Prospective Study of Pre-Gravid Sugar-Sweetened Beverage Consumption and the Risk of Gestational Diabetes Mellitus

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OBJECTIVE — Consumption of sugar-sweetened beverages (SSBs) was related to an elevated risk of type 2 diabetes and insulin resistance in several recent studies among middle- or older-aged populations. Studies on SSB consumption and glucose intolerance among pregnant women, however, are lacking. We therefore examined the association between regular SSB consumption before pregnancy and the risk of gestational diabetes mellitus (GDM).

RESEARCH DESIGN AND METHODS — This was a prospective study among 13,475 U.S. women who reported at least one singleton pregnancy between 1992 and 2001 in the Nurses' Health Study II. GDM was self-reported and validated by medical record review in a subsample. Cox proportional hazards models with multivariate adjustments were applied to examine the association of SSB consumption with GDM risk.

RESULTS — During 10 years of follow-up, 860 incident GDM case subjects were identified. After adjustment for age, parity, race, physical activity, smoking, alcohol intake, prepregnancy BMI, and Western dietary pattern, intake of sugar-sweetened cola was positively associated with the risk of GDM, whereas no significant association was found for other SSBs and diet beverages. Compared with women who consumed <1 serving/month, those who consumed ≥5 servings/week of sugar-sweetened cola had a 22% greater GDM risk (relative risk 1.22 [95% CI 1.01–1.47]).

CONCLUSIONS — Findings from this study suggest that prepregnancy higher consumption of sugar-sweetened cola (≥5 servings/week) is associated with an elevated GDM risk, whereas no significant association with GDM risk was observed for other SSBs and diet beverages.

Diabetes Care 32:2236–2241, 2009

Gestational diabetes mellitus (GDM), defined as glucose intolerance with onset or first recognition during pregnancy, is one of the most common pregnancy complications (1). Women with GDM are at increased risk of pregnancy complications, perinatal morbidity, and type 2 diabetes in the years after pregnancy. Offspring of women with GDM have increased risk of obesity, glucose intolerance, and diabetes in childhood and early adulthood (1). Despite the maternal and infant morbidity associated with GDM, limited attention has been paid to the identification of dietary risk factors for GDM.

Sugar-sweetened beverages (SSBs) are the leading source of added sugars in Americans' diets (2). In animal models and human studies, a high-sugar diet reduces insulin sensitivity (3,4) and insulin secretion (5). Higher consumption of SSBs was associated with an elevated risk of type 2 diabetes (6–8) and insulin resistance (9) among middle- or older-aged adults in several recent epidemiological studies. Studies regarding the impact of habitual SSB consumption on glucose intolerance among pregnant women, however, are lacking. We therefore examined the association of pregravid SSB consumption with GDM risk in a large prospective cohort of U.S. women.

RESEARCH DESIGN AND METHODS

The Nurses' Health Study II (NHS II) is a prospective cohort study of 116,671 female U.S. nurses, originally recruited at age 24–44 years in 1989. This cohort has been, and continues to be, followed with the use of biennial mailed questionnaires to update information on health-related behavior and to determine incident disease outcome. The follow-up rate has been ~90% for every 2-year period. In the present analysis, women were excluded if they did not complete a semiquantitative food frequency questionnaire (SFFQ) in 1991; if more than 70 items on the SFFQ were left blank; if their reported total energy intake was implausible (<500 kcal/day or >3,500 kcal/day); if they reported a multiple gestation (twins or higher-order multiple gestation); if they did not provide physical activity data in 1991; or if they reported a history of diabetes, cancer, cardiovascular disease, or GDM on the 1989 or 1991 questionnaires. The final sample for the current analyses consisted of 13,475 women who reported having at least one singleton pregnancy lasting 6 months or more between 1992 and 2001.

