# Vegetarian Diet, Growth, and Nutrition in Early Childhood: A Longitudinal Cohort Study

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**OBJECTIVES:** The primary objective of this study was to examine the relationships between vegetarian diet and growth, micronutrient stores, and serum lipids among healthy children. Secondary objectives included exploring whether cow's milk consumption or age modified these relationships.

**METHODS:** A longitudinal cohort study of children aged 6 months to 8 years who participated in the TARGet Kids! cohort study. Linear mixed-effect modeling was used to evaluate the relationships between vegetarian diet and BMI z-score (zBMI), height-for-age z-score, serum ferritin, 25-hydroxyvitamin D, and serum lipids. Generalized estimating equation modeling was used to explore weight status categories. Possible effect modification by age and cow's milk consumption was examined.

**RESULTS:** A total of 8907 children, including 248 vegetarian at baseline, participated. Mean age at baseline was 2.2 years (SD 1.5). There was no evidence of an association between vegetarian diet and zBMI, height-for-age z-score, serum ferritin, 25-hydroxyvitamin D, or serum lipids. Children with vegetarian diet had higher odds of underweight (zBMI <-2) (odds ratio 1.87, 95% confidence interval 1.19 to 2.96; P = .007) but no association with overweight or obesity was found. Cow's milk consumption was associated with higher nonhigh-density lipoprotein cholesterol (P = .03), total cholesterol (P = .04), and low-density lipoprotein cholesterol (P = .02) among children with vegetarian diet. However, children with and without vegetarian diet who consumed the recommended 2 cups of cow's milk per day had similar serum lipids.

**CONCLUSIONS:** Evidence of clinically meaningful differences in growth or biochemical measures of nutrition for children with vegetarian diet was not found. However, vegetarian diet was associated with higher odds of underweight.



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Ms Elliott and Dr Maguire designed the research study, performed the statistical analyses, and drafted the initial manuscript; Dr Keown-Stoneman conceptualized and designed the study and contributed to the statistical analyses and interpretation of data; Drs Birken, Jenkins, and Borkhoff conceptualized and designed the study; and all authors reviewed and revised the manuscript critically for important intellectual content, read and approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

WHAT'S KNOWN ON THE SUBJECT: International guidelines about vegetarian diet in infancy and childhood have differing recommendations. Studies which have evaluated the relationship between vegetarian diet and childhood growth and nutritional status have had conflicting findings.

WHAT THIS STUDY ADDS: In this study, children with vegetarian diet had similar mean BMI z-score, height-for-age z-score, serum ferritin, 25-hydroxyvitamin D, and serum lipid measures. However, vegetarian diet was associated with higher odds of underweight.

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Vegetarian diets are becoming increasingly popular for adults and children.<sup>1–3</sup> The 2007–2010 National Health and Nutrition Examination Surveys found that 2.1% of American adults followed a vegetarian diet.<sup>4</sup> Vegetarian diet has been defined as a dietary pattern that excludes meat, whereas a vegan diet excludes meat- and animalderived products such as dairy, egg, and honey.<sup>5,6</sup> Recent dietary guidelines support increasing consumption of plant-based proteins and reducing saturated fat intake.<sup>7</sup> Although vegetarian diet is presumed to be healthy for children,<sup>8</sup> few studies have evaluated the impact of vegetarian diet on childhood growth and nutritional status.

A 2017 systematic review of vegetarian diets for children found conflicting evidence on growth and biochemical measures of nutrition.<sup>5</sup> The authors concluded that recommendations could not be made on the benefits or risks of present-day vegetarian diets with respect to the nutritional status of children.<sup>5</sup> Studies which identified positive growth and nutritional outcomes involved children from Seventh-Day Adventist (SDA) families who may have different lifestyles than typical North American families.<sup>5,9</sup> The few small observational studies which evaluated vegetarian diet in non-SDA children had conflicting findings.<sup>10–15</sup> Limited evidence has led to differing health professional guidelines. North American guidelines suggest well-planned vegetarian and vegan diets are safe for people of all ages.<sup>6,8</sup> However, the Canadian Pediatric Society notes a vegetarian diet can be nutritionally adequate when milk and egg products are provided.<sup>16</sup> Some European guidelines do not recommend vegan diet for children because of the risk of nutrient

insufficiency without appropriate clinical follow-up, serum monitoring, and supplement use.<sup>17–19</sup> The 2020–2025 Dietary Guidelines for Americans includes a healthy vegetarian eating pattern for children aged 12 to 23 months. These guidelines also call for clinician involvement for monitoring the adequacy of vegetarian diet in childhood.<sup>20</sup>

We hypothesized that vegetarian diet in childhood would be associated with lower growth, iron and vitamin D stores because of lower total caloric intake, lower heme-iron intake from animal-based foods, and reduced vitamin D from fortified cow's milk. However, because of lower intake of saturated fat from animal foods, we also hypothesized that children with vegetarian diet would have lower serum lipids.

