




# Specific fruit but not total fruit intake during early pregnancy is inversely associated with gestational diabetes mellitus risk: a prospective cohort study

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## Abstract

**Objectives:** Fruit intake may influence gestational diabetes mellitus (GDM) risk. However, prospective evidence remains controversial and limited. The current study aimed to investigate whether total fruit and specific fruit intake influence GDM risk.

**Design:** A prospective cohort study was conducted. Dietary information was collected by a 3-d 24-h dietary recall. All participants underwent a standard 75-g oral glucose tolerance test at 24–28 gestational weeks. Log-binomial models were used to estimate the association between fruit intake and GDM risk, and the results are presented as relative risks (RR) and 95 % CI.

**Setting:** Southwest China.

**Participants:** Totally, 1453 healthy pregnant women in 2017.

**Results:** Total fruit intake was not associated with lower GDM risk (RR of 1.03 (95 % CI 0.83, 1.27) ( $P_{\text{trend}} = 0.789$ )). The RR of GDM risk was 0.73 for the highest anthocyanin-rich fruit intake quartile compared with the lowest quartile (95 % CI 0.56, 0.93;  $P_{\text{trend}} = 0.015$ ). A higher grape intake had a linear inverse association with GDM risk (Q4 v. Q1: RR = 0.65; 95 % CI 0.43, 0.98;  $P_{\text{trend}} = 0.044$ ), and after further adjustment for anthocyanin intake, the inverse association tended to be non-linear (Q4 v. Q1: RR = 0.65; 95 % CI 0.44, 0.98;  $P_{\text{trend}} = 0.079$ ). However, we did not find an association between glycaemic index-grouped fruit, glycaemic load-grouped fruit or other fruit subtype intake and GDM risk.

**Conclusions:** In conclusion, specific fruit intake (particularly anthocyanin-rich fruit and grapes) but not total fruit intake was inversely associated with GDM risk.

**Keywords**  
Gestational diabetes mellitus  
Fruit  
Anthocyanin  
Glycaemic index  
Glycaemic load

Gestational diabetes mellitus (GDM) is a typical complication of pregnancy and arises due to impaired glucose tolerance. The prevalence of GDM is rising globally, and GDM leads to adverse health consequences for mothers (e.g. caesarean section and pre-eclampsia) and their offspring (e.g. macrosomia and shoulder dystocia) in the short term and an increased risk of type 2 diabetes mellitus (T2DM) in the long term<sup>(1–4)</sup>.

However, lifestyle interventions that address factors such as weight and diet may help reduce the disease burden<sup>(5–8)</sup>. Fruits, a vital component of a balanced diet, are rich in vitamins, minerals, dietary fibre and antioxidant

chemicals such as anthocyanin. Mixed results suggest that increased intake of fruits may prevent several chronic diseases, including diabetes<sup>(9–11)</sup>, but the association between fruit intake and the risk of GDM is still unknown. Nutritional components vary between fruit subtypes and, thus, may have a different impact on diabetes risk. In recent years, a major focus of studies has been on the relationship between fruit subtypes and diabetes risk. Some studies have suggested that specific fruit subtypes and not all fruits may affect the risk of T2DM, due to their different carbohydrate quality and quantity and specific flavonoids content<sup>(12,13)</sup>. Anthocyanin, a typical flavonoid characterised

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by its antioxidative property, may be beneficial for minimising diabetes risk<sup>(14,15)</sup>. Furthermore, anthocyanin is mainly consumed by the Chinese population in the form of fruits, and some studies have suggested that anthocyanin-rich fruits can lower the risk of T2DM<sup>(16,17)</sup>, considering GDM may share the similar pathogenesis with T2DM, we hypothesised that anthocyanin-rich fruit is associated with the risk of GDM; however, the association between anthocyanin-rich fruits and GDM has not been well researched. However, fruits contain carbohydrates (such as glucose, fructose and fibre), which may have an impact on blood glucose. The glycaemic index (GI) and glycaemic load (GL) can reflect the quality and quantity of carbohydrates in fruits. However, there is a lack of evidence regarding whether the GI or GL values of fruits can influence GDM risk, and the current research conclusions are still inconsistent<sup>(18,19)</sup>. Furthermore, variations in nutrients among different individual fruits may influence GDM risk differently. Previous studies suggested that some individual fruits, including apples, bananas, grapes, pears and peaches, have an impact on T2DM risk, and those fruits are commonly consumed in the human population<sup>(12,13,16)</sup>. However, there are few available studies on the relationship between individual fruit intake and GDM risk.

