the effects of beverage intake on changes on body fatness. All statistical analyses were performed in SPSS 20.0 (SPSS Inc) with statistical significance set as *P* ≤0.05 (two-sided).

Results

Descriptive information on anthropometrics, dietary intake, pubertal status, socioeconomic status and physical activity is presented in Table 1. The percentages of children consuming each beverage type were: water (92%), milk (97%), SSBs (57%), fruit juice (37%), and coffee/tea (19%). As expected, anthropometric data increased significantly from baseline to follow-up (*P*<0.0001).

The prospective associations between each beverage intake and change in body fatness measures were presented in Table 2. Regression analyses using the standard multivariate model and the partition model showed SSB intake was significantly associated with change in body fatness. However, no significant association between other types of beverage intake and change in body fatness was found. In model 1 with adjustment for all covariates, SSB intake was directly associated with subsequent 6 y changes in both BMI z-score (β=0.05, *P*=0.02) and Σ4SF (β=0.86, *P*=0.02). Further adjustment for energy intake in Model 2 attenuated the significant association for BMI z-score (β=0.05, *P*=0.06) and Σ4SF (β=0.94, *P*=0.06) in the standard multivariate model. In the energy partition model, adjusting for energy from sources other than beverages did not affect the regression coefficient or the significance of the association (Model 3).

The estimated change in body fatness associated with replacing SSB with water, coffee/tea, milk, and fruit juice are presented in Table 3. With adjustment for all covariates, replacing 100g SSB with 100g water was significantly and inversely associated with subsequent 6-y changes in BMI z-score (β= -0.04, *P*=0.02), WC (β= -0.29, *P*=0.04) and Σ4SF (β= -0.91, *P*=0.02)(Model 1). Substituting coffee/tea for SSB predicted lower increase in WC (β= -0.74, *P*=0.03), but not for BMI z-score and Σ4SF (Model 1). Further adjustment for energy from beverages attenuated the significant effects of replacing SSB with water or coffee/tea (P>0.05, Model 2 in Table 3). Replacing 100g SSB with 100g milk was also inversely associated with changes in BMI z-score (β= -0.05, *P*=0.02), WC (β= -0.33, *P*=0.046) and Σ4SF (β= -0.79, *P*=0.06). Adjusting for total energy intake only slightly reduced the association for BMI z-score (β= -0.05, *P*=0.03), WC (β= -0.31, *P*=0.06) and Σ4SF (β= -0.73, *P*=0.07) (Model 2). Substitution of 100% fruit juice for SSB was not associated with changes in any measure of body fatness. Independent of all covariates, total beverage intake was directly associated with changes in all body fatness measures (Model 2). The effects of replacing SSB with water, milk, 100% fruit juice and coffee/tea on change in body fatness with adjustment for all confounders are illustrated in Figure 1.

Discussion

Current literature on beverage intake and adiposity has focused mainly on SSB, and to a lesser extent on milk, fruit juice, and non-caloric beverages. In this cohort of Danish children, we examined the prospective associations between a variety of beverages and change in body fatness over 6 years. We found SSB intake at age 9 y, but not other beverage types (water, milk, fruit juice, coffee/tea), was directly associated with subsequent 6 y change in body fatness. In particular, BMI z-score and Σ4SF were found to increase by 0.05 units and 0.86mm, respectively over 6 y, for every 100g increase in SSB intake per day. By substituting 100g SSB for 100 g water or milk, beneficial long term effects on body fatness were observed. Substituting SSB with water predicted a decrease in BMI z-score, WC and Σ4SF by 0.04 units, 0.29cm and 0.91 mm, respectively over 6y. Substitution of SSB by milk also resulted in subsequent 6 y decreases in BMI z-score (0.05 units), WC (0.33 cm) and Σ4SF (0.79 mm). Moreover, substituting SSB with coffee/tea predicted significant 6 y decrease in WC (0.74cm).

Our finding that SSB intake was more closely related to change in body fatness compared to other beverage types are consistent with several previous cohort studies that simultaneously examined the associations between a variety of beverages consumed and long term obesity outcomes. Striegel-Moore et al (32) found that among a large cohort of US girls aged 9-10 y with a follow-up of 10 y only regular soft drink intake during childhood was a significant predictor of BMI in late adolescence. However, no evidence of an association was observed for other beverages such as milk, coffee/tea, and fruit juice. Likewise, in a group of non-Hispanic white girls that examined SSB intake at age 5 y, but not milk or fruit juice, predicted increases in % body fat, WC and prevalence of overweight from age 5 to 15 y (33). Similar findings were also demonstrated by Tam et al, in a small group of Australian children, where intake of soft drinks at 8 y, but not fruit juice or milk, was associated with subsequent 5 y excess weight gain (34).