The primary objective of this study was to evaluate the relationship between vegetarian diet and growth, including weight status and height among children aged 6 months to 8 years. Secondary objectives included evaluating the relationship between vegetarian diet and iron stores, vitamin D stores, and serum lipids. In addition, because of the commonness of cow's milk consumption in childhood and the heterogeneity of vegetarian diets, we planned to explore whether cow's milk intake or age modified the associations between vegetarian diet and BMI z-score (zBMI), heightfor-age z-score (zHeight), micronutrient stores, and serum lipids.

# **METHODS**

## **Setting and Participants**

This was a longitudinal cohort study which involved repeated measures in children aged 6 months to 8 years who participated in the TARGet

Kids! cohort study between 2008 and 2019. TARGet Kids! is a primary care, practice-based research network and cohort study in Toronto, Canada.<sup>21</sup> Trained research assistants recruited children from 13 pediatric or family medicine clinics during regularly scheduled health supervision visits. Baseline demographic information, exposure, and outcome data were collected by trained research assistants at health supervision visits using a standardized questionnaire.<sup>21</sup> Children with health conditions affecting growth, chronic conditions (except for asthma), or baseline developmental impairment were excluded.

## **Exposure Variable**

The primary exposure was parentreported vegetarian diet (yes/no) for their child. Similar to the National Health and Nutrition Examination Survey in the United States, vegetarian diet was determined by response to the question: "Please specify your child's diet."<sup>22,23</sup> Those who checked "Vegetarian diet" or "Vegan diet" were classified as vegetarian. Parents were asked to describe their child's diet (vegetarian or nonvegetarian) at each health supervision visit.

## **Outcome Variables**

The primary outcome was zBMI. Secondary outcomes included weight status category, zHeight, serum ferritin, 25-hydroxyvitamin D (25[OH]D), nonhigh-density lipoprotein (HDL) cholesterol (calculated as total cholesterol minus HDL), total cholesterol, low-density lipoprotein (LDL), HDL, and triglycerides. Anthropometric measures were obtained by trained research assistants during each health supervision visit. Weight was measured using a precision digital scale to 2 decimal places (Seca, Hamburg, Germany). Height was

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measured using a length board for participants  $\leq 2$  years and a calibrated stadiometer for those >2 years (Seca, Hamburg, Germany). Weight in kilograms was divided by height in meters squared to determine BMI. zBMI and zHeight were calculated on the basis of World Health Organization (WHO) growth standards, which are standardized by child sex and age, and are believed to represent optimal growth.<sup>24–26</sup> Nonfasting samples were offered by trained phlebotomists during each health supervision visit and sent daily to Mount Sinai Services laboratory in Toronto (mountsinaiservices.com). Previous studies have shown fasting has little impact on serum lipid tests in children.<sup>27,28</sup> Serum ferritin, 25(OH)D, and serum lipids were quantified using a Roche Modular platform (Roche Diagnostics, http://www.roche. com/diagnostics). LDL was calculated using the Friedewald equation.<sup>29</sup>

# **Other Variables**

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Potential confounders were determined a priori from a literature review. These included child age, calendar date, sex, birth weight,<sup>30</sup> breastfeeding duration,<sup>30</sup> sugar-containing beverage intake,<sup>31</sup> cow's milk intake, mother's age at birth,<sup>31</sup> maternal ethnicity (selfreported),<sup>31</sup> self-reported family income,<sup>30</sup> maternal BMI,<sup>31</sup> maternal height (for zHeight),<sup>32</sup> C-reactive protein (CRP) (for serum ferritin),<sup>33</sup> iron supplementation (for serum ferritin),<sup>6</sup> vitamin D supplementation (for 25[OH]D),<sup>6</sup> and zBMI (for serum ferritin,<sup>34</sup> 25[OH]D,<sup>35</sup> and serum lipids<sup>36</sup>). Covariates were collected at each health care visit, along with exposure and outcome measures. Calendar date and child age were included because children were recruited over the course of many years. See Supplemental Information for measurement details.

# **Statistical Analysis**

Descriptive statistics were obtained for the primary exposure, outcomes, and covariates. Baseline was defined as the first clinic visit after 6 months of age.

