

ORIGINAL ARTICLE

Is consumption of sugar-sweetened soft drinks during pregnancy associated with birth weight?

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Funding information

NIH/NINDS, Grant/Award Number: UO1 NS047537-06A1. UO1 NS 047537-01. Ministry of Education and Research, NIH/NIEHS, Grant/Award Number: NO1-ES-75558. Norwegian Ministry of Health, Innlandet Hospital Trust and the Southern and Eastern Norway Regional Health Authority

Abstract

In Norway, there were parallel increases and subsequent decreases in birth weight (BW) and consumption of sugar-sweetened carbonated soft drinks (SSC) during the period 1990–2010, and by an ecological approach, we have suggested that the relationship was causal. The objective of this study was to examine if such a relationship was present in a prospectively followed cohort of pregnant women. The study population included 62,494 term singleton mother–infant dyads in the Norwegian Mother and Child Cohort Study (MoBa), a national prospective cohort study in Norway from 1999 to 2008. The association between SSC consumption and BW was assessed using multiple regression analyses with adjustment for potential confounders. Each 100 ml intake of SSC was associated with a 7.8 g (95% confidence interval [CI]: –10.3 to –5.3) decrease in BW, a decreased risk of BW > 4,500 g (odds ratio [OR]: 0.94, 95% CI: 0.90 to 0.97) and a near significantly increased risk of BW < 2,500 g (OR: 1.05, 95% CI: 0.99 to 1.10). The negative association with SSC consumption was aggravated by smoking, lack of exercise, and obesity. For mothers with gestational diabetes mellitus, we observed an increased risk of BW > 4,500 g (OR: 1.18, 95% CI: 1.00 to 1.39) and a trend towards significant increase in mean BW (25.1 g, 95% CI: –2.0 to 52.2) per 100 ml SSC. Our findings suggest that increasing consumption of rapidly absorbed sugar from SSC had opposite associations with BW in normal pregnancies and pregnancies complicated by gestational diabetes mellitus.

KEYWORDS

birth weight, exercise, gestational diabetes, MoBa, smoking, sugar-sweetened beverages

1 | INTRODUCTION

The prevalence of overweight and obesity (OWOB) among children and adults has reached alarming proportions in high, middle, and low income countries (Ng et al., 2014). High maternal body mass index (BMI), large pregnancy weight gains, and high maternal blood glucose levels are associated with increased risk of giving birth to large infants (Clausen et al., 2005, HAPO Study Cooperative Research Group, 2009), and high birth weight (BW) is associated with OWOB later in life (Yu et al., 2011). Insights into epigenetic mechanisms and fetal

programming may imply that preventive measures before or during pregnancy may make important contributions to curtail the future risk of OWOB (Hanson & Gluckman, 2014).

In Norway, there were parallel increases in mean BW and proportion of large newborns and per capita consumption of sugar-sweetened carbonated soft drinks (SSC) from 1990 to 2000 and subsequent parallel decreases to 1990 levels by 2010. A temporary 50% increase in the national consumption of SSC was associated timewise with a 50% increase in the proportion of babies with BW above 4,500 g (Grundt, Nakling, Eide, & Markestad, 2012). Similar national trends in BW and

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consumption of sugar-sweetened soft drinks have been reported for USA, Denmark, Australia, and Sweden (**Supplementary Appendix**; Supplementary Information 1), but the causes of possible relationships have not been addressed.

A previous study compared data from a large regional pregnancy register, where the time trends for BW were equal to the national Norwegian trends, and simultaneous national statistics on nutrition and exercise, and suggested that the relationship between SSC and BW was positive and causal (Grundt et al., 2012). The aim of this study was to examine if the same relationship was also present in a large pregnancy cohort where detailed information on maternal diet, including consumption of SSC and other sources of sugar, and relevant confounders were collected prospectively.

2 | PARTICIPANTS AND METHODS

2.1 | Participants

The Norwegian Mother and Child Cohort Study (MoBa) is a prospective population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health (Magnus et al., 2006). From 1999 to 2008, pregnant women from all over Norway were recruited by postal invitation prior to routine ultrasound screening at 17–19 weeks of pregnancy. Consent was obtained for 40.6% of all pregnancies (109,258 infants). Data were collected from the Medical Birth Registry of Norway (MBRN) and from questionnaires completed by the mothers at approximately 15 (Q1), 22 (Q2: a Food Frequency Questionnaire), and 30 weeks (Q3) of pregnancy, and 6 months after delivery (Q4). The current study was based on version seven of the quality-assured data files which was released for research on June 16, 2012. Relevant variables were provided by the MoBa data administration, that is, sociodemographic data, parental weight and height, pregnancy complications, maternal diet, exercise and other exposures during pregnancy, and anthropometric measures of the newborn. Details on variable definitions and data sources are presented in the **Supplementary Appendix** (Supplementary Table A).

Prerequisites for study eligibility were birth of live born singleton babies, completed questionnaires (after the introduction of a new Q2 version in March 2002), and contributing data from the MBRN. A total of 75,075 mother–child dyads fulfilled these criteria, but among them, we selected term born infants without malformations born to mothers without extreme energy intakes (<4.5 MJ or >20 MJ per day) because they were probably erroneously recorded, pre-existing diabetes mellitus

or eating disorders, that is, 62,494 mother–infant dyads (83.2%, **Figure 1** and **Tables 1 and 2**). Due to missing information on relevant covariates (**Figure 1**), 55,774 of these cases (89.3%) were included in the multiple regression analyses (**Tables 3 and 4**). The participants were mainly of white Caucasian ethnicity; only 6.2% had a mother tongue other than Norwegian, and on the basis of the information about language, most of them were Caucasians from European/Western countries.

