Original Investigation

# Association Between Artificially Sweetened Beverage Consumption During Pregnancy and Infant Body Mass Index

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**IMPORTANCE** The consumption of artificial sweeteners has increased substantially in recent decades, including among pregnant women. Animal studies suggest that exposure to artificial sweeteners in utero may predispose offspring to develop obesity; however, to our knowledge, this has never been studied in humans.

**OBJECTIVE** To determine whether maternal consumption of artificially sweetened beverages during pregnancy is associated with infant body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]).

**DESIGN, SETTING, AND PARTICIPANTS** This cohort study included 3033 mother-infant dyads from the Canadian Healthy Infant Longitudinal Development (CHILD) Study, a population-based birth cohort that recruited healthy pregnant women from 2009 to 2012. Women completed dietary assessments during pregnancy, and their infants' BMI was measured at 1 year of age (n = 2686; 89% follow-up). Statistical analysis for this study used data collected after the first year of follow-up, which was completed in October 2013. The data analysis was conducted in August 2015.

**EXPOSURES** Maternal consumption of artificially sweetened beverages and sugar-sweetened beverages during pregnancy, determined by a food frequency questionnaire.

**MAIN OUTCOMES AND MEASURES** Infant BMI *z* score and risk of overweight at 1 year of age, determined from objective anthropometric measurements and defined according to World Health Organization reference standards.

**RESULTS** The mean (SD) age of the 3033 pregnant women was 32.4 (4.7) years, and their mean (SD) BMI was 24.8 (5.4). The mean (SD) infant BMI *z* score at 1 year of age was 0.19 (1.05), and 5.1% of infants were overweight. More than a quarter of women (29.5%) consumed artificially sweetened beverages during pregnancy, including 5.1% who reported daily consumption. Compared with no consumption, daily consumption of artificially sweetened beverages was associated with a 0.20-unit increase in infant BMI *z* score (adjusted 95% CI, 0.02-0.38) and a 2-fold higher risk of infant overweight at 1 year of age (adjusted odds ratio, 2.19; 95% CI, 1.23-3.88). These effects were not explained by maternal BMI, diet quality, total energy intake, or other obesity risk factors. There were no comparable associations for sugar-sweetened beverages.

**CONCLUSIONS AND RELEVANCE** To our knowledge, we provide the first human evidence that maternal consumption of artificial sweeteners during pregnancy may influence infant BMI. Given the current epidemic of childhood obesity and widespread use of artificial sweeteners, further research is warranted to confirm our findings and investigate the underlying biological mechanisms, with the ultimate goal of informing evidence-based dietary recommendations for pregnant women.

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Editorial

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The incidence of childhood obesity has more than doubled in the last 30 years.[1] One-third of children in developed countries are now overweight or obese,[2] putting them at increased risk for cardiometabolic disease and mental health disorders.[3] With more than 20% of preschool children classified as overweight or obese,[1] it is clear that obesity is rooted in early life. Evidence from both human and animal studies shows that metabolism, endocrine pathways, and weight gain trajectories are "programmed" during early development,[4] and prenatal nutrition plays a key role in this process.[5]

Added sugar intake is strongly associated with obesity and related comorbidities, prompting population-wide recommendations to reduce sugar consumption.[6] As a result, sugar replacements or nonnutritive sweeteners (NNSs) have become increasingly popular, with more than 50% of Americans reporting NNS consumption in recent surveys and cohort studies.[7] Although few data are available for pregnant women in the United States, cohort studies from Norway[8] and Denmark[9] have found that more than 30% of women report consuming artificially sweetened beverages (ASBs) during pregnancy. Despite the widespread and increasing consumption of NNSs,[10] their long-term effect on human health is poorly understood, and current intake recommendations are unclear, particularly for pregnant women and young children. The American Dietetic Association states that NNSs are safe to consume during pregnancy and childhood within acceptable daily intakes,[11] while the US Institute of Medicine makes no specific recommendation for pregnant women but cautions against NNS use in children, citing a paucity of evidence for the adverse long-term health effects of NNS exposure in early life.[12]

A growing body of literature suggests that chronic NNS consumption may paradoxically increase the risk of obesity and metabolic diseases.[13] Proposed mechanisms for this association include alteration of glucose metabolism,[14] disruption of gut microbiota,[15] or dysregulation of satiety and caloric compensation.[16] However, this evidence has been generated in adult studies,[17] and little is known about the effect of NNS exposure during gestation. Limited results from animal models indicate that NNS consumption during pregnancy may predispose offspring to develop obesity and metabolic syndrome,[18] but to our knowledge, this has never been studied in humans. Cohort studies documenting consumption of ASBs during pregnancy have reported associations with preterm delivery,[8,9,19] allergic disease,[20] and forearm fractures[21] among offspring, but infant body composition has not been evaluated.