For the primary analysis, linear mixed-effects modeling was used to determine the relationship between vegetarian diet and mean zBMI.<sup>37</sup> The model was adjusted for covariates listed above. Restricted cubic splines with 5 knots were chosen a priori to test potential nonlinear effects.<sup>38</sup> Recommended locations for the 5 knots were used and include the following quantile locations of age: 0.05, 0.275, 0.5, 0.725, and 0.95.<sup>38</sup> Subject specific random intercepts were included.

For the secondary analyses, similar linear mixed-effects models were used to evaluate the relationship between vegetarian diet and mean zHeight, serum ferritin, 25(OH)D, and serum lipids. Serum ferritin and triglyceride data were positively skewed and were log-transformed. The populationaveraged association between vegetarian diet and weight status categories, using WHO zBMI cutpoints, was assessed using multinomial generalized estimating equation models.<sup>39</sup> Mutually exclusive weight categories were defined as: underweight (zBMI <-2), normal weight  $(-2 \leq zBMI \leq 1)$ , overweight  $(1 < zBMI \le 2)$ , and obese (zBMI > 2).<sup>40</sup> WHO cutoffs were chosen to allow for evaluation of growth continuously from birth to 8 years of age. Using established cut-points,41-43 biochemical outcomes were also evaluated using generalized estimating equation models.<sup>39</sup> Likelihood ratio tests were used to explore possible effect-modification by age and cow's milk intake in the primary and secondary analyses. Effect modification by age was used to examine changes in growth rate between vegetarians and nonvegetarians. The interaction

term was included in the final model if the likelihood ratio test was P < .30.<sup>38</sup>

Observations with missing report of diet type were excluded from the analysis (54 observations, 0.6%). Observations with missing anthropometric or biochemical outcome measures were excluded from the analysis (Fig 1). Potentially implausible zBMI and zHeight measures were identified and excluded according to WHO-recommended cutpoints of <-5.0 and >+5.0 SD units and <-6.0 and >+6.0 SD units, respectively.<sup>24,44</sup> Observations with 25(OH)D >250 nmol/L were excluded from analyses involving 25(OH)D. Observations with CRP >5 mg/L or a missing CRP measurement were excluded from analysis involving serum ferritin because CRP is a marker of inflammation and serum ferritin can be falsely elevated in states of acute inflammation.45 In addition, observations with serum ferritin  ${>}200~\mu\text{g/L}$  were removed.  $^{45}$ All covariates had <15% missing data. For all other variables, multiple imputation by chained equations on 15 imputed data sets was used and line parameter estimates were pooled using Rubin's Rules (R: mice package).<sup>46,47</sup> The variance inflation factor was <5 for all covariates. Statistical analyses were conducted using R version 3.6.2.48 Parents provided written consent for their child. Ethics approval was granted through the research ethics boards of the Hospital for Sick Children and St. Michael's Hospital.

# **RESULTS**

There were 8907 children, including 248 who were vegetarian at baseline (25 vegan) and 338 who ever reported vegetarian diet between 6 months and 8 years of age. Sixty-nine percent (6175 of 8907) of participants had 2 or more measures. Growth measures were available on 8794 children who were included in the growth



### **FIGURE 1**

Flowchart of participants recruited and exclusion criteria.

analysis and venous blood was obtained on 4673 children who were included in the biochemical analysis. The mean age of children at baseline was 2.2 years (SD 1.5), and 52.4% were male. Children were followed for an average of 2.8 years (SD 1.7). Children with vegetarian diet had longer breastfeeding duration (12.6 months [SD 9.5] vs 10.0 months [SD 7.0]) and were more likely to have Asian ethnicity (33.8% vs 19.0%). Otherwise, children with and without vegetarian diet seemed similar at baseline (Table 1). Children with and without laboratory testing also appeared similar (Supplemental Table 3).

For the primary analysis, there was no evidence of an association between vegetarian diet and mean zBMI (adjusted mean difference 0.01, 95% confidence interval [CI]: -0.07 to 0.09; P = .84) (Table 2). Additionally, there was no evidence of effect modification by age (P = .97) or cow's milk consumption (P = .69) (Supplemental Table 4). Therefore, we did not find evidence of differences in mean zBMI or zBMI growth rates between children with vegetarian diet and nonvegetarian diet. From the adjusted multinomial model, there was evidence that vegetarian diet was associated with higher odds of underweight (odds

ratio [OR] 1.87, 95% CI: 1.19 to 2.96; P = .007), but there was no evidence of an association with overweight (OR 1.13, 95% CI: 0.87 to 1.48; P =.36) or obesity (OR 0.69, 95% CI: 0.39 to 1.22; P = .20) (Table 2 and Fig 2) relative to children with normal weight. Exploratory analysis revealed that underweight children with and without vegetarian diets appeared similar; however, they were younger (2.9 years [SD 2.6] vs 3.8 years [SD 2.5]) and more likely to have Asian ethnicity (29.9% vs 18.0%).

