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Sugar-containing beverage consumption and cardiometabolic risk in preschool children

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ABSTRACT

Objective: Sugar-containing beverages (SCBs) including 100% fruit juice, fruit drinks and soda substantially contribute to total caloric intake in young children. The objective of this study was to examine whether consumption of SCB is associated with cardiometabolic risk (CMR) in preschool children, along with whether 100% fruit juice and sugar sweetened beverage (SSB) is associated with CMR.

Study Design: We used a repeated measures study design examining SCB consumption and CMR outcomes measured concurrently in children 3–6 years of age participating in TARGet Kids!, a primary-care, practice-based research network in Canada (2008–2017). To account for within-person variability, multivariable linear regression models using generalized estimating equation was used to examine the association between SCB consumption and CMR score and the individual CMR score components including systolic blood pressure, waist circumference, high-density lipoprotein cholesterol (HDL-c), triglycerides, and glucose.

Results: After adjusting for sociodemographic, familial and child-related covariates, higher SCB consumption was associated with elevated CMR score [0.05 (95% CI −0.0001 to 0.09), p = 0.05], including lower HDL-c [−0.02 mmol/L (95% CI −0.03 to −0.01), p = 0.01] and higher triglycerides [0.02 mmol/L (95% CI 0.004 to 0.04), p = 0.02]. When examined separately, higher 100% fruit juice [−0.02 mmol/L (95% CI −0.03 to −0.003), p = 0.02] and SSB[-0.03 mmol/L (95% CI −0.06 to −0.001), p = 0.04] consumption were each associated with lower HDL-c.

Conclusion: Higher SCB consumption was associated with small elevations of CMR in preschool children. Our findings support recommendations to limit overall intake of SCBs in early childhood, in effort to reduce the potential long-term burden of CMR.

1. Introduction

Cardiometabolic risk (CMR) factors including higher adiposity, blood pressure, adverse lipids and glycaemia in childhood are associated with increased risk of metabolic syndrome, subclinical atherosclerosis and type 2 diabetes in adulthood (Juonala et al., 2010;

Abbreviations: AAP, American Academy of Pediatrics; CMR, cardiometabolic risk; CVD, Cardiovascular disease; GEE, Generalized estimating equations; HDL-c, high density lipoprotein-cholesterol; NHANES, National Health and Nutrition Examination Survey; SCB, Sugar-containing beverage; SSB, Sugar-sweetened beverage; SBP, Systolic blood pressure; TG, triglycerides; WC, waist circumference; zBMI, Body mass index z-score

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Magnussen et al., 2010; Raitakari et al., 2003). Composite CMR scores have been developed for use in children and have been shown to be associated with high carotid intima media thickness in adulthood (DeBoer and Gurka, 2017; Magnussen et al., 2016). The use of CMR scores in research has been recently highlighted by the American Academy of Pediatrics (AAP) as an approach that captures the clustering that occurs among cardiovascular risk factors and recognizes that risk lies on a continuum (Magge et al., 2017).

Sugar-containing beverages (SCBs) which includes 100% fruit juice, fruit drinks and soda collectively contribute to a quarter of the total calories consumed in diets of preschool children (Fulgoni and Quann, 2012), with 100% fruit juice contributing the most among young children (Garriguet, 2008). Although consumption of fruit drinks and soda, also known as sugar sweetened beverages (SSBs), have been implicated in increased risk of CVD and type 2 diabetes in adults (Singh et al., 2015) and adverse levels of CMR factors in adolescence (Vos et al., 2017), few studies have examined these associations in young children (< 6 years of age) (Bel-Serrat et al., 2013; Kosova et al., 2013). In addition, while some studies have reported higher 100% fruit juice consumption is associated with a modest increase in body mass index (BMI) in young children (Shefferly et al., 2016;Faith et al., 2006;Sonneville et al., 2015;Auerbach et al., 2017), it is unknown whether 100% fruit juice is associated with CMR in preschool children.

To our knowledge only one study examined the association of SCB and CMR in young children (Leermakers et al., 2015). In that study SCB consumption was measured at 1 year of age and was significantly associated with CMR score, but not individual CMR score components at 6 years of age (Leermakers et al., 2015). It is unknown whether prospectively collected SCB consumption is associated with concurrent CMR in preschool children and it is unclear whether 100% fruit juice is associated with CMR. Our primary objective was to examine whether SCB consumption is associated with a continuous CMR score and its 5 individual components in preschool children. We further examined whether 100% fruit juice and SSB, analyzed separately, were associated with CMR.

