

# Dietary Fiber Intake, Dietary Glycemic Load, and the Risk for Gestational Diabetes Mellitus

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**OBJECTIVE** — We aimed to examine whether pregravid dietary fiber consumptions from cereal, fruit, and vegetable sources and dietary glycemic load were related to gestational diabetes mellitus (GDM) risk.

**RESEARCH DESIGN AND METHODS** — This study was a prospective cohort study among 13,110 eligible women in the Nurses' Health Study II. GDM was self-reported and validated by medical record review in a subsample.

**RESULTS** — We documented 758 incident GDM cases during 8 years of follow-up. After adjustment for age, parity, prepregnancy BMI, and other covariates, dietary total fiber and cereal and fruit fiber were strongly associated with GDM risk. Each 10-g/day increment in total fiber intake was associated with 26% (95% CI 9–49) reduction in risk; each 5-g/day increment in cereal or fruit fiber was associated with a 23% (9–36) or 26% (5–42) reduction, respectively. Dietary glycemic load was positively related to GDM risk. Multivariate relative risk for highest versus lowest quintiles was 1.61 (1.02–2.53) (*P* for trend 0.03). The combination of high-glycemic load and low-cereal fiber diet was associated with 2.15-fold (1.04–4.29) increased risk compared with the reciprocal diet.

**CONCLUSIONS** — These findings suggested that prepregnancy diet might be associated with women's GDM risk. In particular, diet with low fiber and high glycemic load was associated with an increased risk. Future clinical and metabolic studies are warranted to confirm these findings.

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Gestational diabetes mellitus (GDM) is among the most common complications of pregnancy. GDM complicates ~7% of all pregnancies, resulting in >200,000 cases annually (1). Recent data have shown a substantial rise in the incidence of GDM from 1991 to 2000 (2) and a doubling from 1994 to 2002 (3). Women with GDM experience increased risk for prenatal morbidity and a considerably elevated risk for impaired glucose

tolerance and type 2 diabetes in the years following pregnancy (1). Children of women with GDM are more likely to be obese and have impaired glucose tolerance and diabetes in early adulthood (1). Few modifiable risk factors for GDM have been identified. Obesity is the major recognized modifiable risk factor thus far. High prepregnancy BMI has been consistently associated with an increased risk of GDM (1,4).

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**Abbreviations:** GDM, gestational diabetes mellitus; SFFQ, semiquantitative food frequency questionnaire.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Substantial evidence from epidemiologic and clinical studies supports the thesis that diet influences glucose homeostasis and that modification of diet can lower the risk of diabetes. Dietary fiber and types of carbohydrate have received particular interest due to their impact on postprandial glucose and insulin responses. Associations of dietary fiber (5–10) and dietary glycemic index and load (5–9) with type 2 diabetes among men and nonpregnant women have been extensively studied in large epidemiological studies. Studies on the role of these dietary factors in the development of GDM are sparse. In a large prospective cohort of U.S. women of reproductive age, we examined whether pregravid intakes of dietary fiber and dietary glycemic load and index were related to GDM risk.

## RESEARCH DESIGN AND METHODS

The Nurses' Health Study II, established in 1989, is a prospective cohort study of 116,671 female U.S. nurses. This cohort has been, and continues to be, followed with the use of biennial mailed questionnaires to update information on health-related behavior and characters and to determine incident disease outcome. The follow-up rate exceeds 90% for every 2-year period. For the analyses presented here, women were excluded if they did not complete a semi-quantitative food frequency questionnaire (SFFQ) in 1991 or if more than nine items on it were left blank; if their reported dietary intake was implausible with regard to total energy intake (i.e., <500 kcal/day or >3,500 kcal/day); if they reported a multiple gestation (i.e., twins or higher-order multiple gestation); or if they reported a history of diabetes, cancer, cardiovascular disease, or GDM on the 1989 or 1991 questionnaire. The final sample for the current analyses consisted of 13,110 women who reported having at least one singleton pregnancy lasting ≥6 months between 1992 and 1998.

## Dietary assessment

Dietary intake information was collected by a 133-food SFFQ designed to assess

average food intake over the previous year. For this analysis, we used information from the SFFQs administered in 1991 and 1995. Women were asked to specify a commonly used unit or portion size for each food and report how often they had consumed that amount of each food on average over the previous year. Nutrient intakes were computed by multiplying the frequency response by the nutrient content of the specified portion sizes. 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 the manufacturer. In the U.S. Department of Agriculture database, dietary fiber was determined by enzymatic-gravimetric methods 985.29 and 991.43 of the Association of Official Analytical Chemists (12).