Therefore, considering that earlier dietary intervention is definitely important for decreasing GDM risk<sup>(20)</sup> and that there is a need to fill in the abovementioned research gap, the aim of our study was to explore whether total fruit and specific fruit intake during the first trimester influence GDM risk. Considering that fruits contain various beneficial nutrients, we hypothesised that total fruit intake is inversely associated with the risk of GDM and that some specific fruit intake is associated with GDM risk.

## Subjects and methods

### Study design and population

This prospective cohort study was conducted in 2017 at Sichuan Provincial Hospital for Women and Children in Southwest China. The inclusion criteria were as follows: (1) gestational age from 6 to 14 weeks; (2) singleton pregnancy and (3) no chronic metabolic disease. At recruitment, a total of 1673 pregnant women were invited to join the study at their first prenatal visits during early pregnancy. Data on baseline characteristics and lifestyle factors were collected from specialised interviewers face to face using a self-designed questionnaire. Dietary information was obtained by 3-d 24-h dietary recall during each trimester, and GDM was diagnosed per the standard 75-g oral glucose tolerance test administered at 24–28 gestational weeks.

In the current study, we set the participants with the lowest fruit intake as the control group and other participants as the exposure group. N1 and N2 are the numbers of participants in the exposure group and control group, respectively. N is the total sample size. According to limited

previous literature reports, we hypothesised that three exposure levels may influence GDM risk differently. Thus, we set N1/N2 = 3:1, aiming to explore the influence of the three levels on GDM risk by comparing them with the lowest fruit intake level (the control group), respectively. Then we used PASS 15.0 software to calculate the sample size ( $\alpha = 0.05$  (two-sided),  $1 - \beta = 0.90$ , N1/N2 = 3:1). The minimum sample size ( $N = N1 + N2$ ) required was 1265 participants. We assumed a 20% dropout rate, resulting in a final included sample size of 1582 participants. At recruitment, a total of 1673 participants were invited to join the study. We excluded participants who did not complete the dietary recall ( $n = 8$ ) or the oral glucose tolerance test ( $n = 155$ ), participants with a GDM history ( $n = 39$ ) and participants who reported extreme total energy intake  $< 500$  or  $> 3500$  kcal/d ( $n = 18$ ). Therefore, 1453 participants were included in the analysis. A flowchart for the inclusion and exclusion of the study participants is shown in Fig. 1. All subjects provided written informed consent when recruited to the cohort.

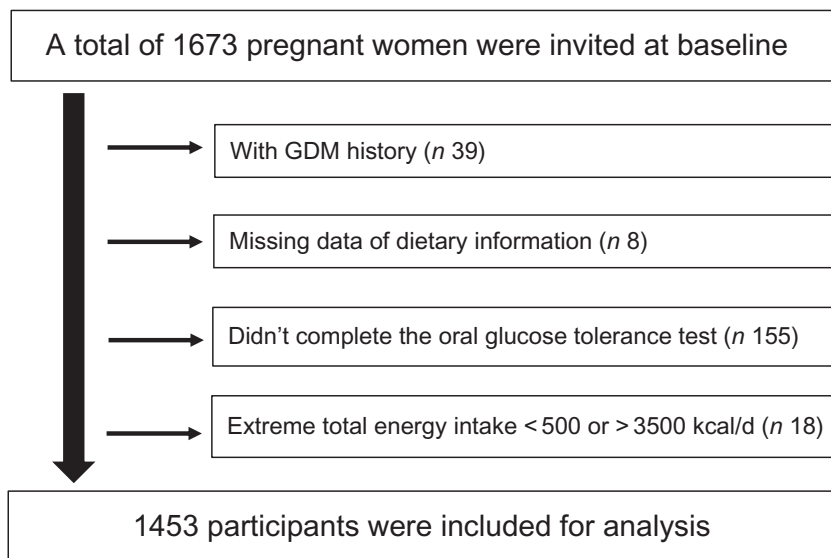
### Dietary assessment

A 3-d 24-h dietary recall (2 weekdays and 1 weekend day) was conducted to collect dietary information during early pregnancy. A face-to-face 24-h dietary recall was initially conducted by specialised interviewers. Interviewers collected detailed information on the meals and snacks that participants ate and drank over the past 24-h period by asking questions. The estimation tools (e.g. standard tools and food atlas) were used to reduce the participants' memory error. Dietary information for the other 2 d was collected from trained interviewers by telephone.

We calculated the average daily total fruit intake per person and then classified fifty-nine individual fruits into two groups based on their anthocyanin content mostly from the USDA Database for Flavonoid Content<sup>(21)</sup> and the Phenol-Explorer database<sup>(22)</sup>. Moreover, for fruits that were not included in either database, we searched the literature to collect relevant information<sup>(23)</sup>. Thus, fruits (e.g. blueberries, strawberries, blackcurrants, mulberries, cherries and grapes) containing very high amounts of anthocyanin ( $\geq 27.01$  mg/100 g) were defined as anthocyanin-rich fruit, and the remaining fruits were classified as non-anthocyanin-rich fruit.