2. Methods

2.1. Study design and population

A repeated measures study was conducted in the TARGet Kids! (The Applied Research Group for Kids) cohort, a primary-care, practice-based research network in Toronto, Canada (www.targetkids.ca) (Carsley et al., 2015). Children < 6 years of age were recruited between July 2008 and May 2017 during their well-child physician visits from 11 primary care practices. Since blood pressure is measured in children 3 years and older in the cohort, we included children 3–6 years of age in the current study. In TARGet Kids! children are followed at their well-child physician visits and are invited to participate in data collection annually. Therefore, we included children who had at least one visit where both SCB intake and CMR factors were measured concurrently. We accounted for the within subject variability from repeated measurements in the statistical analysis. Children were excluded if they had health conditions affecting growth, chronic conditions besides asthma, severe developmental delay or had parents who were non– fluent in English, at recruitment. Children in this study were further excluded if they were missing any of the SCB or CMR score components. The Research Ethics Boards at the Hospital for Sick Children and St. Michael's Hospital approved the study protocol (www.clinicaltrials.gov, NCT01869530) and informed consent was obtained from the parents of participating children.

2.2. Exposures

Parents completed a detailed Nutrition and Health Questionnaire modified from the Canadian Community Health survey (Health Canada, 2006) which included questions on beverage consumption. Parents indicated the frequency of consumption of each beverage in response to *"Circle how many 250-mL cups of each drink your child has currently in a typical day"*, with responses ranging from 0 to 5 or more cups per day. The primary exposure variable of interest was SCBs which was computed as the sum of responses collected from 100% fruit juice (apple, orange, etc), sweetened drinks (Sunny D, Kool aid, etc), soda or pop. Our secondary exposures included each of 100% fruit juice defined as juice without added sugar, and SSBs, defined as the sum of sweetened drinks and soda/pop.

2.3. Outcome measures

Trained research assistants (RA) embedded in each clinic measured systolic blood pressure (SBP) using mercury sphygmomanometers and appropriate child blood pressure cuff sizes (National High Blood Pressure Education Program Working Group on High Blood Pressure in and Adolescents, 2004). Waist circumference (WC) was measured at minimal respiration to the nearest 0.1 cm (Centers for Disease Control and Prevention and National Center for Health Statistics, 2003). Non-fasting blood samples were collected by the RA using standard guidelines as previously described (Anderson et al., 2017) and transported to Mount Sinai Laboratory (http: //www.mountsinaiservices.com) for analysis. Concentrations of glucose were measured using the enzymatic reference method with hexokinase, triglycerides (TG) and high-density lipoprotein cholesterol (HDL-c) were assayed using the enzymatic colorimetric method on the Roche Modular platform. Time of last drink (except for water) and last meal or snack was recorded during the collection of blood. Although we (Anderson et al., 2017) and others (Steiner et al., 2011) have shown that fasting duration has a small impact on CMR biomarkers, including glucose, we accounted for fasting duration to control for any impact of food/beverage intake on blood sugar.

We calculated a continuous CMR score (Eisenmann, 2008), which included measures of SBP, WC, TG, glucose, and HDL-c. First, each CMR score component was standardized using the mean and standard deviations within each age and sex group within the TARGet Kids! cohort. Then, z-score values of each of the five components were summed and divided by the square root of 5 to obtain the CMR score. The inverse z-score for HDL-c was used, as lower levels would be representative of poorer cardiometabolic health. To determine which components of the CMR score were associated with each exposure, we used the non-standardized levels of each to facilitate interpretation of effect estimates.

2.4. Covariates

Covariates were selected a priori based on established evidence implicating each as potential risk factors or associated with SCB and CMR. The RA measured the child's height using a stadiometer (Seca, Hamburg, Germany) and weight using a precision digital scale (SECA model 703). BMI was calculated and age and sex-standardized BMI z-score (zBMI) was calculated according to the World Health Organization growth standards using the igrowup package (WHO, 2011). Parents reported their child's birthweight, as well as parental history of cardiometabolic-related disease (heart disease, hypertension, high cholesterol and/or diabetes), annual household income, maternal education and ethnicity. Unstructured free play outside of school was measured by asking the question *"Aside from time in daycare and school, on a typical weekday, how much time does your child spend outside in unstructured free play"*. Screen time was computed as the sum of the time spent awake in a room with the television, videos or DVDs on, using the computer, playing video games, and playing with handheld devices on a typical weekday and weekend day and a weighted average was calculated.