Ascertainment of GDM

GDM case subjects were identified based on self-reported information in the biennial questionnaire. A previous validation study based on medical record review demonstrated a high validity of self-reported diagnosis of GDM in this cohort (10). In brief, medical records were re-

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Received 11 May 2009 and accepted 28 July 2009.
DOI: 10.2337/dc09-0866

See accompanying editorial, p. 2314.

viewed among a sample of 114 women in the cohort who corroborated on a supplementary questionnaire that they had a first diagnosis of GDM in a singleton pregnancy between 1989 and 1991. Of these women, 94% were confirmed to have a physician diagnosis of GDM. Supplementary questionnaires were also sent to 100 women reporting a pregnancy uncomplicated by GDM during the same interval. A singleton pregnancy during this period was confirmed for 93 responders. Among them, 83% reported a glucose loading test and all (100%) reported frequent urine screening in pregnancy, consistent with a high degree of surveillance in this cohort.

Dietary assessment

Dietary intake information was collected by a 133-item SFFQ designed to assess average food intake over the previous year. Women were asked how often they had consumed a specified amount of each food on average over the previous year. For beverages, one serving (considered as one glass, bottle, or can) was used as the unit for the consumption of SSBs. The original SFFQ included four items for SSBs including "Coke, Pepsi, or other cola with sugar," "caffeine-free Coke, Pepsi, or other cola with sugar," "other carbonated beverages with sugar," and "fruit punch," as well as three items for diet beverages including "low-calorie cola with caffeine," "low-calorie caffeine-free cola," and "other low-calorie beverages." In the primary analysis, we summed the intakes of single items for the above beverage categories to generate the total consumptions of SSBs and of diet beverages. In the secondary analysis, we also created several subgroups under each major beverage category: two subgroups for the SSB category (sugar-sweetened cola including "Coke, Pepsi, or other cola with sugar" and "caffeine-free Coke, Pepsi, or other cola with sugar" and other SSBs including "other carbonated beverages with sugar" and "fruit punch") and two subgroups for the diet beverages category (diet cola including "low-calorie cola with caffeine" and "low-calorie caffeine-free cola" and other diet beverages including "other low-calorie beverages").

Nutrient intakes were computed by multiplying the frequency response by the nutrient content of the specified portion sizes and summing the contributions of all foods. Food composition values were obtained from the Harvard University Food Composition Database, which was derived from U.S. Department of Agriculture sources (11) and supplemented with information from manufacturers. The validity and reliability of SFFQs similar to those used in the NHS II were described elsewhere (11,12). Corrected correlation coefficients between the SFFQ and multiple dietary records were 0.84 for cola-type soft drinks (sugar-sweetened and diet combined), 0.56 for other carbonated soft drinks, and 0.56 for fruit punch in a similar cohort of women (the NHS) (12) and were 0.84 for sugar-sweetened cola, 0.55 for other sugar-sweetened soft drinks, 0.73 for diet cola, and 0.74 for other diet soft drinks in the Health Professionals Follow-Up Study (11).

Assessment of nondietary covariates

Participants' sociodemographic, clinical, and lifestyle information was collected at baseline and updated biennially. BMI was calculated by self-reported weight and height (weight in kilograms divided by the square of height in meters). Self-reports of body weight were highly correlated with technician-measured weight ($r = 0.96$) in a similar cohort (10,13). Physical activity was assessed through mailed questionnaires in 1989, 1991, and 1997. Participants were asked to report weekly activities for each of the following categories: walking or hiking outdoors; jogging; running; bicycling; lap swimming; tennis, squash, or racquetball playing; calisthenics; and other recreation. From this information, weekly energy expenditure in MET hours was calculated and used to represent total discretionary physical activity in the analyses. Family history of diabetes and other diseases was reported in 1989.