We undertook an observational study of mother-infant dyads from the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort to determine the association of ASB consumption during pregnancy and infant body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]) in the first year of life.

### Key Points

**Question** Does maternal consumption of artificially sweetened beverages during pregnancy influence infant body composition?

**Findings** In this population-based birth cohort of 3033 mother-infant dyads, maternal consumption of artificially sweetened beverages during pregnancy was significantly associated with infant body mass index at 1 year of age. After controlling for maternal obesity and diet quality, daily artificially sweetened beverage consumption was associated with a 0.2-unit increase in infant body mass index *z* score and a 2-fold higher risk of overweight.

**Meaning** Exposure to artificial sweeteners in utero may contribute to the development of childhood obesity.

## Methods

### Study Design and Population

We accessed data from the CHILD Study, a national population-based birth cohort of 3542 families across 4 sites in Canada.[22] Women with singleton pregnancies were enrolled between 2009 and 2012 and remained eligible if they delivered a healthy, full-term infant (>35 weeks' gestation with no congenital abnormalities). For the current study, we included 3033 mother-infant dyads who completed the prenatal dietary assessment, of which 2686 (89%) had complete outcome data for infant BMI at 1 year of age and 2413 (80%) had complete data for infant BMI and all essential covariates (maternal BMI and other potential confounders identified through bivariate screening). There was no difference in maternal consumption of sweetened beverages, infant BMI, or essential covariates among dyads with complete data compared with all eligible dyads (eTable 1 in the Supplement). This study was approved by the University of Manitoba Human Research Ethics Board. Written informed consent was obtained from mothers during enrollment.

### Maternal Dietary Assessment

Maternal diet was documented in the CHILD Study using a validated food frequency questionnaire (FFQ)[23,24] administered in the second or (usually) third trimester of pregnancy. The FFQ was modified to address usual food intakes during the current pregnancy. Intake of ASBs was determined from reported consumption of "diet soft drinks or pop" (1 serving = 12 oz or 1 can) and "artificial sweetener added to tea or coffee" (1 serving = 1 packet). Sugar-sweetened beverage (SSB) intake was similarly determined from consumption of "regular soft drinks or pop" (1 serving = 12 oz or 1 can) and "sugar or honey added to tea or coffee" (1 serving = 1 teaspoon or 1 packet). Following the methods of Maslova et al,[20] beverage intakes were classified according to the number of servings per week as never, fewer than 1 per month, 1 or more per week, 2 to 6 per week, or 1 or more per day. Total energy intake (kilocalories per day) and the Healthy Eating Index[25] score were derived from FFQ data using food composition tables from the Nutrition Coding Center nutrient database (University of Minnesota). The Healthy Eating Index[25] is a measure of diet quality in terms of conformance with the 2010 Dietary Guidelines from the US Department of Agriculture; it has 12 components addressing dietary adequacy (9 components) and moderation (3 components), with a maximum score of 100.

### Infant BMI

At 1 year of age (mean [SD] age, 12.5 [1.5] months), infants were weighed to the nearest 0.1 kg and measured to the nearest 0.1 cm by trained study staff according to a standardized protocol during a CHILD Study clinical assessment. Age- and sex-specific BMI-for-age *z* scores and weight-for-length *z* scores were calculated according to the 2006 World Health Organization standards using their "igrowup" package for SAS (SAS Institute).[26] Infants with BMI *z* scores exceeding the 97th percentile were classified as overweight.[27]

### Covariates

Infant sex, birth weight, and gestational age and maternal age were documented from hospital records. Maternal BMI was calculated from measured height and self-reported prepregnancy weight (n = 1845), estimated from measured weight at 1 year after birth if mothers could not recall their prepregnancy weight (n = 868), or imputed by multiple imputation if neither measure was available (n = 320). Validation against prenatal health records (n = 224) showed that prepregnancy weight was slightly underestimated by maternal recall (mean difference, −1.0 kg; 95% CI, −1.5 to −0.4) and slightly overestimated by measured weight at 1 year after birth (mean difference, +1.3 kg; 95% CI, 0.5-2.2). Maternal education and prenatal smoking were ascertained by a questionnaire during pregnancy. Education was dichotomized (postsecondary degree: yes or no), and mothers were considered prenatal smokers if they reported current smoking or quitting smoking at any time during their pregnancy. Maternal diabetes during pregnancy (preexisting or gestational) was determined from hospital records and by maternal report. Breastfeeding and timing of the introduction of solid foods were reported by a standardized questionnaire at 3, 6, and 12 months after birth. Duration of breastfeeding in the first year was evaluated as a continuous variable (age in months at cessation of breastfeeding, or "12 months" if still breastfeeding after 1 year).

