Prospective Study of Dietary Carbohydrates, Glycemic Index, Glycemic Load, and Incidence of Type 2 Diabetes Mellitus in Middle-aged Chinese Women

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Background: Much uncertainty exists about the role of dietary glycemic index and glycemic load in the development of type 2 diabetes mellitus, especially in populations that traditionally subsist on a diet high in carbohydrates.

Methods: We observed a cohort of 64 227 Chinese women with no history of diabetes or other chronic disease at baseline for 4.6 years. In-person interviews were conducted to collect data on dietary habits, physical activity, and other relevant information using a validated questionnaire. Incident diabetes cases were identified via in-person follow-up. Associations between dietary carbohydrate intake, glycemic index, and glycemic load and diabetes incidence were evaluated using multivariable Cox proportional hazards models.

Results: We identified 1608 incident cases of type 2 diabetes mellitus in 297 755 person-years of follow-up. Di-

NCERTAINTY EXISTS ABOUT the role of dietary carbohydrates in the development of type 2 diabetes mellitus (DM).¹ Several²⁻⁵ but not all studies of primarily white populations have linked dietary *glycemic index* (GI), an in vivo measure of carbohydrate quality based on the rapidity of its

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absorption, and *glycemic load* (GL), a measure of the total glycemic effect of carbohydrates in the diet,^{6,7} to an increased risk of type 2 DM. Because bread, potatoes, sugar-sweetened soft drinks, and sweets and desserts are the main sources of dietary GL in Western populations, it has been suggested that the associations between dietary GI and GL and risk of type 2 DM may differ in Chinese and other Asian populations in which rice is the major staple food.⁸

etary carbohydrate intake and consumption of rice were positively associated with risk of developing type 2 diabetes mellitus. The multivariable-adjusted estimates of relative risk comparing the highest vs the lowest quintiles of intake were 1.28 (95% confidence interval, 1.09-1.50) for carbohydrates and 1.78 (95% confidence interval, 1.48-2.15) for rice. The relative risk for increasing quintiles of intake was 1.00, 1.04, 1.02, 1.09, and 1.21 (95% confidence interval, 1.03-1.43) for dietary glycemic index and 1.00, 1.06, 0.97, 1.23, and 1.34 (95% confidence interval, 1.13-1.58) for dietary glycemic load.

Conclusion: High intake of foods with a high glycemic index and glycemic load, especially rice, the main carbohydrate-contributing food in this population, may increase the risk of type 2 diabetes mellitus in Chinese women.

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Little is known about the direct role of dietary GI and GL in the development of type 2 DM in populations that traditionally subsist on diets high in carbohydrates. Using data collected in the Shanghai Women's Health Study, we prospectively examined the relationships between dietary carbohydrates, GI, GL, and carbohydrate-rich foods with the risk of type 2 DM in middle-aged Chinese women.

METHODS

STUDY POPULATION

The Shanghai Women's Health Study is a population-based prospective cohort study of 74 942 women aged 40 to 70 years at baseline. Details of the study have been reported elsewhere.^{9,10} In brief, all eligible women residing in 7 communities between December 28, 1996, and May 23, 2000, were recruited, with a participation rate of 92.7%. In-person interviews were conducted to obtain information on demographics, dietary intake, physical activity,

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disease history, reproductive history, and occupational history. According to a standard protocol anthropometric measurements at baseline including weight, height, and circumferences of waist and hips were taken by trained interviewers who were retired medical professionals.¹⁰ From these measurements, the following variables were created: waist-hip ratio (WHR) (calculated as waist circumference divided by hip circumference) and body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared).

Cohort members were followed up via in-person interviews every 2 years. The first in-person follow-up for all living cohort members was conducted from October 10, 2000, to October 6, 2002. Assessment of disease outcomes was conducted for 74 755 cohort members, with a complete response rate of 99.8%. The second follow-up survey was launched January 17, 2002, and completed November 20, 2004, with a complete response rate of 98.7%. Only 934 participants were unavailable for follow-up during the entire 5-year period. The institutional review boards of all institutions involved in the study approved the study protocols, and written informed consent was obtained from all participants before the interview was conducted. A total of 64 227 participants with no history of chronic disease, which included cardiovascular disease, diabetes mellitus, and cancer, were included in the study.