2.2 | Details of ethics approval

MoBa obtained a license from the Norwegian Data Inspectorate (01/4325), which was extended in 2012, and approved by the Regional Ethical Committee for Medical Research on September 1, 1996 (S-95113) and May 20, 1998 (S-97045).

2.3 | Maternal health and family characteristics

The MoBa questionnaires contained data on socioeconomic factors, maternal pre-pregnancy and pregnancy health and behaviors, paternal health and behaviors, and maternal and newborn outcomes. The MBRN data included information on prior pregnancies, pre-pregnancy health, pregnancy complications, and outcomes.

2.4 | Dietary variables

Intakes of sugar-sweetened and artificially-sweetened beverages and of their respective carbonated subgroups (SSC and ASC) were reported in the Q1, Q2, and Q3 questionnaires, and mean intakes (ml per day) were calculated for the entire pregnancy. Due to the parallel trends of BW and SSC consumption in Norway since 1990 (Grundt et al., 2012), we considered SSC intake to be of special interest and grouped the women into low (<100 ml/day), medium (≥ 100 and <500 ml/day) and high (≥ 500 ml/day) SSC consumers.

Assessments of other food, nutrient, and energy intakes during the pregnancy were based on data from a semiquantitative food frequency questionnaire specifically developed and validated for pregnant women in MoBa (Q2 at 22 weeks of pregnancy, where average intakes during the first half of pregnancy were reported, described in detail elsewhere) (Brantsaeter, Haugen, Alexander, & Meltzer, 2008, Meltzer, Brantsaeter, Ydersbond, Alexander, & Haugen, 2008). Energy intake from protein, fat, carbohydrates, added sugar, and SSC, and intake of micronutrients (vitamins and minerals) was calculated from food frequencies using FoodCalc (Lauritsen, 2002) and the Norwegian Food Composition Table (Rimestad et al., 2001). “Added sugar” was defined as industrially processed

Key messages

- Increasing consumption of sugar-sweetened carbonated beverages during pregnancy was associated with decreasing birth weight. The association was stronger for women who were overweight or obese, physically inactive or smoked.
- In pregnancies complicated by gestational diabetes mellitus, there was an opposite nonsignificant trend of increasing birth weight with increasing consumption of sugar-sweetened carbonated beverages.
- The results suggest that the association between consumption of rapidly absorbed sugar and birth weight may vary dependent on glucose tolerance and other modifiers of fetal growth.

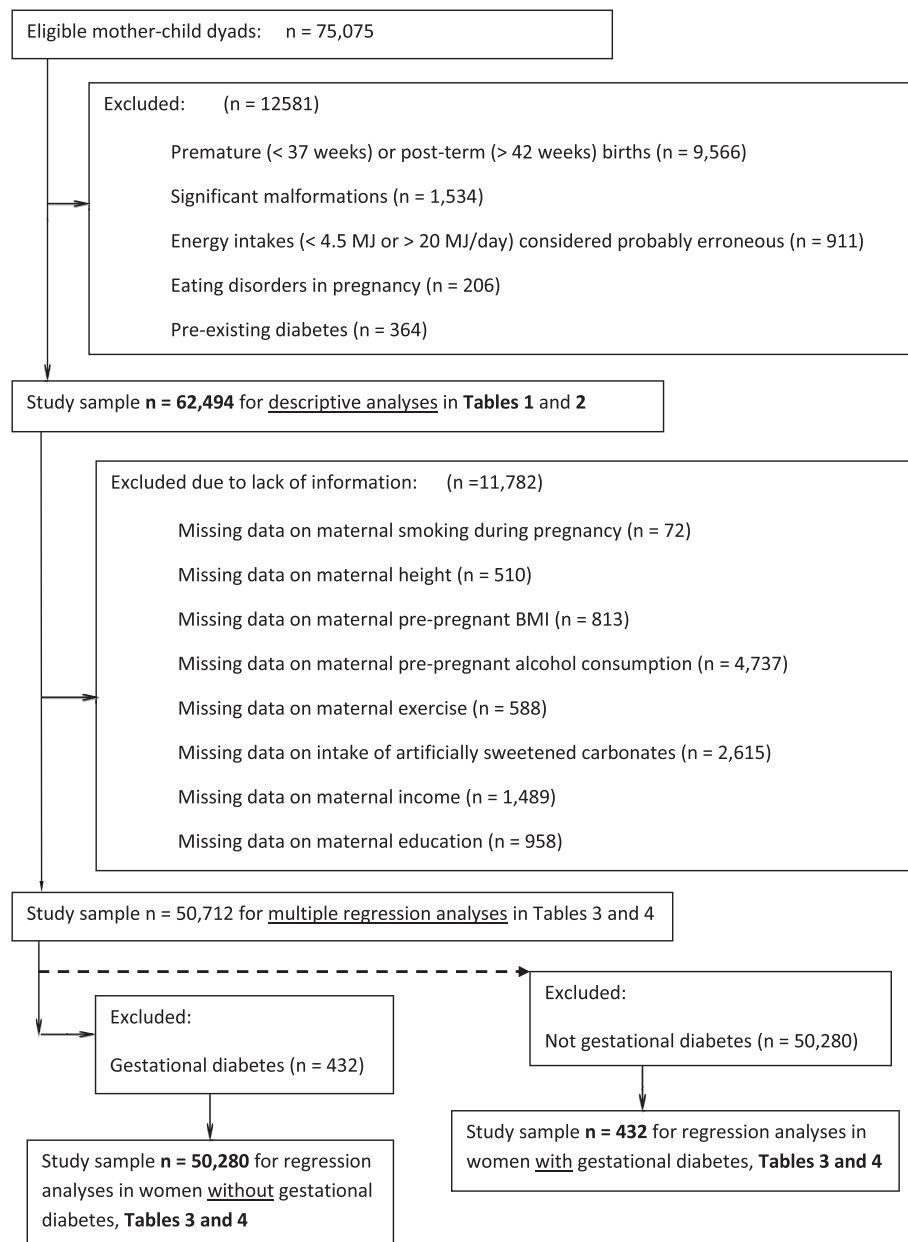


FIGURE 1 Flowchart of inclusions

sugars (e.g., glucose, sucrose, and fructose) added to foods and beverages such as candy, biscuits, juices, cordials, and soft drinks.

