

Dietary Carbohydrate Intake and New-onset Diabetes: A Nationwide Cohort Study in China

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Abstract

Background: The association of carbohydrate intake with diabetes risk remains uncertain. We aimed to evaluate the prospective associations of the amount and types of carbohydrate intake with new-onset diabetes.

Methods: A total of 16,260 non-diabetic participants from the China Health and Nutrition Survey (CHNS) were included. Dietary intake was collected by three consecutive 24-h dietary recalls combined with a household food inventory. Participants with self-reported diabetes, or fasting plasma glucose \geq 7.0 mmol/L or glycated hemoglobin \geq 6.5% during the follow-up were defined having new-onset diabetes.

Results: During a median follow-up of 9 years (158,930 person-years), 1,100 participants developed diabetes. Overall, there was a U-shaped association between percent of energy from carbohydrate intake and new-onset diabetes, with minimal risk at 49-56% of energy from total carbohydrate intake (quartile 2) (*P* for nonlinearity <0.001). Moreover, there was an L-shaped association between high-quality carbohydrate intake and new-onset diabetes (*P* for nonlinearity <0.001), and a J-shaped association of low-quality carbohydrate intake with new-onset diabetes (*P* for nonlinearity <0.001). Furthermore, there was an inverse association between the plant-based low-carbohydrate scores for low-quality carbohydrate and new-onset diabetes. However, a reversed J-shaped association was found between the animal-based low-carbohydrate and new-onset for low-quality carbohydrate scores for low-quality carbohydrate scores for low-quality carbohydrate scores for low-quality <0.001).

Conclusions: There was a U-shape association between percent of total carbohydrate intake and newonset diabetes, with the lowest risk at 49-56% carbohydrate intake. Our findings provide some evidence for the intake of high-quality carbohydrate, and the substitution of plant-based products for low-quality carbohydrate for primary prevention of diabetes.

Background

Diabetes has become a major health concern worldwide due to its high prevalence and related huge burden of disability and mortality. In 2014, global age-standardized diabetes prevalence was 9.0% in men, and 7.9% in women ¹. As such, it is of great clinical and public health importance to identify more modifiable related factors for the primary prevention of diabetes.

International Diabetes Federation (IDF) has emphasized that a healthy diet could be the major preventive measure for diabetes ². Along with fats and protein, carbohydrate is one of the three basic macronutrients. A low-carbohydrate, high-protein, high-fat diet has been suggested as a strategy for weight-loss ³⁻⁵. However, the results regarding the association of carbohydrate intake with diabetes risk are still considerably mixed, including no significant association in most of the studies in western countries, and positive association in some of the Asian countries ^{6,7}. The possible explanations may be that the amount and type of carbohydrate intake differ by geographical and socioeconomic factors.

Western Asian countries usually have a higher percentage of energy from carbohydrate (about 60%), whereas North American and European countries capture lower carbohydrate (usually < 50%) ⁸. Moreover, the dietary patters in Asian countries are substantially different from patterns in Western countries. However, to date, few previous studies have comprehensively examined the amount and type of carbohydrates with incident diabetes. More importantly, few related studies, using the carbohydrate intake data continuously, have been conducted, which may allow for the possibility of non-linear relation of carbohydrate intake and new-onset diabetes.

Considering the above knowledge gaps and the need to provide more evidence for the development of guidelines on amount and type of carbohydrate intake, we aimed to explore the relationships of the amount and type of carbohydrate intake with incident diabetes, and to assess whether replacement carbohydrate with protein and fat affected the risk of diabetes, using data from the China Health and Nutrition Survey (CHNS), a national health and nutrition survey in China.

Materials And Methods

Study design and participants

Details on the study design, sampling methods, response rates and some results of the CHNS have been published elsewhere ⁹⁻¹³. Briefly, CHNS is an ongoing multipurpose longitudinal cohort study initiated in 1989, and has been followed up every 2-4 years. A multistage, random cluster approach was used to draw the sample from 9 provinces (from north to south) and 3 largest autonomous cities in mainland China. The CHNS rounds have been completed in 1989, 1991, 1993, 1997, 2000, 2004, 2006, 2009, 2011 and 2015. In each survey round, demographic, socioeconomic, lifestyle, nutritional and health information were collected.