According to the China Food Composition Table<sup>(24)</sup> and the international GI database<sup>(25)</sup>, we classified individual fruits into four groups based on their GI values and GL values. Low-GI fruits (GI  $< 55$ ): apples, cherries and oranges, etc. and high-GI fruits (GI  $\geq 55$ ) included mangos, pineapples and watermelon, etc., GL values were calculated per 100 g of fruit; low-GL fruits (GL  $< 10$ ) included prunes, peaches and pears, etc. and high-GL fruits (GL  $\geq 10$ ) included litchi, sugarcane and dates, etc.

Furthermore, the five individual fruits (apples, bananas, grapes, pears and peaches) were also studied separately.



**Fig. 1** Flowchart for inclusion and exclusion of the study participants

The average daily food intake was calculated by Nutrition calculator v.2.7.3 based on the China Food Composition Table<sup>(24)</sup>.

#### **Diagnostic criteria of GDM**

The standard 75-g oral glucose tolerance test was performed at 24–28 weeks of gestation. GDM was diagnosed when the glucose concentration threshold met the following criteria recommended by the International Association of Diabetes and Pregnancy Study Groups<sup>(26)</sup>: fasting plasma glucose  $\geq 5.1$  mmol/l, 1-h plasma glucose  $\geq 10.0$  mmol/l or 2-h plasma glucose  $\geq 8.5$  mmol/l.

#### **Measurement of non-dietary factors**

Data on baseline characteristics, including age, occupation, educational level, family income level, gravidity, parity, family history of diabetes, smoking status, alcohol consumption and physical activity, were collected through a self-designed questionnaire. Pre-pregnancy weight was self-reported, while height was measured by trained interviewers. Body mass (kg) was divided by the square of height ( $m^2$ ) to obtain the BMI. Physical activity refers to all types of physical movements that increase energy expenditure due to skeletal muscle contraction, and it was assessed by the validated Pregnancy Physical Activity Questionnaire<sup>(27)</sup>.

#### **Statistical analysis**

Means and standard deviations are used to describe continuous variables with a normal distribution, while those with a skewed distribution are expressed as medians and interquartile ranges. Categorical variables are presented as percentages. Means and medians were compared by using ANOVA, and the Kruskal–Wallis  $H$  test, respectively,

and  $\chi^2$  tests were used for categorical variables. We classified subjects into quartiles according to their daily fruit intake to analyse the participants' baseline characteristics. To adjust for extraneous variation due to total energy intake, the intake of nutrients (e.g. carbohydrate, protein, fat, dietary fibre and anthocyanin) was adjusted for total energy intake by the residual method.

Because the GDM incidence in our cohort was  $>10\%$ , the use of OR to estimate relative risks (RR) was not appropriate<sup>(28)</sup>. Thus, we chose log-binomial models to estimate the RR and 95% CI of GDM risk<sup>(29)</sup>. When the models did not converge, we further used the modified log-Poisson regression to fit the three models<sup>(30)</sup>. When conducting the regression analysis, we selected the confounding variables covariates that were shown to be associated with GDM risk in the literature. Model 1 was adjusted for age (years), pre-pregnancy BMI ( $kg/m^2$ ), educational level ( $\leq 12$ ; 13–15;  $\geq 16$  years), family income level ( $\leq 2999$ ; 3000–4999; 5000–9999;  $\geq 10\,000$  CNY/month), family history of diabetes (yes/no), parity (1;  $\geq 2$ ), smoking (yes/no), alcohol consumption (yes/no), physical activity (MET h/week) and energy (kJ/d). In model 2, we added vegetables (g/d), whole grains (g/d), red meat (g/d) and beverages (0;  $\geq 1$ ). In model 3, we further adjusted for dietary fibre intake (g/d), aiming to examine whether the association between fruit and GDM could be explained by dietary fibre. Other relevant fruit subtypes or individual fruits were mutually adjusted in each model. When we examined individual fruit intake and GDM risk, we further adjusted anthocyanin intake to fit model 4, aiming to investigate whether nutrients other than anthocyanin in fruits could influence GDM risk.  $P_{trend}$  was calculated with the median intake in each quartile as a continuous variable in a separate regression model with adjustments for the same covariates in each model. Considering that the intake



of some fruit subtypes (anthocyanin-rich fruit, high-GI fruit and high-GL fruit) and individual fruit was insufficient for division into quartiles, we coded non-consumers as 0, and consumers were divided into tertiles among these subtypes.