For descriptive purposes, selected food items assumed to reflect overall dietary quality, and dietary patterns were combined into group variables on the basis of the assumption that high consumption of vegetables, fruit, and fish indicated a healthy diet, and high consumption of pizza/pasta, sweet and salty snacks, and processed meat indicated an unhealthy diet. We also included three dietary patterns derived by principal component factor analysis and described as prudent (healthy), Western (unhealthy), and traditional (intermediate) patterns (see Supporting Information 2 and prior description (Englund-Ogge et al., 2014).

2.5 | Physical activity

Leisure physical activity was reported as frequency per month or week for 13 different exercise activities at weeks 15 (Q1) and 30

(Q3), and “exercise during pregnancy” was defined as the mean of the two combined scores. On the basis of the combined frequency score, we also dichotomized exercise into “less than weekly” or “weekly or more”. Previous validation of the exercise data in week 15 showed that reported frequencies were significantly associated with objectively measured physical activity (motion sensor) (Brantsaeter et al., 2010).

2.6 | Newborn characteristics

Gestational age (GA) at birth was generally based on ultrasound assessment at 17–19 weeks of pregnancy (98.3%). BW, crown-head length, and head circumference were measured immediately after birth by midwives. High BW (HBW) was defined as >4,500 g and low BW (LBW) as <2,500 g, large for gestational age (LGA) as a BW above the 90th percentile and small for

TABLE 1 Parental and new-born characteristics of 62,494 participants in the Norwegian Mother and Child Cohort Study 2002–2008, in groups by maternal daily intake of sugar-sweetened carbonated beverages

Characteristic ^a	Maternal daily intake of SSC			p-value ^a
	<100 ml (n = 47,706)	100–500 ml (n = 13,067)	≥500 ml (n = 1,721)	
Mother				
Age, years; mean (SD)	30.7 (4.3)	28.9 (4.5)	27.9 (5.0)	<.001
Height, cm; mean (SD)	168.3 (5.9)	167.9 (6.0)	167.3 (6.1)	<.001
Pre-pregnancy BMI, kg/m ² ; mean (SD)	23.79 (4.04)	24.38 (4.43)	24.94 (4.98)	<.001
Pregnancy weight gain, kg; mean (SD)	14.72 (5.60)	15.00 (6.18)	14.86 (7.38)	<.001
Exercise, times/ week; mean (SD)	2.68 (0.95)	2.37 (0.93)	2.15 (0.95)	<.001
Pre-pregnancy BMI groups; %				<.001
< 18.5 kg/m ² : underweight	2.7	3.4	4.0	
18.5–24.9 kg/m ² : normal weight	68.6	60.9	56.0	
25.0–29.9 kg/m ² : overweight	20.6	24.6	24.9	
≥ 30 kg/m ² : obese	8.0	11.1	20.9	
Primipara; %	44.4	46.4	45.0	<.001
Married or cohabitating; %	97.6	96.4	93.3	<.001
Teenage pregnancy; %	0.4	1.5	3.2	<.001
Education >12 years; %	75.8	58.1	33.8	<.001
High income ^b ; %	42.6	27.4	18.8	<.001
Exercise ≥ once per week; %	65.5	52.6	41.1	<.001
Smoking; %	9.1	18.4	37.8	<.001
Alcohol pre-pregnancy				
> weekly; %	10.1	6.3	4.3	<.001
≥5 units per occasion; %	18.9	29.9	39.7	<.001
Hypertension, pre-existing; %	1.1	1.1	2.1	<.001
Preeclampsia; %	2.9	3.8	3.9	<.001
Gestational diabetes; %	1.0	0.6	0.9	<.01
Glycosuria; %	8.7	10.9	12.8	<.001
Spontaneous onset of labor; %	84.0	83.7	81.2	<.01
Father				
BMI father, kg/m ² ; mean (SD)	25.73 (3.22)	26.02 (3.38)	26.42 (3.91)	<.001
Smoking; %	16.1	25.8	38.0	<.001
Education >12 years; %	60.0	41.9	24.5	<.001
Newborn				
Gestational age, days; mean (SD)	280.1 (7.8)	279.9 (7.9)	279.2 (8.2)	<.001
Birth weight, g; mean (SD)	3,628 (470)	3,631 (480)	3,563 (479)	<.001
Birth length ^c , cm; mean (SD)	50.49 (1.93)	50.46 (1.96)	50.21 (2.04)	<.001
Birth head circ., cm; mean (SD)	35.34 (1.40)	35.36 (1.41)	35.26 (1.41)	.028
Ponderal index, kg/m ³ ; mean (SD)	28.13 (2.48)	28.19 (2.48)	28.06 (2.42)	.041
BW categories, %				<.001
BW < 2,500 g	0.6	0.8	1.6	
BW 2500–4500 g	95.6	95.2	95.9	
BW > 4,500 g	3.8	4.0	2.5	

Note. SSC = sugar-sweetened carbonated beverages; SD = standard deviation; BMI = body mass index; head circ = head circumference; BW = birth weight.

^aMeans are compared with one-way analysis of variance and percents with Pearson's chi-squared test: 58,532–62,494 subjects were included in the various analyses.