In this analysis, we conducted a prospective cohort study using seven waves (1997 to 2015) of the CHNS data. In this cohort, members were surveyed in at least two study rounds, and the first survey round is considered as baseline. We excluded participants who were pregnant, <18 years old, or having diabetes at baseline. Participants with missing dietary carbohydrate data or with extreme dietary energy data (male: >4200 or <600 kcal/day; female: >3600 or <500 kcal/day) were further excluded ¹⁴. Finally, 16,260 participants were included in this analysis (eFigure 1).

The institutional review boards of the University of North Carolina at Chapel Hill and the National Institute of Nutrition and Food Safety, and Chinese Center for Disease Control and Prevention, approved the study. Each participant provided their written informed consent.

Dietary nutrient intakes

Dietary measurements in CHNS are described in detail elsewhere ¹⁵. Briefly, both individual and household level data were collected in each survey round. Dietary information was collected by 3-day dietary recalls through questionnaires, in combination with using a 3-day food-weighed method to assess

cooking oil and condiment consumption. The three consecutive days were randomly allocated from Monday to Sunday and are almost equally balanced across the seven days of the week for each sampling unit. Nutrient intakes were calculated using the China food composition tables (FCTs). The accuracy of 24-hour dietary recall designed to assess energy and nutrient intake has been validated ¹⁵.

In this study, three-day average intakes of dietary macronutrients and micronutrients in each round were calculated. We evaluated energy-adjusted nutrient intake for each nutrient using sex specific linear regression models ¹⁶. Cumulative average intake values of each nutrient were calculated for each participant, using all results up to the last visit prior to the date of new-onset diabetes, or using all results among those without new-onset diabetes, to reduce within-subject variation and represent long-term dietary intake and minimize within-person variation.

Definition of the low-carbohydrate diet (LCD) scores

In our present study, macronutrients were divided into high- and low-quality carbohydrate, plant-based protein and fat, as well as animal-based protein and fat. Food sources constituting these subtypes are shown in the eTable 1 ^{17,18}.

Low-carbohydrate diet (LCD) scores was defined following an established method ¹⁹. First, the study participants were divided into 11 strata each of fat, protein, and carbohydrate intake, expressed as a percentage of energy (eTable 2). For fat and protein, participants in the highest strata received 10 points for that macronutrient and participants in the lowest strata received 0 points. For carbohydrate, the lowest strata received 10 points and the highest 0 points. The scores of three macronutrients were summed to create the overall LCD scores, which ranged from 0-30 (a higher score reflects less intake of carbohydrate and less intake of fat and protein, while a lower score reflects more intake of carbohydrate and less intake of fat and protein).

A total LCD score for low-quality carbohydrate was built based on percentage of energy intake from lowquality carbohydrate, total protein and total fat. Furthermore, we also built a plant-based LCD score for low-quality carbohydrate, based on percentage of energy intake from low-quality carbohydrate, plant protein and plant fat; and an animal-based LCD score for low-quality carbohydrate based on percent of energy from low-quality carbohydrate, animal protein and animal fat. As such, each participant was given the overall, plant-based and animal-based scores. (eTable 1, eTable 2). In detail, a higher total LCD score reflects less intake of low-quality carbohydrate and more intake of total fat and total protein, a higher plant-based LCD score reflects less intake of low-quality carbohydrate and more intake of plant fat and plant protein, and a higher animal-based LCD score reflects less intake of low-quality carbohydrate and more intake of low-quality carbohydrate and more intake of animal fat and animal-based LCD score reflects less intake of low-quality carbohydrate and more intake of animal fat and animal-based LCD score reflects less intake of low-quality carbohydrate and

Assessments of blood pressure and covariates

After the participants had rested for 5 minutes, seated blood pressure was measured by trained research staff using a mercury manometer, following the standard method. Triplicate measurements on the same

arm were taken in a quiet and bright room. The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) of the three independent measures were used in analysis.