DIETARY ASSESSMENT

Dietary intake was assessed twice, during the baseline survey and at the first follow-up survey, via in-person interviews using a food frequency questionnaire (FFQ) designed for and validated in this population.⁹ The Shanghai Women's Health Study FFQ comprises 77 food items and food groups that include 90% of foods commonly consumed in urban Shanghai during the study period. Carbohydrate-rich foods included rice, noodles or steamed bread, bread, potatoes, and sweet potatoes. For women who developed type 2 DM, cancer, or cardiovascular diseases between baseline and the first follow-up FFQ, only dietary data from the baseline FFQ were included in this analysis. For other participants, FFQ data from baseline and follow-up were averaged to reduce random measurement error. The Chinese Food Composition Tables¹¹ were used to estimate intake of nutrients and energy intake (ie, kilocalories per day).

We calculated dietary GI and GL based on the FFQs as described in detail previously.^{6,7,12} We calculated each food's GL by multiplying the carbohydrate content of each food by the food's GI value and the average amount of food consumed per day. We then summed these products over all food items to produce the dietary GL. We derived dietary GI by dividing the dietary GL by the amount of carbohydrate intake, thus establishing a weighted average of GI in each individual's diet.⁶

Glycemic index values (using the glucose level as the reference) were obtained from international tables for GI values¹³ and from the Chinese Food Composition Tables.¹¹ The physiologic interpretation of these variables has been described previously.^{6,7,12} To further reduce measurement error and to adjust for extraneous variation owing to total energy intake, we applied the residual method described by Willett and Stampfer.¹⁴

PHYSICAL ACTIVITY ASSESSMENT

Detailed assessment of physical activity was obtained using a validated questionnaire.¹⁵ The questionnaire evaluated regular exercise and sports participation during the preceding 5 years and collected information on daily living activity such as walking, stair climbing, cycling, household activities, and daily commuting journey to and from work (walking and cycling). We calculated the metabolic equivalent task (MET) value for each

activity using a compendium of physical activity values.¹⁶ One MET hour per day is roughly equivalent to 1 kcal/kg/d or about 15 minutes of participation in an activity of moderate intensity (4 METs) for an average adult.¹⁶ We combined each of the exercise and lifestyle activity indices to derive a quantitative estimate of overall nonoccupational activity (METs–hours per day).

OUTCOME ASCERTAINMENT

Incident type 2 DM was identified through outcome follow-up surveys. A total of 1608 study participants reported having a type 2 DM diagnosis since the baseline survey. We considered type 2 DM to be confirmed if the participants reported having been diagnosed as having type 2 DM and met at least 1 of the following criteria as recommended by the American Diabetes Association¹⁷: fasting glucose level greater than or equal to 126 mg/dL (to convert to millimoles per liter, multiply by 0.0555) on 2 separate occasions or an oral glucose tolerance test value greater than or equal to 200 mg/dL (performed as part of the participant's primary health care), or use of hypoglycemic medication (ie, insulin or oral hypoglycemic drugs). Of the participants with self-reported type 2 DM, 896 met the study outcome criteria and are referred to as having confirmed type 2 DM in this report; all other participants are considered to have probable type 2 DM. We performed analyses of both confirmed and probable type 2 DM cases and found similar results. Thus, in this article, we present results with all type 2 DM cases combined.

STATISTICAL ANALYSIS

Person-years for each participant were calculated as the interval between baseline recruitment to the diagnosis of type 2 DM, censored at death or completion of the second follow-up. The Cox proportional hazards model was used to assess the rate ratio of type 2 DM by intake categories of carbohydrates, GI, GL, and specific food groups. These dietary variables were categorized by quintile distribution, with the lowest quintiles serving as the reference groups. We excluded from this study participants who had extreme values for total energy intake (<500 or >3500 kcal/d; n=36),¹⁸ leaving 64 191 participants for the final analysis. Sociodemographic factors and type 2 DM risk factors were adjusted for in the analyses as potential confounders. These included age (entered as a continuous variable), level of educational achievement (none, elementary school, middle or high school, or college), family income in yuan per year (¥<10000 [<\$1204.80], ¥10000-¥19999 [\$1204.81-\$2409.50], ¥20 000-¥29 999 [\$2409.60-\$3614.30], or ≥30 000 $[\geq$ \$3614.40]; the exchange rate for the US dollar at the time of the baseline survey was 1=8.3, occupation (professional, clerical, manual worker, housewife, or retired), smoking status (smoked at least 1 cigarette per day for more than 6 consecutive months), alcohol consumption (yes or no to having ever consumed beer, wine, or spirits at least 3 times per week), nonoccupational physical activity (quintiles of METshours per day), and hypertension diagnosis (yes or no).