^b>300,000 NOK (approximately 36,000 USD/33,000 EUR);

^cCrown-heel length.

gestational age (SGA) as a BW less than the 10th percentile for GA according to Norwegian percentiles (Skjaerven, Gjessing, & Bakketeig, 2000). Newborn ponderal index was calculated as weight/length³.

2.7 | Statistical analyses

The characteristics of low, medium, and high SSC consumers were explored and compared using one-way analysis of variance (ANOVA)

TABLE 2 Maternal dietary intakes during pregnancy^a for 62,494 participants in the Norwegian Mother and Child Cohort Study 2002–2008, in groups by daily intake (ml) of sugar-sweetened carbonated beverages

Characteristic ^b	Maternal daily intake of SSC			p-value ^b
	<100 ml (n = 47,706) Mean (SD)	100–500 ml (n = 13,067) Mean (SD)	≥500 ml (n = 1,721) Mean (SD)	
Energy intake, kcal/day				
Total	2,249 (570)	2,436 (645)	2,779 (756)	<.001
Fat	704 (208)	760 (228)	803 (216)	<.001
Protein	348 (82)	349 (89)	349 (100)	.11
Carbohydrate ^c	1193 (336)	1321 (386)	1619 (481)	<.001
SSC	8 (10)	86 (42)	343 (155)	<.001
Energy/kg body weight	34.4 (10.7)	36.8 (12.3)	41.7 (15.1)	<.001
Protein/kg/day	5.31 (1.53)	5.26 (1.66)	5.22 (1.90)	<.01
Energy intake, % of total energy				
Fat	30.6 (4.5)	30.5 (4.3)	28.3 (4.8)	<.001
Protein	15.8 (2.0)	14.7 (2.0)	12.8 (2.1)	<.001
Carbohydrate ^c	53.4 (4.6)	54.6 (4.61)	58.6 (5.6)	<.001
Added sugar ^d	9.2 (3.7)	13.2 (4.8)	22.2 (8.0)	<.001
Added sugar (excluding SSC)	8.8 (3.6)	9.3 (4.6)	8.9 (6.8)	<.001
SSC	0.4 (0.5)	3.7 (2.0)	13.0 (6.2)	<.001
Selected beverage groups:				
SSC, ml/day	21 (25)	214 (104)	857 (388)	<.001
Juice and nectar, ml/day	166 (176)	191 (204)	187 (252)	<.001
ASC, ml/day	84 (209)	56 (144)	90 (264)	<.001
Alcohol ≥0.5 units/week (%)	1.7	1.7	1.6	.91
Markers of "healthy diet": ^e				
Fiber, g/day	31.4 (10.3)	29.6 (10.4)	28.8 (11.6)	<.001
Fish, g/day	42.6 (24.8)	37.8 (24.8)	34.5 (26.7)	<.001
Vegetables, g/day	168 (99)	141 (91)	131 (91)	<.001
Fruit, g/day	286 (195)	258 (198)	245 (226)	<.001
Markers of "unhealthy diet": ^f				
Pizza/pasta, g/day	48.3 (21.2)	53.5 (23.0)	58.4 (28.5)	<.001
Meat, processed, g/day	17.3 (10.1)	20.5 (10.7)	23.0 (13.2)	<.001
Sweet and salty snacks, g/day	55.4 (40.7)	69.6 (50.0)	83.7 (67.5)	<.001
Dietary patterns: principal components scores ^g				
Prudent	0.10 (1.00)	-0.31 (0.92)	-0.56 (0.90)	<.001
Western	-0.14 (0.94)	0.40 (1.02)	0.79 (1.18)	<.001
Traditional	-0.02 (0.99)	0.06 (1.03)	0.02 (1.11)	<.001

Note. SSC = sugar-sweetened carbonated beverages; ASC = artificially sweetened carbonated beverages; SD = standard deviation.

^aConsumption of SSC and ASC was the mean of reported intakes at weeks 15, 22, and 30 of pregnancy. Other dietary intakes were based on questionnaires at week 22 when the women reported intakes since the beginning of pregnancy.

^bmeans are compared with one-way analysis of variance and percents with Pearson's chi-squared test: 58,532–62,494 subjects were included in the various analyses, *** = $p < .001$.

^cincluding added sugar (which includes SSC).

^dincluding SSC.

^ehigh consumption indicate healthy diet.

^fhigh consumption indicate unhealthy diet.

^gdiet in principal component factor analysis: Prudent means basically healthy diet, Western basically unhealthy, and Traditional diets in between (SSC excluded, other sugar-sweetened beverages included). All participants have z-scores (mean = 0, SD = 1) on all patterns, with scores ranging from -1 (*weakly adherent to pattern*) to 1 (*closely adherent to pattern*).

for continuous measures and Pearson's chi-squared test for categorical variables. Changes in SSC and ASC intakes from 2002 to 2008 were assessed using student's *t*-test for continuous measures and Pearson's chi-squared test for categorical variables.