To evaluate possible effect modification, we performed stratified analyses according to pre-pregnancy BMI ( $< 24$  v.  $\geq 24$  kg/m<sup>2</sup>) and family history of diabetes (yes v. no). Data were analysed by using STATA 15.0 software. All *P*-values were two-sided, and  $P < 0.05$  was defined as statistically significant.

## Results

Among the 1453 participants (age:  $28.5 \pm 4.0$  years and pre-pregnancy BMI:  $20.7 \pm 2.7$  kg/m<sup>2</sup>), we observed 523 cases of incident GDM. In the cohort, the median total fruit intake was 279.7 (180.8, 415.2) g/d, which is the recommended fruit intake during early pregnancy in China (200~400 g/d). Women who consumed a higher amount of fruit tended to have a lower pre-pregnancy BMI and rate of a family

history of diabetes. Furthermore, women who consumed more fruit also consumed more vegetables, more carbohydrates and more anthocyanins but less fat and protein. We did not observe significant differences in educational level, family income level, gravidity, parity, smoking status, alcohol consumption, whole grain intake, red meat intake, beverage intake and dietary fibre intake among the quartiles of total fruit intake (Table 1).

After adjustments for multivariable socio-demographic and dietary factors, the RR of GDM risk was 0.73 for the highest anthocyanin-rich fruit intake quartile compared with the lowest quartile (95% CI 0.56, 0.93;  $P_{\text{trend}} = 0.015$ ), and each 50-g increment in anthocyanin-rich fruit intake seemed to lower GDM risk by 14% (RR = 0.86; 95% CI 0.77, 0.96) (Table 2). We did not find that total fruit intake and non-anthocyanin-rich fruit intake were significantly associated with GDM risk even after adjusting for dietary fibre intake. Furthermore, neither GI-grouped nor GL-grouped fruit was observed to have an association with GDM risk and further adjustment for dietary fibre intake did not alter the observed results. (Table 3).

**Table 1** Baseline characteristics of 1453 participants according to quartiles of total fruit intake (mean; median; number (percentages))

Characteristic	Overall		Q1		Q2		Q3		Q4		<i>P</i> ‡
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Numbers	1453		364		363		363		363		
Age (years)	28.5		28.8		28.2		28.7		28.4		0.213
Pre-pregnancy BMI (kg/m <sup>2</sup> )	20.7		21.1		20.9		20.4		20.4		<0.001
Education (years)											0.241
≤12	331	22.8	97	26.6	72	18.8	91	23.7	93	24.2	
13–15	525	36.1	136	35.3	150	39.1	132	34.4	134	34.8	
≥16	597	41.1	115	29.9	135	35.2	136	35.4	134	34.8	
Family income (CNY/month)											0.153
≤2999	48	3.3	13	3.4	14	3.9	11	3.0	10	2.8	
3000–4999	424	29.2	116	31.9	101	27.8	99	27.3	108	29.8	
5000–9999	679	46.7	174	47.8	167	46.0	185	51.0	153	42.1	
≥10 000	302	21.0	61	16.8	81	22.3	68	18.7	92	25.3	
Family history of diabetes	144	10.0	35	9.6	38	10.5	40	11.0	31	8.5	0.021
Primigravid	668	46.0	150	41.2	177	48.8	168	46.3	173	47.7	0.180
Primiparity	952	65.5	223	61.3	250	68.9	238	65.6	241	66.4	0.184
Smoking	49	3.4	11	3.0	16	4.4	8	2.2	14	3.9	0.374
Passive smoking	373	25.7	104	28.6	93	25.6	80	22.0	96	26.4	0.238
Alcohol drinking	113	7.8	23	6.3	36	9.9	29	8.0	25	6.9	0.281
Dietary intake											
Energy (kJ/d)	7824.1		7024.9		7670.5		8006.1		8627.4		<0.001
Fruits (g/d)*	279.7		109.6		229.2		340.8		539.7		<0.001
Vegetables (g/d)*	255		224.4		245.2		263.5		278.9		<0.001
Whole grains (g/d)*	0.59		0.0		3.7		4.9		0.0		0.029
Red meat (g/d)*	44.7		41.5		48.7		45.4		43.3		0.257
Drinks	189	13.0	52	14.3	53	14.6	49	13.5	35	9.6	0.168
Carbohydrate (g/d)†	254.8		252.4		248.0		255.5		263.2		<0.001
Protein (g/d)†	57.5		57.7		59.4		56.3		56.6		0.003
Fat (g/d)†	71.5		72.0		73.4		72.0		68.7		<0.001
Dietary fibre (g/d)†	11.8		9.8		11.4		12.5		14.8		0.118
Anthocyanin (mg/d)†	7.1		0.6		7.5		9.3		22.2		<0.001
Physical activity (MET h/week)	106.6		107.9		104.5		104.8		109.0		0.449
GDM	523	36.0	130	35.7	130	35.8	133	36.6	130	35.8	0.993

GDM, gestational diabetes mellitus.

