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Effects of dietary glycemic index and load on children's cardiovascular risk factors

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A B S T R A C T

Purpose: Consumption of foods high in glycemic index (GI) and glycemic load (GL) is associated with cardiovascular (CV) diseases in adulthood. We examined whether GI and GL predict CV risk factors in children after 2 years of follow-up.
Methods: Three 24-hour recalls were administered at baseline, and individual average daily GI and GL scores were calculated in a cohort of 8–10 year-old children. CV risk factors included body mass index z-score (BMIz), percent fat mass, triglycerides (TGs), low-density lipoprotein and high-density lipoprotein (HDL) cholesterol, and systolic and diastolic blood pressure. Main analyses consisted of multiple linear regression adjusted for anthropometric, socioeconomic, and dietary factors.
Results: After 2 years, the highest dietary GL tertile compared with the lowest was associated with increased BMIz (mean difference [MD], 1.1; 95% CI, 0.88–1.31), fat mass (MD, 10.8%; 95% CI, 8.62–13.0), TGs (MD, 0.17 mmol/L; 95% CI, 0.07–0.28), and decreased HDL (MD, −0.13 mmol/L; 95% CI, −0.19 to −0.07). The GL–TG and the GL–HDL associations were mediated by BMIz.
Conclusions: GL predicts increased BMIz, percent fat mass, and TGs and decreased HDL in young children after 2 years. Recommendations to decrease CV risk in children should include lowering foods high in GL.

Introduction

Childhood obesity is epidemic in North America (REF 1 and 2), and it has short-term metabolic and cardiovascular (CV) effects, including increased fasting insulin and triglycerides (TGs), lowered high-density lipoprotein (HDL) cholesterol and increased blood pressure. It has been associated with the development of type II diabetes and hypertension in children and adolescents and may lead to cardiovascular diseases (CVD) later in life [1,2]. Dietary intake, among other factors, has an important influence on obesity and CVD risk factors. Particularly, refined carbohydrates tend to be absorbed faster into the bloodstream, causing excessive insulin secretion and increased hepatic and cellular fat storage [3]. Excess energy intake, specifically in the form of refined carbohydrates, can lead to obesity, worsened blood lipid profiles, and ultimately to CVD [4–6].

The glycemic index (GI) is a measure of blood glycemic response resulting from various qualities of dietary carbohydrates (by definition, a high quality [low GI] carbohydrate does not raise blood glucose as much as a low quality [high GI] carbohydrate, relative to an equal weight of glucose), whereas glycemic load (GL) is an indicator of both quality (GI) and quantity of carbohydrates consumed [7]. GI and GL are associated with adiposity, dyslipidemia, and CVD in adults [8–12]; however, few studies have assessed this association in youth, and the findings have been inconsistent,

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Authors' contributions: K.S. designed the research question for this project, conducted the analysis, interpreted results, and wrote the article. A.B., M.H., K.G.D., and G.P. participated in the research question design (defining outcomes, identifying confounders, and determining appropriate analysis methods) and reviewed and edited the manuscript.

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likely owing to methodological flaws, including dietary measurement error and differential recall, and varying populations compositions [13–17].

The objective of our study was to examine how dietary GI and GL at baseline predict adiposity, lipid profiles, and blood pressure, 2 years later in a cohort of children with obese parents. Identifying longitudinal associations between GI and GL, scores that are easily understandable, and CV risk factors could add to current knowledge on pediatric obesity and CVD prevention and help improve nutritional counseling by dietitians and physicians and potentially also help families make healthy food choices.

Methods

Study population

The design and methods of the QUebec Adipose and Lifestyle InvesTigation in Youth (QUALITY) study have been previously described [18]. A total of 630 children aged 8–10 years and both biological parents, at least one of whom had to be obese, were recruited and, 2 years later, the follow-up included 564 children (89.5% retention). The QUALITY cohort used a school-based sampling strategy to identify potential participants. Caucasian children of Western European ancestry aged 8–10 years with at least one obese biological parent were included. The cohort was restricted to Caucasian families to reduce genetic admixture. Families were excluded if the mother was pregnant or breastfeeding or if the family had plans to move out of province. Children who had any of the following criteria were excluded: (1) type I or type II diabetes; (2) a serious illness, psychological condition, or cognitive disorder; (3) treatment with oral antihypertensive medication or steroids; and (4) following a very restricted diet (<600 kcal/d).

Measurements

Trained dietitians administered three unannounced nonconsecutive 24-hour dietary recalls, including one weekend day over the telephone within 8–12 weeks after the baseline visit. A disposable kit of food portion models (e.g., a graduated cup, a bowl, etc.) was provided to participants at the baseline visit, in conjunction with a training and practice session for children and parents. Interviews were conducted with the child, and parents helped with food descriptions and cooking details. The dietary data collected from 613 participants were entered in the CANDAT Nutrient Analysis Software (Godin and associates, London, Ontario, 2007), which calculates nutrient composition of foods based on the Canadian Nutrition Files. Underreporters of energy intake were identified using the Goldberg equation [19] (Methods A.1-A.2).

The steps for assigning GI and GL to foods in the database were as follows. First, we assigned a value of zero to each food group containing less than or equal to 5 g of carbohydrate per 100 g [20]. Next, if a food was listed in the International table of GI [21], we used the corresponding GI score. Foods without a preassigned GI value in the International table of GI [21] were assigned a GI based on the closest nutritionally matching food [20,22]. Finally, we multiplied every GI value by the available carbohydrate content in each food to obtain a GL score. We obtained an average daily GI and GL for each participant by calculating the sum of the scores by recall day and then averaging the totals of the three dietary recalls.