Demographic and lifestyle information was obtained through questionnaires, including age, sex, smoking status, alcohol consumption, occupation, education level, residence, regions, and concomitant diseases. Body height and weight were measured following a standard procedure with calibrated equipment. Body mass index (BMI) was calculated as weight (kg) by height squared (m²). Physical activity was collected by staff-administered questionnaires exploring all occupational, transportation, domestic and leisure activities in adults.

Study outcome

The participants had been asked to report their diabetes status with a questionnaire-based interview at each follow-up. New-onset diabetes were confirmed if the answer was "yes" to the question "has a doctor ever told you that you suffer from diabetes?". In addition, blood samples were collected and assayed only in 2009. Therefore, in 2009, outcome was also ascertained by an additional criterion: fasting blood glucose \geq 7.0 mmol/L or glycated hemoglobin [HbA1c] \geq 6.5%) ^{20, 21}.

When a participant was first identified with new-onset diabetes in a following survey, the middle date between this and the nearest survey before was used to calculate the follow-up time. For those free of diabetes in all following surveys, the last survey date was used to calculate the follow-up time.

Statistical Analysis

Intake of dietary carbohydrate were expressed as the percentage of total energy using nutrient density method ²² and then categories into quartile (<49, 49 -<56, 56 -<63, \geq 63 of energy intake from carbohydrate intake). Population characteristics are presented as mean ± standard deviations (SDs) for continuous variables, and proportions for categorical variables. Differences in population characteristics by quintile of carbohydrate intake were compared using ANOVA tests, or chi-square tests, accordingly.

We used Cox proportional hazards models to calculate hazard ratios (HRs) and 95% confidence intervals (Cls) for the risk of new-onset diabetes. Model 1 included adjustments for age, sex, and body mass index (BMI). Model 2 included adjustments for age, sex, regions, BMI, smoking status, systolic blood pressure (SBP), diastolic blood pressure (DBP), education level, urban or rural residence, occupation, physical activity, as well as total energy intake, sodium intake, potassium intake and fiber intake. Furthermore, we used a cubic B-spline with 4 knots (20%, 40%, 60%, 80% of carbohydrate intake) to display the potentially non-linear relationship of total, high-quality and low-quality carbohydrate, and total, animal-based and plant-based LCD scores for low-quality carbohydrate with new-onset diabetes in a more intuitive way with adjustments for covariates in Model 2.

Moreover, possible modifications of the association between total, high-quality and low-quality carbohydrate intake and new-onset diabetes were evaluated for the following variables: age (<60 $vs. \geq$ 60

years), sex, BMI (<24 vs. \geq 24 kg/m²), waist circumference (<80 vs. \geq 80 cm), total protein intake ([median] <12 vs. \geq 12 % of energy), and total fat intake ([median] <31 vs. \geq 31 % of energy), and interactions between subgroups and carbohydrate intake were examined by likelihood ratio testing.

We consider a two-side *P* value<0.05 as statistically significant in all analysis. All statistical analyses were conducted using R version 3.6.1.

Results

Baseline characteristics of study participants

In the final analysis, a total number of 16,260 participants were included, as showed in eFigure 1. Mean percent of energy intake as total carbohydrate, high-quality carbohydrate and low-quality carbohydrate was 56.0% (SD: 10.3), 6.6% (SD: 5.2), and 46.1% (SD: 12.6), respectively. Notably, low-quality carbohydrate was the main source of carbohydrate intake, which accounted for 82% of carbohydrate intake.

Table 1 illustrated baseline characteristics of included participants in line with quartile for percent of energy intake from total carbohydrate intake. Mean age of the 16,260 non-diabetic participants was 43 years (SD: 15.3), and 49% was males. In participants with higher intake of total carbohydrate, younger age, lower levels of SBP, DBP and BMI were also shown. Moreover, they were more likely to be smoker and farmer, had higher physically active levels, less likely to be unemployed, live urban residence, receive high school education. For diets, they consumed less fat, protein and sodium, but more fiber.