### Statistical Analysis

The distribution of covariates across categories of beverage intake was examined by univariate analysis using the $\chi^2$ test for binary variables or 1-way analysis of variance for continuous variables. Multivariable regression was used to investigate associations between maternal sweetened beverage intake during pregnancy and infant BMI *z* score (linear regression) or overweight (logistic regression) at 1 year of age. Models included both types of sweetened beverages and were adjusted for infant sex and potential confounders, including known or suspected risk factors for weight gain in addition to those identified in univariate analyses. Results are presented as crude and adjusted β estimates (βs and adjusted βs [aβs]) and odds ratios (ORs and adjusted ORs [aORs]) with 95% CIs. Stratified analyses were planned a priori to determine whether ASB associations differed by infant sex, maternal overweight, or breastfeeding duration; intermediate ASB intake categories were combined to conserve power, and heterogeneity across strata was evaluated by a likelihood ratio test comparing regression models with and without interaction terms. All tests were 2-sided, and statistical significance was considered at $P < .05$. Analyses were conducted for mother-infant dyads with complete data (n = 2413) and confirmed in the full cohort following multiple imputation of missing data (N = 3033). Multiple imputation (20 imputed data sets) was performed with fully conditional specification (chained equations) using all essential covariates and the following auxiliary variables: study site, gestational age, maternal age, and race/ethnicity. All analyses were performed using SAS version 9.4.

## Results

Among 2413 mother-infant dyads with complete data (eTable 1 in the Supplement), the mean (SD) maternal age was 32.5 (4.6) years, and the mean (SD) maternal BMI was 24.8 (5.4); 78.2% of mothers had a postsecondary degree, 7.9% smoked during pregnancy, and 5.8% had diabetes (4.4% developed gestational diabetes and 1.4% had preexisting diabetes). The mean (SD) infant BMI *z* score at 1 year of age was 0.19 (1.05), and 5.1% of infants were overweight. Overall, 29.5% of mothers consumed ASBs during pregnancy, including 5.1% who reported daily consumption, while 77.2% consumed SSBs, including 23.4% who reported daily consumption (**Table 1**).

The distribution of covariates across categories of sweetened beverage intake is shown in Table 1. Both ASB and SSB consumption were associated with maternal smoking, higher maternal BMI, lower maternal diet quality, and shorter breastfeeding duration. Consumption of ASBs was further associated with earlier introduction of solid foods, while SSB consumption was associated with lower maternal education and higher total energy intake. Despite significantly reduced SSB consumption, women who frequently consumed ASBs did not have lower total energy intake. Women with diabetes had higher ASB intake and lower SSB intake.

Associations of maternal consumption of ASBs and SSBs during pregnancy with infant BMI *z* scores at 1 year of age are shown in **Table 2** and **Figure**, A. The highest BMI *z* scores were observed among infants born to mothers reporting daily consumption of ASBs (mean [SD], 0.55 [1.01] vs 0.17 [1.04] for daily consumers vs nonconsumers; β, 0.37; 95% CI, 0.18-0.57). This association was attenuated after adjusting for maternal BMI and further attenuated after adjusting for additional covariates (total maternal energy intake, diet quality, smoking, diabetes, education, infant sex, birth weight, breastfeeding duration, and introduction of solid foods). In fully adjusted models, daily ASB consumption remained significantly associated with higher infant BMI *z* scores (aβ, 0.22; 95% CI, 0.02-0.41). Consumption of SSBs was not associated with infant BMI *z* scores (β, 0.11; 95% CI, −0.02 to 0.23; aβ, 0.07; 95% CI, −0.06 to 0.19 for daily consumers vs nonconsumers). These results were confirmed following multiple imputation of missing data (Table 2), and similar patterns of association were found for weight-for-length *z* scores (eTable 2 in the Supplement).

Comparable results were found for the dichotomous outcome of infant overweight at 1 year of age (**Table 3**; Figure, B). The highest incidence of overweight was observed among infants born to mothers reporting daily consumption of ASBs (10.4% vs 4.5% among daily consumers vs nonconsumers; OR,

