www.jpeds.com • THE JOURNAL OF PEDIATRICS

Lifestyle Habits, Dietary Factors, and the Metabolically Unhealthy Obese Phenotype in Youth

Jean-Baptiste Roberge, MD[1,2], Andraea Van Hulst, PhD[3], Tracie A. Barnett, PhD[1,4], Vicky Drapeau, PhD[5], Andrea Benedetti, PhD[3,6,7], Angelo Tremblay, PhD[8], and Mélanie Henderson, MD, PhD[1,9]

Objective To determine whether lifestyle habits and dietary factors at age 8-10 years predict the development of metabolically unhealthy obesity 2 years later among children who were previously metabolically healthy obese.
Study design The QUebec Adipose and Lifestyle InvesTigation in Youth cohort comprises 630 youth with a parental history of obesity. Metabolically healthy obesity and metabolically unhealthy obesity were defined using cutoffs for the components of pediatric metabolic syndrome. Dietary factors, physical activity, fitness, sedentary behavior, screen time, and sleep duration were measured. Multivariable logistic regressions were used to examine associations.
Results At baseline, 48 participants with metabolically healthy obesity were identified; 2 years later, 19 became metabolically unhealthy obese and 29 remained metabolically healthy obese. Every additional daily portion of fruits and vegetables decreased the risk of converting to metabolically unhealthy obesity by 39% (OR 0.61, 95% CI 0.40-0.94). Cumulating more hours of screen time and diets high in saturated fat and sugar-sweetened beverages and low in protein were associated with a tendency to develop metabolically unhealthy obesity.
Conclusions Fruit and vegetable intake and possibly screen time, saturated fat, sugar-sweetened beverages, and protein intake may be important targets for the prevention of cardiometabolic complications in obese children. *(J Pediatr 2019;204:46-52).*
Trial registration ClinicalTrials.gov: NCT03356262.

Obesity in youth is linked to multiple comorbidities affecting all organ systems and is linked to increased mortality in adults.[1-3] However, not all individuals who are obese have the same risk phenotype. Whereas some have an unfavorable cardiometabolic phenotype (known as "metabolically unhealthy obese"), others have a more favorable cardiometabolic phenotype (known as "metabolically healthy obese"). Children with metabolically unhealthy obesity usually are defined as obese children with at least 1 cardiometabolic risk factor; children with metabolically healthy obesity have no cardiometabolic risk factors.[4] The prevalence of the metabolically healthy obese phenotype in youth is uncertain, given the absence of a standard definition,[5] with estimates ranging from 6 to 74%.[6-18]

Current recommendations for the management and treatment of obesity in youth do not consider the metabolically healthy obese and metabolically unhealthy obese phenotypes.[19] Because most strategies to address obesity in youth have shown limited effectiveness at best,[20] including both home-[21] and community-based[22] youth obesity prevention programs, some authors have proposed that achieving or maintaining the metabolically healthy obese phenotype may be a goal that is easier to achieve compared with weight loss per se for some obese youth.[8,23] Little is known with regard to modifiable determinants of the metabolically healthy obese and metabolically unhealthy obese phenotypes, and findings are often conflicting. Although some cross-sectional studies have shown that physical activity, screen time,[6,8,13] and dietary intake[8] were not related to the metabolically healthy obese phenotype, others have shown that metabolically healthy obesity youth consumed healthier diets,[7] had longer sleep duration,[9] and participated in more moderate-to-vigorous physical activity (MVPA) compared with children with the metabolically unhealthy obese phenotype.[12] However, these studies were cross-sectional and differed substantially in terms of definitions used for the metabolically healthy obese phenotype[9,12,13] and in terms of population characteristics.[6-9,12,13] Studies examining prospective associations between modifiable lifestyle habits in childhood and conversion from metabolically healthy obesity to metabolically unhealthy obesity in early adolescence are needed, particularly as it is known that puberty has a strong impact on cardiometabolic health in obese children.[24]

BMI	Body mass index
HDL	High-density lipoprotein
MVPA	Moderate-to-vigorous physical activity
QUALITY	QUebec Adipose and Lifestyle InvesTigation in Youth

From the [1]Centre de Recherche du Centre Hospitalier Universitaire Sainte-Justine, University of Montreal; [2]Department of Pediatrics, Faculty of Medicine, Université de Montréal; [3]Ingram School of Nursing, McGill University, Montreal; [4]Epidemiology and Biostatistics Unit, Institut national de la recherche scientifique (INRS)—Institut Armand-Frappier, Laval; [5]Department of Physical Education, Université Laval, Québec; [6]Department of Medicine, McGill University; [7]Respiratory Epidemiology and Clinical Research Unit, McGill University Health Centre, Montréal; [8]Department of Kinesiology, Université Laval, Québec; and [9]Division of Endocrinology, Department of Pediatrics, Centre Hospitalier Universitaire Sainte-Justine and Université de Montréal, Montréal, Québec, Canada

Funding and Disclosures available at www.jpeds.com.

https://doi.org10.1016/j.jpeds.2018.08.063

We hypothesize that fitness, lifestyle habits (MVPA, sedentary behavior, and sleep) and dietary factors are determinants of transition from metabolically healthy obesity to metabolically unhealthy obesity in youth and examine whether these factors in childhood predict the development of the metabolically unhealthy obese phenotype in early adolescence among previously metabolically healthy but obese children.