Table 1

Characteristics of study participants by quartiles of energy from carbohydrate intake (% of energy)*

	Quartiles of carbohydrate intake, % of energy				Р
	Q1(< 49)	Q2(49-<56)	Q3(56~63)	Q4(≥63)	value
Ν	4065	4065	4065	4065	
Male, No. (%)	2253 (55.4)	2152 (52.9)	2015 (49.6)	1899 (46.7)	< 0.001
Age, years	45.6 ± 15.6	44.2 ± 15.5	41.9 ± 14.8	40.8 ± 14.9	< 0.001
Systolic blood pressure, mmHg	121.4 ± 17.4	120.0± 17.2	119.0 ± 17.2	118.4 ± 17.2	< 0.001
Diastolic blood pressure, mmHg	78.3 ± 10.7	77.7 ± 10.5	77.2 ± 10.8	76.9±10.9	< 0.001
Body mass index, kg/m ²	23.4 ± 3.4	23.1 ± 3.4	22.7 ± 3.2	22.2 ± 3.1	< 0.001
Smoking, No. (%)	1168 (28.8)	1206 (29.7)	1316 (32.5)	1401 (34.6)	< 0.001
Alcohol drinking, No. (%)	1487 (36.9)	1411 (35.1)	1422 (35.4)	1419 (35.4)	0.300
Urban residence, No. (%)	2304 (56.7)	1940 (47.7)	1317 (32.4)	580 (14.3)	< 0.001
Regions, No. (%)					< 0.001
Central	2246 (55.3)	1799 (44.3)	1687 (41.5)	2087 (51.3)	
North	806 (19.8)	900 (22.1)	924 (22.7)	854 (21)	
South	1013 (24.9)	1366 (33.6)	1454 (35.8)	1124 (27.7)	
Physical activity, MET-h/wk	125.6 ± 115.7	135.0 ± 117.6	163.3 ± 136.5	191.3 ± 141.1	< 0.001
Occupation, No. (%)					< 0.001
Farmer	362 (8.9)	734 (18.2)	1555 (38.7)	2677 (66.8)	
Worker	521 (12.9)	584 (14.5)	512 (12.7)	278 (6.9)	
Unemployed	1587 (39.2)	1375 (34.1)	991 (24.6)	635 (15.8)	
Other	1577 (39)	1337 (33.2)	963 (23.9)	420 (10.5)	

*Variables are presented as Mean \pm SDs for continuous variables or N (%) for categorical variables.