The glycemic index is a relative measure of the glycemic impact of the carbohydrates in different foods (13). The glycemic index values for single food items were based on available databases and publications (14,15), with white bread as the reference food. Total glycemic load was calculated by first multiplying the carbohydrate content of each food by its glycemic index value, then by multiplying this value by the frequency of consumption and summing the values from all food. Dietary glycemic load thus represents the quality and quantity of carbohydrate intake and the interaction between the two. The average glycemic index was calculated for each participant by dividing each person's glycemic load scores by their total daily intake of carbohydrate. Dietary fiber, magnesium, glycemic load, and glycemic index were energy adjusted using the residual method (16). Intakes of carbohydrate, protein, and fatty acids were expressed as nutrient density (percent of total energy intake).

The validity and reliability of SFFQs similar to those used in the Nurses' Health Study II were described elsewhere (17–20). Corrected correlation coefficients between the SFFQ and multiple dietary records for carbohydrate and fiber were 0.64 and 0.56, respectively, in a validation study conducted in a similar cohort (the Nurses' Health Study I [19,20]) and 0.73 and 0.68, respectively, in the Health Professionals Follow-Up Study (18). Correlations were also high for individual carbohydrate-rich food items (e.g., white bread, 0.71; dark bread, 0.77; cold breakfast cereal, 0.79; potatoes, 0.66) (17). The

ability of the SFFQ to assess dietary glycemic index and glycemic load was documented in a study that evaluated the relations of these two variables to plasma concentrations of HDL cholesterol and triacylglycerol in women (21). The concept of glycemic load as a direct measure of postprandial glycemia in healthy subjects has also been previously validated (22).

#### Assessment of nondietary covariates

Participants provided sociodemographic, clinical, and lifestyle information biennially, including age, weight, and smoking status. We calculated BMI (kilograms divided by the square of height in meters; the latter assessed at baseline only). Self-reports of body weight have been shown to be highly correlated with technician-measured weight ( $r = 0.96$ ) in the Nurses' Health Study I (23). Family history of diabetes was reported in 1989 only.

#### Ascertainment of GDM

Diagnosis of GDM was based on self-reported information in the biennial questionnaire. A previous validation study of GDM based on medical record review in this cohort demonstrated a high validity of self-reported diagnosis of GDM (4,24). In brief, we reviewed medical records 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 on medical record review. We also sent supplementary questionnaires to 100 women reporting a pregnancy uncomplicated by GDM during the same interval. Of 93 responders who confirmed a singleton pregnancy during this period, 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.

#### Statistical analysis

In primary analyses, we created measures of cumulative average intakes of dietary fiber, dietary glycemic index, and glycemic load to present long-term intakes of these dietary variables of individual participants before GDM was reported. 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 varia-

tion. Relative risks (RRs) of GDM for each category of nutrient or food intake compared with the lowest category were estimated using Cox proportional hazards analysis stratified by 5-year age categories. We used information on covariates from the baseline or subsequent questionnaires in multivariate analyses. 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 restricted to nulliparous women ( $n = 5,039$ ; 266 GDM cases). In multivariate analyses, we additionally adjusted for age, race/ethnicity (Caucasian, African American, Hispanic, and Asian), family history of diabetes (yes or no), smoking status (never, past, or current), 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  $\geq 35.0$  kg/m<sup>2</sup>), physical activity (quintiles), intakes of total calories (quintiles), alcohol consumption (0, 0.1–4.9, 5.0–9.9, and >10 g/day), protein (quintiles), and fatty acids (quintiles). Covariates were updated during follow-up by using the most recent data for each 2-year follow-up interval.

We evaluated whether associations between dietary factors and GDM risk were modified by BMI (<25, 25–29.9, or  $\geq 30$  kg/m<sup>2</sup>), physical activity (high versus low; dichotomized by median), or family history of diabetes (yes or no) by stratified analyses and by evaluating interaction terms. The significance of linear trends across categories of dietary intake was evaluated using the median value for each category of dietary intake analyzed as a continuous variable in multivariate models. All statistical analyses were performed by using SAS statistical software (version 8.2; SAS Institute, Cary, NC).