The lack of an association between milk intake and change in body fatness is congruent with current literature. The majority of prospective studies found that milk intake, whether reduced fat or low-fat, suggest no association, although several prospective studies have found a protective association between regular milk intake and weight status (35). For instance, Vanselow et al (36), found no association between SSBs and fruit juice and weight gain, but white milk intake at 15 y was inversely associated with subsequent 5 y changes in BMI in a large cohort of US adolescents. The potential biological mechanisms underlying the beneficial effect of milk intake on body weight are as yet unclear. The most prevailing hypothesis is the potential impact of dietary calcium on adipocyte lipid metabolism and fatty acid absorption. Furthermore, accumulating evidence also suggests that whey protein derivatives may affect body weight through their influences on food intake and appetite regulation (35).

With respect to effects of water intake and obesity, most previous studies are short term experimental studies, in which the effect of drinking water on energy intake and/or body weight (as a reference group) was compared with either no beverages or a range of caloric beverages (37). Our study is one of the first studies that directly evaluated the effect of water intake and long term obesity development in children. Consistent with our results, Johnson et al also found no evidence of an association between water intakes at ages 5 and 7 y and changes in fat mass at age 9 y in a cohort of British children (38). However, another two studies conducted in adults have found inverse associations between water and body weight. In a secondary analysis of 12 month weight loss intervention trials among overweight dieting women, individuals who drank >1L water/day had greater loss of body weight and WC (31). Results from a pooled analysis of three prospective cohort studies of white and educated US adults also found water intake was inversely associated long term weight gain (14). The lack of an association for water may be due to possible underestimation of water intake in the current study, because water consumed during the day and unaccompanied with foods tends to be ignored in dietary assessment methods (39).

The underlying mechanism by which SSB intake affects obesity development is not well understood. Results from the standard multivariate model indicate that total energy intake may be a potential mediator of the association between SSB and increased body fatness, because the significant association between SSB intake and body fatness reduced substantially after adjusting for total energy intake. In the energy partition model, adjusting for energy from other sources (non-beverage sources) did not affect the significant association, suggesting that the association between SSB intake and changes in body fatness is independent of energy intake from other sources. Rather, the association may be contributed by both specific energy and non-energy effect of SSB. In other words, the association between SSB intake and adiposity may be caused by additional energy provided by SSBs or non-energy effects of SSB such as the high glycemic load on body weight regulation.

Consistent with results from many short term experimental studies (37) and the recent prospective cohorts studies in a group of adults (14), we found that the substitution of water and milk for SSB demonstrated a beneficial effect on long term change in body fatness. The beneficial effect of replacing SSB by water is likely due to the lower energy content contributed by total beverage intake, as adjustment for total energy from beverage intake attenuated significant effects. By using similar substitution models, the beneficial effect of replacing SSB with water on body weight and fat were also reported by Stookey et al (31) in a group of overweight dieting women over 12 months. Replacing SSB with the same amount of milk (100g) demonstrated a protective effect on body fatness. Controlling for energy from beverages resulted in similar regression coefficients, indicating that factors other than energy (e.g. specific milk constituents) may mediate the effects of replacing milk for SSB on body fatness. The impact of milk constituents such as calcium and milk proteins on body composition and appetite regulation has been widely acknowledged (35).

Scientific evidence regarding 100% fruit juice and body weight gain remains inconclusive. Our findings are consistent with most previous prospective studies that found no evidence of an association between 100% fruit juice and increased adiposity among children (37, 38). Positive associations have only been found among studies with overweight and obese children (39, 40). In our study, replacing fruit juice with SSB was not associated with any measure of body fatness. Given that fruit juice contains comparable amount of natural sugars to SSBs, they may not be a good alternative for SSBs in regard to weight management.

Plain coffee/tea contributes fluid to the diet without contributing energy. Previous evidence, mostly in adults, suggests that plain coffee and tea may have a beneficial effect on weight management (43). However, we found no significant effect of coffee/tea on body fatness, and the beneficial effect of replacing coffee/tea for SSB was only observed for one body fatness measure. It is likely that the low coffee/tea intake of the current population at the age of 9 y may have hindered our ability to find an effect. In addition, we included substitution with plain and sweetened coffee/tea in the analysis, which may differ to other studies where only plain coffee/tea was substituted.