Statistical analysis

In the primary analyses, we created measures of cumulative average intakes of SSB to represent long-term intakes before GDM was diagnosed. For instance, the 1991 intake was used for the follow-up between 1991 and 1995, and the average of the 1991 and 1995 intake was used for the follow-up between 1995 and 1999 to reduce within-person variation. SSB consumption was analyzed both as a categorical variable (0–3 servings/month, 1–4 servings/week, ≥5 servings/week) and a continuous variable (servings/day). Because women with previous GDM were excluded from this study and women with a previous pregnancy uncomplicated by GDM are less likely than nulliparous women (i.e., women whose index pregnancy is their first termed pregnancy) to develop GDM, nulliparous women were overrepresented in the GDM group. To account for this effect, we adjusted for parity in multivariate analyses and performed a secondary analysis by restricting our analysis to nulliparous women. We performed multivariate Cox proportional hazards analyses to estimate relative risks (RRs) and 95% CIs while controlling for potential confounding factors. All models included age and parity. Subsequent models were built with inclusion of potential confounders, including race/ethnicity (Caucasian, African American, Hispanic, and Asian), family history of diabetes (yes or no), smoking status (never, past, or current), physical activity (quintiles), and alcohol consumption (0, 0.1–4.9, 5.0–9.9, and >10 g/day). Because BMI might represent intermediate variables in the relationship between beverage consumption and GDM risk, we adjusted for BMI (<21, 21–22.9, 23.0–24.9, 25.0–26.9, 27.0–28.9, 29.0–30.9, 31.0–32.9, 33.0–34.9, and >35.0 kg/m^2) in separate models. In addition, we constructed dietary pattern scores using key food items that characterized the Western and prudent dietary patterns as described previously (14). The Western dietary pattern included red meat, processed meat, refined grain products, snacks, sweets and desserts (not including SSBs), french fries, and pizza; the prudent dietary pattern included fruits, tomatoes, cabbages, green leafy vegetables, dark-yellow vegetables, legumes, other vegetables, poultry, and fish (14). These simplified dietary pattern variables were highly correlated ($r > 0.92$) with the patterns derived from the factor analysis in our study population (15). The significance of the linear trends across categories of beverage intake was evaluated using the median value for each category of beverage intake and analyzed as a continuous variable in multivariate models.

We evaluated whether associations between consumption of SSBs and the risk of GDM were modified by BMI (<25 or ≥5 kg/m^2), nulliparity (yes or no), smoking habit (never, past, or current smoker), or family history of diabetes (yes or no) using stratified analyses and by evaluating interaction terms. All statistical analyses were performed by using SAS statistical software (version 8.2; SAS Institute, Cary, NC).

RESULTS — During 10 years of follow-up, 860 women reported their first diagnosis of GDM among the 13,475

Table 1—*Baseline (1991) characteristics according to the frequencies of SSB consumption in 13,475 women*

	SSB consumption			
	0–3 servings/month	1–4 servings/week	≥5 servings/week	*P*
n (%)	5,584 (41.4)	3,675 (27.3)	4,216 (31.3)	
Age (years)	31.9 (3.3)	31.5 (3.3)	31.0 (3.2)	<0.001
Ethnicity (%)				
Caucasian	95.1	94.3	93.6	
African American	0.5	0.7	1.3	
Hispanic	1.5	1.3	1.3	
Asian	1.4	1.7	2.0	
Others	1.5	2.0	1.7	<0.001
Husband's education (%)				
High school or less	15.6	18.1	19.5	
College	44.7	47.8	50.4	
Graduate school	39.7	34.1	30.1	<0.001
Family history of diabetes (%)	13.8	11.3	11.0	<0.001
Nulliparous (%)	56.1	61.7	62.3	<0.001
Current smoking (%)	8.3	7.5	10.6	<0.001
Alcohol consumption (g/day)	3.7 ± 5.5	3.0 ± 5.0	2.6 ± 4.8	<0.001
BMI (kg/m^2)	23.6 ± 4.3	23.3 ± 3.1	23.3 ± 4.3	<0.001
Physical activity (h/week)	25.4 ± 30.4	22.0 ± 26.5	21.0 ± 28.1	<0.001
Dietary factors (per day)				
Total calories (kcal)	1,662 ± 504	1,804 ± 500	2,053 ± 544	<0.001
Carbohydrate (% energy)	48.9 ± 7.4	50.0 ± 6.5	53.6 ± 6.7	<0.001
Protein (% energy)	20.3 ± 3.4	19.9 ± 2.4	17.6 ± 2.9	<0.001
Total fat (% energy)	31.3 ± 5.8	31.4 ± 5.2	29.9 ± 5.1	<0.001
Glycemic index*	52.9 ± 3.3	53.8 ± 2.9	55.6 ± 2.7	<0.001
GL*	1.2 ± 0.2	1.2 ± 0.2	1.3 ± 0.2	<0.001
Total fiber (g)*	19.7 ± 6.0	18.1 ± 4.7	17.2 ± 4.3	<0.001
Magnesium (mg)*	338.4 ± 75.8	323.8 ± 67.7	287.7 ± 63.8	<0.001
Potassium (mg)*	3,032 ± 512	2,909 ± 450	2,661 ± 454	<0.001
Calcium (mg)*	1,125 ± 441	1,118 ± 419	978 ± 387	<0.001
Vitamin C (mg)*	260.2 ± 311.1	243.8 ± 254.5	232.6 ± 229.9	<0.001
Vitamin E (mg)*	37.7 ± 110.0	35.4 ± 102.7	27.9 ± 79.3	<0.001
Fruits (servings)	1.3 ± 1.0	1.2 ± 0.9	1.1 ± 0.9	<0.001
Vegetables (servings)	3.4 ± 2.1	3.1 ± 1.8	2.9 ± 1.7	<0.001
Processed meat (servings)	0.9 ± 1.1	1.2 ± 1.2	1.4 ± 1.2	<0.001
Red meat (servings)	0.5 ± 0.4	0.5 ± 0.4	0.6 ± 0.4	<0.001