**RESULTS** — During 8 years of follow-up (1991–1999), 758 women reported a first diagnosis of GDM among the 13,110 study participants. Women who had a pregravid diet that was high in fiber and glycemic load were on average leaner, more physically active, and less likely to smoke. In addition, dietary fiber and glycemic load were positively related to dietary carbohydrate, magnesium, total

Table 1—Baseline (1991) characteristics according to quintiles of dietary total fiber and dietary glyceemic load

Characteristics	Dietary total fiber			Dietary glyceemic load		
	Q1	Q3	Q5	Q1	Q3	Q5
<i>n</i>	2,827	2,587	2,436	2,255	2,749	2,718
Age (years)	30.9 ± 3.2	31.5 ± 3.2	32.2 ± 3.4	31.6 ± 3.2	31.5 ± 3.3	31.4 ± 3.4
BMI (kg/m <sup>2</sup> )	23.7 ± 4.7	23.5 ± 4.2	22.9 ± 3.6	24.1 ± 4.7	23.5 ± 4.1	22.6 ± 3.9
Physical activity (MET hours/week)*	17.0 ± 24.0	22.5 ± 28.2	31.4 ± 36.3	20.8 ± 26.1	22.9 ± 28.9	25.1 ± 32.5
Current smoker	13.6	7.8	6.3	13.8	9.2	6.9
Nulliparous	39.1	37.0	45.4	42.3	38.4	43.2
Race/ethnicity						
Caucasian	92.9	94.7	94.2	94.6	95.7	91.8
African American	1.5	0.8	0.3	0.7	0.8	1.1
Hispanic	1.0	1.4	2.1	1.3	1.3	1.5
Asian	2.3	1.2	2.1	0.9	0.9	3.7
Other	2.3	1.9	1.2	2.5	1.3	1.9
Family history of diabetes	11.2	13.3	12.3	13.8	12.6	11.2
Alcohol consumption (g/day)	3.4 ± 6.6	2.9 ± 4.6	2.7 ± 4.2	5.5 ± 8.6	3.0 ± 4.4	1.7 ± 2.9
Total calories (kcal/day)	1,822 ± 565	1,833 ± 539	1,792 ± 534	1,790 ± 557	1,856 ± 525	1,783 ± 551
Carbohydrate (% energy)	48.0 ± 8.2	49.9 ± 6.0	55.6 ± 6.6	40.6 ± 4.1	49.8 ± 2.8	59.6 ± 4.9
Protein (% energy)	18.7 ± 3.7	19.4 ± 3.0	19.3 ± 3.4	21.8 ± 3.4	19.5 ± 2.7	16.7 ± 2.8
Total fat (% energy)	33.2 ± 5.9	31.4 ± 4.7	27.1 ± 4.8	36.8 ± 4.8	31.5 ± 3.7	25.5 ± 4.0
Trans fat (% energy)	1.8 ± 0.7	1.6 ± 0.5	1.2 ± 0.5	1.8 ± 0.7	1.6 ± 0.6	1.3 ± 0.5
Polyunsaturated fat (% energy)	5.2 ± 1.3	5.6 ± 1.3	5.3 ± 1.3	6.2 ± 1.5	5.5 ± 1.1	4.7 ± 1.1
Monounsaturated fat (% energy)	12.6 ± 2.6	11.8 ± 2.0	10.0 ± 2.1	13.9 ± 2.2	11.9 ± 1.7	9.6 ± 1.8
Saturated fat (% energy)	12.5 ± 2.6	11.3 ± 2.0	9.3 ± 2.0	13.6 ± 2.3	11.4 ± 1.7	9.0 ± 1.8
Energy-adjusted intakes						
Glyceemic load	169.7 ± 35.2	173.7 ± 25.2	190.0 ± 27.8	133.8 ± 12.4	171.1 ± 4.0	216.8 ± 18.3
Glyceemic index	77.9 ± 5.2	77.1 ± 4.2	75.6 ± 4.5	73.2 ± 4.7	76.5 ± 3.7	80.6 ± 3.8
Total fiber (g/day)	12.0 ± 1.6	17.5 ± 0.7	26.3 ± 5.4	15.5 ± 4.0	18.2 ± 4.5	19.7 ± 7.3
Cereal fiber (g/day)	3.8 ± 1.3	5.6 ± 1.8	8.4 ± 5.3	4.2 ± 2.0	5.8 ± 2.6	6.9 ± 4.6
Fruit fiber (g/day)	1.8 ± 1.0	3.2 ± 1.6	5.5 ± 3.0	2.5 ± 1.8	3.4 ± 2.1	3.9 ± 2.8
Vegetable fiber (g/day)	3.8 ± 1.3	6.2 ± 1.8	10.1 ± 4.1	6.2 ± 2.9	6.5 ± 2.9	6.5 ± 3.8
Magnesium (mg/day)	269.2 ± 61.1	314.1 ± 57.5	384.1 ± 76.2	308.6 ± 63.5	322.6 ± 68.4	317.8 ± 86.6
Total iron (mg/day)	27.0 ± 29.3	30.6 ± 29.9	34.5 ± 31.4	25.0 ± 25.8	31.1 ± 30.7	33.7 ± 32.3
Vitamin C (mg/day)	194.6 ± 225.3	239.8 ± 262.6	322.3 ± 332.5	206.0 ± 257.9	235.4 ± 242.4	297.8 ± 320.0
Vitamin E (mg/day)	25.7 ± 73.3	29.5 ± 79.1	45.7 ± 121.7	28.7 ± 80.7	32.0 ± 89.5	39.8 ± 116.0