Anthropometric measurements were collected according to a standardized protocol with participants dressed in light indoor clothing with no shoes, using a stadiometer for height (nearest 0.1 cm), and an electronic scale for weight (nearest 0.1 kg). Height and weight were measured twice, and a third measure was obtained if the first two measures differed by 0.2 cm or 0.2 kg or more. The final value was the average of the two closest measurements. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Age- and sex-specific BMI z-score (BMIz) was obtained using the Centers for Disease Control and Prevention growth charts [23]. Percent body fat was assessed using dual-energy X-ray absorptiometry (Prodigy Bone Densitometer System, DF-14664, GE Lunar Corporation, Madison, WI). At each clinic visit, blood was collected from both children and parents by venipuncture after an overnight fast. Blood samples were centrifuged, aliquoted, and stored at −80 Celsius and were analyzed at the Department of Biochemistry at Center Hospitalier Universitaire Sainte-Justine [18]. TGs and HDL cholesterol concentrations were determined on a Synchron LX20 with Beckman Instruments reagents and expressed as millimoles per liter. Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald equation [24].

Blood pressure was measured on the right arm with participants in seated position, using an oscillometric instrument (Dinamap XL, model CR9340, Critikon Company, FL). Five readings were recorded, and the mean value of the last three readings was used for systolic blood pressure (SBP) and diastolic blood pressure (DBP). Age-, sex-, and height-specific z-scores were calculated following the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents [25].

Physical activity was assessed over a 7-day period using an Actigraph LS 7164 activity monitor (Actigraph LLC, Pensacola, FL). Accelerometry data were downloaded as 1-minute epochs and were processed using standardized quality control and data reduction procedures [26]. Participants were retained if they had at least four days with a minimum of 10 hours of wear time [27]. We used daily step counts to adjust for physical activity. Screen time was assessed by interviewer-administered questionnaire that collected daily hours of television, computer, or video game use. Data on parental education and household income were collected from questionnaires. Sexual maturity was observed by trained nurses and scored according to the Tanner stages [28,29]. We categorized children into prepubertal (stage 1) or pubertal (stages 2 and higher).

Exposure and outcome definition

The outcomes of interest included BMIz, percent fat mass, blood lipids, including TG, HDL, and LDL cholesterol, and SBP z-score and DBP z-score after a 2-year follow-up. Independent variables were baseline GI and GL.

Statistical analyses

Descriptive statistics are reported as mean (SD) or median (interquartile range) for both baseline and follow-up visits. We used multiple imputation (Proc MI in SAS 9.3) to account for missing data of covariates, particularly the physical activity variable that had 15% missing data. All dietary variables were adjusted for energy intake using the residual method [30]. We estimated multiple linear regression models for each outcome of interest, with baseline GI or GL (residuals) as independent variables, adjusted for important confounders measured at baseline (age, sex, pubertal vs. prepubertal, physical activity, family income, parental education, fat and protein intake (residuals), season, and underreporting (ratio of energy intake and estimated energy requirement). Age and sex were not included in the BMIz, SBP z-score, and DBP z-score models because these outcome measures are already adjusted for age and sex. We assessed linearity with adjusted linear regression splines of predicted BMIz, percent fat mass, TG, LDL, HDL, SBP z-score, and DBP z-score as a function of GL, which showed nearly linear relationships between GL and outcomes of interest; therefore, estimates of linear regressions are presented. We tested for interactions between each exposure variables (GI and GL) and sex and with BMI category (under/normal weight vs. overweight/obese) by introducing an interaction term one at a time in adjusted models. As a secondary analysis, we assessed mediation by BMIz at baseline, assuming diet recall was an indicator of usual intake, using the Baron and Kenny approach [31]. Although we chose to adjust for underreporting as a continuous variable to reduce residual confounding, we also conducted additional analyses using a binary parametrization to facilitate comparisons with some authors who used the categorized underreporting variable for adjustment. Because the inclusion of all macronutrients in a model could potentially result in aliasing with the intercept, we conducted a second sensitivity analysis with adjustments for only nondietary variables or only fat intake. We used SAS version 9.3 for analyses and STATA version 13.1 for graphics.

Results

Among the 630 participants recruited at baseline, 66 were lost to follow-up. There were no significant differences between those included and those lost to follow-up in the analyses presented herein with respect to age, BMIz, and sex. Population characteristics at baseline and follow-up are shown in Table 1. After 2 years, children had a higher percent fat mass, spent approximately one additional hour of screen time per day, and were less physically active (Table 1).

In multiple linear regression, GI at baseline did not predict any cardiometabolic risk factors after 2 years (Table 2). GL predicted BMIz (β, 0.03; 95% CI, 0.02–0.03), percent fat mass (β, 0.29; 95% CI, 0.25–0.33), TG (β, 0.005; 95% CI, 0.003–0.007), and HDL cholesterol (β, −0.003; 95% CI, −0.004 to −0.002) after 2 years, but not LDL cholesterol, SBP z-score, and DBP z-score (Table 3). Highest dietary GL tertile compared with the lowest was associated with an increased BMIz (mean difference [MD], 1.1; 95% CI, 0.88–1.31), percent fat mass (MD, 10.8; 95% CI, 8.62–13.0), TGs (MD, 0.17; 95% CI, 0.07–0.28), and decreased HDL (MD, −0.13; 95% CI, −0.19 to −0.07). No statistically significant interactions were found with BMI category or sex.