For the secondary analysis, the adjusted model identified weak evidence of an association between vegetarian diet and zHeight (adjusted mean difference -0.08, 95% CI: -0.17 to 0.001; P = .054). On average, children with vegetarian diet had 0.8 lower zHeight, which is equivalent to 0.3 cm for a 3-year-old child. There was no evidence of an association between vegetarian diet and serum ferritin, 25(OH)D, or serum lipids in the unadjusted or adjusted models (Table 2). Likelihood ratio tests provided evidence that cow's milk intake modified the association between vegetarian diet and serum lipids. Cow's milk intake modified the association between vegetarian diet and mean non-HDL cholesterol (P = .03), mean total cholesterol

(P = .04), and mean LDL cholesterol (P = .02) (Supplemental Tables 4 and 5). Children with vegetarian diet who consumed little to no cow's milk had lower serum lipids than children with nonvegetarian diet. However, children with and without vegetarian diet who consumed the recommended 2 cups of cow's milk per day had similar serum lipids (Fig 3).<sup>49,50</sup> When evaluated categorically, there was no evidence of an association between vegetarian diet and serum ferritin, 25(OH)D, or serum lipids (Table 2). There was no evidence of an interaction by age in any of the models (Supplemental Table 4).

# **DISCUSSION**

In this longitudinal cohort study, associations were not identified between vegetarian and nonvegetarian diets and child zBMI, zHeight, serum ferritin, 25(OH)D, and serum lipids. There was a weak association between vegetarian diet and lower mean zHeight. However, the magnitude was small (0.3 cm for a 3-year-old child) and unlikely to be clinically meaningful. When evaluated categorically, vegetarian diet was associated with higher odds of underweight. Cow's milk consumption was associated with higher serum lipids for children with vegetarian diet; however, serum lipids among children with and without vegetarian diet who consumed the recommended volume of cow's milk per day (2 cups) were similar.49,50

Among SDA populations, positive growth outcomes among children with vegetarian diet have been identified. In a cross-sectional study of 2272 children (n = 1090 vegetarian) aged 6 to 17 years, males with vegetarian diet were, on average, 1.6 cm taller (P < .01) and females had 0.43 lower BMI (P = .01) when compared with

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#### **TABLE 1** Participant Baseline Characteristics