Data are means ± SD or percent. Q1 is the lowest quintile, Q3 is the medium quintile, and Q5 is the highest quintile. \*MET hours/week was calculated using the duration per week of various forms of exercise, weighting each activity by its intensity level. For total fiber, tests for trend were all significant ( $P < 0.01$ ) except for age, parity, race/ethnicity, family history of diabetes, protein, and polyunsaturated fat intake. For glyceemic load, tests for trend were all significant ( $P < 0.01$ ) except for age, parity, race/ethnicity, family history of diabetes, and vitamin E.

iron, vitamin C, and vitamin E and inversely related to alcohol, total fat, and saturated, monounsaturated, and *trans* fatty acids (Table 1).

Dietary total fiber, in particular cereal and fruit fiber, intakes were strongly and inversely associated with GDM risk (Table 2). The associations were most significant comparing women in the two extreme quintiles of dietary intakes. These inverse associations remained significant after further adjustment for the other sources of dietary fiber. Additional adjustment for dietary magnesium, vitamin C, and vitamin E intake did not change the results materially; the multivariate RRs for the highest compared with the lowest quintile were 0.70 (95% CI

0.52–0.96) ( $P$  for trend 0.02) for total fiber, 0.77 (0.59–1.01) ( $P$  for trend 0.03) for cereal fiber, and 0.68 (0.52–0.88) ( $P$  for trend 0.02) for fruit fiber. When total and specific dietary fiber were analyzed as continuous variables, each 10-g/day increment in total fiber was associated with a 26% reduction in GDM risk, each 5-g/day increment in cereal fiber with a 23% reduction in risk, and each 5-g/day increment in fruit fiber with a 26% reduction in risk using multivariate analysis. No significant associations were observed for vegetable fiber and GDM risk in multivariate analysis, although there appears to be a reduction in the risk in the upper quintile. Dietary magnesium was inversely related to GDM risk after adjustment for

BMI, but this inverse association was not statistically significant after further adjustment for other lifestyle and dietary factors (especially dietary fiber). In post hoc analyses, we evaluated whether the observed lower GDM risk was related to fiber from any specific food group. The lower risk appeared predominantly related to higher fiber intake from dark breads. Dietary fruit intakes were significantly and inversely associated with GDM risk; the multivariate RR for the highest compared with the lowest quintile was 0.74 (95% CI 0.57–0.95) ( $P$  for trend 0.03).