Data are means ± SE, unless otherwise indicated. *Energy adjusted.

women included in this study. On average, women in this population consumed fewer SSBs than diet beverages. At baseline, the median intake was 1 serving/week for SSBs and 2–4 servings/week for diet beverages. The percentages of women who reported consuming SSBs of 0–3 servings/month, 2–4 servings/week, and ≥5 servings/week were 41.4, 27.3, and 33.3%, respectively. By volume, 34% of SSBs consumed was from sugar-sweetened cola and 66% was from other SSBs. For diet beverages, the percentages of women who reported consuming 0–3 servings/month, 2–4 servings/week, and ≥5 servings/week were 38.3, 15.3, and 46.4%, respectively. Of diet beverages consumed, 81% was from diet cola and 19% was from other diet beverages. Women with a higher intake of SSBs were on average younger and less likely to have a family history of diabetes or drink alcohol (Table 1). These women tended to consume a diet higher in total calories, total carbohydrates, processed and red meats, and glycemic load but lower in protein, fat, total dietary fiber, fruits and vegetables, and selected minerals and vitamins (magnesium, calcium, potassium, and vitamins C and E).

After adjusting for age and parity (Table 2; model 1), higher SSB intake was positively associated with GDM risk: compared with women who consumed <1 serving/month (reference group), RR for those who consumed ≥5 servings/week was 1.23 (95% CI 1.05–1.45; P_{trend} = 0.005). The positive association between SSBs and GDM risk remained significant after adjustment for other demographic and lifestyle risk factors for GDM, including race, smoking, alcohol intake, physical activity, and family history of diabetes, in model 2 (P_{trend} = 0.04). This association remained strong after additional adjustment for BMI (model 3). When SSB intake was treated as a continuous variable in model 3, each serving/day increment was associated with a 23% (95% CI 1.05–1.43; P_{trend} = 0.01) increase in GDM risk. The association was slightly attenuated and became borderline insignificant (P = 0.06) with additional adjustment of Western dietary pattern (model 4). However, the trend for an elevated risk of GDM associated with increased SSB consumption persisted: the

Table 2—*RR of GDM in relation to SSB consumption* (n = *13,475; case subjects = 860*)