2.5. Data analysis

We utilized the repeated measures data available in our cohort to increase power and improve precision of measures that have high within-person variability, such as blood pressure (Gillman and Cook, 1995) and TG (Marcovina et al., 1994). Generalized estimating equation (GEE) can account for within-subject correlation and does not require all participants to have repeated measures. Therefore, all subjects with at least one measure of SCB consumption and CMR outcomes available at concurrent visits were included in the models. A multivariable linear regression model using GEE was used to assess the association between total SCB intake and CMR score and each individual CMR factor component. In Model 1 we adjusted for important biological risk factors including age and sex. In addition, we adjusted CMR score and SBP analyses for height (since height is an important predictor of childhood blood pressure) (National High Blood Pressure Education Program Working Group on High Blood Pressure in and Adolescents, 2004). All analyses examining CMR score, HDL-c, TG and glucose were additionally adjusted for fasting duration since last drink/meal/snack. In Model 2 we adjusted for the same covariates as in Model 1, but also accounted for birthweight, height, unstructured free play, screen time, annual household income, maternal education, maternal ethnicity, and parental history of cardiometabolic-related disease. We included the adjustment for height for all outcomes in Model 2, together with adjustments for age and sex, to account for potential differences in overall energy intake (Goran et al., 1993). Finally, since BMI may represent an intermediate rather than a confounder in the association for SCB consumption and CMR outcomes (Gillman et al., 2017; Schulze et al., 2004), we additionally adjusted Model 2 for zBMI in a separate model.

Distribution of variables were checked and TG were log transformed to address skewness. Multiple imputation analysis using twenty imputed data sets was performed to allow inclusion of subjects with missing covariate data (up to 15% missing) using the MICE package (van Buuren and Groothuis-Oudshoorn, 2011). The pooled regression estimates and 95% CI were reported for all adjusted analyses. All analyses were two-sided, with alpha set to 0.05 for statistical significance and conducted using R version 3.4.0 (R:https://www.r-project.org/).

3. Results

In total, 4893 children 3–6 years of age were recruited between July 2008 and May 2017. After excluding children who were missing any of the SCB components (fruit juice, fruit drinks and/or soda consumption), or one or more of the five CMR score components, 1778 children who had cocurrent measures of SCB and CMR score available on one or more visits remained for inclusion in the analysis (Fig. 1). Among these