	Nonvegetarian $(n = 8659)$	Vegetarian $(n = 248)$	All participants $(n = 8907)^{a}$
	(11 - 8639)	(11 - 240)	(// - 0907)
Characteristics			
Age, y, mean (SD)	2.2 (1.5)	2.3 (1.5)	2.2 (1.5)
Age, y, n (%)			
<1	1757 (20.3)	40 (16.1)	1797 (20.2)
1–2	4119 (47.6)	125 (50.4)	4244 (47.6)
3–4	989 (11.4)	29 (11.7)	1018 (11.4)
>4	1794 (20.7)	54 (21.8)	1848 (20.7)
Sex, male, <i>n</i> (%)	4528 (52.4)	137 (55.2)	4665 (52.4)
Birth weight, kg, mean (SD)	3.3 (0.6)	3.2 (0.7)	3.3 (0.6)
Breastfeeding duration, mo, mean (SD)	10.0 (7.0)	12.6 (9.5)	10.0 (7.1)
Daily cow's milk intake (cups/d), mean (SD)	1.4 (1.3)	1.2 (1.2)	1.4 (1.3)
Sugar sweetened beverage intake (mL/d), n (%)			
0	4253 (53.4)	127 (56.2)	4361 (53.5)
1–249	1233 (15.5)	33 (14.6)	1266 (15.5)
250–499	1255 (15.8)	38 (16.8)	1293 (15.8)
500-749	1210 (15.3)	28 (12.4)	1238 (15.2)
Iron supplement, yes, $n$ (%)	479 (5.6)	26 (10.6)	505 (5.8)
Vitamin D supplement, yes, n (%)	3578 (41.9)	122 (49.6)	3700 (42.1)
Maternal BMI, mean (SD)	25.0 (5.0)	24.0 (4.2)	25.0 (5.0)
Maternal height, mean (SD)	163.8 (7.2)	163.5 (8.5)	163.8 (7.3)
Maternal age at birth, mean (SD)	33.3 (4.7)	32.8 (4.4)	33.3 (4.7)
Ethnicity, n (%)	00.0 (11)	02.0 (1.1)	00.0 (1.1)
European	4985 (63.3)	126 (55.3)	5111 (63.0)
Asian <sup>b</sup>	1494 (19.0)	77 (33.8)	1571 (19.4)
Mixed ethnicity	471 (6.0)	16 (7.0)	487 (6.0)
Other	929 (11.8)	9 (3.9)	938 (11.6)
	929 (11.0)	9 (3.9)	330 (11.0)
Family income, CAD \$, n (%)	ECO (7 E)	00 (0 4)	E00 (7 C)
<30,000	560 (7.5)	20 (9.4)	580 (7.6)
30 000–79 999	1350 (18.1)	46 (21.7)	1396 (18.2)
80 000-49 999	2339 (31.4)	88 (41.5)	2427 (31.7)
>150 000	3194 (42.9)	58 (27.4)	3252 (42.5)
Vegan diet, yes, n (%)	0 (0)	25 (10.1)	25 (0.3)
zBMI, mean (SD)	0.04 (1.1)	-0.11 (1.2)	0.04 (1.1)
zHeight, mean (SD)	0.32 (1.2)	0.18 (1.3)	0.31 (1.2)
Weight status, n (%)			
Underweight (zBMI $<-2$ )	274 (3.3)	15 (6.2)	289 (3.3)
Normal ( $\geq -2$ zBMI $\leq 1$ )	6600 (78.6)	192 (79.7)	6792 (78.6)
Overweight (>1 zBMI <2)	1169 (13.9)	26 (10.8)	1195 (13.8)
Obese (zBMI $>$ 2)	353 (4.2)	8 (3.3)	360 (4.2)
Serum ferritin ng/mL, mean (SD)	32.6 (22.9)	31.6 (20.3)	32.6 (22.8)
Median	27.0	26.0	27.0
25(OH)D ng/mL, mean (SD)	35.3 (12.4)	34.9 (12.2)	35.3 (12.4)
Non-HDL cholesterol mg/dL, mean (SD)	108.1 (27.0)	104.3 (27.0)	108.1 (27.0)
Total cholesterol mg/dL, mean (SD)	158.3 (27.0)	154.4 (27.0)	154.4 (27.0)
LDL cholesterol mg/dL, mean (SD)	84.9 (27.0)	81.1 (23.2)	84.9 (27.0)
HDL cholesterol mg/dL, mean (SD)	50.2 (11.6)	46.3 (11.6)	50.2 (11.6)
Triglycerides mg/dL, mean (SD)	115.0 (70.8)	115.0 (70.8)	115.0 (70.8)
Median	97.4	97.4	97.4

To convert mg/dL to SI units (mmol/L), divide results by 38.6 for non-HDL, total cholesterol, LDL, and HDL, and 88.6 for triglycerides. To convert 25(0H)D ng/mL to nmol/L, multiply by 2.496. One ng/mL serum ferritin is equivalent to 1 µg/L. CAD, Canadian dollars.

<sup>a</sup> Includes all cases meeting the inclusion criteria of having a measure of diet. Cases were removed from individual analyses if outcome measure of interest was missing. <sup>b</sup> Asian ethnicity included parent-report of West Asian, South Asian, East Asian, and Southeast Asian.

children with nonvegetarian diet.<sup>51</sup> In another cross-sectional study of 1765 children (n = 870 SDA) aged 7 to 18 years, Sabate et al<sup>52</sup> found those following a vegetarian diet were, on average, 2.5 and 2.0 cm

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taller for males and females, respectively. Few studies have evaluated the relationship between vegetarian diet and childhood growth and nutrition among non-SDA populations. Consistent with the results of the current study, 1 cross-sectional study of 430 children (n = 127 vegetarian) aged 1 to 3 years, which also used WHO z-scores to assess growth, did not identify associations between

TABLE 2 Relationship Between Vegetarian Diet, Growth, and Biochemical Measures of Nutrition