	SSB consumption				
	0–3 servings/month	1–4 servings/week	≥5 servings/week	1 serving/day	P_{trend}
All SSBs					
No. case subjects/person-years	323/185,682	229/173,189	208/185,757		
Model1*	1.00	1.01 (0.85–1.20)	1.23 (1.05–1.45)	1.25 (1.07–1.45)	0.005
Model 2†	1.00	1.02 (0.86–1.21)	1.17 (1.00–1.37)	1.18 (1.01–1.37)	0.04
Model 3‡	1.00	1.06 (0.89–1.25)	1.23 (1.05–1.44)	1.23 (1.05–1.43)	0.01
Model 4§	1.00	1.03 (0.87–1.23)	1.16 (0.98–1.37)	1.16 (0.99–1.36)	0.06
Sugar-sweetened cola					
No. case subjects/person-years	544/332,516	168/113,899	148/98,214		
Model1*	1.00	1.12 (0.94–1.33)	1.39 (1.16–1.67)	1.39 (1.16–1.67)	<0.001
Model 2†	1.00	1.07 (0.90–1.28)	1.26 (1.04–1.51)	1.25 (1.04–1.51)	0.02
Model 3‡	1.00	1.11 (0.93–1.32)	1.29 (1.07–1.56)	1.29 (1.07–1.55)	0.007
Model 4§	1.00	1.08 (0.90–1.28)	1.22 (1.01–1.47)	1.22 (1.01–1.47)	0.04
Other SSBs					
No. case subjects/person-years	448/254,751	256/195,695	156/94,182		
Model1*	1.00	1.00 (0.86–1.17)	0.98 (0.81–1.17)	0.97 (0.77–1.22)	0.78
Model 2†	1.00	1.00 (0.86–1.17)	0.95 (0.79–1.14)	0.94 (0.74–1.18)	0.58
Model 3‡	1.00	1.06 (0.90–1.23)	0.99 (0.82–1.19)	0.99 (0.78–1.25)	0.92
Model 4§	1.00	1.02 (0.87–1.19)	0.94 (0.78–1.13)	0.92 (0.73–1.16)	0.48

Data are RR (95% CI) unless otherwise indicated. *Model 1 adjusted for age (5-year category) and parity (0, 1, 2, or ≥3). †Model 2 adjusted for variables in model 1 plus race/ethnicity, cigarette smoking status (never, past, or current), family history of diabetes in a first-degree relative (yes or no), alcohol intake (5 categories: 0, 0.1–5.0, 5.1–15.0, or >15 g/day), and physical activity (quintile). ‡Model 3 adjusted for variables in model 2 plus BMI (9 categories: <21.0, 21.0–22.9, 23.0–24.9, 25.0–26.9, 27.0–28.9, 29.0–30.9, 31.0–32.9, 33.0–34.9, or ≥35.0 kg/m^2). §Model 4 adjusted for variables in model 3 plus Western dietary pattern score (quintile).

RRs (95% CIs) from the lowest to the highest SSB consumption category in model 4 were 1.00 (reference), 1.03 (0.87–1.23), and 1.16 (0.98–1.37). Further controlling for prudent dietary pattern and other beverage consumption including diet beverages and fruit juices did not change the results materially.

In the stratified analysis according to participants' BMI status (<25 or ≥25 kg/m^2), family history of diabetes (yes or no), smoking habit (never, past, or current smoking), or nulliparity (yes or no), the direction of the association between GDM risk and SSB consumption was consistent in each strata. The magnitude of the association, however, appeared to be stronger among nulliparous women ($P_{interaction}$ = 0.004).

Because caramel coloring in cola-type beverages has been positively associated with insulin resistance and inflammation in animals (16), we further examined the associations between two types of SSBs (cola versus noncola) and GDM risk. A positive association with GDM risk was found for sugar-sweetened cola but not for noncola SSBs (Table 2). Compared with women who consumed sugar-sweetened cola of 0–3 servings/month, those who consumed ≥5 servings/week had a 22% increase in GDM risk (RR 1.22 [95% CI 1.01–1.47]; P_{trend} = 0.04) after controlling for other potential confounders (model 4).

We also assessed whether consumption of diet beverages was associated with GDM risk. For total diet beverages, the results did not show any association in all models, regardless of whether consumption was treated as a categorical variable or a continuous variable (Table 3). We further examined the relationship between two types of diet beverages (diet cola or other diet beverages) and risk of GDM. The consumption of other diet beverages showed positive associations in model 2. However, this positive association disappeared after additional adjustment for BMI and other dietary variables in models 3 and 4.

CONCLUSIONS — In this large prospective study, we observed that pregravid consumption of sugar-sweetened cola was significantly and positively associated with GDM risk, after adjustment of known risk factors for GDM including age, family history of diabetes, parity, physical activity, smoking status, alcohol intake BMI, and Western dietary pattern. Compared with women who consumed <1 serving/month, those who consumed ≥5 servings/week of sugar-sweetened cola had a 22% greater GDM risk. No statistically significant elevation in risk was observed for other SSBs and diet beverages.