\*Values are medians.

†Energy-adjusted intake by the residual method.

‡ANOVA, the Kruskal Wallis *H* test or the  $\chi^2$  test were used to estimate the *P* values as appropriate.

**Table 2** Relative risks (RR) of gestational diabetes mellitus (GDM) according to quartiles of total fruit and anthocyanin-grouped fruit

	Q1		Q2		Q3		Q4		<i>P</i> for trend	Per 50 g increment	
	RR	95 % CI	RR	95 % CI	RR	95 % CI	RR	95 % CI		RR	95 % CI
<b>Total fruit</b>											
Median (g)	109.6		229.2		340.8		539.7				
Range (g)	42.3–146.7		207.0–255.0		306.7–375.0		463.0–643.6				
Cases/No. of subjects	130/364		130/363		133/363		130/363				
Model 1*	1.00	Ref	1.01	0.84, 1.23	1.01	0.83, 1.22	0.98	0.80, 1.20	0.797	0.99	0.97, 1.07
Model 2†	1.00	Ref	1.01	0.84, 1.24	1.05	0.87, 1.28	1.01	0.83, 1.24	0.880	1.00	0.97, 1.03
Model 3‡	1.00	Ref	1.02	0.84, 1.24	1.06	0.87, 1.29	1.03	0.83, 1.27	0.789	1.00	0.97, 1.04
<b>Anthocyanin-rich fruit</b>											
Median (g)	0.0		45.6		106.7		216.3				
Range (g)	0.0		32.4–56.0		80.0–124.3		168.0–278.3				
Cases/No. of subjects	273/849		78/201		95/211		77/192				
Model 1*	1.00	Ref	0.93	0.75, 1.15	0.95	0.78, 1.17	0.71	0.55, 0.92	0.009	0.86	0.77, 0.96
Model 2†	1.00	Ref	0.95	0.77, 1.17	0.97	0.79, 1.19	0.72	0.56, 0.93	0.013	0.86	0.77, 0.96
Model 3‡	1.00	Ref	0.95	0.77, 1.18	0.97	0.79, 1.19	0.73	0.56, 0.93	0.015	0.86	0.77, 0.96
<b>Non-anthocyanin-rich fruit</b>											
Median (g)	0.0		198.2		298.3		484.4				
Range (g)	0.0–118.0		170.3–216.5		270.7–327.0		415.0–588.5				
Cases/No. of subjects	127/363		122/364		149/363		125/363				
Model 1*	1.00	Ref	0.94	0.77, 1.15	0.97	0.80, 1.19	1.13	0.93, 1.14	0.149	1.02	0.98, 1.05
Model 2†	1.00	Ref	0.95	0.78, 1.16	0.98	0.80, 1.19	1.14	0.99, 1.37	0.131	1.02	0.98, 1.05
Model 3‡	1.00	Ref	0.96	0.79, 1.17	0.99	0.82, 1.22	1.19	0.97, 1.45	0.067	1.02	0.99, 1.07

\*Adjusted for age (years); pre-pregnancy BMI (kg/m<sup>2</sup>); education level (≤12; 13–15; ≥16 years); family income level (≤2999; 3000–4999; 5000–9999; ≥10 000 CNY/month); family history of diabetes (yes/no); parity (1; ≥2); smoking (yes/no); alcohol drinking (yes/no); physical activity (MET h/week); energy (kJ/d).

†Model 1 plus vegetables (g/d); whole grains (g/d); beverage (0; ≥1).

‡Model 2 plus dietary fibre (g/d), different subtypes of fruit intake were mutually adjusted.

**Table 3** Relative risks (RR) of gestational diabetes mellitus (GDM) according to quartiles of glycaemic index (GI)-grouped and glycaemic load (GL)-grouped fruit