In stratified analyses, there was no evidence indicating that the inverse associations of GDM risk with total, cereal, and

Table 2—Relative risks of GDM according to quintiles of dietary intakes of fiber and magnesium, dietary glycemic load and index, and dietary intakes of carbohydrate

	Quintiles					Each unit increment in fiber intakes	P value for trend
	Q1	Q2	Q3	Q4	Q5		
<b>Total fiber (g/day)</b>							
Range	4.6–14.0	14.1–16.4	16.5–18.7	18.8–21.9	>22.0	Each 10-g/day increment	
Median	12.4	15.4	17.5	20.1	24.8		
Cases/person-years	181/20,397	169/19,801	170/20,282	141/19,815	97/19,337		
RR1 (95% CI)	1.00	0.98 (0.79–1.20)	1.00 (0.81–1.24)	0.83 (0.66–1.03)	0.62 (0.48–0.79)	0.69 (0.58–0.83)	<0.001
RR2 (95% CI)	1.00	0.97 (0.78–1.20)	1.00 (0.80–1.24)	0.84 (0.66–1.07)	0.67 (0.51–0.90)	0.74 (0.51–0.91)	0.005
<b>Cereal fiber (g/day)</b>							
Range	<3.5	3.6–4.5	4.6–5.6	5.7–7.2	>7.2	Each 5-g/day increment	
Median	2.9	4.1	5.1	6.3	8.9		
Cases/person-years	179/18,701	185/19,966	136/20,229	140/20,048	118/20,688		
RR1 (95% CI)	1.00	1.03 (0.83–1.28)	0.80 (0.64–1.00)	0.87 (0.69–1.08)	0.69 (0.54–0.87)	0.72 (0.60–0.87)	<0.001
RR2 (95% CI)	1.00	1.03 (0.83–1.29)	0.82 (0.65–1.03)	0.89 (0.70–1.13)	0.76 (0.59–0.99)	0.76 (0.62–0.90)	0.02
RR3 (95% CI)	1.00	1.04 (0.84–1.30)	0.83 (0.65–1.04)	0.89 (0.71–1.15)	0.76 (0.59–0.98)	0.77 (0.64–0.91)	0.02
<b>Fruit fiber (g/day)</b>							
Range	<1.5	1.6–2.3	2.4–3.4	3.5–4.8	>4.8	Each 5-g/day increment	
Median	1.1	2.0	2.9	4.1	6.2		
Cases/person-years	200/19,749	137/19,360	160/20,343	150/20,922	111/19,258		
RR1 (95% CI)	1.00	0.73 (0.59–0.91)	0.81 (0.66–0.99)	0.75 (0.61–0.93)	0.57 (0.45–0.72)	0.63 (0.51–0.78)	<0.001
RR2 (95% CI)	1.00	0.74 (0.60–0.93)	0.85 (0.69–1.05)	0.81 (0.65–1.02)	0.66 (0.51–0.86)	0.73 (0.58–0.93)	0.01
RR3 (95% CI)	1.00	0.75 (0.60–0.94)	0.86 (0.69–1.07)	0.82 (0.65–1.04)	0.67 (0.51–0.87)	0.74 (0.58–0.95)	0.02
<b>Vegetable fiber (g/day)</b>							
Range	<4.1	4.2–5.4	5.5–6.8	6.9–8.8	>8.8	Each 5-g/day increment	
Median	3.3	4.8	6.1	7.7	10.6		
Cases/person-years	168/20,201	163/20,591	161/19,734	140/18,826	126/19,280		
RR1 (95% CI)	1.00	1.02 (0.83–1.26)	0.99 (0.80–1.23)	0.95 (0.76–1.19)	0.77 (0.61–0.98)	0.77 (0.61–0.98)	0.03
RR2 (95% CI)	1.00	1.04 (0.84–1.28)	1.00 (0.80–1.24)	0.97 (0.77–1.22)	0.83 (0.64–1.08)	0.83 (0.64–1.08)	0.13
RR3 (95% CI)	1.00	1.06 (0.86–1.32)	1.04 (0.83–1.29)	1.01 (0.80–1.28)	0.87 (0.67–1.13)	0.87 (0.67–1.13)	0.24
<b>Magnesium (mg/day)</b>							
Range	<257	257–290	291–323	324–368	>368	Each 5-g/day increment	
Median	234	275	307	343	409		
Cases/person-years	175/18,930	154/19,375	138/20,205	152/20,538	139/20,584		
RR1 (95% CI)	1.00	0.86 (0.69–1.07)	0.76 (0.61–0.96)	0.81 (0.65–1.01)	0.74 (0.59–0.93)	0.74 (0.59–0.93)	0.02
RR2 (95% CI)	1.00	0.86 (0.68–1.08)	0.76 (0.60–0.97)	0.84 (0.66–1.07)	0.78 (0.60–1.01)	0.78 (0.60–1.01)	0.11
RR3 (95% CI)	1.00	0.92 (0.73–1.17)	0.86 (0.67–1.11)	0.99 (0.76–1.29)	0.96 (0.72–1.28)	0.96 (0.72–1.28)	0.39