We conducted stratified analysis by WHR, BMI, and physical activity categories. We also defined a group at high risk for insulin resistance or type 2 DM on the basis of the following criteria: WHR at least 0.85, BMI at least 25, and being in the lower quartile of physical activity METs. We then examined the effect of dietary GI and GL according to risk status for insulin resistance. The log-likelihood ratio test was used to evaluate the significance of these interaction terms. All analyses were performed using commercially available software (SAS version 9.1; SAS Institute Inc, Cary, North Carolina), and all tests of statistical significance were based on 2-sided probability.

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Table 1. Characteristics of the Population by Quintiles of Energy-Adjusted Glycemic Load^a

Characteristic	Q1	Q2	Q3	Q4	Q5
Dietary data					
Intake, kcal/d	1773.2	1643.9	1609.5	1602.6	1784.1
Carbohydrate, g/d	263.5	269.1	276.3	287.1	337.6
Total fat, g/d	42.5	32.1	27.6	23.9	21.
Protein, g/d	84.1	69.6	63.7	59.3	59.
Fiber, g/d	13.8	11.5	10.5	9.7	9.3
Other data					
Age, mean, y	49.1	49.8	50.5	51.6	53.8
Obesity					
Central ^b	14.9	15.8	18.2	20.5	27.
World Health	2.9	3.2	3.7	4.2	7.4
Organization ^c					
Asian ^d	9.9	10.4	11.8	13.6	19.8
Smoking status	2.2	1.7	2.0	2.0	3.
Alcohol consumption	3.8	2.1	2.0	1.6	1.
Exercise	37.2	34.1	32.1	31.1	29.9
Education level					
None	7.4	10.9	15.9	21.1	36.
Elementary school	36.6	37.4	39.8	41.2	38.
Middle or high school	36.1	34.5	29.9	26.3	18.4
College	19.8	17.0	14.4	11.3	6.3
Income, ¥ ^e					
<10000	11.7	12.3	14.5	16.3	21.0
10 000-19 999	33.5	36.3	37.0	40.4	42.
20 000-29 999	30.3	30.5	30.3	27.9	24.0
\geq 30 000	24.4	20.9	18.1	15.3	11.
Occupation					
Professional	25.9	24.2	21.4	17.3	10.0
Clerical	14.9	14.0	13.3	12.4	10.5
Manual worker	22.9	23.3	23.5	23.1	21.9
Housewife or retired	36.2	38.5	41.8	47.2	56.9
Hypertension	15.2	17.3	18.3	20.2	23.3

Abbreviation: Q, quintile.

^aData are given as percentage of participants unless otherwise indicated. P<.001 for all characteristics, by analysis of variance or χ^2 test.

^bWaist-hip ratio greater than or equal to 0.85.

^cBody mass index greater than or equal to 30 (calculated as weight in kilograms divided by height in meters squared).

^dBody mass index greater than 27.5.

^eTo convert yuan to US dollars, divide by 8.3.

RESULTS

At baseline, dietary GL was positively associated with the intake of carbohydrates and inversely associated with the intake of fat, protein, and fiber. Participants in the higher quintiles of GL were more likely to be older, less educated, have a lower annual income, be housewives or retired at the time of the survey, and to have ever smoked, and they were less likely to exercise or have ever consumed alcohol (**Table 1**). Glycemic load was also positively associated with overall and central obesity. The top 10 contributors to dietary GL in this population were rice (73.9%), noodles and steamed bread (7.3%), sweets and desserts (3.3%), bread (2.6%), watermelon (1.4%), apples (0.8%), candy (0.7%), potatoes (0.6%), milk (0.5%), and bananas (0.4%).

During an average of 5 years of follow-up (297755 person-years), 1608 incident cases of type 2 DM were documented. High carbohydrate intake was associated

Table 2. Association of Carbohydrate Level, Glycemic Index, Glycemic Load, and Food Groups With High Glycemic Index With Risk of Type 2 Diabetes Mellitus