Mediation analysis showed total effects of baseline GL on TG and HDL after 2 years that were attenuated when BMIz was included in the model to evaluate the direct effect (TG: β , 0.003; 95% CI, 0.001–0.007; and HDL: β, −0.001; 95% CI, −0.003 to 0.001), indicating that BMIz mediated the association between GL and TG and GL and HDL (Fig. 1A and B).

Our sensitivity analyses revealed similar results to our main analysis of GI and GL when adjusting for underreporting as a binary variable (Tables B.1-B.2); however, the impact of GL on risk factors was attenuated when adjusting for only nondietary variables or only fat intake (Table B.3).

Discussion

CV risk factors tend to track over time, with research supporting the idea that worse cardiometabolic risk profiles in childhood will result in deleterious cardiometabolic profiles in adulthood [32]. The American Academy of Pediatrics recommends prevention of CVD by maintaining healthy weight and blood lipid levels in childhood [33]. Our study revealed an association between high-dietary GL and overall worse cardiometabolic profiles 2 years later in children at risk for obesity.

Specifically, GL but not GI predicted increased adiposity and unhealthy blood lipids in our population of 8- to 10-year-old children after 2 years. In addition, the association between GL and blood lipids was mediated by BMIz, indicating that the association

Table 1
Population characteristics of children in the QUALITY cohort at baseline and first follow-up visit

Characteristic	Baseline ($n = 630$)	Follow-up ($n = 564$)
Age (y), mean (SD)	9.6 (0.9)	11.7 (0.9)
Male (%)	54.4	55.5
BMI category (%)		
Underweight (z-score <−2)	0.3	0.9
Normal weight (z-score ≥−2 and <1)	56.7	58.3
Overweight (z-score ≥1 and < 2)	30.0	28.4
Obese (z-score ≥2)	13.0	12.4
Tanner stage (%)		
Prepubertal	78.4	33.2
Pubertal	21.6	66.8
Percent fat mass, median (IQR)	25.3 (17.4–35.2)	27.8 (19.4–36.4)
Screen time (h/d), median (IQR)	2.2 (1.3–3.7)	2.9 (1.9–4.4)
SBP z-score, median (IQR)	−0.79 (−1.26 to −0.35)	−0.85 (−1.37 to −0.39)
DBP z-score, median (IQR)	−1.09 (−1.40 to −0.83)	−1.09 (−1.39 to −0.80)
Triglycerides, median (IQR)	0.7 (0.6–1.0)	0.7 (0.5–0.9)
HDL cholesterol, median (IQR)	1.2 (1.0–1.3)	1.1 (1.0–1.3)
LDL cholesterol, median (IQR)	2.3 (2.0–2.7)	2.2 (1.9–2.6)
Parent education		
No parent with high school diploma	1.4	0.8
1 or 2 parents with high school diploma	6.4	6.4
1 or 2 parents with community college or equivalent	37.8	42.9
1 or 2 parents with university degree	54.4	49.9
Family income, mean (SD)	42,360 (18,574)	48,643 (22,191)
Glycemic index, mean (SD)	52.2 (4.2)	—
Glycemic load, mean (SD)	110.1 (30.8)	—
Carbohydrate intake (g), mean per day (SD)	221.3 (56.0)	—
Energy intake (kcal), mean per day (SD)	1681.8 (388.4)	—
Sugar-sweetened beverages (mL), median (IQR)	67.9 (0.0–189.5)	—
Number of snacks, median (IQR)	5 (3–6)	—
Physical activity (counts per minute), median (IQR)*	559.1 (459.0–675.1)	462.3 (374.5–587.3)

IQR = interquartile range.
* Accelerometry data only completed for $n = 535$ at baseline and $n = 418$ at follow-up visit.

Table 2
Longitudinal association between dietary glycemic index at baseline and cardiometabolic risk outcomes after 2 years of follow-up in children from the QUALITY cohort

Outcome	Continuous GI*	Tertiles of GI†		
		1	2	3
BMI z-score				
Mean difference (95% CI)	0.11 (−0.08 to 0.31)	0	−0.01 (−0.22 to 0.19)	0.10 (−0.11 to 0.30)
Adjusted mean difference (95% CI) ‡	−0.11 (−0.30 to 0.08)	0	−0.14 (−0.34 to 0.05)	−0.11 (−0.31 to 0.08)
Fat mass (%)				
Mean difference (95% CI)	0.66 (−1.30 to 2.61)	0	−0.86 (−2.92 to 1.20)	0.38 (−1.64 to 2.40)
Adjusted mean difference (95% CI)	−0.78 (−2.65 to 1.10)	0	−1.43 (−3.34 to 0.49)	−1.03 (−2.30 to 0.90)
Triglycerides (mmol/L)				
Mean difference (95% CI)	0.05 (−0.03 to 0.01)	0	−0.02 (−0.11 to 0.06)	0.07 (−0.02 to 0.15)
Adjusted mean difference (95% CI)	0.005 (−0.08 to 0.09)	0	−0.05 (−0.13 to 0.04)	0.02 (−0.07 to 0.11)
LDL cholesterol (mmol/L)				
Mean difference (95% CI)	0.02 (−0.10 to 0.14)	0	0.01 (−0.12 to 0.13)	0.03 (−0.09 to 0.15)
Adjusted mean difference (95% CI)	0.003 (−0.12 to 0.13)	0	−0.01 (−0.14 to 0.11)	0.02 (−0.11 to 0.14)
HDL cholesterol (mmol/L)				
Mean difference (95% CI)	−0.04 (−0.09 to 0.01)	0	−0.02 (−0.01 to 0.03)	−0.03 (−0.08 to 0.02)
Adjusted mean difference (95% CI)	−0.003 (−0.05 to 0.05)	0	−0.002 (−0.05 to 0.05)	0.003 (−0.05 to 0.05)
SBP z-score				
Mean difference (95% CI)	0.08 (−0.07 to 0.23)	0	0.06 (−0.09 to 0.22)	0.07 (−0.08 to 0.23)
Adjusted mean difference (95% CI)‡	0.02 (−0.14 to 0.17)	0	0.01 (−0.15 to 0.17)	0.01 (−0.15 to 0.17)
DBP z-score				
Mean difference (95% CI)	0.07 (−0.02 to 0.16)	0	0.04 (−0.06 to 0.13)	0.07 (−0.02 to 0.17)
Adjusted mean difference (95% CI)‡	0.03 (−0.06 to 0.13)	0	0.02 (−0.08 to 0.11)	0.03 (−0.07 to 0.13)