Glycemic load									
Range	<148.2	148.2–164.1	164.2–178.4	178.5–196.6	>196.6				
Median	136.7	156.8	171.1	186.0.6	211.7				
Cases/person-years	210/19,543	174/19,298	128/20,439	145/22,458	139/19,894				
RR1 (95% CI)	1.00	0.86 (0.69–1.08)	0.70 (0.55–0.88)	0.83 (0.66–1.03)	0.84 (0.67–1.05)				0.16
RR2b (95% CI)*	1.00	0.99 (0.76–1.28)	0.89 (0.65–1.22)	1.21 (0.84–1.74)	1.61 (1.02–2.53)				0.03
Glycemic index									
Range	<72.9	72.9–75.8	75.9–78.1	78.2–80.7	>80.7				
Median	70.9	74.5	76.9	79.3	82.6				
No. of cases	147	143	154	145	169				
Person-years	19,308	19,708	20,305	20,616	19,695				
RR1 (95% CI)	1.00	1.07 (0.84–1.36)	1.19 (0.95–1.50)	1.13 (0.90–1.43)	1.40 (1.12–1.77)				0.04
RR2b (95% CI)†	1.00	1.05 (0.82–1.33)	1.14 (0.90–1.45)	1.06 (0.82–1.36)	1.30 (1.00–1.68)				0.07
Carbohydrate									
Range (% energy)	<43.7	43.7–47.8	47.9–51.4	51.5–55.7	55.8–85.0				
Median	40.9	46.0	49.6	53.3	59.1				
No. of cases	227	162	137	144	134				
Person-years	19,857	18,559	19,898	20,964	20,354				
RR1 (95% CI)	1.00	0.73 (0.58–0.91)	0.71 (0.57–0.89)	0.73 (0.58–0.91)	0.70 (0.56–0.88)				0.01
RR2b (95% CI)‡	1.00	0.75 (0.58–0.97)	0.75 (0.55–1.02)	0.84 (0.57–1.21)	1.00 (0.62–1.63)				0.97

RR1: adjusted for age (5-year category), parity (0, 1, 2, or  $\geq 3$ ), and BMI (nine categories: <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  $\geq 35.0$  kg/m<sup>2</sup>). RR2: adjusted for variables in model 1, race/ethnicity, cigarette smoking status (never, past, or current), family history of diabetes in a first-degree relative (yes or no), alcohol intake (0, 0.1–5.0, 5.1–15.0, or >15 g/day), physical activity (quintile), total energy (quintile), protein intake (quintile), saturated fat, and polyunsaturated, monounsaturated, and *trans* fatty acids (quintile). RR2b: adjusted for variables in model 1, race/ethnicity, cigarette smoking status (never, past, or current), family history of diabetes in a first-degree relative (yes or no), parity (0, 1, 2, or  $\geq 3$ ), alcohol intake (0, 0.1–5.0, 5.1–15.0, or >15 g/day), physical activity (quintile), total energy (quintile), dietary cereal fiber, fruit and vegetable fiber (quintile), and intakes of protein (quintile). RR3: adjusted for variables in model 2 and the other fiber types (cereal, fruit, or vegetable). \*Additional adjustment for saturated fat and polyunsaturated, monounsaturated, and *trans* fatty acids (quintile). †Additional adjustment for saturated fat and polyunsaturated and *trans* fatty acids (quintile) and carbohydrates (quintile). ‡Additional adjustment for saturated fat and polyunsaturated and *trans* fatty acids (quintile) and glycemic index (quintile).

fruit fiber varied significantly according to BMI, physical activity, or family history of diabetes. Additionally, we restricted our analysis to nulliparous women and obtained similar results. To avoid potential bias due to undiagnosed nongestational diabetes before GDM developed, we eliminated women with GDM who reported the occurrence of nongestational diabetes in the next-round questionnaire ( $n = 20$ ); the results did not change materially.