	Q1		Q2		Q3		Q4		<i>P</i> for trend	Per 50 g increment	
	RR	95 % CI	RR	95 % CI	RR	95 % CI	RR	95 % CI		RR	95 % CI
<b>Low-GI fruit</b>											
Median (g)	54.0		171.8		273.7		445.7				
Range (g)	0.0–91.8		148.0–200.0		239.6–303.1		381.6–547.8				
Cases/No. of subjects	125/365		124/361		133/365		141/362				
Model 1*	1.00	Ref	0.95	0.78, 1.16	1.02	0.84, 1.24	1.05	0.87, 1.27	0.466	1.00	0.98, 1.02
Model 2†	1.00	Ref	0.95	0.78, 1.16	1.02	0.84, 1.24	1.05	0.86, 1.27	0.517	0.99	0.98, 1.02
Model 3‡	1.00	Ref	0.96	0.78, 1.16	1.04	0.85, 1.26	1.18	0.88, 1.32	0.335	1.00	0.98, 1.02
<b>High-GI fruit</b>											
Median (g)	0.0		30.0		61.2		159.0				
Range (g)	0.0		20.0–36.0		50.0–78.0		122.0–220.0				
Cases/No. of subjects	210/549		73/185		119/311		121/363				
Model 1*	1.00	Ref	1.03	0.78, 1.35	1.06	0.82, 1.37	0.89	0.67, 1.19	0.512	0.95	0.86, 1.05
Model 2†	1.00	Ref	0.95	0.79, 1.37	1.08	0.83, 1.39	0.90	0.67, 1.20	0.569	0.95	0.86, 1.05
Model 3‡	1.00	Ref	1.04	0.79, 1.36	1.08	0.84, 1.40	0.90	0.67, 1.20	0.584	0.95	0.86, 1.05
<b>Low-GL fruit</b>											
Median (g)	87.7		210.7		319.0		508.3				
Range (g)	13.0–132.5		187.5–234.0		288.0–351.6		440.0–617.6				
Cases/No. of subjects	129/364		123/364		136/365		135/361				
Model 1*	1.00	Ref	0.96	0.79, 1.18	1.09	0.90, 1.32	1.06	0.87, 1.29	0.383	1.00	0.98, 1.02
Model 2†	1.00	Ref	0.96	0.79, 1.17	1.09	0.90, 1.32	1.05	0.87, 1.27	0.419	0.99	0.91, 1.09
Model 3‡	1.00	Ref	0.97	0.79, 1.18	1.11	0.91, 1.35	1.09	0.89, 1.34	0.259	1.00	0.98, 1.02
<b>High-GL fruit</b>											
Median (g)	0.0		35.0		59.2		108.0				
Range (g)	0.0		25.0–36.0		52.0–66.0		90.0–135.8				
Cases/No. of subjects	351/982		76/199		50/136		46/136				
Model 1*	1.00	Ref	1.12	0.92, 1.36	1.01	0.81, 1.27	0.94	0.73, 1.20	0.843	1.00	0.98, 1.02
Model 2†	1.00	Ref	1.12	0.92, 1.37	1.03	0.82, 1.29	0.94	0.73, 1.21	0.893	1.00	0.92, 1.09
Model 3‡	1.00	Ref	1.13	0.93, 1.38	1.03	0.82, 1.29	0.95	0.73, 1.22	0.935	1.00	0.92, 1.09

\*Adjusted for age (years); pre-pregnancy BMI (kg/m<sup>2</sup>); education level (≤12; 13–15; ≥16 years); family income level (≤2999; 3000–4999; 5000–9999; ≥10 000 CNY/month); family history of diabetes (yes/no); parity (1; ≥2); smoking (yes/no); alcohol drinking (yes/no); physical activity (MET h/week); energy (kJ/d).

†Model 1 plus vegetables (g/d); whole grains (g/d); beverage (0; ≥1).

‡Model 2 plus dietary fibre (g/d) and different subtypes of fruit intake were mutually adjusted.