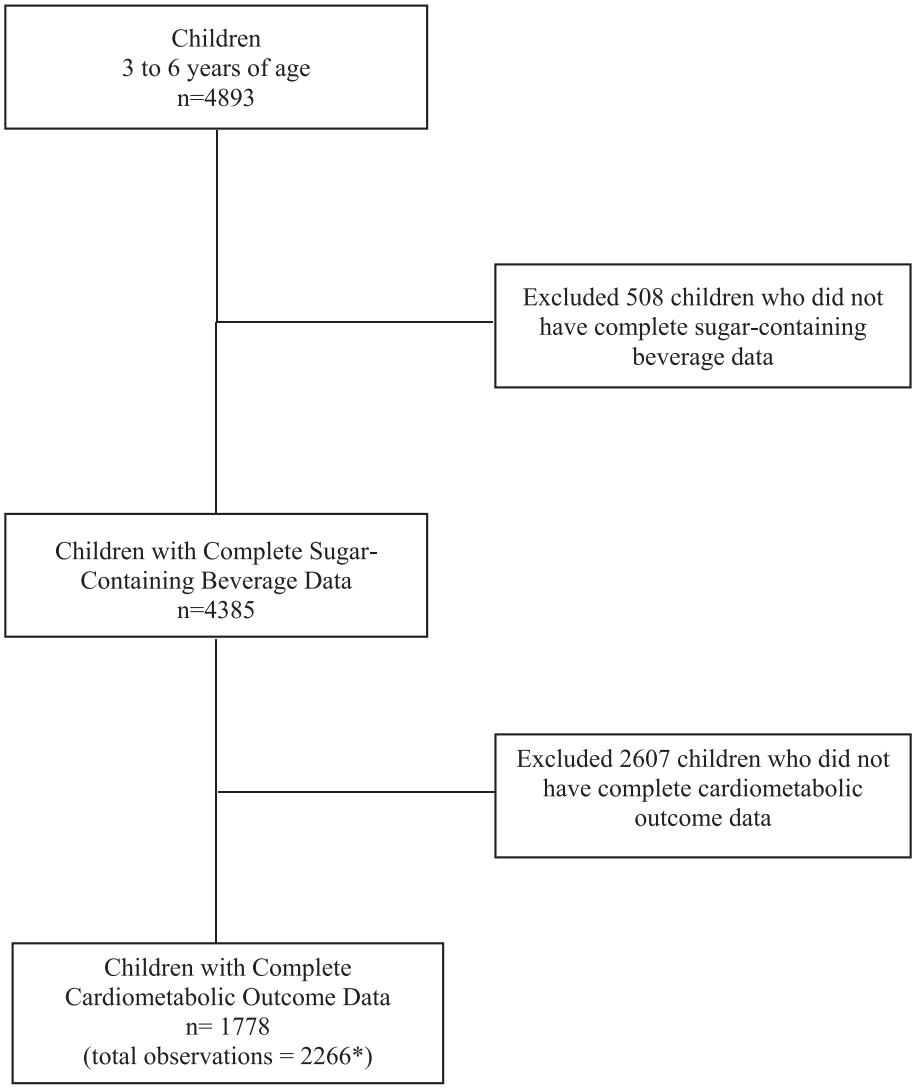

Fig. 1. Participant Flow Chart *402 children had more than 1 visit with a concurrent SCB and CMR observation, resulting in 2266 observations.

children, 402 (23%) had more than one concurrent SCB consumption and CMR outcomes measured over multiple visits, resulting in 2266 observations available for analysis. Among children who had more than one measure, they were followed for an average of 19.8 months (range 2–46 months). On average, children consumed 1 cup of SCB per day (range 0–12 cups), with the majority from 100% fruit juice (0.86 cups per day, range 0–5 cups) and the remainder (0.12 cups per day, range 0–7 cups) from SSBs. Baseline descriptive characteristics are shown in Table 1. The average age of children in the current study at the first visit was 51.0 ± 12.1 months and 53% were male. The majority of mothers were of European descent (69%) and 16% of parents reported history of cardiometabolic-related disease. Overall participants were similar to non-participants (those children who did not have complete SCB or CMR data available) (Table 1).

In GEE multivariable linear regression analysis (Table 2) SCB consumption was positively associated with CMR score ($p = 0.05$) after adjusting for all covariates in Model 2. For every one cup higher SCB intake per day, CMR score was 0.05 SD units (95% CI −0.0001, 0.09) higher. When each CMR component was examined separately, higher SCB consumption was associated with lower HDL-c ($p = 0.01$). Each additional cup of SCB consumed per day was associated with a 0.02 mmol/L (95% CI −0.03, −0.01) lower HDL-c. In addition, higher SCB consumption was associated with higher log TG ($p = 0.02$). The effect size at 0.98 mmol/L (the median level in our study) was equivalent to a 0.02 mmol/L higher TG for one additional SCB cup/d consumed. When we additionally adjusted Model 2 for child's zBMI, the association for SCB consumption with CMR score was attenuated to 0.03 SD units (95% CI −0.01, 0.08), but the association for SCB with HDL-c [-0.02 mmol/L (95% CI −0.03, −0.01)] and log TG [0.02 (95% CI 0.002, 0.04)] remained. When the analysis for the additionally adjusted model without the inclusion of height was repeated, the overall results were not materially different from the results mentioned above.

Higher consumption of 100% fruit juice was not significantly associated with higher CMR score ($p = 0.22$), but was associated with lower HDL-c ($p = 0.02$). Every one cup higher consumption of 100% fruit juice was associated with 0.02 mmol/L (95% CI −0.03, −0.003) lower HDL-c in Model 2 (Table 3). Additional adjustment of Model 2 for zBMI did not materially change the association observed between 100% fruit juice and HDL-c [−0.02 mmol/L (95% CI −0.03, −0.002)]. When the additionally adjusted model without the inclusion of height was repeated, the overall results did not materially differ from the results mentioned above.

In Model 2, higher SSB was associated with a 0.13 SD unit (95% CI 0.03, 0.23) higher CMR score ($p = 0.01$). When examining each CMR score component separately, higher SSB consumption was associated with a 0.03 mmol/L lower HDL-c ($p = 0.04$) (Table 3). Slight attenuation was observed for the association with CMR score [0.10 (95% CI 0.01, 0.20)] after additionally adjusting for zBMI, while results for HDL-c remained unchanged −0.03 mmol/L (95% CI −0.06, −0.001). However, when the analysis for the additionally adjusted model without the inclusion of height was repeated, the overall results were not different with the exception of a slight attenuation in result for the association between SSB and HDL-c [-0.03 (95%CI −0.06, 0.001)].

4. Discussion

In this cohort of almost 1800 preschool children, higher SCB consumption was associated with higher CMR score. Specifically SCB was associated with lower HDL-c and higher levels of TG, together

Table 1
Baseline Characteristics of Participant and Non-Participant Children.