Dietary glycemic load was significantly and positively associated with GDM risk after adjustment for nondietary and dietary covariates. When fat, protein, and total energy intake were held constant, dietary glycemic load represented the effect of substituting high-glycemic index carbohydrate for low-glycemic index carbohydrate on GDM risk (model 2 for glycemic load, Table 2). Total carbohydrate intake was inversely associated with GDM risk after adjustment for age and BMI. However, this association, which might be due to a more healthy diet and lifestyle related to the greater health consciousness typically associated with a low-fat high-carbohydrate diet, disappeared after additional adjustment for lifestyle and other dietary factors. The association between dietary glycemic index alone and GDM risk was not statistically significant.

We also examined the joint effect of dietary glycemic load and cereal fiber. After adjustment for age, BMI, physical activity, dietary factors, and other covariates, compared with women with a high intake of cereal fiber and low dietary glycemic load, those with low cereal fiber intake and high glycemic load had a 2.15-fold (95% CI 1.04–4.29) higher risk of GDM ( $P$  for interaction 0.02).

**CONCLUSIONS** — In this large prospective study of women, pregravid consumptions of dietary total fiber and cereal and fruit fiber were significantly and inversely associated with GDM risk. In contrast, dietary glycemic load was positively associated with GDM risk. These associations were most significant comparing women in the upper and lower quintiles of dietary intakes.

Uncomplicated pregnancy is characterized by progressive hyperlipidemia, insulin resistance, and a deterioration of glucose tolerance in the third trimester. In women with GDM, direct measures of insulin sensitivity during the third trimester have identified exaggerated resistance to insulin's ability to stimulate glucose utili-

zation (25,26) and to suppress both glucose production (25,26) and fatty acid levels (25). When studied postpartum, women who had GDM have greater insulin resistance than women who had uncomplicated pregnancies (26,27). Further, sequential measurements of insulin sensitivity performed in the same women before pregnancy, early in the second trimester, and in the third trimester have documented insulin resistance in both lean and obese women who developed GDM later (26). These findings indicated that most women who develop GDM had underlying insulin resistance to which the insulin resistance of pregnancy was partially additive (28). 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.

There are several possible mechanisms that may explain the relationship between dietary fiber and glucose homeostasis. Increased dietary fiber may reduce appetite and lower total energy intake, thus reducing adiposity and improving insulin sensitivity (29,30). Fiber intake may also delay gastric emptying (30) and slow glucose absorption, resulting in lesser absorption of glucose and lesser increases in insulin levels (29,31). The beneficial effect of fiber on glucose homeostasis may be also due to delayed gastric emptying rate, slowed digestion, and absorption of food rich in fiber (30) and the subsequently reduced rate of glucose absorption and plasma insulin levels (29,31). These benefits have been attributed primarily to soluble fiber, which creates a gel-like substance in the stomach (32). Whole-grain and bran products from wheat and corn, the major source of cereal fiber in our cohort, typically contain insoluble fiber. Other characteristics of these sources of cereal fiber might also be important in glucose and lipid metabolism (e.g., the physical form and degree of processing whole grains and the presence of organic acids, enzyme inhibitors, and other bioactive compounds). Epidemiological studies are unlikely to yield detailed evaluations of these pathways, and thus experimental studies are clearly warranted (33).

We are unaware of published studies that comprehensively examined the association of total dietary fiber and specific

sources of fiber with GDM risk. The inverse relationship between total fiber and cereal fiber and the risk of GDM in the present study is consistent with findings from those studies of type 2 diabetes (5–10). In addition, an inverse association with circulating levels of C-reactive protein (34,35) and a positive association with adiponectin (36) have been reported for total dietary fiber and cereal fiber. Both biomarkers have been associated with risks of GDM (37,38). Notably, different from published studies on type 2 diabetes, fruit fiber was strongly associated with a reduced risk of GDM in the present study. In addition to fruit fiber, fruits comprise other components that were associated with reductions in GDM risk. It is plausible that the observed association between fruit fiber and GDM risk may be mediated through other components. For example, dietary vitamin C and plasma ascorbic acid levels have been inversely associated with GDM risk (39). However, the association between fruit fiber and GDM risk remained significant after adjustment for dietary intakes of vitamin C and E and magnesium in the present study, although the association was slightly attenuated. Future studies are warranted to confirm these findings and decipher underlying mechanisms for the observed associations. Similar to most previous studies on type 2 diabetes (5–10), we did not observe a significant association of vegetable fiber intakes with GDM risk. Taken together, these findings suggest that effects of dietary fiber may vary depending on food source.