Q1(< 49) 554 (13.8) 517 (12.9)	Q2(49≺56) 704 (17.7)	Q3(56-<63) 826 (20.7)	Q4(≥ 63)	value < 0.001
517 (12.9)	704 (17.7)	826 (20 7)		
517 (12.9)	704 (17.7)	826 (20 7)		
		220 (20.7)	1153 (29.2)	
	640 (16.1)	864 (21.7)	1077 (27.3)	
1152 (28.7)	1289 (32.4)	1396 (35.1)	1256 (31.9)	
1788 (44.6)	1348 (33.9)	896 (22.5)	456 (11.6)	
2040.3 ± 549.7	2117.2 ± 486.4	2172.3 ± 470.0	2219.7± 513.9	< 0.001
42.6 ± 6.1	53.0 ± 1.9	59.5 ± 2.0	68.7±4.3	< 0.001
5.9 ± 3.9	6.3±4.3	6.4 ± 5.0	7.9 ± 6.8	< 0.001
31.8 ± 8.7	43.0 ± 6.9	50.4 ± 6.7	59.1 ± 8.2	< 0.001
43.9 ± 6.7	34.2 ± 2.8	28.3 ± 2.6	19.9 ± 4.4	< 0.001
13.5±3.1	12.7 ± 2.2	12.1 ± 1.9	11.4±1.5	< 0.001
8.8 ± 5.1	9.9 ± 4.9	10.8 ± 5.6	12.6 ± 6.0	< 0.001
5.4 ± 3.4	5.1 ± 2.4	5.0 ± 2.6	4.8 ± 3.0	< 0.001
1.7±0.6	1.6±0.5	1.6±0.6	1.7 ± 0.6	< 0.001
3.6 ± 2.5	3.3±1.8	3.2 ± 1.8	3.1 ± 2.0	< 0.001
	549.7 42.6 ± 6.1 5.9 ± 3.9 31.8 ± 8.7 43.9 ± 6.7 13.5 ± 3.1 8.8 ± 5.1 5.4 ± 3.4 1.7 ± 0.6 3.6 ± 2.5	549.7 486.4 42.6 ± 6.1 53.0 ± 1.9 5.9 ± 3.9 6.3 ± 4.3 31.8 ± 8.7 43.0 ± 6.9 43.9 ± 6.7 34.2 ± 2.8 13.5 ± 3.1 12.7 ± 2.2 8.8 ± 5.1 9.9 ± 4.9 5.4 ± 3.4 5.1 ± 2.4 1.7 ± 0.6 1.6 ± 0.5 3.6 ± 2.5 3.3 ± 1.8	549.7 486.4 470.0 42.6 ± 6.1 53.0 ± 1.9 59.5 ± 2.0 5.9 ± 3.9 6.3 ± 4.3 6.4 ± 5.0 31.8 ± 8.7 43.0 ± 6.9 50.4 ± 6.7 43.9 ± 6.7 34.2 ± 2.8 28.3 ± 2.6 13.5 ± 3.1 12.7 ± 2.2 12.1 ± 1.9 8.8 ± 5.1 9.9 ± 4.9 10.8 ± 5.6 5.4 ± 3.4 5.1 ± 2.4 5.0 ± 2.6 1.7 ± 0.6 1.6 ± 0.5 1.6 ± 0.6 3.6 ± 2.5 3.3 ± 1.8 3.2 ± 1.8	549.7 486.4 470.0 513.9 42.6 ± 6.1 53.0 ± 1.9 59.5 ± 2.0 68.7 ± 4.3 5.9 ± 3.9 6.3 ± 4.3 6.4 ± 5.0 7.9 ± 6.8 31.8 ± 8.7 43.0 ± 6.9 50.4 ± 6.7 59.1 ± 8.2 43.9 ± 6.7 34.2 ± 2.8 28.3 ± 2.6 19.9 ± 4.4 13.5 ± 3.1 12.7 ± 2.2 12.1 ± 1.9 11.4 ± 1.5 8.8 ± 5.1 9.9 ± 4.9 10.8 ± 5.6 12.6 ± 6.0 5.4 ± 3.4 5.1 ± 2.4 5.0 ± 2.6 4.8 ± 3.0 1.7 ± 0.6 1.6 ± 0.5 1.6 ± 0.6 1.7 ± 0.6

Associations of dietary carbohydrate intake (% of energy) with new-onset diabetes

Over a median follow-up of 9 years (inter-quartile range (IQR): 4–15 years, 158, 930 person-years), 1100 (6.8%) participants developed new-onset diabetes, of which, 640 were those with self-reported new-onset diabetes during follow-up period.

Overall, the association between percent of energy from total carbohydrate intake and new-onset diabetes followed a U-shape (P for nonlinearity < 0.001): a percentage of energy in 49–56% (quartile 2) from total carbohydrate intake showed the lowest risk of new-onset diabetes (Fig. 1A, Table 2).

Table 2 Relative risk of new-onset diabetes according to quartiles of energy from carbohydrate intake

Carbohydrate intake, % energy	No. of case	Person-years	Model 1	Model 2	
			HR (95%CI)	HR (95%Cl)	
Total carbohydrate					
Quartile					
Q1(< 49)	238	29333	1.24(1.03, 1.49)	1.20(0.99, 1.45)	
Q2(49-< 56)	260	39266	ref	ref	
Q3(56-<63)	286	44030	1.19(0.99, 1.42)	1.26(1.05, 1.51)	
Q4(≥ 63)	316	44030	1.44(1.21, 1.72)	1.67(1.37, 2.05)	
Category					
Q1(< 49)	238	29333	1.24(1.03, 1.49)	1.21(1.00, 1.47)	
Q2(49-< 56)	260	39266	ref	ref	
Q3-4(≥ 56)	602	87721	1.31(1.12, 1.52)	1.40(1.19, 1.66)	
High quality carbohydrate					
Quartile					
Q1(< 3)	332	36988	ref	ref	
Q2(3-<5)	257	44069	0.64(0.54, 0.75)	0.59(0.49, 0.70)	
Q3(5-<8)	222	41343	0.51(0.43, 0.61)	0.44(0.36, 0.53)	
Q4(≥ 8)	289	36530	0.68(0.57, 0.80)	0.54(0.44, 0.65)	
Low quality carbohydrate					
Quartile					
Q1(< 38)	224	26777	1.21(1.01, 1.46)	1.19(0.97, 1.45)	
Q2(38-<47)	263	39873	ref	ref	
Q3(47-<55)	295	45362	1.23(1.03, 1.47)	1.39(1.16, 1.67)	
Q4(≥ 55)	318	46919	1.57(1.32, 1.88)	1.95(1.60, 2.37)	