Methods

Data were from the baseline evaluation (2005-2008) and first follow-up assessment (2007-2011) of the QUALITY (QUebec Adipose and Lifestyle InvesTigation in Youth) study, an ongoing longitudinal investigation of the natural history of obesity and cardiovascular risk in youth (ClinicalTrials.gov: NCT03356262). Participants were recruited in schools located within 75 km of 3 metropolitan areas in Québec, Canada. White children, aged 8-10 years, with at least 1 obese biological parent were eligible. A total of 630 children completed the baseline evaluation, and 564 completed a follow-up visit 2 years later. A detailed description of the study design and methods is available elsewhere.[25] All participants and their parents provided written informed assent and consent, respectively. The study was approved by the ethics boards of the Centre Hospitalier Universitaire Sainte-Justine and the Québec Heart and Lung Institute.

Children underwent a physical examination by a trained nurse. Weight, height, and waist circumference were measured according to standardized protocols.[26] Body mass index (BMI) percentiles were computed using age- and sex-specific BMI reference values from the World Health Organization.[27] Waist circumference was converted to age- and sex-specific percentiles using British reference values.[28] Body composition, expressed as total body percent fat mass, was assessed using dual-energy radiograph absorptiometry (DF+14664; GE Lunar Corporation, Madison, Wisconsin). Pubertal development was determined according to nurse-assessed Tanner stages.[29,30]

Systolic and diastolic blood pressure were measured using an appropriately sized cuff and an automated oscillometric blood pressure monitor, doing 5 repeat measures at 1-minute intervals (Dinamap model CR9340; Critikon Co, Tampa, Florida). Participants were seated and at rest for 5 minutes before the measurements. The average of the last 3 measures was computed and transformed to age-, sex-, and height-specific z scores.[31]

Participants underwent a 2-hour oral glucose tolerance test after a 12-hour overnight fast. An oral glucose dose of 1.75 g/kg of body weight (up to a maximum of 75 g) was ingested, after which blood samples were collected at 0, 30, 60, 90, and 120 minutes. Plasma insulin was measured using an ultrasensitive Access immunoassay system (Beckman Coulter Inc, Brea, California). The glucose oxidase method was used to compute the plasma glucose concentrations on the Beckman Coulter Synchron LX20 automat. Insulin sensitivity was measured with the Matsuda insulin sensitivity index.[32] Insulin secretion was measured by the ratio of the area under the curve of insulin to glucose over the first 30 minutes and 120 minutes.[33] Lipids (triglycerides and high-density lipoprotein [HDL] cholesterol) were determined enzymatically on a Synchron LX20 (Beckman Coulter) with Beckman Instruments reagents.

We defined metabolically unhealthy obesity as children with a BMI ≥97th percentile and at least 1 of the following risk factors based on the cut-offs from Cook et al for components of pediatric metabolic syndrome: triglycerides ≥1.24 mmol/L, fasting glucose ≥6.1 mmol/L, HDL cholesterol ≤1.03 mmol/L, and blood pressure > 90th percentile.[34] The metabolically healthy obese phenotype was defined as a BMI ≥97th percentile and the absence of any components of the metabolic syndrome. Our primary outcome was the development of metabolically unhealthy obesity at age 10-12 years in previously metabolically healthy but obese children at age 8-10 years.

Dietary intake data were obtained using the average of three 24-hour diet recalls administered by a nutritionist over the telephone within 4-6 weeks of the baseline visit, including 2 week days and 1 weekend day, using the US Department of Agriculture's Automated Multiple Pass Method.[35] Participants received a small, disposable kit of food portion models and a short training session at the clinic visit to prepare them for subsequent recalls. Foods reported on the recalls were entered into the CANDAT research system (Godin and Associates, London, Ontario, Canada) and converted to macronutrients using the 2007 Canadian Nutrient File. Carbohydrate, total fat, saturated fat, and protein intake were calculated as a percentage of total daily kilocalorie intake and fiber intake as grams per day. Daily servings of fruits and vegetables were based on the portion sizes from the 2007 Canada's Food Guide.[36] Sugar-sweetened beverage intake, which excluded 100% fruit juices, was measured as the average number of 100-mL portions per day.

Physical activity was assessed using 7-day accelerometry (Actigraph LS 7164 activity monitor; Actigraph, Pensacola, Florida) in the week following the baseline clinic visit. An epoch length of 1 minute was applied. Standardized quality control and data reduction procedures were also undertaken.[37] Valid days required a minimum of 10 hours of wear time,[38] and only participants with a minimum of 4 valid days were retained for analyses.[39] Total minutes spent daily in MVPA was derived using validated cut-points for pediatric populations and an average daily MVPA over the total number of valid days of wear was computed.[40] Nonwear time was defined as any period of 0 counts that lasted at least 60 minutes, accepting 1-2 consecutive minutes where count values were between 1 and 100, inclusively.[38] Children were instructed to remove the accelerometer when going to bed and to put it back on after awakening. Sleep duration was thus defined as the mean nightly nonwear time over the past 7 days. Sedentary behavior was defined using (1) sedentary time by accelerometry data based on the average minutes per day at an activity count of <100 counts/minute[38] and (2) self-reported daily hours of screen time, including TV viewing, computer use, and video games.