Dietary Data	No. of Incident Cases	Person-Years	RR ^a (95% CI)
Carbohydrates ^b			
Q1	239	59 334	1 [Reference]
Q2	246	59 954	0.96 (0.80-1.15
Q3	244	60 037	0.87 (0.73-1.05
Q4	336	59 403	1.09 (0.92-1.29
Q5	540	59014	1.28 (1.09-1.50
Glycemic index ^b			
Q1	238	58 641	1 [Reference]
Q2	279	61 410	1.04 (0.87-1.24
Q3	281	59 366	1.02 (0.86-1.22
Q4	335	59757	1.09 (0.92-1.29
Q5	472	58 568	1.21 (1.03-1.43
Glycemic load ^b			,
Q1	221	59 256	1 [Reference]
Q2	256	60 085	1.06 (0.88-1.27
Q3	253	60 003	0.97 (0.81-1.17
Q4	349	59628	1.23 (1.03-1.46
Q5	526	58769	1.34 (1.13-1.58
Staple food items			
Q1	221	58734	1 [Reference]
Q2	286	59 566	1.13 (0.94-1.35
Q3	260	59 931	0.96 (0.80-1.16
Q4	339	59 966	1.13 (0.94-1.37
Q5	499	59 545	1.37 (1.11-1.69
Rice, ^c g/d			
<200	179	53 200	1 [Reference]
200-249	311	82 809	1.04 (0.86-1.25
250-299	486	93 493	1.29 (1.08-1.54
\geq 300	629	68 241	1.78 (1.48-2.15
Tubers			
Q1	444	58 217	1 [Reference]
Q2	286	59650	0.67 (0.58-0.78
Q3	239	60 083	0.56 (0.48-0.66
Q4	309	60 169	0.69 (0.60-0.80
Q5	327	59 622	0.67 (0.58-0.78

Abbreviations: CI, confidence interval; Q, quintile; RR, relative risk. ^a Adjusted for age, kilocalories per day consumed, body mass index (calculated as weight in kilograms divided by height in meters squared), waist-hip ratio, smoking status, alcohol consumption, physical activity, income level, education level, occupation, and diagnosis of hypertension.

^bEnergy adjusted. ^cRice could not be categorized by quintiles of intake because of the nature

of the distribution of the variable.

with a moderately increased risk of type 2 DM (**Table 2**). The relative risk (RR) across quintiles was 1.00, 0.96, 0.87, 1.09, and 1.28 (95% confidence interval [CI], 1.09-1.50). The percentage of energy contributed by carbohydrates was also associated with an increase in the risk of type 2 DM (RR for quintiles of energy contributed by carbohydrates: 1.00, 0.89, 0.94, 1.14, and 1.31 [95% CI, 1.10-1.50]).

Both dietary GI and GL were positively associated with the risk of type 2 DM. The adjusted RR for type 2 DM across increasing quintiles of intake was 1.00, 1.04, 1.02, 1.09, and 1.21 (95% CI, 1.03-1.43) for dietary GI and 1.00, 1.06, 0.97, 1.23, and 1.34 (95% CI, 1.13-1.58) for dietary GL.

A high intake of staples (rice, noodles and steamed bread, and bread) was associated with a greater risk of developing type 2 DM. Compared with women in the low-

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Table 3. Stratified Analysis of Intake of Carbohydrates, Glycemic Index, Glycemic Load, and Rice by Waist-Hip Ratio and Risk of Type 2 Diabetes Mellitus^a

	Waist-H	Waist-Hip Ratio			
	< 0.85	≥0.85			
Dietary Data	RR (95% CI)	RR (95% CI)			
Carbohydrates ^b					
Q1	1 [Reference]	1 [Reference]			
Q2	0.89 (0.71-1.12)	1.05 (0.78-1.42)			
Q3	0.80 (0.63-1.01)	1.02 (0.76-1.36)			
Q4	0.97 (0.78-1.22)	1.26 (0.96-1.65)			
Q5	1.23 (1.00-1.52)	1.38 (1.07-1.79)			
Interaction, 0.40					
Glycemic index ^c					
Q1	1 [Reference] ^d	1 [Reference] ^e			
Q2	0.96 (0.77-1.20)	1.23 (0.93-1.63)			
Q3	0.85 (0.67-1.06)	1.32 (1.01-1.74)			
Q4	1.05 (0.84-1.30)	1.19 (0.91-1.56)			
Q5	1.17 (0.94-1.45)	1.35 (1.05-1.75)			
Interaction, 0.07					
Glycemic load ^c					
Q1	1 [Reference]	1 [Reference]			
Q2	0.94 (0.75-1.19)	1.27 (0.94-1.72)			
Q3	0.88 (0.69-1.11)	1.19 (0.88-1.60)			
Q4	1.08 (0.87-1.35)	1.46 (1.10-1.94)			
Q5	1.26 (1.02-1.56)	1.54 (1.17-2.02)			
Interaction, 0.34					
Rice, g/d ^c					
<200	1 [Reference]	1 [Reference]			
200-249	0.91 (0.72-1.15)	1.27 (0.94-1.72)			
250-299	1.23 (0.98-1.54)	1.41 (1.05-1.88)			
\geq 300	1.64 (1.28-2.10)	2.04 (1.51-2.10)			
Interaction, 0.39					

Abbreviations: CI, confidence interval; Q, quintile; RR, relative risk. ^aUnless otherwise indicated, all P_{trend} < .001.