Overall our findings are accordant with current beverage recommendations to reduce intake of SSB. Furthermore, the long term benefits of replacing water or milk for SSB on body fatness development demonstrated in our study indicate that reducing SSB by replacement with water and milk may be effective strategies in the prevention and management of childhood obesity. Additionally, it may be more effective for public health campaigns to advocate "replacing water and milk for SSB" instead of "reducing SSB intake" alone.

There are several strengths to our study. To our knowledge, no study to date has examined the long term effects of replacing SSB with other beverages on childhood obesity. Our results have a good generalizability, because the mean energy intake of the 9 year-olds children (9.1MJ) in the current sample is comparable to the mean energy intake (9.1MJ) of a national representative sample of children aged 4 to 14 y, according to the 1995 Danish National Surveys (40). The assessment of a variety of beverages allows us to examine individual effects of beverage intakes on body fatness. We were able to account for age, gender, socioeconomic status, physical activity, and pubertal status, which have been considered as important confounders in evaluating childhood obesity. To adjust for the confounding effects of energy intake, we applied two energy adjustment methods. These allowed us to differentiate the effects of total energy intake as well as the specific energy and non-energy effects of SSB on the estimated association. Finally, anthropometric data were objectively measured, which eliminates the possibility of reporting bias.

Our study also has a number of limitations. First, our study has a small sample size, which may have limited power to detect effects. Second, the dietary intake was measured by a single 24-hr recall with a parent-assisted food record, which only provides a snapshot of usual intake, and is unable to account for day to day variations of dietary intake. However, this dietary assessment method was shown to be a suitable measure of dietary intakes at a group level among children of 3rd grade (41). Nevertheless, the 24hr recall is prone to reporting bias, even though we excluded extreme under-reporters as identified by the Goldberg method. Under-reporting is of particular concern, as it may distort diet and disease relationships. Evidence show underreporting is more common in overweight and obese participants (42, 43), and foods that are perceived as unhealthy and consumed as snacks are more likely to be under-reported (44). On the other hand, reporting bias in the present study most likely attenuated not inflated our current significant findings, suggesting that the observed associations are indeed present. Third, the crude measure of self-reported physical activity may have resulted in residual confounding. However, the fact that similar results were obtained from the sensitivity analysis using accelerometer measurements, makes this possibility less likely. Fourth, the main analyses were based on beverage intake at baseline, individuals who have changed their beverage intake pattern may have been misclassified, which would tend to attenuate the observed associations. Lastly, although we managed to control for many important confounders, there may be other possible residual and unmeasured confounding.

Conclusion

In conclusion, our results indicate that SSB consumption was directly associated with long term change in body fatness in children. No evidence of an association was found for other beverages. Additionally, the replacement of SSBs with water and milk demonstrated beneficial effects on body fatness. Our findings support the current recommendations to limit SSB consumption, and replacing SSBs for water and milk may be beneficial for long term weight management in children. Further long term randomized controlled trials are needed to further elucidate the effects of replacing water or milk for SSB on obesity development.

Conflict of interest

The authors have no conflicts of interest.

Acknowledgements

References

1. Hu FB. Resolved: there is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. Obes Rev. 2013. doi: 10.1111/obr.12040. PubMed PMID: 23763695.

2. Mattes R, Shikany J, Kaiser K, Allison D. Nutritively sweetened beverage consumption and body weight: a systematic review and meta-analysis of randomized experiments. obesity reviews. 2011;12:346-65. doi: 10.1111/j.1467-789X.2010.00755.x.

3. Drewnowski A, Bellisle F. Liquid calories, sugar, and body weight. The American Journal of Clinical Nutrition. 2007;85:651-61.

4. Banchman C, Baranowski T, Nicklas T. Is There an Association Between Sweetened Beverages and Adiposity? Nutrition Reviews. 2006;64(4):153-74.

5. World Health Organization. Diet, Nutrition and the Prevention of Chronic Diseases: report of a Joint WHO/FAO Expert Consultation. Geneva: WHO2003. Available from: http://www.fao.org/docrep/005/AC911E/ac911e07.htm#bm07.2.5.

6. Davis M, Gance-Cleveland B, Hassink S, Johnson R, Paradis G, Resnicow K. Recommendations for prevention of childhood obesity. Pediatrics. 2007;120(Suppl 4):S229-53.

7. Daniels MC, Popkin BM. Impact of water intake on energy intake and weight status: a systematic review. Nutrition reviews. 2010;68(9):505-21. doi: 10.1111/j.1753-4887.2010.00311.x. PubMed PMID: 20796216; PubMed Central PMCID: PMC2929932.