Both dietary glycemic index and load were used to characterize the capability of diet to induce postprandial glycemia. Although metabolic studies on the effect of glycemic index and load on insulin sensitivity and secretion have shown mixed results, regular consumption of meals higher in glycemic index was found to increase 24-h blood glucose and insulin secretion levels (40,41). Similarly, increases in dietary glycemic load induced both hyperglycemia and hyperinsulinemia (22). Very few studies in this regard have been conducted among pregnant women. An association of low dietary glycemic index with lower levels of plasma glucose and HbA<sub>1c</sub> was reported among pregnant women in a clinical trial (42) and in an observational study (43). Findings from large prospective epidemiological studies on the association between glycemic index and load and type 2 diabetes risk have also been inconsistent. Higher glycemic

index (5–7) and glycemic load (7) were related to significantly elevated risk of diabetes after adjustment for covariates, including cereal fiber in the Nurses' Health Study I and II and the Health Professionals Follow-Up Study. However, no significant associations were observed in the Iowa Women's Health Study (8), and in the Atherosclerosis Risk in Communities study (9), a borderline significant association was reported only with glycemic load after adjustment for cereal fiber. We are not aware of epidemiologic studies on the association between glycemic index/load and GDM risk. Dietary glycemic load was a stronger predictor of GDM risk than glycemic index or the amount of carbohydrate alone in the present study, which may suggest the importance of both the quality and quantity of carbohydrate in determining a pregnant woman's susceptibility to GDM. In joint analyses, the lowest risk of GDM was observed among those who consumed the highest amount of cereal fiber and lowest glycemic load.

The SFFQ, similar to the questionnaires used in the Nurses' Health Study II cohort, has been validated against multiple weeks of food records completed over the previous year and showed good correlations (17). Misclassification of dietary exposure such as dietary fiber, glycemic index, and glycemic load is inevitable. However, 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 and would not explain the positive results. Our use of cumulative averages of dietary intakes reduced the influence of random error. Our study participants, on average, have higher mean intakes of fiber than the general U.S. populations, which is probably due to a more healthy diet and lifestyle related to the greater health consciousness of these health professionals. Nonetheless, even among this population high in fiber intakes, we observed significantly reduced risk of GDM associated with higher fiber intake. The Nurses' Health Study II cohort does not represent random samples of U.S. women. It will be important to confirm these findings in other populations. The relative socioeconomic homogeneity of this population, on the other hand, tends to reduce the impact of unknown confounders. Conceivably, women with "classic" GDM risk factors, such as obesity and advanced age, might be screened more carefully for GDM than

women without such risk factors, artifactually increasing the observed risks associated with such characteristics. However, in a previous study (24) that evaluated GDM self-reports, we found a high level of surveillance for GDM regardless of risk factor status and noted no significant bias in screening based on risk factor profile. Our validation study also indicated a high degree of accuracy of self-reported GDM compared with medical record review (4,24). Because of the observational nature of the current study, we cannot rule out the possibility of residual confounding by unmeasured factors. We, however, carefully controlled for major well-documented risk factors for GDM and still observed significant associations of dietary fiber and glycemic load with GDM risk.

Dietary information during pregnancy was not collected in the current study. It is plausible that much of the beneficial effect of the high-fiber low-glycemic load diet that we observed for pregravid period reflected continued consumption patterns during pregnancy. Limited data (44) indicated that intakes of dietary fiber and food high in fiber in periconception period and early pregnancy were highly correlated with those in the second trimester of pregnancy, although women generally increased their caloric intake in pregnancy to meet fetal needs. The current study addresses the relationship between dietary factors and GDM only. Maternal glucose was one of the major energy sources for fetal growth (45,46), and lower dietary glycemic index during pregnancy was associated with reduced infant birth weight (43). Further studies are needed to examine associations between these dietary factors in pregnancy and other pregnancy outcomes, including fetal growth and development.

In summary, although the observational design of the present study does not prove causality, our findings suggest that pregravid diet was associated with women's susceptibility to GDM. In particular, a diet with low fiber and high glycemic load was associated with an increased GDM risk. Future clinical and metabolic studies are warranted to confirm these findings.

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