Table 1. Maternal and Infant Characteristics According to Maternal Consumption of ASBs and SSBs During Pregnancy

| Characteristic | Frequency of Beverage Consumption, Mean (SD) | | | | *P* Value[a] |
|---|---|---|---|---|---|
| | <1/mo | ≤1/wk | 2-6/wk | ≥1/d | |
| ASBs | | | | | |
| Total, No. (%) | 1702 (70.5) | 404 (16.7) | 185 (7.7) | 122 (5.1) | |
| Maternal age, y | 32.4 (4.6) | 32.7 (4.7) | 32.0 (4.3) | 32.5 (4.7) | .32 |
| Maternal BMI | 24.2 (5.0) | 25.5 (5.5) | 26.5 (6.6) | 28.0 (6.5) | <.001 |
| Maternal diet quality, HEI score/100 | 73.1 (8.6) | 73.9 (7.7) | 72.2 (9.0) | 71.6 (7.7) | .02 |
| Maternal energy intake, cal/d | 2016 (706) | 1969 (681) | 1985 (699) | 2050 (877) | .57 |
| Infant birth weight, g | 3461 (480) | 3463 (468) | 3395 (553) | 3482 (409) | .33 |
| Infant gestational age, wk | 39.2 (1.4) | 39.2 (1.4) | 39.1 (1.5) | 39.0 (1.3) | .18 |
| Breastfeeding duration in first year, mo | 9.1 (4.0) | 8.7 (4.0) | 7.9 (4.2) | 6.7 (4.6) | <.001 |
| Introduction of solid foods <4 mo, No. (%) | 305 (17.9) | 79 (19.6) | 39 (21.1) | 34 (27.9) | .04 |
| Maternal smoking in pregnancy, No. (%) | 113 (6.6) | 29 (7.2) | 25 (13.5) | 24 (19.7) | <.001 |
| Maternal diabetes in pregnancy, No. (%)[b] | 78 (4.6) | 26 (6.4) | 16 (8.6) | 21 (17.2) | <.001 |
| Maternal postsecondary education, No. (%) | 1335 (78.4) | 326 (80.7) | 136 (73.5) | 89 (73.0) | .10 |
| Maternal SSB consumption, No. (%) | 1337 (78.6) | 324 (80.2) | 134 (72.4) | 68 (55.7) | <.001 |
| SSBs | | | | | |
| Total, No. (%) | 550 (22.8) | 629 (26.1) | 670 (27.8) | 564 (23.4) | |
| Maternal age, y | 33.5 (4.3) | 31.9 (4.6) | 31.8 (4.7) | 32.8 (4.7) | <.001 |
| Maternal BMI | 24.3 (5.4) | 24.4 (4.9) | 25.1 (5.7) | 25.2 (5.7) | .003 |
| Maternal diet quality, HEI score/100 | 75.8 (7.5) | 74.2 (7.5) | 72.1 (8.9) | 70.3 (8.9) | <.001 |
| Maternal energy intake, cal/d | 1906 (641) | 1905 (626) | 2030 (693) | 2194 (837) | <.001 |
| Infant birth weight, g | 3439 (462) | 3449 (472) | 3479 (499) | 3460 (487) | .49 |
| Infant gestational age, wk | 39.2 (1.3) | 39.2 (1.4) | 39.2 (1.4) | 39.2 (1.3) | .69 |
| Breastfeeding duration in first year, mo | 9.1 (3.9) | 9.2 (3.9) | 8.9 (4.1) | 8.0 (4.3) | <.001 |
| Introduction of solid foods <4 mo, No. (%) | 91 (16.5) | 114 (18.1) | 136 (20.3) | 116 (20.6) | .25 |
| Maternal smoking in pregnancy, No. (%) | 20 (3.6) | 40 (6.4) | 45 (6.7) | 86 (15.2) | <.001 |
| Maternal diabetes in pregnancy, No. (%)[b] | 46 (8.4) | 30 (4.8) | 36 (5.4) | 29 (5.1) | .04 |
| Maternal postsecondary education, No. (%) | 470 (85.5) | 501 (79.7) | 512 (76.4) | 403 (71.5) | <.001 |
| Maternal ASB consumption, No. (%) | 185 (33.6) | 181 (28.8) | 180 (26.9) | 165 (29.3) | .07 |

Abbreviations: ASB, artificially sweetened beverage; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HEI, Healthy Eating Index; SSB, sugar-sweetened beverage.

[a] Comparisons by $\chi^2$ test for binary variables or by analysis of variance for continuous variables.

[b] Maternal diabetes includes preexisting and gestational diabetes.