Outcome Variables <sup>a,b</sup>	Exposure Variable: Vegetarian, yes		
	Unadjusted Estimate (95% Cl; <i>P</i> )	Adjusted Estimate (95% Cl; <i>P</i> )	
Continuous outcomes			
zBMI <sup>c,d</sup>	-0.01 (-0.09 to 0.07; .79)	0.01 (-0.07 to 0.09; .84)	
zHeight <sup>c,e</sup>	-0.10 (-0.19 to -0.02; .02)	-0.08 (-0.17 to 0.001; .05)	
25(OH)D (ng/mL) <sup>d,f</sup>	-0.82 (-2.57 to 0.93; .36)	-1.05 (-2.73 to 0.64; .22)	
Non-HDL cholesterol (mg/dL) <sup>d,g</sup>	-2.70 (-6.56 to 1.16; .15)	-3.09 (-6.95 to 0.77; .10)	
Total cholesterol (mg/dL) <sup>d,g</sup>	-3.09 (-7.34 to 0.77; .11)	-3.47 (-7.72 to 0.39; .08)	
LDL (mg/dL) <sup>d,g</sup>	-2.32 (-5.79 to 1.54; .23)	-2.70 (-6.18 to 1.16; .15)	
HDL (mg/dL) <sup>d,g</sup>	-0.39 (-2.70 to 1.16; .47)	-0.77 (-2.70 to 1.16; .46)	
Back transformed results			
Triglycerides (mg/dL) <sup>d,g,h</sup>	0.98 (0.90 to 1.06; .60)	0.98 (0.91, 1.06; .66)	
Ferritin (ng/mL) <sup>d,h,i</sup>	1.02 (0.93 to 1.11; .71)	0.99 (0.91, 1.08; .82)	
Categorical outcomes			
Weight status categories <sup>d</sup>			
Underweight ( $<$ -2)	1.94 (1.19 to 3.16; .008)	1.87 (1.19 to 2.96; .007)	
Overweight (>1-<2)	1.06 (0.82 to 1.37; .65)	1.13 (0.87 to 1.48; .36)	
Obese (>2)	0.68 (0.41 to 1.14; .14)	0.69 (0.39 to 1.22; .20)	
Serum ferritin <14 ng/mL <sup>d,i</sup>	1.02 (0.59 to 1.75; .95)	1.11 (0.64 to 1.93; .72)	
25(0H)D <20 ng/mL <sup>d,f</sup>	1.52 (0.87 to 2.66; .14)	1.45 (0.82 to 2.56; .20)	
Non-HDL cholesterol $\geq$ 145 mg/dL <sup>d,g</sup>	0.46 (0.18 to 1.22; .12)	0.46 (0.17 to 1.23; .12)	
Total cholesterol $\geq$ 200 md/dL <sup>d,g</sup>	0.73 (0.35 to 1.51; .39)	0.72 (0.34 to 1.53; .39)	
$LDL \ge 130 \text{ mg/dL}^{d,g}$	0.41 (0.13 to 1.31; .13)	0.40 (0.12 to 1.30; .12)	
$HDL \leq 40 mg/dL^{d,g}$	1.38 (0.96 to 2.00; .08)	1.42 (0.98 to 2.05; .06)	
Triglycerides $\geq$ 100 mg/dL <sup>d,g</sup>	0.90 (0.64 to 1.26; .55)	0.92 (0.65 to 1.29; .63)	

To convert mg/dL to SI units (mmol/L), divide results by 38.6 for non-HDL, total cholesterol, LDL and HDL, and 88.6 for triglycerides. To convert 25(0H)D ng/mL to nmol/L, multiply by 2.496; 1 ng/mL serum ferritin is equivalent to 1 µg/L. Each row shows results from separate models.

<sup>b</sup> Time as child age in restricted cubic splines, 5 knots.

<sup>c</sup> zBMI and zHeight are reported in z-score units.

<sup>d</sup> Adjusted for child age, calendar date (restricted cubic splines, 5 knots), sex, birth weight, breastfeeding duration, cow's milk intake, sugar-containing beverage intake, maternal age at birth, maternal ethnicity, maternal BMI, and self-reported family income. Children with normal weight were considered the reference group

<sup>e</sup> Adjusted for child age, calendar date (restricted cubic splines, 5 knots), sex, birth weight, breastfeeding duration, cow's milk intake, sugar-containing beverage intake, maternal age at birth, maternal ethnicity, maternal height, and self-reported family income.

<sup>f</sup> Adjusted for zBMI and vitamin D supplement use

<sup>g</sup> Adjusted for zBMI

<sup>h</sup> Because of log transformations, the effects of these results are multiplicative, and therefore a Cl containing 1 indicates no evidence of an association.