8. Pereira M. Diet beverages and the risk of obesity, diabetes, and cardiovascular disease: a review of the evidence. Nutrition reviews. 2013;71(7):433-40.

9. Muckelbauer R, Libuda L, Clausen K, Toschke AM, Reinehr T, Kersting M. Promotion and provision of drinking water in schools for overweight prevention: randomized, controlled cluster trial. Pediatrics. 2009;123(4):e661-7. Epub 2009/04/02. doi: 10.1542/peds.2008-2186. PubMed PMID: 19336356.

10. Dennis EA, Dengo AL, Comber DL, Flack KD, Savla J, Davy KP, et al. Water consumption increases weight loss during a hypocaloric diet intervention in middle-aged and older adults. Obesity (Silver Spring, Md). 2010;18(2):300-7. Epub 2009/08/08. doi: 10.1038/oby.2009.235. PubMed PMID: 19661958; PubMed Central PMCID: PMC2859815.

11. de Ruyter J, Olthof M, Seidell J, Katan M. A Trial of Sugar-free or Sugar-Sweetened Beverages and Body Weight in Children. N Eng J Med. 2012;367(15):1397-406. doi: 10.1056/NEJMoa123034.

12. Ebbeling C, Feldman H, Chomitz V, Antonelli T, Gortmaker S, Osganian S, et al. A Randomized Trial of Sugar-Sweetened Beverages and Adolescent Body Weight. N Eng J Med. 2012;367(15):1407-16.

13. Alaba C, Ebbeling C, Cifuentes M, al e. Effects of replacing the habitualconsumption of sugar-sweetened beverages with milk in Chilean children. Am J Clin Nutr. 2008;88:605-11.

14. Pan A, Malik VS, Hao T, Willett WC, Mozaffarian D, Hu FB. Changes in water and beverage intake and long-term weight changes: results from three prospective cohort studies. Int J Obes (Lond). 2013. doi: 10.1038/ijo.2012.225. PubMed PMID: 23318721; PubMed Central PMCID: PMC3628978.

15. Wang Y, Ludwig D, Sonneville K, Gortmaker S. Impact of Change in Sweetened Caloric Beverage Consumption on Energy Intake Among Children and Adolescents. Arch Pediatr Adolesc Med. 2009;163(4):336-43.

16. Riddoch C, Edwards D, Page A, Froberg K, Anderssen S, Wedderkopp N. The European Youth Heart Study-Cardiovascular Disease Risk Factor in Children: Rationale, Aims, Study Design, and

Validation of Method. Journal of Physical Activity and Helath. 2005;2:115-29.
17. Kynde I, Johnsen NF, Wedderkopp N, Bygbjerg IB, Helge JW, Heitmann BL. Intake of total dietary sugar and fibre is associated with insulin resistance among Danish 8-10- and 14-16-year-old girls but not boys. European Youth Heart Studies I and II. Public Health Nutr. 2010;13(10):1669-74. Epub 2010/03/20. doi: 10.1017/S1368980010000285. PubMed PMID: 20236560.
18. Hare-Bruun H, Nielsen B, Kristensen P, Moller N, Togo P, Heitmann B. Television viweing, food preferences, and food habits among children: A prospective epidemiological study. BMC Public Health. 2011;11:311.
19. Goldberg G, Black A, Jebb Sea. Critical evaluation of energy intake data using fundamental principles of energy physiology: 1. Derivation of cut-off limits to identify underrecording. Eur J Clin Nutr 1991;45(569-81).
20. Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. Human nutrition Clinical nutrition. 1985;39 Suppl 1:5-41. PubMed PMID: 4044297.
21. Danish Institute for Food and Veterinary Research, Ministry of Family and Consumer Affairs. Danish Food Composition Databank. Søborg: DFVR; 2006.
22. Cole T, Green P. Smoothing reference centile curves: the LMS method and penalized likelihood. . Stat Med. 1992;11:1305-19.
23. Andersen L. Physical activity and clustered cardiovascular risk in children: a cross-sectional study(The European Youth Health Study). Lancet. 2006;368:299-304.
24. Olsen N, Andersen LB, Wedderkopp N, Kristensen P, Heitmann B. Intake of Liquid and Solid Sucrose in Relation to Changes in Body Fatness over 6 Years among 8- to 10-Year-Old Children: The European Youth Heart Study. Obes Facts. 2012;5(4):506-12. PubMed Central PMCID: PMC 22854439.
25. Groth M, Fagt S, Brùndsted L. Social determinants of dietary habits in Denmark. European Journal of Clinical Nutrition. 2001;55:959-66.
26. Tanner J. Normal growth and techniques of growth assessment. Clin Endocrinol Metab. 1986;15:411-51.
27. Katz M. Multivariable Analysis: A practical guide for clinicians. New York: Cambridge University Press; 1999.
28. Willet W. Nutritional Epidemiology. 3rd ed. New York: Oxford University Press; 2013.
29. Hu F, Stampfer M, Rimm E, Ascherio A, Rosner B, Spiegelman D, et al. Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. Am J Epidemiol. 1999;149:531-40.
30. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. Am J Epidemiol. 1986;124(1):17-27. Epub 1986/07/01. PubMed PMID: 3521261.
31. Stookey JD, Constant F, Popkin BM, Gardner CD. Drinking water is associated with weight loss in overweight dieting women independent of diet and activity. Obesity (Silver Spring). 2008;16(11):2481-8. doi: 10.1038/oby.2008.409. PubMed PMID: 18787524.
32. Striegel-Moore R, Thompson D, Affenito S, Franko D, Obarzanek E, Barton Bea. Correlates of beverage intake in adolescent girls: the National Heart, Lung, and Blood Institute Growth and Health Study. J Pediatr. 2006;148:183-7.
33. Fiorito L, Marini M, Francis L, Smiciklas-Wright H, Birch L. Beverage intake of girls at age 5 y predicts adiposity and weight status in childhood and adolescence. Am J Clin Nutr. 2009;90:935-42.
34. Tam C, Garnett S, Cowell C, Campbell K, Cabrera G, Baur L. Soft drink consumption and excess weight gain in Australian school students: results from the Nepean study. International Journal of