Table 2. Maternal Consumption of ASBs and SSBs During Pregnancy and Infant BMI *z* Score at 1 Year

| Maternal Beverage Consumption | Infant BMI *z* Score (n = 2413) | | β (95% CI) | | | |
|---|---|---|---|---|---|---|
| | No. | Mean (SD) | Crude (n = 2413) | Adjusted for Maternal BMI (n = 2413) | Adjusted for Maternal BMI and Covariates[a] (n = 2413) | Adjusted for Maternal BMI and Covariates and Multiple Imputation (N = 3033)[a,b] |
| ASBs | | | | | | |
| <1/mo | 1702 | 0.17 (1.04) | 0 [Reference] | 0 [Reference] | 0 [Reference] | 0 [Reference] |
| ≤1/wk | 404 | 0.13 (1.04) | −0.04 (−0.15 to 0.08) | −0.07 (−0.18 to 0.05) | −0.08 (−0.19 to 0.03) | −0.07 (−0.18 to 0.04) |
| 2-6/wk | 185 | 0.29 (1.06) | 0.13 (−0.03 to 0.29) | 0.07 (−0.09 to 0.23) | 0.04 (−0.12 to 0.20) | 0.02 (−0.13 to 0.17) |
| ≥1/d | 122 | 0.55 (1.01) | 0.37 (0.18 to 0.57)[c] | 0.28 (0.09 to 0.47)[c] | 0.22 (0.02 to 0.41)[c] | 0.20 (0.02 to 0.38)[c] |
| SSBs | | | | | | |
| <1/mo | 550 | 0.21 (1.07) | 0 [Reference] | 0 [Reference] | 0 [Reference] | 0 [Reference] |
| ≤1/wk | 629 | 0.13 (1.03) | −0.05 (−0.17 to 0.07) | −0.06 (−0.17 to 0.06) | −0.05 (−0.17 to 0.07) | −0.05 (−0.16 to 0.07) |
| 2-6/wk | 670 | 0.15 (1.05) | −0.03 (−0.15 to 0.09) | −0.06 (−0.17 to 0.06) | −0.04 (−0.16 to 0.07) | −0.04 (−0.16 to 0.07) |
| ≥1/d | 564 | 0.29 (1.02) | 0.11 (−0.02 to 0.23) | 0.08 (−0.04 to 0.20) | 0.07 (−0.06 to 0.19) | 0.05 (−0.07 to 0.17) |

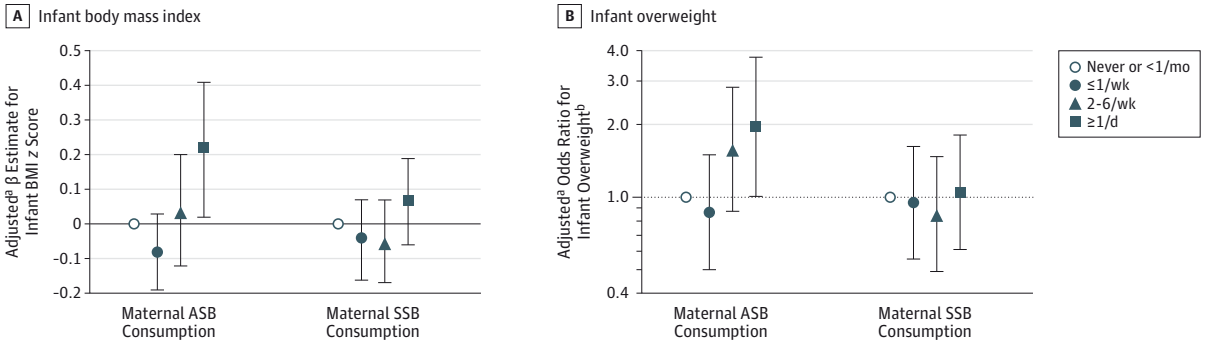
Abbreviations: ASBs, artificially sweetened beverages; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); SSBs, sugar-sweetened beverages.

[a] Covariates include maternal total energy intake, Healthy Eating Index score, maternal postsecondary education, maternal smoking and diabetes during pregnancy, breastfeeding duration, infant sex, and introduction of solid foods before 4 months. All models are mutually adjusted for both beverage types.

[b] Multiple imputation of missing outcome and covariate data with fully conditional specification.

[c] Significant confidence intervals.

Figure. Maternal Consumption of Artificially Sweetened Beverages (ASBs) and Sugar-Sweetened Beverages (SSBs) and Infant Body Composition at 1 Year of Age for 2413 Mother-Infant Dyads




BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared). Error bars indicate 95% CIs.

[a] Mutually adjusted for both types of beverages, maternal total energy intake, Healthy Eating Index score, maternal postsecondary education, maternal smoking and diabetes during pregnancy, breastfeeding duration, infant sex, and introduction of solid foods before 4 months.

[b] Overweight in infants was defined as a BMI *z* score exceeding the 97th percentile for age and sex.