<sup>1</sup> Adjusted for CRP, zBMI, and iron supplement use.

vegetarian diet and weight-forheight, height-for-age, or weight-forage z-scores.<sup>10</sup> Similarly, other prospective cohort studies found no association between vegetarian diet and childhood growth. A study of 2875 children (n = 29 vegetarian) found no differences in height, weight, or BMI among male or females aged 6 to 11 years.<sup>12</sup> A matched pairs prospective cohort study which followed 100 children (n = 50 vegetarian) aged 7 to11 years in England for 1 year also found no association between vegetarian diet and weight, height,

or BMI.<sup>11</sup> However, these studies had small sample sizes and likely insufficient power to detect clinically meaningful differences in child anthropometric measures, particularly for weight status categories.

Since the predominant source of iron and vitamin D in most children's diets is meat and cow's milk, respectively,<sup>53–55</sup> we hypothesized that children with vegetarian diet would have lower serum ferritin and 25(OH)D, which we did not find. Several small crosssectional and prospective cohort studies also did not find associations between vegetarian diet and serum ferritin or 25(OH)D.56,57 However, Thane et al,<sup>57</sup> in a cross-sectional study of 345 children aged 1.5 to 3 years (n = 11 vegetarian), found that children with vegetarian diet had lower serum ferritin relative to children with nonvegetarian diet. A Polish study involving 40 children (n = 22 vegetarian) aged 2 to18 years found that children with vegetarian diet had lower serum ferritin (9.61 vs 36.1  $\mu$ g/L, P = .01) and a higher prevalence of iron deficiency (36.4%, *n* = 8 vs 11.1%, n = 2, P = .02).<sup>15</sup> However, these children were older (up to 18 years) and the relationship between vegetarian diet and iron stores may be more pronounced with longer duration of exposure.<sup>15</sup> In addition, these studies were conducted in European countries, which, because of cultural differences, may have influenced the dietary pattern of both vegetarian and nonvegetarian diets.

Our serum lipid finding is consistent with a cross-sectional study of 42 children (n = 24 vegetarian) aged 2 to 18 years in Poland, which also did not find an association.<sup>14</sup> However, a Slovakian cross-sectional study of 52 (n = 26 vegetarian) children aged 11 to 14 years found that those with vegetarian diet had lower total cholesterol (4.38 [SD 0.08] mmol/L versus 4.96 mmol/L [SD 0.09], P <.001) and LDL (2.64 mmol/L [SD 0.09] vs 3.07 mmol/L [SD 0.12], *P* <.01), but found no association with HDL or triglycerides.<sup>13</sup> These findings may indicate that the relationship between vegetarian diet and serum lipids is more pronounced in older children who may have a longer duration of exposure.

A relationship between cow's milk and serum lipids has been previously

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## **FIGURE 2**

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Vegetarian diet and growth, micronutrient, and serum lipid measures. zBMI, weight status, serum ferritin, 25(0H)D, and serum lipids models adjusted for child age, calendar date (restricted cubic splines, 5 knots), sex, birth weight, breastfeeding duration, cow's milk intake, sugar sweetened beverage intake, maternal age at birth, maternal ethnicity, maternal BMI, and self-reported family income. Serum ferritin adjusted for CRP, zBMI, and iron supplement use. 25(0H)D adjusted for zBMI and vitamin D supplement use. Serum lipids adjusted for zBMI. zHeight model adjusted for child age, calendar date (restricted cubic splines, 5 knots), sex, zBMI, birth weight, breastfeeding duration, cow's milk intake, sugar-containing beverage intake, maternal age at birth, maternal ethnicity, maternal height, and self-reported family income. Time as child age in restricted cubic splines, 5 knots. Shaded area represents 95% CI.

reported.<sup>58</sup> In the current study, we identified a stronger relationship between cow's milk intake and serum non-HDL cholesterol, total cholesterol, and LDL-cholesterol among children with vegetarian diet than children without vegetarian diet. It is unclear whether these differences persist into older childhood or adulthood. We speculate that cow's milk may be among the main sources of saturated fat for children with vegetarian diet. It is unclear what biological mechanism influences the serum lipid sensitivity we observed. We have considered that children with vegetarian diet who do not consume cow's milk may drink a larger

volume of plant-based milks, which have been identified to have a lipidlowering effect in adults.<sup>59</sup> However, we also found similar serum lipid measures among vegetarian and nonvegetarian children consuming the recommended 2 cups of cow's milk per day.<sup>49,50</sup>

Strengths of this study include a large, ethnically diverse cohort of healthy urban children, with 248 children at baseline with vegetarian diet. Detailed data allowed us to account for numerous clinically important potential confounders with simultaneous measurement of exposure and outcome measures. The use of parent-report of vegetarian diet is also a strength. Several studies have identified that dietary recall alone underestimates the proportion of people who selfreport vegetarian diet because of occasional consumption of red meat, poultry, fish, or dairy.<sup>4,10,60-64</sup>