Ages 8 to 10 y at baseline.
All crude models were adjusted for underreporting (ratio of energy intake and estimated energy requirement). All multiple linear regression models were adjusted for pubertal versus nonpubertal status, screen time, physical activity (CPM), family income, parent education (four categories), ratio of energy intake and estimated energy requirement, fat and protein intake (residuals), and season.
* Continuous model: every 10 unit increase in GI at baseline is associated with a mean increase in outcome of x.
† Tertile model: consuming a dietary GI in the highest tertile compared with the lowest reference tertile at baseline is associated with an increased outcome of x after 2 y of follow-up interpretation.
‡ Age and sex were not included in the BMI z-score, SBP z-score, and DBP z-score models.

is mainly explained by BMI. We did not observe any associations with GI and carbohydrate quality, but did observe associations with GL and carbohydrate quality and quantity, implying that it is important to consider both quality and quantity of carbohydrates, rather than quality alone when selecting dietary carbohydrates.

GL may exert harmful effects via several pathways. The consumption of high GI foods induces immediate hyperglycemia

Table 3
Longitudinal association between dietary glycemic load at baseline and cardiometabolic risk outcomes after 2 y of follow-up in children from the QUALITY cohort, ages 8–10 years at baseline

Outcome	Continuous GL*	Tertiles of GI†		
		1	2	3
BMI z-score				
Mean difference (95% CI)	0.01 (0.001 to 0.002)	0	0.10 (−0.11 to 0.30)	0.54 (0.32 to 0.75)
Adjusted mean difference (95% CI)‡	0.03 (0.02 to 0.03)	0	0.37 (0.19 to 0.55)	1.10 (0.88 to 1.31)
Fat mass (%)				
Mean difference (95% CI)	0.11 (0.07 to 0.18)	0	1.34 (−0.69 to 3.36)	4.78 (2.60 to 6.70)
Adjusted mean difference (95% CI)	0.29 (0.25 to 0.33)	0	4.12 (2.32 to 5.93)	10.8 (8.62 to 13.0)
Triglycerides (mmol/L)				
Mean difference (95% CI)	0.001 (−0.001 to 0.003)	0	0.08 (−0.16 to 0.01)	0.03 (−0.06 to −0.13)
Adjusted mean difference (95% CI)	0.005 (0.003 to 0.007)	0	−0.01 (−0.10 to 0.08)	0.17 (0.07 to 0.28)
LDL cholesterol (mmol/L)				
Mean difference (95% CI)	−0.0004 (−0.003 to 0.002)	0	0.02 (−0.10 to 0.15)	−0.03 (−0.17 to 0.10)
Adjusted mean difference (95% CI)	0.002 (−0.001 to 0.0001)	0	0.07 (−0.06 to 0.20)	0.07 (−0.08 to 0.23)
HDL cholesterol (mmol/L)				
Mean difference (95% CI)	−0.001 (−0.002 to 0.0001)	0	0.02 (−0.03 to 0.07)	−0.05 (−0.11 to 0.004)
Adjusted mean difference (95% CI)	−0.003 (−0.004 to −0.002)	0	−0.02 (−0.07 to 0.03)	−0.13 (−0.19 to −0.07)
SBP z-score				
Mean difference (95% CI)	0.001 (−0.002 to 0.004)	0	−0.04 (−0.19 to 0.12)	−0.01 (−0.18 to 0.16)
Adjusted mean difference (95% CI)‡	0.004 (0.000 to 0.008)	0	0.02 (−0.14 to 0.18)	0.07 (−0.12 to 0.26)
DBP z-score				
Mean difference (95% CI)	0.0003 (−0.002 to 0.002)	0	0.03 (−0.06 to 0.13)	0.03 (−0.07 to 0.14)
Adjusted mean difference (95% CI)‡	−0.0001 (−0.002 to 0.003)	0	0.04 (−0.06 to 0.14)	0.03 (−0.09 to 0.14)

All crude models were adjusted for underreporting (ratio of energy intake and estimated energy requirement). All multiple linear regression models were adjusted for age, sex, pubertal versus nonpubertal status, screen time, physical activity (CPM), family income, parent education (four categories), ratio of energy intake and estimated energy requirement, energy (residual method), fat and protein intake (residuals), and season.
* Continuous model: every 10-unit increase in GL at baseline is associated with a mean increase in outcome of x.
† Tertile model: consuming a dietary GL in the highest tertile compared with the lowest reference tertile at baseline is associated with an increased outcome of x after 2 y of follow-up interpretation.
‡ Age and sex were only included in the percent fat mass, TG, LDL, and HDL models.