^bAdjusted for age, kilocalories per day consumed, body mass index (calculated as weight in kilograms divided by height in meters squared), smoking status, alcohol consumption, physical activity, income level, education level, occupation, and diagnosis of hypertension. P_{trend} = .01.

^cEnergy adjusted.

^d P_{trend} =.08.

 $e P_{trend} = .06.$

est quintile of intake, the multivariable-adjusted RR of type 2 DM across quintiles was 1.00, 1.13, 0.96, 1.13, and 1.37 (95% CI, 1.11-1.69) for staples. The positive association was evident for rice consumption, the top dietary GL contributor. The RR comparing the extreme categories of rice intake (<200 g/d vs \geq 300 g/d) was 1.78 (95% CI, 1.48-2.15). Note that 100 g of raw rice is equivalent to 250 g of cooked rice (1 cup of rice); thus, 300 g of raw rice is equivalent to 3 cups of cooked rice and 200 g of raw rice is equivalent to 2 cups of cooked rice. Intake of tubers was associated with a lower risk of type 2 DM. The multivariate adjusted RR of type 2 DM across quintiles of potato and sweet potato intake was 1.00, 0.82, 0.69, 0.78, and 0.72 and 1.00, 0.54, 0.63, 0.48, and 0.51, respectively.

In our population, having a high WHR (≥ 0.85) or a high BMI (≥ 25) was associated with higher risk of type 2 DM (RR, 1.76 [95% CI, 1.59-1.96] and 2.31 [95% CI, 2.06-2.58], respectively). Therefore, we conducted analyses stratified by categories of WHR and BMI. Dietary car-

Table 4. Stratified Analysis of Intake of Carbohydrates, Glycemic Index, Glycemic Load, and RIce by Body Mass Index and Risk of Type 2 Diabetes Mellitus^a

	Body Mass Index ^b			
	≤25	>25		
Dietary Data	RR (95% CI)	RR (95% CI)		
Carbohydrates ^c				
Q1	1 [Reference]	1 [Reference]		
Q2	0.86 (0.65-1.13)	1.05 (0.82-1.32		
Q3	0.80 (0.60-1.06)	0.94 (0.74-1.20		
Q4	0.73 (0.55-0.97)	1.32 (1.06-1.65		
Q5	1.22 (0.94-1.58)	1.41 (1.14-1.73		
Interaction, 0.01 Glycemic index ^d	, , , , , , , , , , , , , , , , , , ,	, , , , , , , , , , , , , , , , , , ,		
Q1	1 [Reference] ^e	1 [Reference] ^f		
Q2	1.01 (0.77-1.33)	1.04 (0.83-1.30		
Q3	0.86 (0.65-1.15)	1.12 (0.90-1.39		
Q4	1.00 (0.76-1.32)	1.14 (0.92-1.41		
Q5	1.08 (0.82-1.43)	1.30 (1.06-1.60		
Interaction, 0.57 Glycemic load ^d	, , , , , , , , , , , , , , , , , , ,	,		
Q1	1 [Reference] ^g	1 [Reference]		
Q2	0.88 (0.66-1.16)	1.19 (0.93-1.51		
Q3	0.78 (0.59-1.05)	1.13 (0.89-1.44		
Q4	0.86 (0.65-1.14)	1.50 (1.20-1.88		
Q5	1.18 (0.91-1.55)	1.52 (1.22-1.89		
Interaction, 0.04				
Rice, g/d				
<200	1 [Reference] ^h	1 [Reference]		
200-249	0.81 (0.60-1.08)	1.18 (0.93-1.51		
250-299	1.17 (0.89-1.53)	1.34 (1.06-1.69		
\geq 300 Interaction, 0.40	1.39 (1.02-1.90)	2.05 (1.61-2.61		

Abbreviations: CI, confidence interval; Q, quintile; RR, relative risk.