Model 1: Adjusted for age, sex, BMI;

Model 2: Adjusted for age, sex, BMI, region, smoking, SBP, DBP, education, urban or rural residence, occupation, physical activity, sodium intake, potassium intake, fiber intake, and energy intake.

However, an L-shape association was found for high-quality carbohydrate intake (*P* for nonlinearity < 0.001) (Fig. 1B). Comparing with those in the 1st quartile of high-quality carbohydrate intake, the

adjusted HRs (95%Cls) were 0.59(0.49, 0.70) in 2nd quartile, 0.44(0.36, 0.53) in 3rd quartile, and 0.54(0.44, 0.65) in 4th quartile, respectively (Table 2).

In contrast, there was a J-shape association between low-quality carbohydrate intake and new-onset diabetes (*P* for nonlinearity < 0.001) (Fig. 1C). Comparing with those in the 2nd quartile of low-quality carbohydrate intake, the adjusted HRs (95%Cls) was 1.19(0.97, 1.45) in the 1st quartile and 1.95(1.60, 2.37) in the 4th quartile, respectively (Table 2).

Similar trends were found for the associations of total (eFigure 2A), high-quality (eFigure 2B), and lowquality carbohydrate (eFigure 2C) intake with self-reported new-onset diabetes during follow-up period.

Associations of LCD scores for low-quality carbohydrate with new-onset diabetes

There was a reversed J-shaped association between animal-based LCD scores for low-quality carbohydrate and new-onset diabetes (*P* for nonlinearity < 0.001): the adjusted HRs were 1.93 (95%CI,1.38-2.70) and 1.39 (95%CI,1.01-1.92) for the 1st and 10th decile of the LCD scores, respectively, compared with the 8th decile (Fig. 2B, eTable 3). Similar trends were found for the total LCD scores for low-quality carbohydrate (Fig. 2A, eTable 3).

However, for plant-based LCD scores for low-quality carbohydrate, the adjusted HRs (95%Cls) of newonset diabetes was 2.21 (1.53–3.20) in the 1st decile and 0.88 (0.67–1.17) in the 10th decile, compared with those in the 8th decile (Fig. 2C, eTable 3).

Association of dietary fat and protein intake (% of energy) with new-onset diabetes

We further examined the association between each macronutrient and new-onset diabetes in multivariate nutrient density models. Overall, there were U-shaped associations of the percentage energy from animal-(eFigure 3A) or plant-based (eFigure 3B) fat, animal- (eFigure 3C) or plant-based (eFigure 3D) protein intake with new-onset diabetes (All *P* for nonlinearity < 0.001).

Stratified Analyses

In the stratified analyses, age, sex, BMI, waist circumference, the percentage energy from total protein and total fat did not significantly modify the association between the percentage energy from total, high-quality and low-quality carbohydrate intake with the risk of new-onset diabetes (All *P*-interactions > 0.05) (eTable 4).

Discussion

Findings from a large sample, nation-wide, prospective study in China showed a U-shaped association between percent of energy from total carbohydrate intake and new-onset diabetes, with the minimal risk observed at 49–56% carbohydrate intake (quartile 2). The increased risks of new-onset diabetes were

mainly found in those with lower intake of high-quality carbohydrate or higher intake of low-quality carbohydrate. Furthermore, there was an L-shape association between the plant-based LCD scores for low-quality carbohydrate and new-onset diabetes. However, there was a reversed J-shaped association between animal-based LCD scores for low-quality carbohydrate and new-onset diabetes.