Obesity. 2006;30:1091-3.
35. Dougkas A, Reynolds C, Givens I, Elwood P, Minihane A. Associations between dairy consumption and body weight: a review of the evidence and underlying mechanisms. Nutr Res Rev 2011;15:1-24.
36. Vanselow M, Pereira M, Neumark-Sztainer D, Raatz S. Adolescent beverage habits and changes in weight over time: findings from Project EAT. Am J Clin Nutr. 2009;90(6):1489-95. PubMed Central PMCID: PMC19864412.
37. Daniels M, Popkin B. Impact of water intake on energy intake and weight status: a systematic review. Nutr Rev. 2010;2010(68):2481-8.
38. Johnson L, Mander A, Jones Lea. Is sugarsweetened beverage consumption associated with increased fatness in children? Nutition 2007;23:557-63.
39. Nissensohn M, Castro-Quezada M, Serra-Majem L. Beverage and water intake of healthy adults in some European countries. International journal of food sciences and nutrition. 2013;Early Online: 1-5.
40. Fagt S, Biltoft-Jensen A, Matthiessen J, Groth M, Christensen T, Trolle E. Dietary Habits in Denmark 1995-2006: National Food Institute, Technical University of Denmark; 2008. Available from: http://www.food.dtu.dk/upload/f%C3%B8devareinstituttet/food.dtu.dk/publikationer/tilbagevendende_publikationer/kostunders%C3%B8gelser/danskernes_kostvaner_1995-2006.pdf.
41. Lytle LA, Nichaman MZ, Obarzanek E, Glovsky E, Montgomery D, Nicklas T, et al. Validation of 24-hour recalls assisted by food records in third-grade children. The CATCH Collaborative Group. J Am Diet Assoc. 1993;93(12):1431-6. PubMed PMID: 8245378.
42. Lioret S, Touvier M, Balin M, Huybrechts I, Dubuisson C, Dufour A, et al. Characteristics of energy under-reporting in children and adolescents. Br J Nutr. 2011;105(11):1671-80.
43. Livingstone M, Robson P, Wallace J. Issues in dietary intake assessment of children and adolescents. Br J Nutr. 2004 92(Suppl 2):S213-22.
44. Lafay L, Mennen L, Basdevant A, Charles M, Borys J, Eschwège E, et al. Does energy intake underreporting involve all kinds of food or only specific food items? Results from the Fleurbaix Laventie Ville Sante (FLVS) study. . Int J Obes Relat Metab Disord 2000;24(11):1500-6.