Fitness, by means of peak oxygen consumption, was measured during an adapted standard incremental exercise test[41] on an electromagnetic bicycle to volitional exhaustion with indirect calorimetry measurements throughout the test. The measure was considered as a true maximum value if a respiratory exchange ratio greater than 1.0 was attained and/or a heart rate of ≥185 beats/min was reached.[42] Peak oxygen consumption was expressed as a function of lean body mass.

Statistical Analyses

Means and proportions of baseline attributes were compared between youth with metabolically healthy obesity and metabolically unhealthy obesity at follow-up using independent samples *t* tests for continuous variables and χ^2 tests for categorical variables. Multivariable logistic regression analysis was then used to estimate the risk of developing the metabolically unhealthy obese phenotype at age 10-12 years for each lifestyle/dietary factor measured at age 8-10 years. Given the small sample size, model stability was assessed by examining changes in beta coefficients and SEs following the addition of covariates one at the time. All models were minimally adjusted for sex, age at follow-up, and MVPA at baseline. Because preliminary analyses revealed no significant changes when Tanner stage or season of physical activity assessment were adjusted for, they were excluded from subsequent analyses for statistical parsimony. Models examining the associations of fiber, sugar-sweetened beverages, and fruit and vegetable intake additionally were adjusted for total kilocalorie intake. We accounted for missing data using multiple imputation via chained equations (PROC MI) in 20 imputed data sets.[43] All statistical analyses were performed using SAS, version 9.4 (SAS Institutes Inc, Cary, North Carolina).

Results

Of the 630 QUALITY participants at baseline, 181 were obese. Most of these children who were obese were metabolically unhealthy obese at baseline and remained metabolically unhealthy obese at follow-up (Figure). A total of 69 participants were identified as metabolically healthy obese at baseline; of these, 21 were excluded from the current analysis because they were no longer obese at follow-up (n = 15), were lost to follow-up (n = 5), or had missing outcome data at follow-up (n = 1). The final sample thus included 48 participants (36 boys and 12 girls) who were obese at baseline and follow-up but otherwise metabolically healthy at baseline. At follow-up, 19 (39.6%) of these were newly categorized as being metabolically unhealthy obese (Figure). As shown in Table I, participants with metabolically unhealthy obesity were older, engaged in more screen time, and had a lower Matsuda insulin sensitivity index at baseline compared with participants who remained metabolically healthy obese. No differences in pubertal development or percent fat mass were found.

Of the 19 participants who developed the metabolically unhealthy obese phenotype at age 10-12 years, 13 (68%) had developed 1 metabolic risk factor and 6 (32%) had developed 2 metabolic risk factors. The most common risk factor was low HDL cholesterol (Table II).

Using multivariable logistic regression models, we examined associations between the metabolically unhealthy obese phenotype and baseline fitness, lifestyle habits, and dietary factors (Table III). In case-complete analyses, we found that every additional serving of fruits and vegetables per day decreased the odds of converting to the metabolically unhealthy obese phenotype by 39% (OR 0.61, 95% CI 0.40-0.94). Other predictors were associated with a borderline increased odds of becoming metabolically unhealthy obese, namely screen time (OR 1.40, 95% CI 0.95-2.07), saturated fat intake (OR 1.41, 95% CI 0.98-2.04), and sugar-sweetened beverages intake (OR 1.80, 95% CI 0.93-3.47), or a borderline

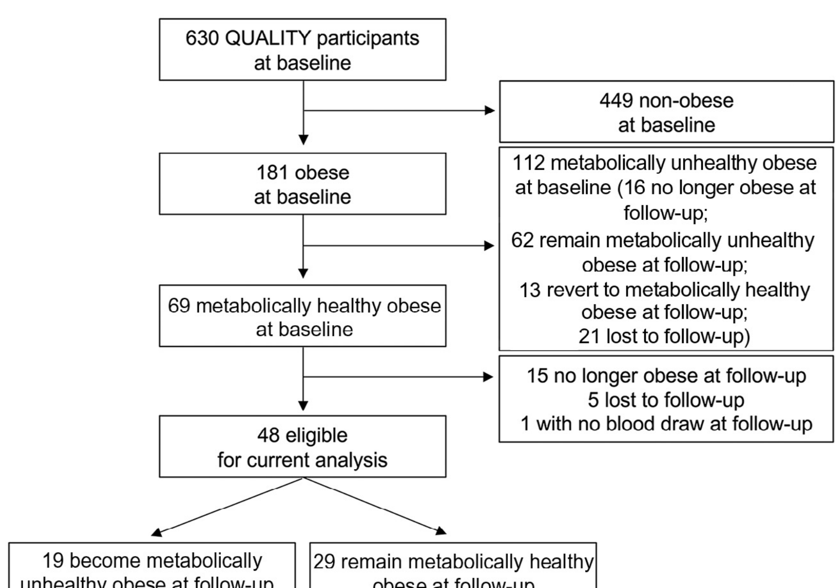

Figure. Flowchart of study participants.