A previous meta-analysis of eight studies in western countries showed that the pooled estimate of RR was 0.97 (95% Cl 0.90–1.06) per 50 g per day of total dietary carbohydrate intake (P=0.5). However, there was a substantial heterogeneity between the cohort studies ⁶. After that, controversial findings had still been reported, with positive associations in obese Japanese men, middle-aged Korean adults, or Chinese women ^{23–25}, while no associations in Korea or USA population ^{26–28}. Of note, among Chinese women, the corresponding relative risks (RR) for risk of type 2 diabetes were 0.96, 0.87, 1.09, 1.28 for participants in quintile 2, quintile 3, quintile 4, quintile 5, respectively, compared those in quintile 1 of carbohydrate intake. That is to say that this study also showed a U-shaped trend between carbohydrate intake and diabetes risk. Overall, the above studies suggested that the association between carbohydrate intake and diabetes risk remains inconclusive. The discrepant findings may be partly due to the difference of the amount and type of carbohydrate intake in different population. Moreover, previous studies, which usually assumed linearity between carbohydrate intake and diabetes, seemed to have overlooked some valuable information.

Based on data of a large-scale sample, multi-center, prospective, nationwide cohort in China, our study provided a chance to examine the continuous association of the amount and type of carbohydrate intake (% of energy) with new-onset diabetes in a population with a wide range of carbohydrate intake. We provided some new insights in this field. First, there was a U-shaped association of the percentage of energy consumed from total carbohydrate with new-onset diabetes: with the lowest risk observed at 49– 56% (quartile 2) carbohydrate intake. Consistently, previous studies also reported the U-shape associations of percent of energy from carbohydrate intake with mortality ¹⁴ and new-onset hypertension ²⁹, with lowest incidence risk at 50–60% and 50–55% of carbohydrate intake, respectively. Second, the increased new-onset diabetes risk was mainly observed in those with lower intake of high-quality carbohydrate on the risk of cardiovascular disease and mortality ³⁰. Ley SH et al also recommended the dietary patterns rich in high-quality carbohydrate and lower in low-quality carbohydrate foods for diabetes prevention and management ³¹.

These findings might be in reasonable explication. Extreme low dietary carbohydrate is not recommended because of its essential role in maintaining normal physiological function, including primary fuel use by the brain and central nervous system, sources of water-soluble vitamins and minerals as well as fiber and so on ³². Moreover, high-quality carbohydrate, including fruits, and non-starch vegetables, etc., is abundant in antioxidants, and phytochemicals. These ingredients can regulate glucose by accelerating hepatic insulin response and decreasing hepatic glucose output in healthy participants ^{33,34}. However,

low-quality carbohydrate, including refined grains, starchy vegetables, and sugars, was absorbed mainly as glucose that may possibly easily increase plasma glucose and insulin response ³⁵.

Furthermore, we found that there was an L-shape association between the plant-based LCD scores for low-quality carbohydrate and new-onset diabetes. Consistently, previous studies had reported inverse associations of LCD scores that favored plant-derived protein and fat intake with the risk of mortality ^{14,36}, hypertension ²⁹ and coronary heart diseases ^{19,37}. Moreover, although a positive association of LCD scores favoring animal-derived protein and fat sources with mortality ¹⁴ had been reported, our study showed that there seemed to be a reversed J-shaped association of animal-based LCD scores for low-quality carbohydrate with new-onset diabetes. On the one hand, these results suggested that due to the high intake of low-quality carbohydrate in this population, the possible unfavorable effect associated with moderate animal fats and proteins intake may be still lower than the detrimental effect of high intake of low-quality carbohydrate intake on the new-onset diabetes. On the other hand, our results really indicated that substitution of plant-based products for low-quality carbohydrate may be a more appropriate strategy for prevention of diabetes.

Some limitations are needed considering. First, due to the observational design, although broad covariates have been included in the adjustments, residual confounding from unmeasured or unrecorded risk factors cannot be excluded. Second, fasting glucose and HbA1c were only available in round 2009, the incident rate of type 2 diabetes might be underestimated. Third, dietary measurements in CHNS were derived from self-reported dietary 24-hour recalls, which may be affected by recall bias. Nevertheless, it's one of the most common methods for dietary intake data, and has been used by some precious important cohorts ^{8,14,22}. More importantly, the accuracy of 24-hour dietary recall for the evaluation of energy and nutrient intake has been validated by lots of previous studies ^{15,38,39}. In addition, CHNS was conducted in China, the generalization of our results to other ethnics and population still needs more studies. Further confirmation of our findings in future studies is necessary.