Table 1. Descriptive analysis of characteristics of participants at baseline and follow-up[1]

	1997(n=385)	2003(n=385)
Continuous variables	Mean±SD	Mean±SD
Age(years)[2]	9.6±0.4	15.7±0.3
Height(cm)[2]	138.9±6.4	170.3±8.9
Weight(kg)[2]	33.3±6.0	61.7±11.0
Body mass index(kg/m^2)[2]	17.2±2.3	21.2±3.0
BMI z-score (SD)[2]	0.4±1.1	0.5±1.0
Waist circumference(cm)[2]	58.2±5.5	74.2±7.7
Sum of four skinfolds(mm)[2]	36.2±16.9	44.5±21.0
Energy intake(MJ/d)	9.1±2.3	
Protein intake (g/d)	69.6±20.0	
Fat intake (g/d)	80.1±27.5	
Carbohydrate intake (g/d)	288.5±80.7	
Fibre intake (g/d)	18.6±7.6	
Water (g/d)	453.1±351.5	
Milk(g/d)	481.2±290.9	
SSB(g/d)	154.0±204.9	
Fruit juice (g/d)	62.4±139.0	
Coffee/tea(g/d)	22.8±72.1	
Categorical variables	%	
Gender		
Boys	43.9	
Girls	56.1	
Pubertal status		
Stage 1	83.7	
Stage 2	15.7	
Stage 3	0.6	
Socioeconomic Status		
Low	46.6	
High	53.4	
Physical activity		
Inactive	45.4	
Active	54.6	

[1]values were expressed as Mean ± standard deviation or percentage. SSB: sugar sweetened beverages

[2] P<0.0001

Table 2. Regression analysis of baseline beverage intake and subsequent 6-y changes in body fatness from 9 to 15 years[1]

	Change in BMIz $_{9\text{-}15}$		Change in WC $_{9\text{-}15}$		Change in Σ4SF $_{9\text{-}15}$	
	β±SE	**P**	**β±SE**	**P**	**β±SE**	**P**
Water (100g/d)						
Crude model [a]	-0.005±0.01	0.64	-0.02±0.09	0.85	-0.28±0.24	0.24
Model 1[b]	-0.000±0.01	0.96	-0.08±0.09	0.34	-0.08±0.22	0.73
Model 2 [c]	-0.001±0.01	0.91	-0.06±0.09	0.49	-0.05±0.22	0.82
Milk (100g/d)						
Crude model [a]	-0.02±0.01	0.23	-0.10±0.11	0.34	-0.38±0.29	0.20
Model 1 [b]	-0.003±0.01	0.79	-0.13±0.11	0.22	0.04±0.26	0.87
Model 2 [c]	-0.001±0.01	0.95	-0.05±0.12	0.65	0.12±0.29	0.67
Model 3 [d]	-0.003±0.01	0.81	-0.09±0.11	0.41	0.09±0.26	0.74
SSB (100g/d)						

Crude model [a]	0.03±0.02	0.12	0.30±0.15	0.05	0.52±0.41	0.20
Model 1 [b]	0.05±0.02	0.02	0.22±0.15	0.14	0.86±0.37	0.02
Model 2 [c]	0.05±0.02	0.06	0.30±0.15	0.18	0.94±0.39	0.06
Model 3 [d]	0.05±0.02	0.01	0.25±0.15	0.09	0.88±0.37	0.02
Fruit juice (100g/d)						
Crude model [a]	0.02±0.03	0.42	-0.06±0.22	0.78	0.49±0.59	0.41
Model 1 [b]	0.02±0.03	0.39	-0.01±0.22	0.59	0.47±0.54	0.38
Model 2 [c]	0.03±0.03	0.34	-0.01±0.23	0.96	0.58±0.57	0.31
Model 3 [d]	0.03±0.03	0.35	-0.01±0.22	0.95	0.60±0.56	0.28
Coffee/tea(100g/d)						
Crude model [a]	-0.04±0.06	0.43	-0.31±0.41	0.45	-0.67±1.11	0.55
Model 1 [b]	-0.02±0.05	0.67	-0.39±0.41	0.34	-0.09±1.01	0.93
Model 2 [c]	-0.02±0.05	0.64	-0.44±0.41	0.28	-0.04±1.02	0.97
Model 3 [d]	-0.02±0.05	0.65	-0.41±0.41	0.31	-0.06±1.01	0.95

[1]All beverages were included simultaneously in the same model, BMIz (body mass index z-score), WC (waist circumference), Σ4SF (sum of four skinfolds), SSB (sugar-sweetened beverages), SE (standard error)

[a] Crude models included beverage intakes and changes in BMI/WC/Σ4SF

[b] Model 1: adjusted for baseline age, BMIz/WC/Σ4SF, gender, physical activity, socioeconomic status, pubertal status, and gender×socioeconomic status.