^aAdjusted for age, kilocalories per day consumed, waist-hip ratio, smoking status, alcohol consumption, physical activity, income level, education level, occupation, and diagnosis of hypertension. Unless otherwise indicated, all

 $P_{\text{trend}} < .001.$ ^bCalculated as weight in kilograms divided by height in meters squared. ^C P_{trend} = .24.

d Energy adjusted.

 $e P_{trend} = .62.$

 $^{\rm f}P_{\rm trend}$ < .01.

 $^{9}P_{\text{trend}}=.20.$

 $^{h}P_{trend} = .001.$

bohydrate intake, GI, GL, and rice intake were associated with an increased risk of type 2 DM across all WHR and BMI categories (Table 3 and Table 4). The effect of carbohydrate intake, GI, GL, and rice intake was slightly stronger in participants with higher WHR and BMI. Significant multiplicative interactions were observed between carbohydrates and BMI and between GI and BMI.

Those in the lower quartile of physical activity participation (as measured in METs) had a modestly higher risk than all other participants (RR, 1.16; 95% CI, 1.04-1.30). The association of carbohydrates, rice, GI, and GL with type 2 DM seemed to be more pronounced in participants with low activity levels, and tests for interaction were significant for GL and physical activity (Table 5). We further evaluated dietary associations in analyses stratified by risk of insulin resistance or type 2 DM (defined as participants having a WHR ≥ 0.85 ,

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Table 5. Stratified Analysis of Intake of Carbohydrates, Glycemic Index, Glycemic Load, and Rice by Physical Activity Level and Risk of Type 2 Diabetes Mellitus^a

	Low Physical Activity	Medium/High Physical Activity RR (95% Cl)	
Dietary Data	RR (95% CI)		
Carbohydrates ^b			
Q1	1 [Reference]	1 [Reference]	
Q2	0.88 (0.62-1.25)	0.99 (0.80-1.22)	
Q3	0.87 (0.61-1.24)	0.87 (0.70-1.07)	
Q4	1.11 (0.79-1.54)	1.07 (0.88-1.31)	
Q5	1.54 (1.13-2.10)	1.19 (0.99-1.44)	
Interaction, 0.39			
Glycemic index ^b			
Q1	1 [Reference] ^c	1 [Reference] ^d	
Q2	1.16 (0.82-1.64)	1.01 (0.82-1.23)	
Q3	1.21 (0.86-1.70)	0.97 (0.79-1.18)	
Q4	1.41 (1.01-1.97)	1.01 (0.83-1.23)	
Q5	1.45 (1.04-2.01)	1.15 (0.96-1.39)	
Interaction, 0.51			
Glycemic load ^b			
Q1	1 [Reference]	1 [Reference] ^e	
Q2	0.91 (0.63-1.30)	1.12 (0.91-1.39)	
Q3	0.87 (0.60-1.26)	1.01 (0.82-1.25)	
Q4	1.43 (1.02-1.99)	1.16 (0.95-1.42)	
Q5	1.66 (1.20-2.29)	1.24 (1.02-1.51)	
Interaction, 0.05			
Rice, g/d			
<200	1 [Reference]	1 [Reference]	
200-249	1.01 (0.70-1.46)	1.04 (0.84-1.29)	
250-299	1.60 (1.14-2.26)	1.19 (0.97-1.46)	
≥300 Interaction, 0.63	2.44 (1.69-3.52)	1.59 (1.28-1.98)	

Abbreviations: CI, confidence interval; Q, quintile; RR, relative risk. ^aAdjusted for age, kilocalories per day consumed, body mass index, waist-hip ratio, smoking status, alcohol consumption, income level, education level, occupation, and diagnosis of hypertension. Unless otherwise indicated, all $P_{\text{trend}} < .001$.

^bEnergy adjusted.

- $^{\rm C}P_{\rm trend} = .01.$ $^{d}P_{\text{trend}}=.11.$
- $e P_{trend} = .02.$

BMI \geq 25, and being in the lower quartile of physical activity METs). We found that carbohydrates, dietary GL, and rice were more strongly related to the risk of type 2 DM in women who also had a high risk of insulin resistance, although results of tests for multiplicative interaction were not significant (**Table 6**). This analysis was adjusted for age, total daily energy intake, alcohol intake, smoking status, education level, income level, occupation, and diagnosis of hypertension.

COMMENT

In this large prospective study of middle-aged Chinese women, staple foods, rice in particular, were associated with an increased risk of developing type 2 DM. Carbohydrate intake, dietary GI, and dietary GL were all positively associated with the risk of type 2 DM.