The relationships between intakes of sugar from SSC (per 100 ml increments) and BW were examined by multiple linear regression analyses for the continuous BW variable with adjustment for possible confounders. In developing the linear model, potential

TABLE 3 Unadjusted and adjusted relationships in linear regression analyses between consumption of sugar-sweetened carbonated beverages, per 100 ml, and birth weight presented in strata according to maternal gestational diabetes mellitus, pre-pregnancy BMI category, exercise, and smoking^a

GDM	Model	Stratum	All (n)	SSC intake (n)		b ^d (grams)	95% CI
				100–500 ml	>500 ml		
No	Unadjusted		61,944	12,986	1,706	-6.0	(-8.2, -3.9)
	Adjusted ^b		50,280	10,496	1325	-7.8	(-10.3, -5.3)
	BMI-category ^c	UW	1,398	340	50	-3.9	(-16.9, 9.1)
		NW	33,650	6,377	742	-5.3	(-8.5, -2.1)
		OWOB	15,162	3,764	529	-10.1	(-14.0, -6.1)
	Exercise	<1 time/week	26,321	6,657	951	-9.5	(-12.5, -6.5)
		≥1 time/week	23,959	3,839	374	-3.8	(-8.0, 0.5)
	Smoking	Nonsmokers	44,385	8,569	819	-5.5	(-8.6, -2.3)
		Smokers	5,895	1,927	506	-11.0	(-15.1, -6.9)
	Yes	Unadjusted		550	81	15	15.4
Adjusted ^b			432	67	11	25.1	(-2.0, 52.2)

Note. BMI = body mass index (kg/m²); b = regression coefficient; CI = confidence interval; GDM = gestational diabetes mellitus; SSC = sugar-sweetened carbonated beverages; UW = underweight (BMI: <18.5 kg/m²); NW = normal weight (BMI: 18.5–25 kg/m²); OWOB = overweight (25–30 kg/m²) or obese (BMI: >30 kg/m²).

^aInteractions with SSC intake in final model: GDM ($p < .01$), pre-pregnant BMI ($p < .01$), exercise ($p = .08$), and smoking ($p = .07$).

^bAdjusted for potential confounders in the final model: maternal height and pre-pregnancy BMI, age, parity, education and income, diet patterns, i.e. three principal component variables, exercise, smoking, volume of alcohol intake per occasion prior to pregnancy, ASC intake, spontaneous labour, and offspring year of birth.

^cPre-pregnancy.

^dGrams change in BW per 100 ml increase in consumption of SSC.

TABLE 4 Associations in multinomial logistic regression analyses between maternal consumption of sugar-sweetened carbonated beverages, per 100 ml, and the birth weight categories <2500, 2500–4500, and >4500 g, for 61,944 newborns in the Norwegian Mother and Child Cohort Study 2002–2008. Illustration of interactions in strata by maternal gestational diabetes mellitus, pre-pregnancy BMI category, exercise, and smoking^a

BW < 2,500 g ^b						
GDM	Model	Stratum	All (n)	BW < 2,500 (n)	OR ^c	95% CI
No	Unadjusted		61,944	430	1.08	(1.04, 1.12)
	Adjusted ^d		20,280	356	1.05	(0.99, 1.10)
	BMI category ^e	UW	1,398	21	1.10	(0.95, 1.27)
		NW	33,650	246	1.02	(0.95, 1.09)
		OWOB	15,162	89	1.08	(1.00, 1.17)
	Exercise	<1 time/week	26,280	170	1.07	(1.01, 1.13)
		≥1 time/week	23,930	186	0.99	(0.90, 1.09)
	Smoking	Nonsmokers	44,321	289	1.02	(0.95, 1.11)
		Smokers	5,889	67	1.07	(1.01, 1.13)
	BW > 4,500 g					
GDM	Model	Stratum	All (n)	BW > 4,500 (n)	OR ^c	95% CI
No	Unadjusted		61,944	2,228	0.98	(0.95, 1.01)
	Adjusted ^d		50,280	1,793	0.94	(0.90, 0.97)
	BMI category ^e	UW	1,398	7	1.13	(0.86, 1.49)
		NW	33,650	892	0.96	(0.91, 1.01)
		OWOB	15,162	893	0.93	(0.88, 0.97)
	Exercise	<1 time/week	26,280	1,073	0.93	(0.89, 0.97)
		≥1 time/week	23,930	719	0.96	(0.90, 1.02)
	Smoking	Nonsmokers	44,321	1,608	0.94	(0.90, 0.98)
		Smokers	5,889	184	0.93	(0.87, 1.00)
	Yes	Unadjusted		550	45	1.10
Adjusted ^d			432	36	1.18	(1.00, 1.39)

Note. BMI = body mass index (kg/m²); GDM = gestational diabetes mellitus; OR = odds ratio; CI = confidence interval; UW = underweight (BMI: <18.5 kg/m²); NW = normal weight (BMI: 18.5–25 kg/m²); OWOB = overweight (25–30 kg/m²) or obese (BMI: >30 kg/m²).

^aPresentation in strata based on interactions with SSC intake in the study's final multivariable linear regression model (pre-pregnancy BMI ($p < .01$), exercise ($p = .02$), smoking ($p = .02$), and GDM ($p = .01$), see (Table 3);

^bAnalysis for LBW risk was not done for the GDM stratum because there was only one LBW infant among GDM women.

^cOdds ratio per 100 ml increase in consumption of sugar-sweetened carbonated beverages, birth weight 2,500–4,500 g is the reference.

^dAdjusted for potential confounders: maternal height and pre-pregnancy BMI, age, parity, education and income, diet patterns, i.e. three principal component variables, exercise, smoking, volume of alcohol intake per occasion prior to pregnancy, ASC intake, spontaneous labour, and offspring year of birth.

^ePre-pregnancy.

confounders were considered for inclusion if they were associated with both SSC and BW with a p -value <.10 in separate bivariate analyses.

The influence of possible confounders of the relationship between SSC intake and BW was explored using a manual forward stepwise method. The sequence of covariate inclusion (**Supplementary**

Appendix; Supplementary Table B) was guided by the magnitude of change seen in the association (regression coefficient) between SSC intake and BW, and not by the strength and significance (p -value) of their associations with BW in the multiple regression analyses. Variables that changed the regression coefficient by more than 2% in multiple regression analyses were kept in the model. The resulting set of variables was used as our final model in all multiple regression analyses.