[c] Model 2 : standard multivariate model, adjusted further for total energy upon model 1

[d] Model 3: energy partition model, adjusted further for energy from non-beverage sources upon model 1

Table 3 Regression analysis results for effects of substituting water, coffee/tea, milk or fruit juice for SSBs on changes in body fatness from ages 9 to 15 y[1]

	Change in BMIz $_{9\text{-}15}$		Change in WC $_{9\text{-}15}$		Change in Σ4SF $_{9\text{-}15}$	
	β±SE	P	β±SE	P	β±SE	P
Water (100g/d)						
Crude model[a]	-0.03±0.02	0.23	-0.31±0.16	0.05	-0.80±0.43	0.07
Model 1[b]	-0.04±0.02	0.02	-0.29±0.16	0.04	-0.91±0.40	0.02
Model 2[c]	-0.04±0.03	0.13	-0.47±0.17	0.08	-1.11±0.59	0.07
Coffee/tea (100g/d)						
Crude model[a]	-0.06±0.06	0.12	-0.61±0.42	0.15	-1.19±1.14	0.30
Model 1[b]	-0.07±0.05	0.18	-0.74±0.42	0.03	-0.82±1.04	0.43
Model 2[c]	-0.07±0.06	0.23	-0.99±0.46	0.11	-0.98±1.15	0.27
Milk (100g/d)						
Crude model[a]	-0.05±0.02	0.03	-0.40±0.17	0.02	-0.89±0.45	0.05
Model 1[b]	-0.05±0.02	0.02	-0.33±0.17	0.046	-0.79±0.41	0.06
Model 2[c]	-0.05±0.02	0.03	-0.31±0.17	0.06	-0.73±0.41	0.07
Fruit juice (100g/d)						
Crude model[a]	-0.01±0.03	0.81	-0.36±0.24	0.14	-0.30±0.66	0.97
Model 1[b]	-0.02±0.03	0.53	-0.23±0.25	0.33	-0.29±0.63	0.65
Model 2[c]	-0.02±0.03	0.54	-0.27±0.26	0.37	-0.31±0.63	0.62
Total beverages (100g/d)						
Crude model[a]	0.03±0.02	0.12	0.30±0.15	0.05	0.52±0.41	0.20
Model 1[b]	0.04±0.02	0.01	0.22±0.15	0.06	0.86±0.38	0.02
Model 2[c]	0.05±0.03	0.15	0.43±0.26	0.09	1.03±0.64	0.11

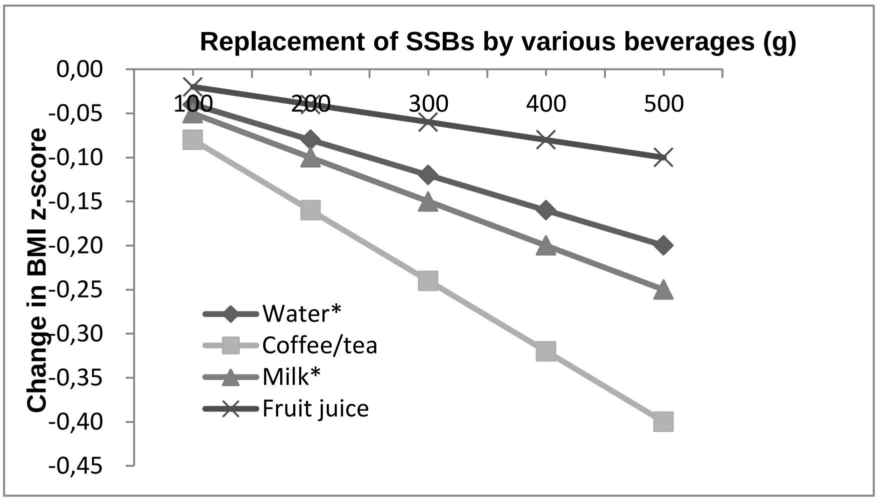
[1]BMIz (body mass index z-score), WC (waist circumference), Σ4SF (sum of four skinfolds), SSBs (sugar-sweetened beverages), β (regression coefficient), SE (standard error)