Table I. Comparison of lifestyle habits, dietary factors, and insulin dynamics at age 8-10 years in relation to metabolically healthy obese and metabolically unhealthy obese phenotypes at age 10-12 years in participants with no risk factors at baseline (QUALITY cohort)

Characteristics	Metabolically healthy obesity (n = 29)	Metabolically unhealthy obesity (n = 19)	*P* value
Age, y, mean (SD)	**9.2 (1.0)**	**9.9 (0.8)**	**.01**
Sex, % male	*65.5*	*89.5*	*.06*
Pubertal, %	13.8	21.1	.51
Percent fat mass, mean (SD)	37.2 (6.7)	37.3 (5.8)	.98
MVPA, min/d, mean (SD)	48.8 (22.9)	42.4 (22.8)	.39
Accelerometer measured sedentary behavior, min/d, mean (SD)	369.5 (68.9)	393.9 (110.1)	.43
Screen time, h/d, mean (SD)	**2.3 (2.0)**	**4.1 (2.0)**	**.005**
Sleep duration, h/d, mean (SD)	10.4 (0.8)	10.4 (1.0)	.95
Peak oxygen consumption, mL/min/kg of LBM	59.8 (6.9)	57.9 (4.0)	.29
Total kilocalorie intake, kcal/d, mean (SD)	1684.6 (452.9)	1844.0 (339.7)	.20
Carbohydrate, %, mean (SD)	52.1 (6.7)	52.3 (5.3)	.90
Fat intake, %, mean (SD)	32.8 (5.6)	32.7 (4.8)	.99
Saturated fat intake, %, mean (SD)	*10.7 (2.5)*	*12.2 (2.9)*	*.07*
Protein intake, %, mean (SD)	16.7 (3.8)	16.1 (3.1)	.58
Fiber intake, g/d, mean (SD)	13.6 (3.8)	13.9 (3.4)	.81
Sugar-sweetened beverages, mL/d, mean (SD)	*107.2 (114.9)*	*198.9 (208.5)*	*.09*
Fruit and vegetable portions, mean (SD)	5.0 (2.3)	3.9 (2.1)	.10
Matsuda ISI, mean (SD)	**7.9 (2.6)**	**6.2 (2.7)**	**.03**
AUC I/G$_{30\ min}$, mean (SD)	34.6 (15.9)	40.6 (14.4)	.20
AUC I/G$_{120\ min}$, mean (SD)	*33.8 (13.2)*	*41.2 (11.5)*	*.06*

AUC I/G$_{30\ min}$, area under the curve of insulin to glucose over the first 30 minutes; *AUC I/G$_{120\ min}$*, area under the curve of insulin to glucose over the first and 120 minutes; *ISI*, insulin sensitivity index; *LBM*, lean body mass.
The *P* value indicates the statistical significance of a *t* test comparing mean values between metabolically healthy obesity and metabolically unhealthy obesity for continuous variables. The χ^2 test was used for categorical variables.
Values in bold indicate statistical significance with *P* less than .05 and italic indicate *P* less than .10.

decreased odds of becoming metabolically unhealthy obese with greater protein intake (OR 0.73, 95% CI 0.51-1.02). Estimates were largely similar when imputed data sets were used, albeit with an attenuation toward the null, particularly for associations with dietary factors. For screen time, the association was strengthened when imputed data were used: every additional hour of screen time increased the odds of converting to the metabolically unhealthy obese phenotype by 50% (OR 1.50; 95% CI 1.02-2.20).

Table II. Prevalence of adverse risk factors defining participants as metabolically unhealthy obese at 10-12 years (n = 19)

Risk factors	% (n)
HDL cholesterol ≤1.03 mmol/L	26 (5)
Triglycerides ≥1.24 mmol/L	5 (1)
SBP >90th percentile for age, sex, and height	89 (17)
Fasting glucose ≥6.1 mmol/L	11 (2)
DBP >90th percentile for age, sex, and height	0 (0)

DBP, diastolic blood pressure; *SBP*, systolic blood pressure.

Discussion

Using a prospective longitudinal design, our study showed that metabolically healthy obese children who ate fewer daily portions of fruits and vegetables were more likely to become metabolically unhealthy obese two years later. The QUALITY study includes a small number of children who were metabolically healthy obese at baseline, of which the majority (60%) remained metabolically healthy obese two years later. Indeed, most of the obese children in the QUALITY study were metabolically unhealthy obese at baseline (112 out of 181), as reported by others.[5] Given the small sample size of this study, findings should be replicated using a larger sample of participants followed over time.