Variable	Participant		Non-Participant	
	n	mean ± SD or n (%)	n	mean ± SD or n (%)
Age (months)	1778	50.98 ± 12.10	3115	46.59 ± 10.45*
Sex (Male)	1778	949 (53.40)	3115	1617 (51.90)
Birthweight (kg)	1567	3.27 ± 0.66	2507	3.28 ± 0.65
zBMI (SD units)	1774	0.23 ± 1.01	2996	0.28 ± 1.05
Average Weekday Free Play (mins/day)	1694	55.98 ± 54.84	2571	57.34 ± 57.12
Average Screen Time (mins/day)	1681	85.70 ± 76.00	2156	83.72 ± 78.93
Maternal Ethnicity	1565		2723	
European		1085 (69.30)		1937 (71.10)
East/Southeast Asian		170 (10.90)		303 (11.10)
South Asian		131 (8.40)		197 (7.20)
Other		179 (11.40)		286 (10.50)
Maternal Education	1739		3032	
College/ University		1584 (91.10)		2741 (90.40)
High school		136 (7.80)		257 (8.50)
Public School		19 (1.10)		34 (1.10)
Annual Household Income ($, CAD)	1473		2204	
< $30,000		83 (5.60)		114 (5.20)
$30,000 to 79,999		237 (16.10)		383 (17.40)
$80,000 to 149,999		436 (29.60)		689 (31.30)
≥$150,000		717 (48.70)		1018 (46.20)
Parental Cardiometabolic-related disease	1612	264 (16.40)	2442	387 (15.80)
SCB Consumption (cups/day)	1778	0.98 ± 1.17	2852	1.10 ± 1.26*
SSB Consumption (cups/day)	1778	0.12 ± 0.50	2544	0.16 ± 0.59*
100% Fruit Juice (cups/day)	1778	0.86 ± 0.92	2810	0.97 ± 0.99*
Cardiometabolic Risk Score	1778	0.02 ± 1.16	153	0.06 ± 1.19
Individual CMR Components	1778			
Systolic Blood Pressure (mmHg)		87.92 ± 7.77	1983	87.18 ± 7.61*
Waist Circumference (cm)		52.64 ± 4.21	2816	52.35 ± 4.29*
High Density Lipoprotein-cholesterol (mmol/L)		1.37 ± 0.33	540	1.38 ± 0.33
Triglycerides (mmol/L)		1.13 ± 0.64	542	1.10 ± 0.57
Glucose (mmol/L)		4.58 ± 0.71	547	4.60 ± 0.69

Mean ± SD and n (%) are shown. Differences between participants and non-participants were compared using chi-square tests for categorical variables and t-tests for continuous variables.
*$p < 0.05$ comparing participants with non-participants.

Table 2
Linear Regression Analyses for the Association between each additional cup of Sugar-Containing Beverage (SCB) Consumption and Cardiometabolic Risk Outcomes.

Variable	Model 1[a]		Model 2[b]		Additionally Adjusted for zBMI[c]	
	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
Cardiometabolic Risk Score	0.03 (−0.02, 0.07)	0.27	0.05 (−0.0001, 0.09)	0.05	0.03 (−0.01, 0.08)	0.11
*Individual CMR Outcomes**						
Systolic Blood Pressure (mmHg)	0.22 (−0.07, 0.51)	0.14	0.14 (−0.17, 0.46)	0.37	0.12 (−0.18, 0.42)	0.44
Waist Circumference (cm)	0.08 (−0.10, 0.26)	0.38	0.06 (−0.12, 0.25)	0.51	−0.01 (−0.15, 0.14)	0.93
High Density Lipoprotein-cholesterol (mmol/L)	−0.01 (−0.02, 0.002)	0.11	−0.02 (−0.03, −0.01)	0.01	−0.02 (−0.03, −0.01)	0.01
Log (Triglycerides, mmol/L)	0.02 (−0.0002, 0.04)	0.05	0.02 (0.004, 0.04)	0.02	0.02 (0.002, 0.04)	0.03
Glucose (mmol/L)	−0.02 (−0.05, −0.003)	0.03	−0.02 (−0.05, 0.01)	0.14	−0.02 (−0.05, 0.01)	0.12

*Values shown for each individual CMR outcome is in the original units, except for triglycerides which was log transformed.
CMR: cardiometabolic risk; HDL-c: high density lipoprotein-cholesterol; SBP: Systolic blood pressure; TG: triglycerides; WC: waist circumference; zBMI: Body mass index z-score
[a] Adjusted for age and sex. (CMR score and SBP were each further adjusted for height; CMR score, HDL-c, log-TG, and glucose were each further adjusted for fasting hours).
[b] Adusted for age, sex, height, birthweight, unstructured free play, screen time, household income, maternal education, maternal ethnicity and parental history of cardiometabolic-related disease. (CMR score, HDL-c, log-TG, and glucose were each further adjusted for fasting hours).
[c] Adjusted for all covariates in Model 2 as well as child's zBMI.