Table 3. Maternal Consumption of ASBs and SSBs During Pregnancy and Infant Overweight[a] at 1 Year

| | Infant Overweight (n = 2413) | | Odds Ratio (95% CI) | | | |
|---|---|---|---|---|---|---|
| Maternal Beverage Consumption | Total No. | No. (%) | Crude (n = 2413) | Adjusted for Maternal BMI (n = 2413) | Adjusted for Maternal BMI and Covariates[b] (n = 2413) | Adjusted for Maternal BMI and Covariates and Multiple Imputation (N = 3033)[b,c] |
| ASBs | | | | | | |
| <1/mo | 1702 | 77 (4.5) | 1 [Reference] | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| ≤1/wk | 404 | 17 (4.2) | 0.93 (0.55-1.60) | 0.88 (0.52-1.52) | 0.86 (0.50-1.49) | 0.93 (0.58-1.50) |
| 2-6/wk | 185 | 15 (8.1) | 1.85 (1.04-3.30)[d] | 1.68 (0.93-3.01) | 1.57 (0.87-2.83) | 1.41 (0.82-2.40) |
| ≥1/d | 122 | 13 (10.7) | 2.43 (1.30-4.55)[d] | 2.08 (1.09-3.96)[d] | 1.94 (1.00-3.76)[d] | 2.19 (1.23-3.88)[d] |
| SSBs | | | | | | |
| <1/mo | 550 | 31 (5.6) | 1 [Reference] | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| ≤1/wk | 629 | 27 (4.3) | 0.84 (0.49-1.44) | 0.83 (0.49-1.43) | 0.85 (0.49-1.46) | 1.03 (0.62-1.71) |
| 2-6/wk | 670 | 32 (4.8) | 0.92 (0.55-1.53) | 0.88 (0.53-1.48) | 0.94 (0.56-1.61) | 1.03 (0.62-1.71) |
| ≥1/d | 564 | 32 (5.7) | 1.08 (0.65-1.80) | 1.03 (0.62-1.73) | 1.04 (0.60-1.80) | 1.24 (0.76-2.01) |

Abbreviations: ASBs, artificially sweetened beverages; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); SSBs, sugar-sweetened beverages.

[a] Overweight in infants was defined as a BMI *z* score exceeding the 97th percentile for age and sex.

[b] Covariates include maternal total energy intake, Healthy Eating Index score, maternal postsecondary education, maternal smoking and diabetes during pregnancy, breastfeeding duration, infant sex, and introduction of solid foods before 4 months. All models are mutually adjusted for both beverage types.

[c] Multiple imputation of missing outcome and covariate data with fully conditional specification.

[d] Significant confidence intervals.

2.43; 95% CI, 1.30-4.55). As with infant BMI *z* score, these associations were attenuated but remained significant after adjusting for maternal BMI and additional covariates (aOR, 1.94; 95% CI, 1.00-3.76). Maternal SSB intake was not associated with infant overweight (OR, 1.08; 95% CI, 0.65-1.08; aOR, 1.04; 95% CI, 0.60-1.80 for daily consumers vs nonconsumers).

Stratified analyses were conducted to explore whether the observed associations of maternal ASB consumption and infant BMI differed according to breastfeeding duration, infant sex, or maternal BMI (**Table 4**). In this exploratory analysis, results suggest that effects from ASB consumption on infant overweight were confined to those who were not breastfed for at least 6 months (aOR, 2.58; 95% CI, 1.10-6.07 for daily ASB consumption compared with aOR, 1.07; 95% CI, 0.31-3.67 for infants breastfed >6 months; *P* for interaction = .09). Effects of ASBs also differed by sex, with effects found only in male infants (aOR, 3.07; 95% CI, 1.41-6.69 in male infants compared with aOR, 0.45; 95% CI, 0.09-2.33 in female infants; *P* for interaction = .02). The effect of maternal ASB consumption on infant BMI *z* score was similar among normal-weight (aOR, 2.21; 95% CI, 0.81-6.06) and overweight (aOR, 1.96; 95% CI, 0.81-4.76) mothers (*P* for interaction = .35).

## Discussion

Our findings in the population-based CHILD birth cohort indicate that maternal consumption of ASBs during pregnancy

Table 4. Maternal Consumption of ASBs During Pregnancy and Infant BMI Stratified By Maternal Prepregnancy Weight Status, Infant Sex, or Breastfeeding Duration