Comparing our findings with those of previous studies is challenging, given that they have relied on cross-sectional designs and differ substantially in terms of definitions for the metabolically unhealthy obese and metabolically healthy obese phenotypes and in methods used to measure lifestyle habits.[5,8,15] Our findings regarding diet as a modifiable predictor of the cardiometabolic phenotype shed new light on the current body of evidence.[7,44] We observed that children who are metabolically healthy obese and who ate fewer portions of fruits and vegetables were more likely to develop the metabolically unhealthy obese phenotype 2 years later. This finding differs from previous cross-sectional studies in youth[7,9,12] and in adults[45,46] but is in keeping with other cross-sectional studies in adults. Specifically, among women who are obese and aged 19-44 years, those with the metabolically healthy obese phenotype were found to eat more whole fruits compared with those with the metabolically unhealthy obese phenotype.[7] Two additional studies found an association between the metabolically healthy obese phenotype in adults with specific eating patterns characterized by a high fruit consumption.[47,48]

In line with our findings, Prince et al reported intake of saturated fat to be associated with the metabolically unhealthy obese profile in youth.[12] Others have reported opposite findings: total fat intake, saturated fat intake, mono- and polyunsaturated fat intake, as well as dairy products have been shown to be cross-sectionally associated with the metabolically healthy obese profile.[7,8] However, these associations may be due to reverse causation by which youth with the metabolically unhealthy obese profile may be currently eating better to address their unfavorable cardiometabolic phenotype.[8] With its prospective design, our study clarifies the directionality of the associations between dietary intake and the metabolically unhealthy obese and metabolically healthy obese phenotypes.

We also found that lower protein intake at age 8-10 years was associated with a tendency to develop metabolically unhealthy obese phenotype at age 10-12 years. Prince et al showed statistically but not clinically significant associations between protein intake among youth who were overweight and

Table III. Lifestyle habits and dietary factors at 8-10 years of age and prediction of metabolically unhealthy obesity at age 10-12 years in participants with no risk factors at baseline (QUALITY cohort)

	Complete case data		Imputed data	
Predictors at 8-10 y	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Sleep duration, h/d	1.93 (0.72-5.17)	.19	1.92 (0.72-5.11)	.19
MVPA, min/d	0.82 (0.60-1.13)	.22	0.84 (0.62-1.14)	.27
Accelerometer measured sedentary behavior, 10 min/d	0.99 (0.91-1.10)	.89	1.00 (0.91-1.10)	.98
Peak oxygen consumption, mL/min/kg of LBM	0.84 (0.68-1.03)	.10	0.95 (0.82-1.10)	.46
Screen time, h/d	*1.40 (0.95-2.07)*	*.09*	**1.50 (1.02-2.20)**	**.04**
Carbohydrates intake, %	1.11 (0.93-1.23)	.35	1.09 (0.96-1.24)	.18
Fat intake, %	1.02 (0.87-1.19)	.85	0.95 (0.84-1.09)	.49
Saturated fat intake, %	*1.41 (0.98-2.04)*	*.06*	1.14 (0.87-1.51)	.34
Protein intake, %	*0.73 (0.51-1.02)*	*.06*	0.81 (0.62-1.05)	.11
Fiber intake, 10 g/d*	0.33 (0.02-5.04)	.42	0.96 (0.10-9.28)	.97
Sugar sweetened beverages intake, 100 mL/d	*1.80 (0.93-3.47)*	*.08*	1.46 (0.83-2.55)	.19
Fruits and vegetables, portions/d*	**0.61 (0.40-0.94)**	**.04**	0.76 (0.54-1.06)	.11

Each predictor examined in a separate model while adjusting for age, sex, and MVPA.
*Denotes models additionally adjusted for total kilocalorie intake.
Values in bold indicate statistical significance with *P* less than .05 and italic indicate *P* less than .10.

obese and the metabolically healthy obese status according to 2 different definitions.[12] Different sources of dietary protein may be differently associated with the cardiometabolic phenotype. The consumption of meat was shown to be a strong independent predictor of the metabolically healthy obese phenotype in Chinese children and adolescents who were obese in a study by Li et al.[9] In the adult literature, Matta et al found that a diet with a high intake of chicken, fish, and meat and a low intake of high-fat dairy products was not associated with the metabolically healthy obese phenotype.[48] In contrast, Hankinson et al found a greater intake of protein from vegetable sources in women with metabolically healthy obesity compared with metabolically unhealthy obesity, an association that became nonsignificant after adjusting for multiple comparisons.[45]

Results from studies looking at specific dietary components are conflicting likely because of difficulties related to accurately measuring diet[7-9] and due to the limitations inherent to interventional studies with short periods of exposure to specific diets. Nonetheless, there is some evidence suggesting that participants with metabolically healthy obesity have a better compliance with the dietary pyramid recommendations in both the pediatric[7] and adult[46] populations. The observation that fruit and vegetable intake was no longer associated with the development of the metabolically unhealthy obese phenotype when using imputed data in the present study might relate to the fact that dietary intake is difficult to measure.[49] Multiple imputation on data that are measured with some degree of nondifferential misclassification error could lead to further imprecision in measurements and bias associations towards the null.