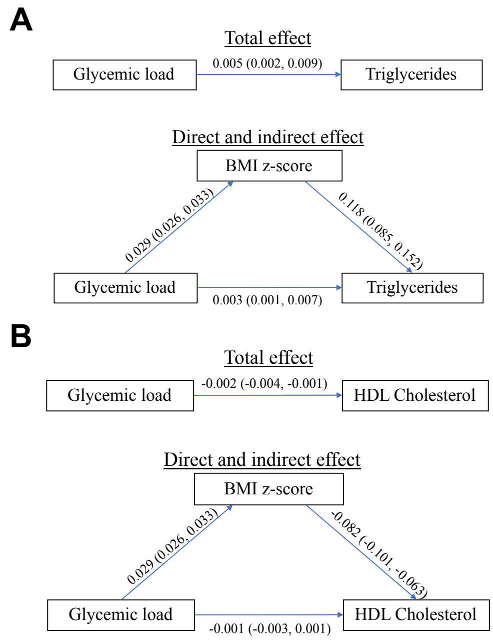

Fig. 1. The total, direct, and indirect effects of glycemic load on triglycerides (A) and HDL cholesterol (B) considering adiposity (BMI z-score) as a mediator (β [95% CI]). Direct effects can be interpreted as follows: for every 10-unit increase in glycemic load, β can be interpreted as the unit change in triglycerides or HDL cholesterol independent of BMI z-score

because of the quick uptake of glucose in the bloodstream [34,35]. This provokes a hyperinsulinemic response to restore normal blood glucose levels, resulting in a relative hypoglycemic state [34,35]. This insulin-induced relative hypoglycemic state may provoke prolonged hyperphagia and overeating, even after normal blood glucose levels have been restored [34,35]. Moreover, the hyperinsulinemia state leads to a preferential behavioral selection of high-GL foods, creating a cycle of hypoglycemia and hyperphagia resulting in weight gain and obesity [34–37]. Following a high-GL meal, a counterregulatory hormonal response is triggered to restore normal glucose levels. This response stimulates processes that elevate free fatty acid concentrations to levels higher than observed with a low-GL diet [7,38,39]. In turn, increased lipid accumulation in adipose tissues leads to weight gain, increased inflammation, and decreased vasodilation, factors known to worsen CVD risk factors [40,41].

We observed increasing BMIz and percent fat mass in children with increasing GL, but not GI. After 2 years, those who consumed a dietary GL in the highest tertile were more than one full BMIz higher and had 10% greater percent fat mass compared with children in the lowest tertile. Nine previous studies, including two longitudinal studies, have examined the association between GI and GL and adiposity in children and have reported inconsistent results. Analyses from the Dortmund Nutrition and Anthropometric Longitudinally Designed Study cohort found no association between change in GI and GL and concurrent changes in BMIz and percent body fat [16]. Consistent with our results, a longitudinal study in 2353 Australian children aged 12 years [13] showed no association between GI and change in adiposity, but observed a 0.77 kg/m^2 increase in BMI for every 50.89 unit (1 SD) increase in dietary GL in girls. We did not observe differences between sexes. This discrepancy may be because of age and cultural differences between the Australian cohort and the QUALITY cohort. The remaining seven studies were cross-sectional. Two cross-sectional studies found higher GI but not GL to be associated with greater adiposity in children [42,43], and one study found associations with both GI and GL [44]. The other four studies found no associations [15–17,45]. In addition to inherent methodological limitations of cross-sectional studies such as reverse causation, the studies mentioned previously also had other methodological problems, including confounding by underreporting [13,17,44], measurement error resulting from an insufficient number of nutritional recalls [44], and selection bias because of selective inclusion criteria and high rates of nonresponse [13,42,45]. Furthermore, the divergent results may be explained by differences in study populations, which varied by age, ethnic origins, and dietary culture of children.

Our results showed an association between high-dietary GL, but not GI, with worsened blood lipids after 2 years, specifically higher TG and lower HDL. Physiologically, elevated insulin levels lead to increased hepatic fat synthesis. This results in an accumulation of TG and cholesterol esters in the blood [46]. Population studies in adults have reported indirect associations between high-GI and high-GL diets and high insulin secretion, resulting in increased TG [8,47,48] and LDL cholesterol [47] and decreased HDL cholesterol [8,48,49]. However, only two cross-sectional studies have examined the association between GI and GL and lipid profiles of children and reported inconsistent results [50,51]. In addition, the association between dietary GL and blood lipids was mediated by BMIz; however, there was evidence of a possible direct effect of dietary GL on TG by pathways that do not include BMIz. The mediating role of adiposity should be further examined in other observational studies with various indicators of adiposity.

Our study is one of the few studies to assess the longitudinal association of GI and GL on CV risk factors in children and the first to examine mediation by BMI. In addition, the QUALITY cohort data were rigorously collected using the most recent measurement tools and provides a large number of covariates.