Using the same final model, the trichotomized BW outcome (LBW, normal BW, and HBW) was examined by multinomial logistic regression. Normal BW was defined as being between 2,500 and 4,500 g.

We also performed sensitivity analyses, by exploring interactions and influences of a range of possible confounders. Possible interactions between pairs of explanatory variables that were identified on the basis of previous evidence and theoretical assumptions, and were tested for impact in the final model, using $p < .10$ as the level of significance. In the process of evaluating significant interactions, we simplified continuous covariates into categorical variables as necessary, to allow stratified analyses. Exposure variables in the final model were investigated for multicollinearity (using variance inflation factor, tolerance, and variance proportions).

We additionally performed analyses to evaluate influence of a range of variables considered to be of possible relevance on the relationship between SSC and BW. In the final model, we firstly substituted SSC with other indices of carbohydrate intakes (total carbohydrate energy, added sugar energy including beverages, and volumes of all sugar-sweetened beverages) in order to assess the associations with other sources of carbohydrates than SSC. In the same way, we tested the influence of artificially sweetened beverages and artificially sweetened carbonated beverages (ASC). Secondly, we tested the inclusion of other possible confounders, for example, variables that were left out of the model due to high number of missing values. Thirdly, we tested the inclusion of covariates considered to be likely mediators for the associations between SSC and BW. Fourthly, women tend to repeat reproductive outcomes, and reproductive history may be associated with both exposures and outcomes (Louis et al., 2006). We therefore repeated the multiple regression analysis with adjustment for clustering due to multiple participations, that is, individuals with repeated births, in the MoBa study population. Finally, using the final regression model, we substituted BW with other measures of body size and proportions as outcomes, that is, crown-heel length, head circumference, and ponderal index.

Multiple linear regression analysis with adjustment for clustering was performed using StataCorp Stata/IC 14.0 for Windows. All other analyses were performed using IBM SPSS Statistics for Windows Version 21 (Release 21.0.0.0).

3 | RESULTS

Of the 62,494 pregnancies, 47,706 (76%) women had SSC intakes less than 100 ml, 13,067 (21%) between 100 and 500 ml and 1,721 (2.8%) 500 ml or more per day (Table 1). For women who reported daily SSC consumption both before and during pregnancy ($n = 18,190$), the mean intake of SSC was 44% lower during pregnancy than before (data not

shown). From 2003 to 2008, the proportion of women who drank 100 ml per day or more during pregnancy decreased from 31.1% to 17.6% ($p < .01$), and the proportion who drank 500 ml or more decreased from 3.9% to 1.8% ($p < .01$, data not shown).

Increasing consumption of SSC from <100 ml to ≥ 500 ml per day was associated with lower maternal age, higher pre-pregnancy BMI, single motherhood, teenage pregnancy, lower education and income, smoking, less exercise, and less frequent but higher intake per occasion of alcohol before pregnancy (Table 1). However, the proportion of women who drank alcohol during pregnancy did not differ between the SSC intake groups (1.6–1.7%, Table 2), and the different SSC groups had similar intakes of vitamins and other micronutrients (data not shown). Mean GA, BW, crown-heel length, ponderal index, and proportions of HBW infants decreased with increasing consumption of SSC, while the proportion of LBW infants increased (Table 1).

Total daily energy intake, energy per kilogram body weight, proportion of energy from carbohydrates and added sugar, and preferences for food items associated with unhealthy diets increased with increasing intakes of SSC (Table 2). However, energy from proteins did not differ between the groups, and protein intake per kilogram per day differed minimally between groups. Variation in consumption of added sugar was mainly due to the differences in SSC intakes (Table 2).

When adjusting for possible confounders in the final multiple linear regression model (maternal height and pre-pregnancy BMI, age, parity, education and income, diet patterns, that is, three principal component variables, exercise, smoking, volume of alcohol intake per occasion prior to pregnancy, ASC intake, spontaneous labor, and offspring year of birth), the mean decrease in BW per 100 ml increase in SSC was 7.8 g (95% confidence interval [CI]: 5.3 to 10.3 g) among women without gestational diabetes mellitus (GDM; Table 3). In the adjusted multinomial logistic regression analyses, the risk of BW < 2,500 g tended to increase (odds ratio [OR]: 1.05, 95% CI: 0.99 to 1.10), and the risk of BW > 4,500 g decreased (OR: 0.94, 95% CI: 0.90 to 0.97) with increasing consumption of SSC (Table 4). The respective results were similar for the outcomes SGA and LGA infants (not shown).

Among the 550 GDM pregnancies, one infant had an LBW and 45 had HBWs, and with increasing consumption of SSC, there was an opposite but nonsignificant trend of increasing BW (25 g per 100 ml, 95% CI: -2 to 52; Table 3), and a significant higher risk of HBW (OR 1.18 per 100 ml, 95% CI: 1.00 to 1.39) (Table 4).

There were significant interactions between SSC consumption on one hand and maternal GDM, BMI, exercise, and smoking on the other. When stratified by these variables, using three BMI categories (underweight [UW], normal weight [NW], overweight or obese [OWOB]) and dichotomized variables for exercise (less than weekly/weekly or more) and smoking (no/yes [occasionally or daily]), the mean BW reduction per 100 ml SSC varied from 3.8 to 11.0 g across pregnancies that were not complicated by GDM (Table 3). The negative associations were stronger for smokers, physically inactive, and OWOB women, and these groups also had a higher risk of LBW and lower risk of HBW (Table 4).

In bivariate regressions, none of the possible confounders had associations with SSC stronger than 0.24 (Pearson's r), and there was

no strong multicollinearity between the covariates in the final multiple linear regression model.