Our findings suggest that screen time in children who are obese may be predictive of the metabolically unhealthy obese phenotype in early adolescence. This association is in line with Ekelund et al, who showed that TV viewing is associated with cardiovascular risk factors in adolescents.[50] Our group has previously found that a greater screen time is associated with deleterious insulin sensitivity over time in children as they enter puberty.[51] In contrast, Camhi et al did not find an association between screen time and the metabolically healthy obese or metabolically unhealthy obese phenotype in adolescents.[6] In our study, time spent in sedentary behavior measured by accelerometry was not associated with the cardiometabolic phenotype 2 years later. This suggests that screen time, as a specific type of sedentary behavior, may have deleterious cardiometabolic effects that differ from those of other types of sedentary behaviors. In keeping with this, our group and others have previously reported on the distinction between screen time, other forms of sedentary behavior, and physical activity in pediatric[39,50-52] and adult[53-55] populations.

We observed no association between physical activity and the metabolically unhealthy obese or metabolically healthy obese phenotype. Other than the study of Prince et al,[12] cross-sectional studies have reported findings similar to ours.[6,8] Overall, results from both cross-sectional[46,56] and longitudinal[57,58] studies looking at associations between physical activity and the metabolic syndrome in obese adults are conflicting.

The major strength of this study is its prospective longitudinal design. Another strength is the fact that the QUALITY cohort used a population-based sampling strategy for recruitment as opposed to sampling in clinics.[25] The participants are hence more representative of obese children from the general population. Several limitations should be noted. First, the sample was small (n = 48); consequently, we likely had power only to detect strong associations. Given this, we discuss some of the potential exposures associated with a tendency to develop the metabolically unhealthy obese phenotype over time, even if the associations did not reach our prespecified *P* value for statistical significance (.05). Second, the generalizability of our study is restricted to white children with obesity. Similarly, children from the QUALITY cohort have been shown to be of higher socioeconomic status compared with a representative sample of Québec children of similar age.[25] This might have underestimated the predictive effects of the factors we studied. Third, to minimize confounding bias, models were adjusted for multiple confounders. This may have resulted in an overspecification of models, thus making findings less generalizable to other populations. Fourth, measurement error of dietary intake is a limitation. Having both the child and the parents interviewed during these recalls may have limited under-reporting.[59] Future longitudinal and interventional studies with larger, more diverse sample sizes are needed to replicate our findings and to explore the effect of modifying these lifestyle habits on the prevention of metabolic complications. ■

We acknowledge the contributions of Dr Marie Lambert, who initiated the QUALITY cohort. The cohort integrates members of TEAM PRODIGY, an interuniversity research team including Université de Montréal, Concordia University, Centre INRS - Institut Armand-Frappier, Université Laval, and McGill University. The research team is grateful to all the children and their families who took part in this study, as well as the technicians, research assistants, and coordinators involved in the QUALITY cohort project.

Submitted for publication Apr 18, 2018; last revision received Jul 30, 2018; accepted Aug 22, 2018

Reprint requests: Mélanie Henderson, MD, PhD, Centre de recherche du Centre Hospitalier Universitaire Sainte-Justine, 3175, Ch. de la Côte-Sainte-Catherine, Montréal, QC H3T 1C5, Canada. E-mail: melanie.henderson.hsj@gmail.com