| Maternal ASB Consumption | Infant BMI *z* Score | | | Infant Overweight[a] | |
|---|---|---|---|---|---|
| | No. | Mean (SD) | Adjusted β (95% CI)[b] | No. (%) | Adjusted OR (95% CI)[b] |
| Prepregnancy weight status | | | | | |
| Normal-weight mothers | | | | | |
| <1/mo | 1147 | 0.09 (1.04) | 0 [Reference] | 40 (3.5) | 1 [Reference] |
| ≤6/wk | 336 | 0.08 (1.05) | −0.05 (−0.17 to 0.08) | 17 (5.1) | 1.32 (0.73 to 2.40) |
| ≥1/d | 47 | 0.38 (1.02) | 0.16 (−0.14 to 0.46) | 5 (10.6) | 2.21 (0.81 to 6.06) |
| Overweight mothers[c] | | | | | |
| <1/mo | 555 | 0.32 (1.04) | 0 [Reference] | 37 (6.7) | 1 [Reference] |
| ≤6/wk | 253 | 0.31 (1.03) | −0.05 (−0.20 to 0.10) | 15 (5.9) | 0.83 (0.44 to 1.56) |
| ≥1/d | 75 | 0.67 (1.00) | 0.28 (0.02 to 0.53) | 8 (10.7) | 1.96 (0.81 to 4.76) |
| *P* value for interaction[d] | | | .92 | | .35 |
| Infant sex | | | | | |
| Female infants | | | | | |
| <1/mo | 807 | 0.16 (1.04) | 0 [Reference] | 37 (4.6) | 1 [Reference] |
| ≤6/wk | 269 | 0.12 (0.96) | −0.09 (−0.23 to 0.05) | 8 (3.0) | 0.59 (0.26 to 1.30) |
| ≥1/d | 51 | 0.42 (0.85) | 0.08 (−0.21 to 0.37) | 2 (3.9) | 0.45 (0.09 to 2.33) |
| Male infants | | | | | |
| <1/mo | 895 | 0.17 (1.04) | 0 [Reference] | 40 (4.5) | 1 [Reference] |
| ≤6/wk | 320 | 0.23 (1.11) | 0.01 (−0.12 to 0.14) | 24 (7.5) | 1.63 (0.95 to 2.79) |
| ≥1/d | 71 | 0.65 (1.11) | 0.30 (0.04 to 0.56) | 11 (15.5) | 3.07 (1.41 to 6.69) |
| *P* value for interaction[d] | | | .29 | | .02 |
| Breastfeeding duration | | | | | |
| Breastfed <6 mo | | | | | |
| <1/mo | 365 | 0.44 (1.05) | 0 [Reference] | 30 (8.2) | 1 [Reference] |
| ≤6/wk | 153 | 0.39 (1.03) | −0.06 (−0.26 to 0.14) | 9 (5.9) | 0.66 (0.30 to 1.46) |
| ≥1/d | 54 | 0.78 (1.02) | 0.32 (0.02 to 0.63) | 10 (18.5) | 2.58 (1.10 to 6.07) |
| Breastfed ≥6 mo | | | | | |
| <1/mo | 1337 | 0.09 (1.03) | 0 [Reference] | 47 (3.5) | 1 [Reference] |
| ≤6/wk | 436 | 0.11 (1.04) | −0.04 (−0.15 to 0.07) | 23 (5.3) | 1.38 (0.82 to 2.32) |
| ≥1/d | 68 | 0.37 (0.98) | 0.14 (−0.12 to 0.39) | 3 (4.4) | 1.07 (0.31 to 3.67) |
| *P* value for interaction[d] | | | .75 | | .09 |

Abbreviations: ASBs, artificially sweetened beverages; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); OR, odds ratio.

[a] Overweight in infants was defined as a BMI *z* score exceeding the 97th percentile for age and sex.

[b] Covariates include maternal sugar-sweetened beverage consumption, total energy intake, Healthy Eating Index score, maternal postsecondary education, maternal smoking and diabetes during pregnancy, breastfeeding duration, infant sex, and introduction of solid foods before 4 months.

[c] Overweight in women was defined as a BMI greater than 25.

[d] *P* values determined by likelihood ratio test comparing regression models with vs without interaction terms.

is associated with higher infant BMI and an increased risk of infant overweight at 1 year of age. Infant birth weight was not affected, suggesting that maternal ASB consumption influenced postnatal weight gain rather than fetal growth. Compared with no ASB consumption during pregnancy, daily ASB consumption was associated with a 0.2-unit increase in infant BMI *z* score and a 2-fold increased risk of infant overweight at 1 year. These associations were independent of maternal BMI, diabetes, total energy intake, diet quality, and other known obesity risk factors. No comparable associations were identified for SSB consumption.

To our knowledge, this is the first human study to evaluate the association of maternal sweetened beverage consumption during pregnancy and infant BMI. Increasing evidence shows that a predisposition to metabolic disease may be acquired or "programmed" early in life.[4,5] This has been demonstrated in both human and animal studies in which offspring of mothers with high caloric intake are at increased risk of developing metabolic conditions later in life.[28,29] Interestingly, rodent studies have shown that maternal NNS consumption in pregnancy also predisposes offspring to obesity, with NNS-exposed offspring exhibiting stronger preferences for sweet foods, increased postnatal weight gain, altered lipid profiles, and increased insulin resistance in adulthood.[30-32] To our knowledge, our results provide the first human evidence to support these findings, suggesting that prenatal NNS exposure may contribute to infant weight gain and early childhood obesity.