**Table 4** Relative risks (RR) of gestational diabetes mellitus (GDM) according to quartiles of individual fruit intake

	Q1		Q2		Q3		Q4		<i>P</i> for trend	Per 50 g increment	
	RR	95 % CI	RR	95 % CI	RR	95 % CI	RR	95 % CI		RR	95 % CI
<b>Apple</b>											
Median (g)	0.0		34.5		69.0		207.0				
Range (g)	0.0		24.0–34.5		69.0–96.0		144.0–207.0				
Cases/No. of subjects	220/665		27/68		133/358		143/362				
Model 1*	1.00	Ref	1.23	0.91, 1.66	1.13	0.95, 1.35	1.17	0.99, 1.38	0.070	1.02	0.98, 1.06
Model 2†	1.00	Ref	1.22	0.91, 1.63	1.14	0.96, 1.36	1.16	0.98, 1.37	0.087	1.02	0.98, 1.05
Model 3‡	1.00	Ref	1.22	0.91, 1.63	1.15	0.97, 1.37	1.19	0.99, 1.41	0.054	1.02	0.98, 1.06
Model 4§	1.00	Ref	1.22	0.91, 1.64	1.15	0.97, 1.37	1.18	0.99, 1.40	0.093	1.02	0.98, 1.06
<b>Banana</b>											
Median (g)	0.0		36.0		54.0		90.0				
Range (g)	0.0		30.0–36.0		49.7–60.0		78.0–111.5				
Cases/No. of subjects	380/1055		70/186		28/83		45/129				
Model 1*	1.00	Ref	1.06	0.87, 1.29	0.88	0.65, 1.21	0.95	0.74, 1.23	0.669	0.98	0.88, 1.08
Model 2†	1.00	Ref	1.09	0.90, 1.34	0.90	0.66, 1.21	0.95	0.74, 1.22	0.739	0.98	0.89, 1.08
Model 3‡	1.00	Ref	1.10	0.90, 1.34	0.89	0.66, 1.21	0.95	0.74, 1.22	0.795	0.98	0.89, 1.09
Model 4§	1.00	Ref	1.10	0.90, 1.35	0.90	0.66, 1.22	0.96	0.75, 1.24	0.791	0.98	0.89, 1.09
<b>Grape</b>											
Median (g)	0.0		25.8		66.7		166.7				
Range (g)	0.0		16.7–33.3		50.0–71.7		120.0–200.0				
Cases/No. of subjects	418/1135		39/106		41/103		25/108				
Model 1*	1.00	Ref	1.03	0.79, 1.35	1.10	0.86, 1.42	0.64	0.45, 0.91	0.025	0.92	0.85, 0.99
Model 2†	1.00	Ref	1.03	0.79, 1.34	1.13	0.88, 1.44	0.66	0.46, 0.93	0.038	0.93	0.86, 1.00
Model 3‡	1.00	Ref	1.03	0.78, 1.35	1.12	0.87, 1.46	0.65	0.43, 0.98	0.044	0.93	0.86, 1.00
Model 4§	1.00	Ref	1.03	0.79, 1.37	1.13	0.87, 1.47	0.65	0.44, 0.98	0.079	0.92	0.84, 1.01
<b>Pear</b>											
Median (g)	0.0		75.0		150.0		238.5				
Range (g)	0.0		51.0–102.0		112.0–153.0		198.8–306.0				
Cases/No. of subjects	410/1135		55/161		18/55		40/102				
Model 1*	1.00	Ref	0.96	0.77, 1.19	0.92	0.63, 1.34	1.05	0.81, 1.37	0.927	0.99	0.96, 1.04
Model 2†	1.00	Ref	0.96	0.77, 1.20	0.96	0.66, 1.41	1.07	0.83, 1.39	0.768	1.00	0.96, 1.04
Model 3‡	1.00	Ref	0.98	0.78, 1.22	0.99	0.68, 1.45	1.17	0.88, 1.56	0.777	1.01	0.96, 1.06
Model 4§	1.00	Ref	0.98	0.78, 1.22	0.99	0.68, 1.46	1.16	0.87, 1.56	0.423	1.01	0.96, 1.06
<b>Peach</b>											
Median (g)	0.0		57.2		120.0		230.0				
Range (g)	0.0		36.0–63.3		96.0–126.8		190.0–292.7				
Cases/No. of subjects	432/1192		29/89		32/98		30/74				
Model 1*	1.00	Ref	0.93	0.67, 1.28	0.97	0.73, 1.29	1.16	0.88, 1.54	0.486	1.03	0.99, 1.07
Model 2†	1.00	Ref	0.93	0.67, 1.28	0.97	0.73, 1.28	1.16	0.87, 1.55	0.485	1.03	0.98, 1.07
Model 3‡	1.00	Ref	0.93	0.67, 1.28	0.97	0.73, 1.28	1.16	0.87, 1.54	0.400	1.03	0.99, 1.08
Model 4§	1.00	Ref	0.93	0.67, 1.28	0.98	0.74, 1.30	1.18	0.88, 1.58	0.421	1.03	0.99, 1.08
<b>Other fruits</b>											
Median (g)	0.0		72.9		162.7		314.0				
Range (g)	0.0		52.7–95.9		136.5–187.6		254.7–400.0				
Cases/No. of subjects	361		374		355		363				
Model 1*	1.00	Ref	1.16	0.96, 1.41	1.12	0.92, 1.37	1.08	0.88, 1.32	0.791	1.00	0.98, 1.02
Model 2†	1.00	Ref	1.18	0.97, 1.42	1.14	0.93, 1.40	1.08	0.89, 1.32	0.822	1.00	0.98, 1.02
Model 3‡	1.00	Ref	1.18	0.97, 1.42	1.14	0.94, 1.40	1.08	0.88, 1.32	0.673	1.00	0.98, 1.03
Model 4§	1.00	Ref	1.18	0.98, 1.43	1.15	0.94, 1.41	1.10	0.89, 1.35	0.696	1.00	0.98, 1.03

\*Adjusted for age (years); pre-pregnancy BMI (kg/m<sup>2</sup>); education level ( $\leq 12$ ; 13–15;  $\geq 16$  years); family income level ( $\leq 2999$ ; 3000–4999; 5000–9999;  $\geq 10\ 000$  CNY/month); family history of diabetes (yes/no); parity (1;  $\geq 2$ ); smoking (yes/no); alcohol drinking (yes/no); physical activity (MET h/week); energy (kJ/d).