References

1. Ebbeling CB, Pawlak DB, Ludwig DS. Childhood obesity: public-health crisis, common sense cure. Lancet 2002;360:473-82.
2. Li S, Chen W, Srinivasan SR, Bond MG, Tang R, Urbina EM, et al. Childhood cardiovascular risk factors and carotid vascular changes in adulthood: the Bogalusa Heart Study. JAMA 2003;290:2271-6.
3. Must A, Strauss RS. Risks and consequences of childhood and adolescent obesity. Int J Obes Relat Metab Disord 1999;23(suppl 2):S2-11.
4. Primeau V, Coderre L, Karelis AD, Brochu M, Lavoie ME, Messier V, et al. Characterizing the profile of obese patients who are metabolically healthy. Int J Obes (Lond) 2011;35:971-81.
5. Bluher S, Schwarz P. Metabolically healthy obesity from childhood to adulthood—does weight status alone matter? Metabolism 2014;63:1084-92.
6. Camhi SM, Waring ME, Sisson SB, Hayman LL, Must A. Physical activity and screen time in metabolically healthy obese phenotypes in adolescents and adults. J Obes 2013;2013:984613.
7. Camhi SM, Whitney Evans E, Hayman LL, Lichtenstein AH, Must A. Healthy eating index and metabolically healthy obesity in U.S. adolescents and adults. Prev Med 2015;77:23-7.
8. Heinzle S, Ball GD, Kuk JL. Variations in the prevalence and predictors of prevalent metabolically healthy obesity in adolescents. Pediatr Obes 2015;11:425-33.
9. Li L, Yin J, Cheng H, Wang Y, Gao S, Li M, et al. Identification of genetic and environmental factors predicting metabolically healthy obesity in children: data from the BCAMS study. J Clin Endocrinol Metab 2016;101:1816-25.
10. Li S, Chen W, Srinivasan SR, Xu J, Berenson GS. Relation of childhood obesity/cardiometabolic phenotypes to adult cardiometabolic profile: the Bogalusa Heart Study. Am J Epidemiol 2012;176(suppl 7):S142-9.
11. Mangge H, Zelzer S, Puerstner P, Schnedl WJ, Reeves G, Postolache TT, et al. Uric acid best predicts metabolically unhealthy obesity with increased cardiovascular risk in youth and adults. Obesity (Silver Spring) 2013;21:E71-7.
12. Prince RL, Kuk JL, Ambler KA, Dhaliwal J, Ball GD. Predictors of metabolically healthy obesity in children. Diabetes Care 2014;37:1462-8.
13. Senechal M, Wicklow B, Wittmeier K, Hay J, MacIntosh AC, Eskicioglu P, et al. Cardiorespiratory fitness and adiposity in metabolically healthy overweight and obese youth. Pediatrics 2013;132:e85-92.
14. Vukovic R, Milenkovic T, Mitrovic K, Todorovic S, Plavsic L, Vukovic A, et al. Preserved insulin sensitivity predicts metabolically healthy obese phenotype in children and adolescents. Eur J Pediatr 2015;174:1649-55.
15. Bervoets L, Massa G. Classification and clinical characterization of metabolically "healthy" obese children and adolescents. J Pediatr Endocrinol Metab 2016;29:553-60.
16. Ding WQ, Yan YK, Zhang MX, Cheng H, Zhao XY, Hou DQ, et al. Hypertension outcomes in metabolically unhealthy normal-weight and metabolically healthy obese children and adolescents. J Hum Hypertens 2015;29:548-54.
17. Weghuber D, Zelzer S, Stelzer I, Paulmichl K, Kammerhofer D, Schnedl W, et al. High risk vs. "metabolically healthy" phenotype in juvenile obesity—neck subcutaneous adipose tissue and serum uric acid are clinically relevant. Exp Clin Endocrinol Diabetes 2013;121:384-90.
18. Zamrazilova H, Weiss R, Hainer V, Aldhoon-Hainerova I. Cardiometabolic health in obese adolescents is related to length of obesity exposure: a pilot study. J Clin Endocrinol Metab 2016;101:3088-95.
19. Lau DC, Douketis JD, Morrison KM, Hramiak IM, Sharma AM, Ur E. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children [summary]. CMAJ 2007;176:S1-13.
20. Tataranni PA. Treatment of obesity: should we target the individual or society? Curr Pharm Des 2003;9:1151-63.
21. Bleich SN, Segal J, Wu Y, Wilson R, Wang Y. Systematic review of community-based childhood obesity prevention studies. Pediatrics 2013;132:e201-10.
22. Showell NN, Fawole O, Segal J, Wilson RF, Cheskin LJ, Bleich SN, et al. A systematic review of home-based childhood obesity prevention studies. Pediatrics 2013;132:e193-200.
23. Kuzik N, Carson V, Andersen LB, Sardinha LB, Grontved A, Hansen BH, et al. Physical activity and sedentary time associations with metabolic health across weight statuses in children and adolescents. Obesity (Silver Spring) 2017;25:1762-9.
24. Reinehr T, Wolters B, Knop C, Lass N, Holl RW. Strong effect of pubertal status on metabolic health in obese children: a longitudinal study. J Clin Endocrinol Metab 2015;100:301-8.
25. Lambert M, Van Hulst A, O'Loughlin J, Tremblay A, Barnett TA, Charron H, et al. Cohort profile: the Quebec adipose and lifestyle investigation in youth cohort. Int J Epidemiol 2012;41:1533-44.
26. Lohman TG, Roche AF, Martorell R. Anthropometric standardization reference manual. Champaign (IL): Human Kinetics Books; 1988.
27. de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. Bull World Health Organ 2007;85:660-7.
28. McCarthy HD, Jarrett KV, Crawley HF. The development of waist circumference percentiles in British children aged 5.0-16.9 y. Eur J Clin Nutr 2001;55:902-7.
29. Marshall WA, Tanner JM. Variations in the pattern of pubertal changes in boys. Arch Dis Child 1970;45:13-23.
30. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Arch Dis Child 1969;44:291-303.
31. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004;114:555-76.
32. Henderson M, Rabasa-Lhoret R, Bastard JP, Chiasson JL, Baillargeon JP, Hanley JA, et al. Measuring insulin sensitivity in youth: how do the different indices compare with the gold-standard method? Diabetes Metab 2011;37:72-8.
33. Henderson M, Baillargeon JP, Rabasa-Lhoret R, Chiasson JL, Hanley J, Lambert M. Estimating insulin secretion in youth using simple indices derived from the oral glucose tolerance test. Diabetes Metab 2012;38:309-15.
34. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third