contributing to higher CMR score. When examined by type of SCB consumed, 100% fruit juice and SSB were each associated with lower HDL-c. Despite the well-documented association for SSB with obesity and CMR in adults (Singh et al., 2015) and pervasiveness of 100% fruit juice in the diets of preschoolers (Fulgoni and Quann, 2012; Garriguet, 2008), little is known regarding the impact of SCB consumption on CMR outcomes in young children.

Our findings demonstrating that higher consumption of SCB was associated with higher CMR score is consistent with a prior study by Leermakers et al which examined the association between SCB at 1 year of age with CMR score at 6 years of age in the Generation R cohort (Leermakers et al., 2015). Although the previous study did not detect any significant associations with the individual risk score components, possibly related to the long time-lag between the exposure and outcome, SCB tended to be positively associated with TG and inversely associated with HDL-c in fully-adjusted models (Leermakers et al., 2015), in line with our results. We have extended Leermakers and colleagues work by examining 100% fruit juice and SSBs separately and observed that higher consumption of each was associated with lower HDL-c and higher consumption of SSB was associated with higher CMR score. Similarly, in the IDEFICS cohort soft drink consumption was associated with higher CVD risk score among a sub-sample of 2–6 year old children in the study, however individual components were not examined (Bel-Serrat et al., 2013). A cross-sectional study investigating SSB intake and cardiometabolic markers in children between the ages of 3 and 11 years old using the NHANES data reported a significant

Table 3
Linear Regression Analyses for the Association between each additional cup of 100% Fruit Juice and Sugar-Sweetened Beverages (SSB) Consumption separately with Cardiometabolic Risk Outcomes.

Variable	Model 1[a]		Model 2[b]		Additionally Adjusted for zBMI[c]	
	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
100% Fruit Juice consumption						
Cardiometabolic Risk Score	0.02 (−0.04, 0.08)	0.48	0.04 (−0.02, 0.10)	0.22	0.02 (−0.03, 0.08)	0.37
*Individual CMR Outcomes**						
Systolic Blood Pressure (mmHg)	0.11 (−0.26, 0.48)	0.56	0.09 (−0.30, 0.49)	0.65	0.07 (−0.32, 0.45)	0.73
Waist Circumference (cm)	0.10 (−0.13, 0.32)	0.40	0.03 (−0.20, 0.26)	0.80	−0.04 (−0.24, 0.15)	0.65
High Density Lipoprotein-cholesterol (mmol/L)	−0.01 (−0.03, 0.002)	0.08	−0.02 (−0.03, −0.003)	0.02	−0.02 (−0.03, −0.002)	0.02
Log (Triglycerides, mmol/L)	0.02 (−0.003, 0.05)	0.09	0.02 (−0.001, 0.05)	0.06	0.02 (−0.003, 0.05)	0.08
Glucose (mmol/L)	−0.03 (−0.06, −0.0003)	0.05	−0.02 (−0.06, 0.01)	0.16	−0.03 (−0.06, 0.01)	0.14
Sugar−Sweetened Beverage (SSB) consumption						
Cardiometabolic Risk Score	0.07 (−0.03, 0.17)	0.17	0.13 (0.03, 0.23)	0.01	0.10 (0.01,0.19)	0.02
*Individual CMR Outcomes**						
Systolic Blood Pressure (mmHg)	0.85 (0.22, 1.48)	0.01	0.47 (−0.20, 1.14)	0.17	0.42 (−0.22, 1.07)	0.20
Waist Circumference (cm)	0.11 (−0.33, 0.55)	0.63	0.25 (−0.16, 0.66)	0.23	0.14 (−0.10, 0.38)	0.27
High Density Lipoprotein- cholesterol (mmol/L)	−0.01 (−0.03, 0.02)	0.67	−0.03 (−0.06, −0.001)	0.04	−0.03 (−0.06, −0.001)	0.04
Log (Triglycerides, mmol/L)	0.03 (−0.01, 0.08)	0.17	0.04 (−0.01, 0.09)	0.08	0.04 (−0.01, 0.09)	0.11
Glucose (mmol/L)	−0.03 (−0.08, 0.01)	0.16	−0.02 (−0.07, 0.03)	0.49	−0.02 (−0.07, 0.03)	0.44