Our study has potential limitations. First, the QUALITY study had some losses to follow-up. However, because only 10% of children were lost to follow-up, our results should not have been significantly altered. Second, although the 24-hour recall is a strong measurement tool for dietary intake, especially when conducted on three or more nonconsecutive days, it can result in measurement error because it relies on memory and recall. However, the use of disposable containers and rulers to help with portion estimations and the involvement of parents at each interview should reduce recall bias. In addition, the fact that interviews were unannounced should considerably reduce reporting bias. In addition, to account for differential reporting, we adjusted for underreporting. Food consumed from the school cafeteria were not observed by the parents; however, studies have shown that by the age of 8–10 years, children are capable of reporting their food intake during a 24-hour recall as reliably as with the help of their parents [52–54]. As well, although random error can result from intra-individual variation in intake from day to day, because the interviews were repeated on three nonconsecutive days and averaged across those days, random error should be reduced. Third, although we adjusted for a variety of dietary and nondietary confounders, there is still a potential for residual confounding by variables strongly correlated with dietary GI or GL that may also explain or mask an association. Although there are inconsistencies between studies regarding the inclusion of all macronutrients in a model potentially resulting in aliasing with the intercept [55], in our study, we do not believe this was an issue because the correlation between GL and percent carbohydrates was only 37%. Fourth, because we only had two timepoints available, we had to use baseline BMIz as the mediator for our mediation analysis. We had to assume that the three nonconsecutive 24-hour recalls represent short-term usual/habitual dietary intake. In addition, we had to remain cautious in our causal interpretation of the results of the mediation analysis because the causal inference assumptions of consistency, exchangeability, and positivity may not be met [56]. Finally, our results are principally generalizable to Caucasian children at risk of obesity. Further research examining these associations among children of different ethnic backgrounds would be informative.

Conclusion

In our longitudinal cohort of children initially aged 8–10 years, GL, but not GI, predicted 2-year increases in BMI, fat mass, and TG and decreases in HDL cholesterol. Our results highlight the important role of GL, specifically carbohydrate quality and quantity, in CV risk factors in children. Dietary recommendations for children in the prevention of obesity and CVD should focus on lowering GL.

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Supplementary Data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.annepidem.2019.10.005.

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Appendix. Methods A.1

Calculation of ratio of energy intake to estimated energy requirements and cutoff for underreporters using Goldberg equation[2,3]

The values used for the Goldberg equation were derived as follows: we used the Schofield equation (Supplemental methods 2) to calculate individual basal metabolic rates (BMRs) with a coefficient of variation of 8.5; we chose a value of 1.65 for physical activity level with a coefficient of variation of 15[25] and a within-subject variation in energy intake of 23.[24] Individuals with an energy intake (EI):BMR ratio less than a cutoff of 1.11 were considered underreporters, whereas those with values greater than 2.46 were considered overreporters. Only 2 participants were overreporters, which we chose to include in the adequate reporters, given that no difference in results was observed after excluding these 2 participants.

Goldberg's equation

$$EI_{rep}:BMR > PAL \times \exp\left[s.d._{min} \times \frac{S/100}{\sqrt{n}}\right] S = \sqrt{\frac{CV_{wEI}^2}{d} + CV_{wB}^2 + CV_{tP}^2}$$

Values used for calculation of confidence limit: EI:BMR: Ratio of energy intake and calculated BMR; CVwBMR = 8 (the coefficient of variation of repeated BMR measurements for Schofield); CVwEI = 23 (the within-subject coefficient of variation in energy intake, 23 recommended for schoolchildren); CVtP = 15 (the total variation in PAL, WHO reports 15 for this); PAL = 1.65.

Calculated cutoff values:

Underreporter: EI:BMR ≤ 1.11.
Overreporter: EI:BMR > 2.46.

Methods A.2

Calculation of basal metabolic rate (estimated energy requirement) using the Schofield WH equation[1]

Gender	Equation
Male	BMR = 19.6 * Wt + 130.3 * Ht + 414.9
Female	BMR = 16.97 * Wt + 161.8 * Ht + 371.2

Wt = weight; Ht = height.
Calculated using baseline weight and height because dietary data were only available at baseline.

Table B1
Analysis using binary variable for underreporting in longitudinal association between dietary glycemic index at baseline and cardiometabolic risk outcomes after 2 years of follow-up in children from the QUALITY cohort, ages 8–10 at baseline

Outcome	Continuous	Tertiles of glycemic index		
	GI	1	2	3
BMI z-score				
Mean difference (95% CI)	0.08 (−0.11, 0.28)	0	−0.01 (−0.22, 0.19)	0.06 (−0.15, 0.26)
Adjusted mean difference (95% CI)*	−0.04 (−0.23, 0.16)	0	−0.07 (−0.27, 0.13)	−0.06 (−0.27, 0.13)
Fat mass (%)				
Mean difference (95% CI)	0.35 (−0.16, 0.23)	0	−0.82 (−2.79, 1.16)	−0.04 (−2.06, 1.99)
Adjusted mean difference (95% CI)	−0.13 (−0.21, 0.18)	0	−0.82 (−2.79, 1.40)	−0.60 (−2.60, 1.40)
Triglycerides (mmol/L)				
Mean difference (95% CI)	0.04 (−0.04, 0.13)	0	−0.02 (−0.11, 0.06)	0.06 (−0.03, 0.14)
Adjusted mean difference (95% CI)	0.01 (−0.07, 0.09)	0	−0.04 (−0.12, 0.05)	0.02 (−0.06, 0.11)
LDL cholesterol (mmol/L)				
Mean difference (95% CI)	0.02 (−0.10, 0.13)	0	0.002 (−0.12, 0.12)	0.02 (−0.10, 0.14)
Adjusted mean difference (95% CI)	0.001 (−0.12, 0.12)	0	−0.01 (−0.14, 0.11)	0.01 (−0.12, 0.14)
HDL cholesterol (mmol/L)				
Mean difference (95% CI)	−0.03 (−0.08, 0.02)	0	−0.03 (−0.08, 0.03)	−0.03 (−0.08, 0.02)
Adjusted mean difference (95% CI)	−0.01 (−0.06, 0.04)	0	−0.01 (−0.06, 0.04)	−0.004 (−0.05, 0.05)
SBP z-score				
Mean difference (95% CI)	0.08 (−0.08, 0.23)	0	0.07 (−0.09, 0.22)	0.07 (−0.09, 0.23)
Adjusted mean difference (95% CI)*	0.05 (−0.11, 0.21)	0	0.03 (−0.12, 0.19)	0.03 (−0.13, 0.19)
DBP z-score				
Mean difference (95% CI)	0.07 (−0.02, 0.16)	0	0.04 (−0.06, 0.13)	0.08 (−0.02, 0.17)
Adjusted mean difference (95% CI)*	0.04 (−0.06, 0.13)	0	0.02 (−0.07, 0.12)	0.04 (−0.06, 0.14)