National Health and Nutrition Examination Survey, 1988-1994. Arch Pediatr Adolesc Med 2003;157:821-7.
35. Moshfegh AJ, Borrud L, Perloff B, LaComb RP. Improved method for the 24-hour dietary recall for use in national surveys. FASEB J 1999;13:A603.
36. Health Canada. Eating well with Canada's food guide. Ottawa (Ontario, Canada): Government of Canada; 2007.
37. Colley R, Connor Gorber S, Tremblay MS. Quality control and data reduction procedures for accelerometry-derived measures of physical activity. Health Rep 2010;21:63-9.
38. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. Med Sci Sports Exerc 2008;40:181-8.
39. Henderson M, Gray-Donald K, Mathieu ME, Barnett TA, Hanley JA, O'Loughlin J, et al. How are physical activity, fitness, and sedentary behavior associated with insulin sensitivity in children? Diabetes Care 2012;35:1272-8.
40. Evenson KR, Catellier DJ, Gill K, Ondrak KS, McMurray RG. Calibration of two objective measures of physical activity for children. J Sports Sci 2008;26:1557-65.
41. Skinner J. Exercise testing and exercise prescription for special cases: theoretical basis and clinical application. 3rd ed. Baltimore (MD): Lippincott Williams & Wilkins; 2005.
42. Docherty D. Measurement in pediatric exercise science. Champaign (IL): Human Kinetics; 1996.
43. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. Stat Med 2011;30:377-99.
44. Gilardini L, Pasqualinotto L, Di Matteo S, Caffetto K, Croci M, Girola A, et al. Factors associated with early atherosclerosis and arterial calcifications in young subjects with a benign phenotype of obesity. Obesity (Silver Spring) 2011;19:1684-9.
45. Hankinson AL, Daviglus ML, Van Horn L, Chan Q, Brown I, Holmes E, et al. Diet composition and activity level of at risk and metabolically healthy obese American adults. Obesity (Silver Spring) 2013;21:637-43.
46. Phillips CM, Dillon C, Harrington JM, McCarthy VJ, Kearney PM, Fitzgerald AP, et al. Defining metabolically healthy obesity: role of dietary and lifestyle factors. PLoS ONE 2013;8:e76188.
47. Bell LK, Edwards S, Grieger JA. The relationship between dietary patterns and metabolic health in a representative sample of adult Australians. Nutrients 2015;7:6491-505.
48. Matta J, Nasreddine L, Jomaa L, Hwalla N, Mehio Sibai A, Czernichow S, et al. Metabolically healthy overweight and obesity is associated with higher adherence to a traditional dietary pattern: a cross-sectional study among adults in Lebanon. Nutrients 2016;8:432.
49. Burrows TL, Martin RJ, Collins CE. A systematic review of the validity of dietary assessment methods in children when compared with the method of doubly labeled water. J Am Diet Assoc 2010;110:1501-10.
50. Ekelund U, Brage S, Froberg K, Harro M, Anderssen SA, Sardinha LB, et al. TV viewing and physical activity are independently associated with metabolic risk in children: the European Youth Heart Study. PLoS Med 2006;3:e488.
51. Henderson M, Benedetti A, Barnett TA, Mathieu ME, Deladoey J, Gray-Donald K. Influence of adiposity, physical activity, fitness, and screen time on insulin dynamics over 2 years in children. JAMA Pediatr 2016;170:227-35.
52. Sigman A. Time for a view on screen time. Arch Dis Child 2012;97:935-42.
53. King WC, Chen JY, Courcoulas AP, Mitchell JE, Wolfe BM, Patterson EJ, et al. Objectively-measured sedentary time and cardiometabolic health in adults with severe obesity. Prev Med 2016;84:12-8.
54. Kim J, Tanabe K, Yokoyama N, Zempo H, Kuno S. Objectively measured light-intensity lifestyle activity and sedentary time are independently associated with metabolic syndrome: a cross-sectional study of Japanese adults. Int J Behav Nutr Phys Act 2013;10:30.
55. Bankoski A, Harris TB, McClain JJ, Brychta RJ, Caserotti P, Chen KY, et al. Sedentary activity associated with metabolic syndrome independent of physical activity. Diabetes Care 2011;34:497-503.
56. Korhonen PE, Korsoff P, Vahlberg T, Kaaja R. Lifestyle of metabolically healthy obese individuals. Prim Care Diabetes 2015;9:179-83.
57. Ortega FB, Lee DC, Katzmarzyk PT, Ruiz JR, Sui X, Church TS, et al. The intriguing metabolically healthy but obese phenotype: cardiovascular prognosis and role of fitness. Eur Heart J 2013;34:389-97.
58. Rhee EJ, Lee MK, Kim JD, Jeon WS, Bae JC, Park SE, et al. Metabolic health is a more important determinant for diabetes development than simple obesity: a 4-year retrospective longitudinal study. PLoS ONE 2014;9:e98369.
59. Hill RJ, Davies PS. The validity of self-reported energy intake as determined using the doubly labelled water technique. Br J Nutr 2001;85:415-30.

Funding and Disclosures

The QUALITY cohort is funded by the Canadian Institutes of Health Research (#OHF-69442, #NMD-94067, #MOP-97853, #MOP-119512), the Heart and Stroke Foundation of Canada (#PG-040291), and Fonds de la Recherche du Québec - Santé. M.H. and A.B. hold Fonds de Recherche du Québec - Santé Junior 2 salary awards. T.B. holds a Senior salary award from the same institution. M.H. also holds a Diabetes Junior Investigator Award from the Canadian Society of Endocrinology and Metabolism—AstraZeneca. V.D. is the recipient of the 2015 Yogurt in Nutrition Initiative grant and has received grants from Danone and Dairy Farmers of Canada. These funding agencies were not involved in the study design, the collection, analysis, and interpretation of data, the writing of the report, and the decision to submit the manuscript for publication. The authors declare no conflicts of interest.