Our study confirms previous research showing that ASB consumption is associated with obesity, diabetes, smoking, and poor diet quality,[33,34] all of which are established maternal risk factors for obesity in offspring.[35,36] Maternal ASB consumption was also correlated with 2 additional risk factors for childhood obesity: shorter breastfeeding duration and earlier introduction of solid foods.[36,37] Importantly, controlling for these

factors did not explain the observed association between maternal consumption of ASBs during pregnancy and infant BMI at 1 year of age, suggesting an independent effect of in utero exposure to artificial sweeteners.

We examined effects from ASB consumption in several predefined subgroups. As expected, overweight mothers reported higher ASB consumption and their infants had higher BMI *z* scores on average; however, effects from ASB consumption were similar in normal-weight and overweight mothers. Our sex-stratified analyses revealed that effects from ASB consumption were only seen in male infants, consistent with findings by Collison et al[31] in which aspartame exposure commencing in utero was associated with excess weight gain in male but not female mice. Sex specificity has been reported for other obesogenic exposures in early life, with males being disproportionately affected by maternal smoking,[38] antibiotic exposure,[39,40] and formula feeding.[41] This sexual dimorphism may be related to sex differences in gut microbiota,[42] which contribute to host metabolism and weight gain.[43] Our findings may support this intriguing hypothesis because NNSs have been shown to modify gut microbiota,[15] although this has not yet been demonstrated for prenatal NNS exposure in humans.

We also performed stratified analyses according to breastfeeding duration because a recent study showed that NNSs are commonly detected in human milk,[44] indicating another possible route of early-life NNS exposure. However, we found that effects from ASB consumption were confined to infants who were breastfed for shorter durations, indicating that NNS exposure through lactation likely does not explain the observed associations with infant BMI. In fact, our results suggest that breastfeeding may mitigate the potentially adverse effects of NNS exposure in utero, although we were underpowered to definitively test this interaction and we lacked information on post partum NNS consumption.

Interestingly, in contrast to our findings for ASB consumption, we found that SSB consumption during pregnancy was not associated with infant BMI. These results support the hypothesis that NNSs are responsible for the observed effects rather than other beverage ingredients or additives, such as caffeine or artificial coloring. There is a paucity of human data on the effects of SSB intake during pregnancy,[45] although animal studies indicate that high maternal sucrose or fructose intake have adverse metabolic effects on offspring.[29,45] Further human research is warranted to explore the potential metabolic effects of maternal SSB consumption during pregnancy.

The major strengths of our study are the standardized prospective evaluation of maternal sweetened beverage consumption during pregnancy and the objective measurement of infant BMI in a large population-representative cohort of mother-infant dyads. A limitation of our study is the potential for measurement error in self-reported dietary outcomes because our FFQ has not been specifically validated for beverage intakes. We also could not distinguish between different types of NNSs or account for NNSs in solid foods. Although misclassification is always a concern with FFQs for dietary assessment, these tools generally differentiate well between low and high consumers, and any misclassification is expected to be nondifferential, leading to an underestimation of true effect estimates. However, one cannot rule out differential reporting of consumption of ASBs and SSBs between normal-weight and overweight or obese mothers. Another potential limitation concerns the uncertainty about the best anthropometric measure of body fat in infants, with Canadian authorities favoring weight-for-length over BMI *z* scores for infants younger than 2 years.[27] At the same time, World Health Organization and European authorities promote the use of BMI as defined by the World Health Organization Multicenter Growth Reference Study[26] for all ages.[46] Moreover, a large (N = 15 488) longitudinal North American study[47] of both measures at 1, 6, 12, 18, and 24 months of age has confirmed their equivalence as predictors of obesity risk at school entry. Finally, as with all observational studies, we cannot exclude the possibility that our results may be influenced by residual and unmeasured confounding factors, although we clinical for a number of important factors, including maternal BMI, smoking, education, total energy intake, diet quality, breastfeeding duration, and early introduction of solid foods.

## Conclusions

To our knowledge, our results provide the first human evidence that artificial sweetener consumption during pregnancy may increase the risk of early childhood overweight. Given the current epidemic of childhood obesity[1,2] and the widespread consumption of artificial sweeteners,[7,10] further research is warranted to replicate our findings in other cohorts, evaluate specific NNS and longer-term outcomes, and study the underlying biological mechanisms.

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