A positive association between carbohydrate intake and glucose intolerance (determined with an oral glucose tolerance test) has previously been reported in a prospec-

Table 6. Dietary Carbohydrates, Glycemic Index, Glycemic Load, and Rice and Risk of Type 2 Diabetes Mellitus Stratified by Risk of Insulin Resistance^a

	Low	High
Dietary Data	RR (95% CI)	RR (95% CI)
Carbohydrates ^b		
Q1	1 [Reference]	1 [Reference] ^c
Q2	0.94 (0.78-1.13)	1.22 (0.61-2.44)
Q3	0.88 (0.73-1.06)	1.18 (0.58-2.40)
Q4	1.10 (0.92-1.31)	1.58 (0.82-3.02)
Q5	1.41 (1.20-1.67)	2.04 (1.11-3.75)
Interaction, 0.90	· · · · ·	· · ·
Glycemic index ^b		
Q1	1 [Reference]	1 [Reference] ^d
Q2	1.05 (0.88-1.25)	0.92 (0.46-1.85
Q3	0.98 (0.82-1.17)	1.63 (0.89-2.98
Q4	1.08 (0.90-1.28)	1.55 (0.86-1.17)
Q5	1.32 (1.11-1.57)	1.32 (0.73-2.36
Interaction, 0.05		
Glycemic load ^b		
Q1	1 [Reference]	1 [Reference] ^c
Q2	1.06 (0.88-1.27)	1.17 (0.56-2.42)
Q3	0.97 (0.80-1.17)	1.44 (0.72-2.89)
Q4	1.21 (1.01-1.45)	2.20 (1.14-4.23)
Q5	1.49 (1.25-1.76)	1.93 (1.03-3.63)
Interaction, 0.37		
Rice, g/d		
<200	1 [Reference] ^e	1 [Reference]
200-249	1.02 (0.84-1.24)	1.21 (0.62-2.39)
250-299	1.32 (1.10-1.58)	1.27 (0.65-2.46)
\geq 300	1.95 (1.60-2.37)	2.60 (1.34-5.06
Interaction, 0.90		

Abbreviations: CI, confidence interval; Q, quintile; RR, relative risk. ^aHigh risk includes participants with body mass index greater than 23 (calculated as weight in kilograms divided by height in meters squared), waist-hip ratio 0.85 or greater, and in the lower guartile of physical activity

metabolic equivalents; low risk includes all other participants. Unless otherwise indicated, all $P_{\text{trend}} < .001$. ^bAdjusted for age, kilocalories per day consumed, smoking status, alcohol

consumption, income level, education level, occupation, and diagnosis of hypertension.

tive study of 175 elderly Dutch men and women.¹⁹ Diets high in refined carbohydrates may lead to hypertension, dyslipidemia (low high-density lipoprotein cholesterol and high triglyceride levels), and high levels of Creactive protein,^{12,20} metabolic intermediaries of insulin resistance. Dietary GI was positively associated with a 2-hour glucose tolerance test in male participants of the Health, Aging and Body Composition cohort study.²¹ High dietary GL and GI were positively associated with several metabolic risk factors in a female Japanese population, in which rice is a major contributor to diet,²² as it is in our study. High dietary GL was associated only with 2-hour incremental glucose concentrations at baseline in the Insulin Resistance Atherosclerosis Study²³ but not with other measures of glucose metabolism at baseline or follow-up or with insulin sensitivity.²⁴ However, the FFQ used in that study and the database used to measure GI had low validity (r=0.37 compared with 24-hour dietary recall).25

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 $^{^{\}rm C}P_{\rm trend}$ < .01. ^d P_{trend} =.20.

^e P_{trend}=.001

High dietary GL has been associated with a higher incidence of insulin resistance as determined by the homeostasis model assessment scores in the Framingham Offspring Study cohort²⁶ and with other health outcomes such as dyslipidemia and coronary heart disease.^{6,27} In a recent report from a 12-week randomized trial of 129 overweight men and women comparing 4 different dietary GLs, participants in the 2 diets with a moderately reduced GL were twice as likely to achieve a weight loss of 5% or more.²⁸ As pointed out by Liu,²⁹ a weight loss of 5%, although modest, was associated with a 58% reduction in the 4-year cumulative incidence of diabetes in overweight and obese men and women with impaired glucose tolerance.30