Although the underlying mechanism remains unclear, available evidence suggests that the main defect in the pathogenesis of GDM is relatively diminished insulin secretion coupled with pregnancy-induced insulin resistance (17). Thus, pregnancy-related metabolic challenges unmask a predisposition to glucose metabolic disorders in some women. Factors that contribute to insulin resistance or impaired insulin secretion before pregnancy and in early pregnancy can have a deleterious effect during pregnancy and be risk factors for GDM.

Several possible explanations may help to understand the positive association between sugar-sweetened cola consumption and GDM risk. First, consuming a large amount of sugar-sweetened cola could contribute to a high–glycemic load (GL) diet by providing a large amount of rapidly absorbable sugars. High-GL foods or diets were observed to induce a greater postprandial plasma glucose response. Although results from human metabolic studies on the impact of GL on insulin sensitivity and secretion are still inconclusive, findings from well-designed studies tend to suggest that a lower-GL diet may improve insulin sensitivity in both normal individuals and patients with im-

Table 3—*RR of GDM in relation to diet beverage consumption* (n = *13,475, cases = 860)*

	Diet beverage consumption				
	0–3 servings/month	1–4 servings/week	≥5 servings/week	1 serving/day	P_{trend}
All diet beverages					
No. case subjects/person-years	158/71,233	268/175,901	434/297,495		
Model1*	1.00	0.86 (0.69–1.06)	1.03 (0.89–1.19)	1.06 (0.94–1.18)	0.36
Model 2†	1.00	0.90 (0.73–1.11)	1.08 (0.93–1.25)	1.08 (0.97–1.21)	0.17
Model 3‡	1.00	0.82 (0.66–1.01)	0.86 (0.73–1.00)	0.91 (0.81–1.03)	0.12
Model 4§	1.00	0.85 (0.68–1.05)	0.87 (0.74–1.02)	0.92 (0.81–1.04)	0.20
Diet cola					
No. case subjects/person-years	356/472,125	322/42,326	182/30,178		
Model1*	1.00	0.92 (0.75–1.13)	1.03 (0.88–1.20)	1.04 (0.92–1.17)	0.53
Model 2†	1.00	0.97 (0.79–1.19)	1.07 (0.91–1.25)	1.06 (0.94–1.20)	0.34
Model 3‡	1.00	0.87 (0.71–1.07)	0.86 (0.73–1.00)	0.90 (0.79–1.02)	0.10
Model 4§	1.00	0.90 (0.72–1.12)	0.86 (0.72–1.02)	0.90 (0.78–1.03)	0.07
Other diet beverages					
No. case subjects/person-years	552/71,788	217/461,344	91/11497		
Model1*	1.00	1.00 (0.83–1.20)	1.28 (1.01–1.64)	1.34 (0.98–1.81)	0.06
Model 2†	1.00	1.06 (0.88–1.26)	1.34 (1.05–1.71)	1.44 (1.06–1.95)	0.02
Model 3‡	1.00	0.94 (0.79–1.13)	1.13 (0.88–1.44)	1.13 (0.83–1.53)	0.45
Model 4§	1.00	0.99 (0.82–1.20)	1.18 (0.91–1.51)	1.21 (0.88–1.66)	0.24

Data are RR (95% CI) unless otherwise indicated. *Model 1 adjusted for age (5-year category) and parity (0, 1, 2, or ≥3). †Model 2 adjusted for variables in model 1 plus race/ethnicity, cigarette smoking status (never, past, or current), family history of diabetes in a first-degree relative (yes or no), alcohol intake (5 categories: 0, 0.1–5.0, 5.1–15.0, or >15g/day), and physical activity (quintile). ‡Model 3 adjusted for variables in model 2 plus BMI (9 categories: <21.0, 21.0–22.9, 23.0–24.9, 25.0–26.9, 27.0–28.9, 29.0–30.9, 31.0–32.9, 33.0–34.9, or ≥35.0 kg/m^2.) §Model 4 adjusted for variables in model 3 plus Western dietary pattern score (quintile) and SSBs.