*Values shown for each individual CMR outcome is in the original units, except for triglycerides which was log transformed.
CMR: cardiometabolic risk; HDL-c: high density lipoprotein-cholesterol; SBP: Systolic blood pressure; TG: triglycerides; WC: waist circumference; zBMI: Body mass index z-score
[a] Adjusted for age and sex. (CMR score and SBP were each further adjusted for height; CMR score, HDL-c, TG, and glucose were each further adjusted for fasting hours).
[b] Adusted for age, sex, height, birthweight, unstructured free play, screen time, household income, maternal education, maternal ethnicity and parental history of cardiometabolic-related disease. (CMR score, HDL-c, log-TG, and glucose were each further adjusted for fasting hours).
[c] Adjusted for all covariates in Model 2 as well as child's zBMI.

association between increased SSB intake and lower HDL-c, observed in their larger subsample of 9–11 year old children (Kosova et al., 2013).

The AAP recently released a policy statement recommending that 100% fruit juice consumption be limited to ½ cup per day in 1–3 year olds and up to ½ - ¾ cup in 4–6 year olds (Heyman et al., 2017). Children participating in NHANES between the ages of 1–5 years were reported to consume on average 1 to 1 ½ cups per day of 100% fruit juice (Fulgoni and Quann, 2012). Slightly lower amounts were observed in the Canadian Community Health Survey in which 100% juice consumption in children between the ages of 1–8 years was estimated to be 0.6–0.8 cups per day (Garriguet, 2008). Similar mean intake (0.86 cup/d) was observed in our study with average intake slightly above the limit set by the AAP (Heyman et al., 2017). Overall, dietary guidelines recommend providing children with whole fruit instead of 100% fruit juice since 100% fruit juice lacks the fibre that whole fruit provides (Heyman et al., 2017). However, given that 100% fruit juice, like whole fruit, contains vitamins and other beneficial nutrients, parents generally perceive fruit juice to be healthy (Munsell et al., 2016). To our knowledge there are no randomized controlled trials comparing the impact of consuming fruit juice derivatives to the equivalent consumption of the whole fruit on CMR outcomes in young children.

In addition to water, fruit juices contain sucrose, fructose, glucose, and sorbitol (Heyman et al., 2017) and levels of fructose in 100% fruit juice have been shown to be similar to the fructose content of SSB (Walker et al., 2014). The adverse associations observed for SCB with TG and HDL-c may be related to the fructose content of SCB, since fructose drives hepatic TG synthesis and accumulation (Lim et al., 2010; Lustig et al., 2016) which can lead to increased HDL-c catabolism (Lamarche et al., 1999). In a randomized, double-blind, crossover two-day feeding study in older children, increases in plasma TG and decreases in HDL-c were observed after randomization to an *iso*-caloric fructose vs glucose beverage (Jin et al., 2012). We demonstrated that associations for SCB, 100% fruit juice and SSB with HDL-c and TGs were unchanged after adjusting for objectively measured zBMI, which is consistent with other studies suggesting that beverages high in sugar can negatively contribute to cardiometabolic health through direct metabolic mechanisms (Leermakers et al., 2015).

For every additional cup of SCB consumed, HDL-c was 0.02 mmol/L lower in our cohort of preschool children. A similar effect size was observed among 3–11 year old children participating in NHANES (Kosova et al., 2013). Overall effect sizes for CMR score and each outcome we observed were greater for SSB compared to 100% fruit juice. Long-term studies are needed to quantify the clinical significance of chronic exposure to small reductions in HDL-c related to dietary exposures in childhood. Given that cumulative exposure to lower HDL-c levels from childhood through adulthood has been shown to be associated with higher atherosclerosis in adults (Li et al., 2003) establishing health promoting habits in early childhood represents an important strategy for long-term CVD risk reduction. There is less compelling evidence on changes in TG levels in children and long-term clinical impact compared to HDL-c. For example, in a study of using data from 4 child to adult cohorts, the odds of increased carotid intimal medial thickness, a non-invasive measure of early artherosclerosis, were higher in adults who had increased HDL-c but not TG in later childhood (Koskinen et al., 2018)

The potential health risks associated with 100% fruit juice have been debated (Abrams and Daniels, 2017). Most prior studies have focused on adverse effects of fruit juice on dental caries and adiposity (Heyman et al., 2017). A recent *meta*-analysis reports that 100% fruit juice is associated with a small increase in zBMI specifically among children ≤ 6 years of age (Auerbach et al., 2017). In our study, we did not observe a significant association of any of the SCBs with WC. Similarly no association was observed in the preschool-aged subgroup of NHANES participants (Kosova et al., 2013).