Whether greater dietary intake of high GI foods directly increases the risk of type 2 DM remains contentious, with some studies reporting a positive association²⁻⁵ and others reporting no association.³¹ Differences in study methods and rigor may be the key factor influencing the study results. Positive associations between dietary GI, GL, and diabetes risk have been reported in the 3 major cohorts of primarily white participants who had high follow-up rates and repeated dietary measurements, specifically, the Nurses' Health Studies I and II and the Health Professionals Follow-up Study.³⁻⁵ The Atherosclerosis Risk in Communities Study found an association between GL and type 2 DM of borderline significance after adjustment for intake of cereal fiber.³² The 2 studies reporting a negative association, the Melbourne Collaborative Cohort Study² and the Iowa Women's Health Study,³¹ had only a single dietary measurement. In addition, for the Melbourne Collaborative Cohort Study, no information was provided about the validity of the dietary assessment, and the authors mentioned that the reproducibility of the dietary questionnaire used in that study was low.2 Ascertainment of diabetes outcome was documented to be poor in the Iowa Women's Health Study.31

In general, most prospective studies have reported no association between carbohydrate intake and type 2 DM.3-5,31-33 The amount and sources of carbohydrate intake in previous studies, primarily of white participants, seem to differ substantially from that observed in the present study. In our population, the amount of carbohydrates consumed by participants is much higher than in previous studies of primarily white participants. For example, the cutoff points for quintiles of carbohydrates were 192.1, 210, 225, and 243 g/d in the Iowa Women's Health Study,³¹ whereas in our study, quintile cutoff points were 233.3, 261.5, 287.1, and 321.9 g/d. The cutoff points of carbohydrates (percent of total energy per day) in the Nurses' Health Study I were 44.4%, 48.3%, 57.7%, and 55.9%,⁵ whereas in our study, they were 62.9%, 66.5%, 69.5%, and 72.9%.

In our study, rice consumption was strongly related to the risk of type 2 DM, similar to findings of other prospective studies conducted in the United States,²⁰ but rice consumption was not related to risk of type 2 DM in crosssectional data from the United Kingdom or prospective data from Australia.^{2,34} In our study, potato intake was associated with a lower risk of type 2 DM. Other studies have reported a positive association3-5,35 or no association,^{2,34,36} and another reported a beneficial effect of potatoes on glucose tolerance.³⁷ Dietary patterns in Shanghai, China, are different from patterns in Western populations. In Shanghai, rice is a main staple food, whereas potatoes are consumed as a vegetable (ie, in lower quantities). In the Da Qing study for diabetes prevention conducted in China, a diet high in fruit and vegetables was associated with a lower incidence of diabetes.³⁸ In our study, the median intake of raw rice was 250 g/d, contributing 73.9% of dietary GL, whereas the median intake of potatoes was 8.1 g/d, contributing only 0.6% of dietary GL. In Western populations, potatoes are often consumed fried or with a large amount of fat and are part of a Western dietary pattern that has been found to be associated with a higher risk of type 2 DM.^{39,40} The difference in the intake amount and preparation method of potatoes between the Chinese and Western diets may have contributed to inconsistent findings between our study and others conducted in Western populations.

It has been reported that the adverse effects of a high dietary GL are more evident in overweight or obese women, who, it is presumed, were already more insulin resistant at baseline.^{6,7} However, data on the joint effect between overall and central obesity and GI and GL on type 2 DM and other metabolic risk factors for insulin resistance and coronary heart disease are sparse and inconsistent.^{2,3,5-7,41} In the present study, we observed a stronger effect of carbohydrate intake, rice intake, GI, and GL in women with higher WHR and BMI, although results of most of the tests for multiplicative interaction were not significant. With longer follow-up, we expect to have more statistical power to verify these findings in future years.

In conclusion, in this large population-based cohort study, we found that a diet high in carbohydrates and with a high GI was associated with a higher risk of type 2 DM, in particular in participants with high WHR and BMI. Given that a large part of the world's population consumes rice and carbohydrates as the mainstay of their diets, these prospective data linking intake of refined carbohydrates to increased risk of type 2 DM may have substantial implications for public health.

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Author Contributions: Dr Shu had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Gao, Zheng, and Shu. Acquisition of data: Gao, Yang, and Li. Analysis and interpretation of data: Villegas, Liu, and Shu. Drafting of the manuscript: Villegas. Critical revision of the manuscript for important intellectual content: Liu, Gao, Yang, Li, Zheng, and Shu. Statistical analysis: Villegas. Obtained funding: Zheng and Shu. Administrative, technical, and material support: Gao, Yang, and Li. Study supervision: Yang, Li, and Shu.

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