Study limitations include potential reverse causality, where changes in outcomes, such as poor growth, could have affected dietary choices. However, we did not find that the associations changed over time. In addition, the participants of this study were urban children with health care-seeking parents. These characteristics may limit generalizability to families where



various levels of cow's milk volume						
	Serum Lipid Outcome Variable <sup>a</sup>					
	Non-HDL Cholesterol	Total Cholesterol	LDL Cholesterol			
	(mg/dL)	(mg/dL)	(mg/dL)			
Daily Cow's Milk	Estimated Difference <sup>b</sup> (95%	Estimated Difference <sup>b</sup> (95%	Estimated Difference <sup>b</sup> (95%			
Consumption	CI; P value)	CI; P value)	CI; P value)			
0 cups	-7.72 (-12.74, -2.70; 0.003)	-8.11 (-13.51, -2.70; 0.004)	-7.34 (-11.97, -2.32; 0.004)			
1 cup	-4.25 (-8.11, -0.77; 0.02)	-4.63 (-8.88, -0.77; 0.02)	-3.86 (-7.72, -0.39; 0.04)			
2 cups	-1.16 (-5.41, 3.09; 0.59)	-1.54 (-6.18, 2.70; 0.46)	-0.77 (-4.63, 3.47; 0.77)			
3 cups	1.93 (-3.86, 8.11; 0.48)	1.54 (-4.63, 7.72; 0.64)	2.70 (-2.70, 8.11; 0.34)			
4 cups	5.41 (-2.70, 13.51; 0.19)	4.63 (-3.86, 16.60; 0.29)	6.18 (-1.54. 13.51; 0.12)			
5 cups	8.49 (-1.93, 18.92; 0.11)	7.72 (-3.47, 18.92; 0.17)	9.27 (-0.77, 19.31; 0.07)			
<sup>a</sup> All models were adjusted for child age, calendar date (restricted cubic splines, 5 knots), sex, zBMI, birthweight, breastfeeding duration, cow's milk intake, sugar-containing beverage intake, maternal age at birth, maternal ethnicity, maternal BMI, and						
self-reported family income. Not adjusted for multiple comparisons. Time as child age in restricted cubic splines, 5 knots.						
bestimated difference between those with vegetarian diet relative to those without vegetarian diet.						
<sup>c</sup> Shaded area represents 95% CI.						
To convert mg/dL to SI units (mmol/L) divide results by 38.6.						

#### FIGURE 3

Effect modification by cow's milk intake of the relationship between vegetarian diet and non-HDL, total, and LDL cholesterol.

the choice of following a vegetarian diet is motivated by lower income or reduced access to healthful, plant-based alternatives. Although adjustment for numerous potential confounders was made, detailed measures of dietary intake and physical activity were not available. In addition, information on parental dietary intake was not available. Although adjustment was made for ethnicity, it is possible that the

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growth standards used may overestimate underweight in Asian American populations. Although the sample size was larger than previous studies, there were too few children to conduct meaningful subgroup analysis for children with vegan diet type or very young age. Finally, with an average follow-up duration of 2.8 years, longer-term outcomes could not be evaluated.

Although clinical trial data would help to determine causality, such trials are unlikely to be possible. Prospectively collected data from unselected populations may be the best available evidence about vegetarian diets for children. Larger longitudinal cohort studies with more detailed measures of dietary intake and longer duration of follow-up are needed to fully assess growth and nutritional outcomes. Evidence for specific dietary requirements for children with vegetarian diet may improve alignment among health professional organizations. In addition, it is important to further understand motivations for vegetarian diet, such as income, and the effect these variables may have on growth and nutritional status. Exploration into socioeconomic status and the influence it may have on vegetarian dietary patterns and quality are important next steps. Lastly, larger longitudinal cohort studies would allow for the evaluation of the different types of vegetarian diet.

# **CONCLUSIONS**

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Guidelines currently differ on the adequacy of vegetarian diet in childhood. In this study, we did not find evidence of clinically meaningful differences in growth or biochemical measures of nutrition for children with vegetarian diet. However, vegetarian diet was associated with higher odds of underweight, underscoring the need for careful dietary planning for underweight children when considering vegetarian diets.

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# **ABBREVIATIONS**

25(OH)D: 25-hydroxyvitamin D CI: confidence interval CRP: C-reactive protein HDL: high-density lipoprotein LDL: low-density lipoprotein OR: odds ratio SDA: Seventh-Day Adventist WHO: World Health Organization zBMI: BMI z-score zHeight: height-for-age z-score

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