4.1. Strengths and limitations

We made use of available repeated measures of SCB intake and CMR in a relatively large cohort of healthy preschool children. The repeated measures design was used to maximize the power of our analysis, especially for variables such SBP (Gillman and Cook, 1995) and TG (Marcovina et al., 1994), which exhibit high within-person variability. We note that the majority of children in our study had only one concurrent SCB and CMR score observation available. Future studies are also needed to determine how changes in the type of SCB consumed over time are associated with CMR in children to determine the long-term relationship between SCB consumption on CMR. The questionnaire we used to quantify typical consumption of SCB included separate questions to measure intakes of 100% fruit juice, fruit drink, and soda, enabling analysis of 100% fruit juice on its own. Nonetheless, we acknowledge that there is potential for misclassification between reporting 100% fruit juice and fruit drinks. Our participants reported consuming 0.86 cups/d of 100% fruit juice, which is consistent with data from the Canadian Community Health Survey, which used an interviewer-administered 24-hr recall (Garriguet, 2008). With blood measures being collected during routine primary health care visits, blood measures were non-fasting which remains to be a limitation. There is evidence suggesting that fasting prior to blood measure collection made very little difference in children, we did however adjust for fasting hours (Andersen et al., 2017). Given that this was an observational study, causality cannot be implied and we cannot rule out residual confounding. Although we adjusted for several important covariates, the lack of adjustment for unmeasured confounders poses a risk for residual confounding. The questionnaire that we used was designed to capture usual beverage consumption rather than overall dietary intake. We were therefore unable to adjust for diet quality or for total energy intake. However, we adjusted for age, sex and height to account for potential differences in overall energy intake (Goran et al., 1993). In addition, associations for lipids were unchanged after inclusion of zBMI in the model. Future randomized trials are necessary to rule out reverse causation and residual confounding for the association between SCB consumption and cardiometabolic risk. Although the continuous CMR score has been shown to be predictive of subclinical atherosclerosis in older children (Magnussen et al., 2010), no studies have determined the validity of the CMR score in preschool children and various definitions have been used to define the CMR score (Kamel et al., 2018). Thus, comparison of the effect size observed for CMR in our study with those observed in other studies is limited. Since participants were from families with reports of high household income and education, results from this study might not be generalizable to children in other settings.

In conclusion, higher SCB intake was associated with higher CMR score, lower HDL-c and higher TG in preschool children. Both 100% fruit juice and SSB consumption were each associated with lower HDL-c levels in early childhood independent of child zBMI. Although small elevations in CMR were observed in this young cohort, childhood dietary habits are likely to persist into adulthood (Fiorito et al., 2010; Mikkila et al., 2005). Therefore, promoting positive dietary preferences at a young age may contribute to more favourable life-long dietary habits to minimize long-term CMR. Longitudinal studies are needed to replicate our findings and evaluate the clinical impact of long-term exposures to modest elevations in CMR.

Clinical Trial Registration: www.clinicaltrials.gov, NCT01869530

Conflict of Interest

CSB received a research grant from the Centre for Addiction and Mental Health Foundation (CAMH 2017–2020). JLM received an unrestricted research grant for a completed investigator-initiated study from the Dairy Farmers of Canada (DFC; 2011–2012) and Ddrops provided non-financial support for an investigator initiated study on vitamin D and respiratory tract infections (2011–2015). Upon completion of this study, KME was hired as an employee of Nutrigenomix

Inc. PCP reports receiving a grant from Hospital for Sick Children Foundation during the conduct of the study. PCP reports receiving the following grants unrelated to this study: a grant from CIHR (FRN # 115059) for an ongoing investigator-initiated trial of iron deficiency in young children, for which Mead Johnson Nutrition provides non-financial support (Fer-In-Sol® liquid iron supplement) (2011–2017); and grants for completed investigator-initiated studies from Danone Institute of Canada (2002–2004 and 2006–2009), Dairy Farmers of Ontario (2008–2010). These agencies had no role in the design, collection, analyses or interpretation of the results of this study or in the preparation, review, or approval of the manuscript. The other authors have no conflicts of interest to disclose.

CRediT authorship contribution statement

Karen M. Eny: Conceptualization, Methodology, Writing - original draft, Writing - review & editing. **Nivethika Jeyakumar:** Conceptualization, Methodology, Formal analysis, Writing - review & editing. **David W.H. Dai:** Methodology, Software, Writing - review & editing. **Jonathon L. Maguire:** Writing - review & editing. **Patricia C. Parkin:** Writing - review & editing. **Catherine S. Birken:** Supervision, Conceptualization, Methodology, Writing - review & editing. **:** .

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