When substituted for SSC in the adjusted final model (one variable at the time), carbohydrate energy intake (both including and excluding energy from SSC) was not associated with BW (data not shown). Added sugar energy and sugar-sweetened beverage volumes were both significantly associated with BW, but not when SSC energy or volume was subtracted (data not shown). Artificially sweetened beverages (mean reduction in BW of -2.0 g per 100 ml, 95% CI: -3.6 to -0.4) and ASC (mean reduction in BW of -3.8 grams per 100 ml, 95% CI: -5.9 to -1.7) were both significantly associated with BW, but the magnitude of their estimated associations were considerably weaker than for SSC (26% and 50% of that of SSC, respectively, data not shown).

For other possible confounders, adjustment for the variable "prior GDM pregnancies," which was missing for 32,820 (53%) of the cases, increased the estimated negative association between SSC intake and BW from 7.6 to 10.2 g per 100 ml (34% change) among women without prior or current GDM, whereas adjustment for paternal education had minimal impact.

When adding (separately) to the final model variables considered likely *mediators* of an association between SSC intake and BW, the following weakened the association estimate: pregnancy weight gain (from -7.8 g to -6.3 g) and gestational age (from -7.8 g to -6.6 g). Total energy intake in kcal/kg, GDM, glycosuria, preeclampsia, and isolated hypertension had minimal impact (less than 2% reduction in the *b* for SSC on BW). Adjustment for clustering due to multiple participations did not change the association between SSC and BW.

Using the exposure variables of the final multiple linear regression model, consumption of SSC (per 100 ml) was also significantly associated with reductions in crown-heel length (cm) (-0.02 , 95% CI: -0.03 to -0.01), head circumference (cm) (-0.01 , 95% CI: -0.02 to -0.01), and ponderal index (kg/m^3) (-0.02 , 95% CI: -0.04 to -0.01).

4 | DISCUSSION

4.1 | Main findings

After adjusting for potential confounders, the consumption of added sugar from SSC was associated with lower mean BWs and with other measures of reduced fetal growth, such as higher proportions of LBW babies and lower proportions of HBW babies in pregnancies not complicated by GDM. The largest negative associations were observed for women who were OWOB, smokers, or inactive. In contrast, increasing consumption of SSC was significantly associated with increased risk of HBW and tended to be associated with increasing mean BW in GDM pregnancies.

4.2 | Strengths and limitations

The strengths of our study include its prospective design, large sample size, and broad and detailed information on sociodemographic, health, and lifestyle characteristics. Although we were able to adjust for numerous factors related to BW, including offspring year of birth, which may capture relevant nonmeasured time trends, we cannot

exclude residual confounding. The consumption of SSC was associated with poorer general health and less healthy habits, including diet. High SSC intake may therefore be a strong marker of a less healthy lifestyle involving a number of unmeasured factors, which may, at least in part, explain the negative association with BW. The proportion of energy from protein decreased with increasing consumption of SSC, but neither the energy intake from protein (per kilogram per day) nor total micronutrient intakes differed materially between the groups suggesting that the high SSC consumers did not experience nutritional deficiencies. As our data were largely based on information provided by mothers, the possibility of recall and report bias cannot be excluded. However, such bias is likely to be nondifferential and may result in attenuation of the observed associations (Marshall & Hastrup, 1996). The low participation rate in MoBa (40.6%) may have introduced a selection bias because the women were older and better educated, and the proportion of smokers was lower than among pregnant women in general. However, despite differences in prevalence estimates, no bias was found in eight other selected exposure-outcome associations in this cohort (Nilsen et al., 2009).

4.3 | Interpretation

Our findings for non-GDM pregnancies were contrary to our hypothesis based on our previous research, and the assumption that a high intake of rapidly absorbed sugar would lead to increased fetal growth, due to relative fetal hyperinsulinemia secondary to elevated maternal, and thus fetal, blood glucose levels (Pedersen, 1952). Both higher BWs and higher risks of a LGA infant have been reported among the offspring of women on high glycemic index and high glycemic load diets (Knudsen, Heitmann, Halldorsson, Sorensen, & Olsen, 2013; Moses et al., 2006). We are not aware of other studies reporting specific associations between SSC and BW in humans. Our results are, however, in line with the results of one study in which the consumption of a high sugar diet was associated with reduced BW and an increased risk of an SGA infant (Lenders et al., 1994).

It has been suggested that impaired fetal growth that is not associated with maternal undernutrition may be caused by other factors related to maternal diet, for example, dyslipidemia and insulin resistance, and environmental factors, for example, smoking. Such factors may contribute to decreased fetal nutrition and oxygenation through oxidative stress that may lead to microvascular endothelial dysfunction and/or disturbed development and function of the placenta, and by reduced blood flow to the placenta due to macrovascular vessel dysfunction from atherosclerosis (Henriksen & Clausen, 2002, Pereira et al., 2015, Reynolds et al., 2006). We suggest that such mechanisms may also explain the unexpected negative association between SSC intake and BW in the non-GDM pregnancies. A likely mechanism may be that rapid uptake of sugar results in glycemic spikes which, if occurring frequently, may decrease vascular function by inducing oxidative stress, inflammation, and endothelial dysfunction (Node & Inoue, 2009). In other circumstances, intake of soft drinks with sugar has also been negatively associated with vascular function in terms of elevated blood pressure and increased risks of coronary heart disease (Brown et al., 2011, Huang, Huang, Tian, Yang, & Gu, 2014), preeclampsia (Borgen et al., 2012; Clausen et al., 2001), and preterm

delivery in some (Englund-Ogge et al., 2012, Petherick, Goran, & Wright, 2014), but not in another study (Halldorsson, Strom, Petersen, & Olsen, 2010). Women who exercise little or smoke may be more vulnerable to such effects (Di Francescomarino, Sciarilli, Di Valerio, Di Baldassarre, & Gallina, 2009, Gordon, Lavoie, Arsenault, Ditto, & Bacon, 2008).