paired glucose intolerance. In crossover studies where insulin sensitivity was measured by euglycemic-hyperinsulinemic clamp, a low-GL diet was found to lead to higher whole-body glucose uptake than the high-GL diet in men with type 2 diabetes (18). In a recent meta-analysis on intervention studies, a 20% improvement in insulin sensitivity was estimated from 18 studies in healthy individuals as well as diabetic or obese individuals (19). In addition, higher-GL diet has been related to an elevated GDM risk in the NHS II population (20). Second, higher sugar intake itself may lead to impaired pancreatic β-cell function. A recent study found that higher sugar intake (~50% of sugar derived from SSBs) was inversely associated with insulin secretion (measured by acute insulin response) and β-cell function (measured by disposition index) after adjusting for body composition and other confounders among children (5). The underlying mechanism for this association is unclear. It has been proposed that consumption of foods high in sugar could lead to the accumulation of reactive oxygen species in β-cells that will subsequently cause β-cell damage and dysfunction (21). Third, caramel coloring in cola-type soft drinks is rich in advanced glycation end products (AGEs). Emerging evidence suggests that AGEs may be positively associated with insulin resistance and inflammation (16). That may help to explain why a stronger association was observed for consumption of sugar-sweetened cola than other SSBs. However, we did not find associations between diet cola and GDM risk, suggesting that AGEs alone may not be a major contributor to the observed association between sugar-sweetened cola consumption and risk of GDM. Due to the observational nature of the present study, it is unlikely to yield detailed evaluations of the underlying mechanisms. Further studies to explore whether AGEs and sugars together could have a synergistic effect on insulin resistance or β-cell damage are needed.

Our study has several strengths including the prospective design, large sample size, and repeated measurements of exposure variables and covariates. However, several limitations of our study should be considered. First, the SFFQ, similar to those used in the NHS II cohort, has been validated against multiple weeks of food records completed over the previous year and showed good correlations (11,12). Although misclassification of dietary SSB intake is inevitable, these dietary data could not have been influenced by the subsequent development of GDM because of the prospective design of this study. This would be expected to attenuate the observed associations, which would not explain the positive results. Our use of cumulative averages of dietary intakes reduced the influence of random errors. Second, because of the observational nature of our study, we cannot prove the causality of the observed association and rule out the impact of residual confounding, although we controlled for most known risk factors of GDM. However, this population is relatively homogeneous regarding socioeconomic status and occupational environments, which tended to reduce the impact of unknown or unmeasured confounders. Third, we did not collect dietary information during pregnancy in this population. Women might change their diets after knowing they are pregnant and receiving dietary counseling or due to the change of their appetite (22,23). It is possible that such changes may have an acute effect on GDM risk or may modify the effects of pregravid beverage consumption on GDM risk. However, there is evidence suggesting that such a pregnancy-related change in dietary intake is item specific and is not substantially for SSBs. For instance, in a prospective study among 2,128 pregnant women (24), SSB consumption did not

change appreciably from the last menstrual period before pregnancy to 26–28 weeks of pregnancy. Lastly, participants in the NHS II cohort do not represent a random sample of U.S. women: the majority of our study participants are health professionals and tend to have a slightly healthier diet and lifestyle than the general U.S. population. Nonetheless, even among this population with low SSB intakes (mean 0.52 vs. 2.18 servings/day in national representative samples) (25), we observed significantly elevated risk of GDM associated with the consumption of sugar-sweetened cola. It will be important to confirm our findings in other populations.

In summary, findings from this large prospective study suggest that higher consumption of sugar-sweetened cola (≥5 servings/week) is significantly associated with an elevated risk of GDM. This is particularly relevant given the widespread use of sugar-sweetened cola. However, consumption of diet beverages was not significantly associated with GDM risk. Further studies in other populations regarding the relation between the consumption of SSBs and risk of GDM as well as other pregnancy-related outcomes are warranted.

Acknowledgments— The NHS II was funded by National Institutes of Health Grants CA50385 and DK58845. L.C., E.Y., and C.Z. were supported by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland.

No potential conflicts of interest relevant to this article were reported.

Parts of this article were presented in abstract form at the 69th Scientific Sessions of the American Diabetes Association, New Orleans, Louisiana, 5–9 June 2009.

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