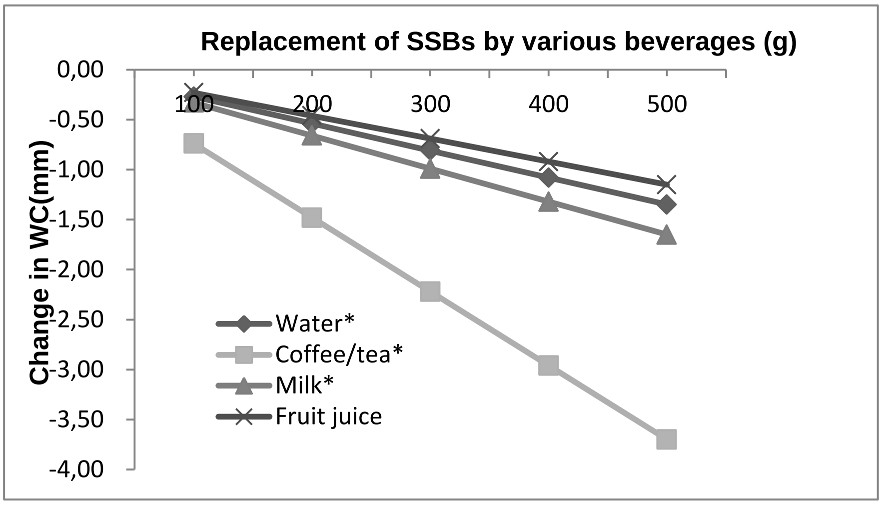
[a] Crude models included water intake (100g/d), milk intake (100g/d), fruit juice intake (100g/d), coffee/tea (100g/d)), total beverages (100g/d), and excluded SSBs from the model (reference category). By keeping the intake of total beverages, coffee/tea, milk and juice constant, a unit increase in water implies a corresponding decrease in SSBs.

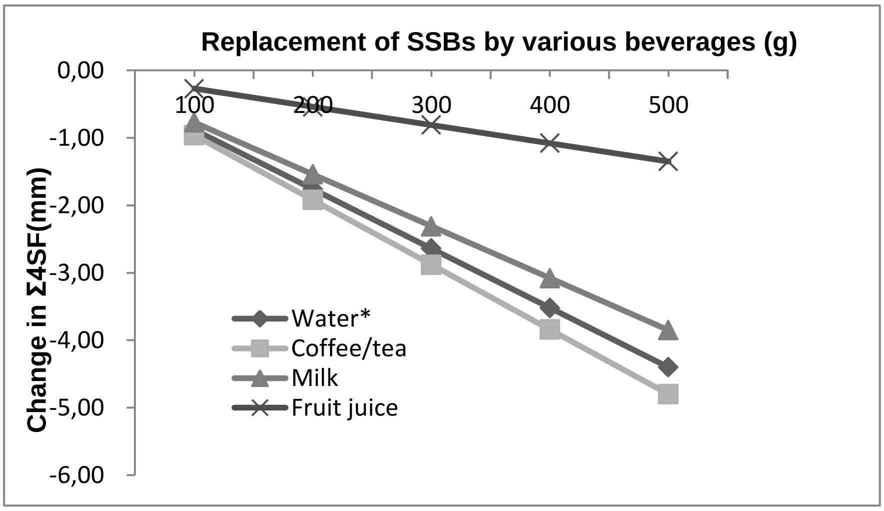
[b] Model 1: adjusted for age, gender, baseline BMIz/WC/Σ4SF, puberty, socioeconomic status, physical activity, energy from food (non-beverages sources, MJ/d) and gender×socioeconomic status.

[c] Model 2: additionally adjusted for energy from beverage sources (MJ/d)

Figure 1. The effects of replacing SSBs with water, milk, 100% fruit juice and coffee/tea on change in body fatness (BMIz, WC, and Σ4SF), adjusting for age, gender, baseline BMIz/WC/Σ4SF, puberty, socioeconomic status, physical activity, energy from food (non-beverages sources, MJ/d) and gender×socioeconomic status (* indicates P<0.05).


Replacement of SSBs by various beverages (g)
Change in BMI z-score
0,00
-0,05
-0,10
-0,15
-0,20
-0,25
-0,30
-0,35
-0,40
-0,45
100
200
300
400
500
Water*
Coffee/tea
Milk*
Fruit juice


Replacement of SSBs by various beverages (g)
Change in WC(mm)
0,00
-0,50
-1,00
-1,50
-2,00
-2,50
-3,00
-3,50
-4,00
100
200
300
400
500
Water*
Coffee/tea*
Milk*
Fruit juice


Replacement of SSBs by various beverages (g)
Change in Σ4SF(mm)
0,00
-1,00
-2,00
-3,00
-4,00
-5,00
-6,00
100
200
300
400
500
Water*
Coffee/tea
Milk
Fruit juice