All crude models were adjusted for underreporting (ratio of energy intake and estimated energy requirement). All multiple linear regression models were adjusted for pubertal versus nonpubertal status, screen time, physical activity (CPM), family income, parent education (4 categories), ratio of energy intake and estimated energy requirement, fat and protein intake (residuals), and season.

* Age and sex were not included in the BMI z-score, SBP z-score, and DBP z-score models. Interpretation: †Continuous model: every 10-unit increase in GI at baseline is associated with a mean increase in outcome of x. Tertile model: ‡consuming a dietary GI in the highest tertile compared with the lowest reference tertile at baseline is associated with an increased outcome of x after 2 years of follow-up.

Table B2
Analysis using binary variable for underreporting in longitudinal association between dietary glycemic load at baseline and cardiometabolic risk outcomes after 2 years of follow-up in children from the QUALITY cohort, ages 8–10 at baseline

Outcome	Continuous GL	Tertiles of glycemic load		
		1	2	3
BMI z-score				
Mean difference (95% CI)	0.01 (0.001, 0.002)	0	0.14 (−0.06, 0.35)	0.36 (0.15, 0.57)
Adjusted mean difference (95% CI)*	0.009 (0.001, 0.01)	0	0.21 (0.01, 0.42)	0.44 (0.22, 0.66)
Fat mass (%)				
Mean difference (95% CI)	0.06 (0.02, 0.10)	0	1.87 (−0.20, 3.95)	3.11 (0.99, 5.23)
Adjusted mean difference (95% CI)	0.09 (0.05, 0.13)	0	2.52 (0.52, 4.52)	4.36 (2.24, 6.47)
Triglycerides (mmol/L)				
Mean difference (95% CI)	0.001 (−0.001, 0.002)	0	−0.05 (−0.14, 0.04)	0.03 (−0.06, −0.12)
Adjusted mean difference (95% CI)	0.002 (0.0001, 0.004)	0	−0.01 (−0.11, 0.07)	0.08 (−0.01, 0.16)
LDL cholesterol (mmol/L)				
Mean difference (95% CI)	0.0001 (−0.002, 0.002)	0	0.05 (−0.08, 0.17)	0.01 (−0.12, 0.13)
Adjusted mean difference (95% CI)	0.001 (−0.001, 0.004)	0	0.09 (−0.04, 0.22)	0.06 (−0.07, 0.20)
HDL cholesterol (mmol/L)				
Mean difference (95% CI)	−0.0003 (−0.001, 0.001)	0	0.01 (−0.04, 0.06)	−0.03 (−0.08, 0.03)
Adjusted mean difference (95% CI)	−0.0001 (−0.002, 0.0004)	0	0.002 (−0.05, 0.05)	−0.04 (−0.10, 0.01)
SBP z-score				
Mean difference (95% CI)	−0.001 (−0.004, 0.003)	0	−0.03 (−0.20, 0.13)	−0.08 (−0.24, 0.09)
Adjusted mean difference (95% CI)*	−0.004 (−0.004, 0.003)	0	−0.02 (−0.19, 0.14)	−0.08 (−0.25, 0.09)
DBP z-score				
Mean difference (95% CI)	0.0002 (−0.002, 0.002)	0	0.03 (−0.07, 0.13)	0.03 (−0.07, 0.13)
Adjusted mean difference (95% CI)*	−0.0004 (−0.002, 0.002)	0	0.03 (−0.07, 0.13)	0.002 (−0.10, 0.11)

All crude models were adjusted for underreporting (ratio of energy intake and estimated energy requirement). All multiple linear regression models were adjusted for age, sex, pubertal versus nonpubertal status, screen time, physical activity (CPM), family income, parent education (4 categories), ratio of energy intake and estimated energy requirement, energy (residual method), fat and protein intake (residuals), and season.

* Age and sex were only included in the percent fat mass, TG, LDL, and HDL models. Interpretation: †Continuous model: every 10-unit increase in GL at baseline is associated with a mean increase in outcome of x. Tertile model: ‡consuming a dietary GL in the highest tertile compared with the lowest reference tertile at baseline is associated with an increased outcome of x after 2 years of follow-up.