In conclusion, our study indicated that there was a U-shaped association between percentage of dietary carbohydrate intake and new-onset diabetes in general Chinese adults, with minimal risk observed at 49–56% (quartile 2) of carbohydrate intake. The increased risks were mainly observed in participants with lower intake of the high-quality carbohydrate or higher intake of low-quality carbohydrate. Moreover, there was an L-shaped association between plant-based LCD scores for low-quality carbohydrate and new-onset diabetes. If further confirmed, our findings support the intake of high-quality carbohydrate, and the substitution of plant-based products for low-quality carbohydrate for prevention of diabetes.

Abbreviations

CHNS: China Health and Nutrition Survey; IDF: International Diabetes Federation; FCT: food composition table; LCD: low-carbohydrate diet; SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index; HbA1c: glycated hemoglobin; SD:standard deviation; CI: confidence interval; IQR: interquartile range.

Declarations

Ethics approval and consent to participate:

The institutional review boards of the University of North Carolina at Chapel Hill and the National Institute of Nutrition and Food Safety, and Chinese Center for Disease Control and Prevention, approved the study. Each participant provided their written informed consent.

Consent for publication:

Not applicable.

Availability of data and materials:

The datasets analysed during the current study are available in the CHNS official website.

Competing interests:

The authors declare that they have no competing interests.

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Authors' Contributions:

Chun Zhou, Xianhui Qin, Yuanyuan Zhang, Huan Li, Panpan He, and Qinqin Li designed the research; Chun Zhou, Zhuxian Zhang, Mengyi Liu, and Xianhui Qin conducted the research; Chun Zhou, Chengzhang Liu and Mengyi Liu performed the data management and statistical analyses; Chun Zhou and Xianhui Qin wrote the manuscript; All authors revised and approved the final manuscript.

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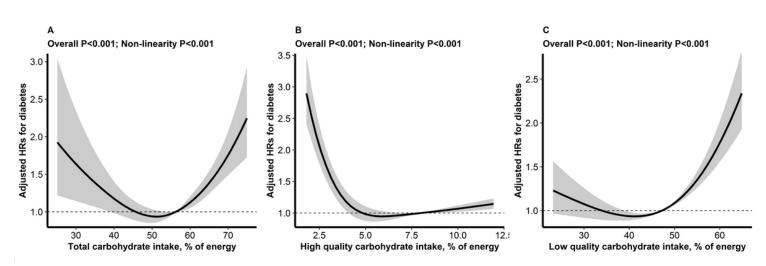
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Figures

Associations between percent of energy from carbohydrate intake and new-onset diabetes (A: total carbohydrate, B: high-quality carbohydrate, C: low-quality carbohydrate) * * Adjusted for age, sex, BMI, region, smoking, SBP, DBP, education, urban or rural residence, occupation, physical activity, sodium intake, potassium intake, fiber intake, and energy intake.

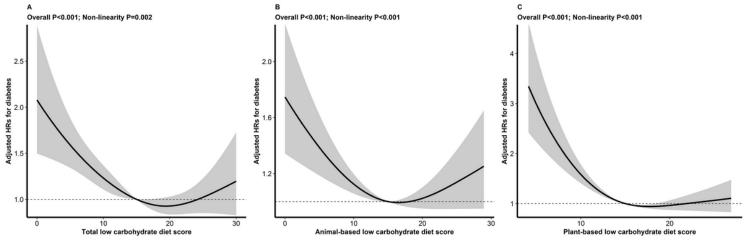


Figure 2

Associations between low-carbohydrate diet (LCD) scores for low-quality carbohydrate and new-onset diabetes (A: total LCD scores, B: animal-based LCD scores, C: plant-based LCD scores) * *Adjusted for age, sex, BMI, region, smoking, SBP, DBP, education, urban or rural residence, occupation, physical activity, sodium intake, potassium intake, fiber intake, and energy intake.

Supplementary Files

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