The positive association between intake of SSC and BW as a continuous measure in women with GDM may have been insignificant due to the small size of the group and few individuals with high SSC consumption. We suggest that the opposite associations between SSC and BW measures for non-GDM and GDM pregnancies may be due to an effect of relatively higher glucose loads to the fetus in the GDM pregnancies because of reduced glucose tolerance in the mothers, while the women without GDM had sufficient insulin response and capacity to control blood glucose levels following SSC intakes. Further, we speculate that the seemingly stronger negative association among women who were OWOB, smokers or more sedentary, may imply that SSC had a more pronounced effect in pregnancies of women with higher cardiovascular risk status and thereby increased risk of affected blood supply to the placenta. In GDM, the growth promoting effect of glucose may have been stronger than a potential negative effect on circulation. We believe that these findings support a hypothesis that the association between rapidly absorbed sugars and BW may vary according to both vascular or placental function and glucose tolerance.

We have previously shown that temporary increases in mean BW and HBW babies in Norway occurred in parallel to a marked increase and subsequent decrease in national consumption of SSC, and we suggested a causal relationship (Grundt et al., 2012). This study may seem to contradict that hypothesis, but it may still be true. In this study, fewer participants had pre-pregnancy diabetes or were diagnosed with GDM than both nonparticipants and the participants in our previous cohort study where data were available for all pregnant women within a region (Grundt et al., 2012, Nilsen et al., 2009). As SSC consumption decreased and leisure time exercise increased in Norway during the recruitment period to the MoBa study (Grundt et al., 2012), glucose tolerance among pregnant women was probably generally better. Furthermore, women with increased cardio-metabolic risk factors, such as obesity, reduced glucose tolerance, or GDM, may have been early adopters of the trend to reduce intakes of SSC. This may have been reinforced by modified behavior as the study participants were recruited early in pregnancy and therefore sensitized to important health issues while responding to questionnaires and experiencing close follow-up until delivery. The 44% reduction in mean SSC intake from pre-pregnancy levels may reflect such behavioral changes. The temporary change in mean BW and rate of large babies in Norway from 1990 to 2010 may, therefore, have been the result of a shifting balance between the proportion of women with combined high SSC intake, strained beta-cell function, and reduced glucose tolerance, and women without such characteristics.

The estimated 7.8 g reduction in BW per 100 ml SSC (Table 3) may seem small but may be significant on a population basis. A daily SSC consumption of 1 L, which was the reported median intake in a Mexican study (Martinez, 2014), as compared to no SSC intake, would mean a reduction in BW of 78 g, that is, approximately the effect of 3.5 pre-

pregnancy BMI-units (Grundt et al., 2012, Stamnes Koeppe et al., 2012) and 40% of the effect of smoking (Valero De Bernabe et al., 2004). In a smoking non-GDM mother with a daily SSC consumption of 1 L, the 7% increased risk per 100 ml SSC of giving birth to a LBW infant (OR: 1.07, Table 4) would correspond to an approximate doubling of the risk, and similarly, in a GDM mother, the 18% increased risk per 100 ml SSC of having an HBW infant (OR: 1.18, Table 4) would correspond to an approximate 5-doubling of the risk.

Artificially sweetened beverages have been associated with increased risk of premature birth (Englund-Ogge et al., 2012; Halldorsson et al., 2010). Our finding of a statistically significant negative association between artificially sweetened beverages and BW may support such a relationship.

5 | CONCLUSIONS

In this population-based cohort study, there was a dose dependent negative association between SSC consumption during pregnancy and BW, and increasing SSC consumption was associated with an increasing risk of LBW and a decreasing risk of HBW in non-GDM pregnancies. These associations were more pronounced for women who were OWOB, reported little or no exercise, or smoked. In pregnancies complicated by GDM, the relationships between SSC consumption and BW tended to be opposite to those of the non-GDM pregnancies. Likely mechanisms for these different associations are discussed. Our results may indicate that women at risk of LBW births, for example, smokers, as well as women at risk of having HBW births, for example, due to impaired glucose tolerance as in GDM, may benefit from limiting sugar intake from SSC.

ACKNOWLEDGMENTS

We are grateful to all the families in Norway who are participating in this ongoing cohort study.

SOURCE OF FUNDING

This study was supported by unrestricted grants from the Innlandet Hospital Trust and the Southern and Eastern Norway Regional Health Authority. The Norwegian Mother and Child Cohort Study is supported by the Norwegian Ministry of Health and the Ministry of Education and Research, NIH/NIEHS (contract no. NO1-ES-75558), NIH/NINDS (grant no.1 UO1 NS 047537-01 and grant no. 2 UO1 NS047537-06A1), and Norwegian Research Council/FUGE (grant no. 151918/S10).

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTIONS

JHG: Conceptualization and design of the study, statistical analyses, interpretation of results, and initial drafting and writing the paper. GEE: Planning, statistical analyses, interpretation of results, and writing of the paper. ALB: Planning, interpretation of results, and writing the

paper. MH: Providing file for data analyses, design of the study, interpretation of results, and writing the paper. TM: Conceptualization and design of the study, interpretation of results, and writing the paper. JHG had primary responsibility for design, writing, and final content. All authors read and approved the final version of the paper.

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How to cite this article: Grundt JH, Eide GE, Brantsæter A-L, Haugen M, Markestad T. Is consumption of sugar-sweetened soft drinks during pregnancy associated with birth weight? *Matern Child Nutr.* 2017;13:e12405. <https://doi.org/10.1111/mcn.12405>