Table B3
Longitudinal association between dietary glycemic load at baseline and cardiometabolic risk outcomes after 2 years of follow-up in children from the QUALITY cohort, ages 8–10 years at baseline, comparing different adjusted models

Outcome	Continuous GL[‖]	Tertiles of glycemic load[¶]		
		1	2	3
BMI z-score				
Crude model (95% CI)[*]	0.01 (0.001, 0.002)	0	0.10 (−0.11, 0.30)	0.54 (0.32, 0.75)
Model adjusted for nondietary factors (95% CI)[†]	0.01 (0.008, 0.02)	0	0.08 (−0.12, 0.28)	0.48 (0.26, 0.69)
Model adjusted for nondietary factors and fat (95% CI)[‡]	0.03 (0.01, 0.04)	0	0.15 (−0.05, 0.36)	0.66 (0.40, 0.91)
Fully adjusted model (95% CI)[§]	0.03 (0.02, 0.05)	0	0.37 (0.19, 0.55)	1.10 (0.88, 1.31)
Fat mass (%)				
Crude model (95% CI)[*]	0.11 (0.07, 0.18)	0	1.34 (−0.69, 3.36)	4.78 (2.60, 6.70)
Model adjusted for nondietary factors (95% CI)[†]	0.12 (0.08, 0.15)	0	1.53 (−0.42, 4.37)	5.14 (3.05, 7.22)
Model adjusted for nondietary factors and fat (95% CI)[‡]	0.18 (0.13, 0.23)	0	2.00 (−0.002, 4.00)	6.53 (4.10, 8.96)
Fully adjusted model (95% CI)[§]	0.29 (0.25, 0.33)	0	4.12 (2.32, 5.93)	10.8 (8.62, 13.0)
Triglycerides (mmol/L)				
Crude model (95% CI)[*]	0.001 (−0.001, 0.003)	0	0.08 (−0.16, 0.01)	0.03 (−0.06, 0.13)
Model adjusted for nondietary factors (95% CI)[†]	0.001 (−0.001, 0.003)	0	−0.07 (−0.17, 0.02)	0.02 (−0.08, 0.13)
Model adjusted for nondietary factors and fat (95% CI)[‡]	0.003 (0.001, 0.005)	0	−0.05 (−0.14, 0.04)	0.08 (−0.03, 0.19)
Fully adjusted model (95% CI)[§]	0.005 (0.003, 0.007)	0	−0.01 (−0.10, 0.08)	0.17 (0.07, 0.28)
LDL cholesterol (mmol/L)				
Crude model (95% CI)[*]	−0.0004 (−0.003, 0.002)	0	0.02 (−0.10, 0.15)	−0.03 (−0.17, 0.10)
Model adjusted for nondietary factors (95% CI)[†]	−0.001 (−0.002, 0.001)	0	0.03 (−0.10, 0.15)	−0.03 (−0.16, 0.11)
Model adjusted for nondietary factors and fat (95% CI)[‡]	0.001 (−0.002, 0.004)	0	0.05 (−0.08, 0.17)	0.01 (−0.14, 0.17)
Fully adjusted model (95% CI)[§]	0.002 (−0.001, 0.0001)	0	0.07 (−0.06, 0.20)	0.07 (−0.08, 0.23)
HDL cholesterol (mmol/L)				
Crude model (95% CI)[*]	−0.001 (−0.002, 0.001)	0	0.02 (−0.03, 0.07)	−0.05 (0.11, 0.004)
Model adjusted for nondietary factors (95% CI)[†]	−0.001 (−0.002, 0.001)	0	0.03 (−0.02, 0.08)	−0.03 (−0.09, 0.02)
Model adjusted for nondietary factors and fat (95% CI)[‡]	−0.002 (−0.003, −0.0003)	0	0.01 (−0.04, 0.06)	−0.07 (−0.13, −0.01)
Fully adjusted model (95% CI)[§]	−0.003 (−0.004, −0.002)	0	−0.02 (−0.07, 0.03)	−0.13 (−0.19, −0.07)
SBP z-score				
Crude model (95% CI)[*]	0.001 (−0.002, 0.004)	0	−0.04 (−0.19, 0.12)	−0.01 (−0.18, 0.16)
Model adjusted for nondietary factors (95% CI)[†]	0.001 (−0.002, 0.005)	0	−0.02 (−0.17, 0.14)	−0.009 (−0.18, 0.16)
Model adjusted for nondietary factors and fat (95% CI)[‡]	0.003 (−0.001, 0.007)	0	−0.009 (−0.17, 0.15)	0.02 (−0.17, 0.22)
Fully adjusted model (95% CI)[§]	0.004 (0.000, 0.008)	0	0.02 (−0.14, 0.18)	0.07 (−0.12, 0.26)
DBP z-score				
Crude model (95% CI)[*]	0.0003 (−0.002, 0.002)	0	0.03 (−0.06, 0.13)	0.03 (−0.07, 0.14)
Model adjusted for nondietary factors (95% CI)[†]	0.0003 (−0.002, 0.002)	0	0.03 (−0.06, 0.13)	0.03 (−0.08, 0.13)
Model adjusted for nondietary factors and fat (95% CI)[‡]	−0.001 (−0.004, 0.001)	0	0.01 (−0.09, 0.11)	−0.02 (−0.14, 0.10)
Fully adjusted model (95% CI)[§]	−0.0001 (−0.002, 0.003)	0	0.04 (−0.06, 0.14)	0.03 (−0.09, 0.14)

[*] All crude models were adjusted for underreporting (ratio of energy intake and estimated energy requirement).
[†] Models adjusted for nondietary factors including age, sex, pubertal versus nonpubertal status, screen time, physical activity (CPM), family income, parent education (4 categories), ratio of energy intake and estimated energy requirement, season, energy (residual method).
[‡] Model additionally adjusted fat intake (residuals).
[§] Fully adjusted model adjusted for same factors as previous models as well as protein intake (residuals). Age and sex were only included in the percent fat mass, TG, LDL, and HDL models.
[‖] Interpretation: Continuous model: every 10-unit increase in GL at baseline is associated with a mean increase in outcome of x.
[¶] Tertile model: consuming a dietary GL in the highest tertile compared with the lowest reference tertile at baseline is associated with an increased outcome of x after 2 years of follow-up.

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