†Model 1 plus vegetables (g/d); whole grains (g/d); beverage (0;  $\geq 1$ ).

‡Model 2 plus dietary fibre (g/d).

§Model 3 plus anthocyanin intake and relevant individual fruits were mutually adjusted in each model.

We also examined individual fruit intake and GDM risk. A higher grape intake had inverse linear association with GDM risk after additional adjustment for dietary fibre intake

(Q4 *v.* Q1: RR = 0.65; 95 % CI 0.43, 0.98;  $P_{\text{trend}} = 0.044$ ) (Table 4). After further adjustment for anthocyanin intake, the inverse association remained significant but tended to



be non-linear (Q4 *v.* Q1: RR = 0.65; 95 % CI 0.44, 0.98;  $P_{\text{trend}} = 0.079$ ). There was no association between apple, banana, pear, peach or other fruit intake and GDM risk.

Stratified analysis showed that the association between fruit subtype intake and GDM risk was consistent among the pre-pregnancy BMI subgroup (<24 (kg/m<sup>2</sup>)) (see online Supplemental Table 1) and family history of diabetes subgroup (none) (see online Supplemental Table 2).

## Discussion

We found that anthocyanin-rich fruit and grape intake during early pregnancy was inversely associated with GDM risk in this prospective cohort study. In addition, an association between total fruit intake, non-anthocyanin-rich fruit, GI-grouped and GL-grouped fruits and other individual fruit intake and GDM risk was not observed.

No association between total fruit intake during early pregnancy and GDM risk was observed in our cohort. Evidence regarding the association between fruit intake during pregnancy and GDM is incomplete and inconsistent. One study reported that total fruit intake may increase GDM risk<sup>(18)</sup>, while another found that total fruit intake may lower GDM risk<sup>(19)</sup>. It should be noted that both studies were conducted during the second trimester, and the time between exposure measurement and GDM diagnosis was very close (3.8–6.5 weeks). Thus, the causality remains unclear. Consistent with our findings, in the Nurses' Health Study II, no association between pre-pregnancy total fruit intake and GDM risk was observed<sup>(31)</sup>. Although dietary variation is common among populations, several large prospective studies found no association between total fruit intake and T2DM risk in women<sup>(13,32–36)</sup>. Whether total fruit intake has an impact on GDM risk needs further investigation.

Equally worth discussing is whether fruit groups or individual fruit can influence GDM risk; the evidence is quite limited and incomplete. To the best of our knowledge, no previous studies have explored the association between anthocyanin-rich fruit intake and GDM risk. In our study, anthocyanin-rich fruit intake was inversely associated with GDM risk. Anthocyanins, a typical flavonoid, are consumed by human populations in the form of red, blue and purple natural foods<sup>(37)</sup> and have aroused interest in recent human health studies. Because purple vegetables, purple sweet potato and red wine are consumed at very low levels in the Chinese population, and because anthocyanins are easily damaged by high temperature through the cooking process, raw fruits are the main food source of anthocyanins. Epidemiological studies have suggested that anthocyanin and anthocyanin-rich fruit may prevent T2DM risk. A meta-analysis involving eighteen prospective studies indicated that diets rich in flavonoids (including anthocyanins) are key to preventing T2DM<sup>(17)</sup>. In addition, a higher anthocyanin-rich fruit intake was inversely

associated with T2DM risk in three large prospective studies<sup>(16)</sup>. Several mechanisms can explain the inverse association between anthocyanin-rich fruit intake and GDM risk. First, high anthocyanin levels in these fruits can be a vital component to prevent GDM risk. During normal pregnancy, mothers experience increased insulin resistance and reduced insulin sensitivity<sup>(38)</sup>. Pancreatic  $\beta$ -cells can maintain blood glucose balance by increasing insulin secretion. However, once  $\beta$ -cells are dysfunctional or lose mass, they can lead to blood glucose homeostasis imbalance, resulting in hyperglycaemia and even GDM. Anthocyanins can improve the mass and function of  $\beta$ -cells by acting on specific receptors or enzymes<sup>(39)</sup> and modulating the insulin signalling pathway<sup>(40)</sup>, thus reducing insulin resistance and increasing insulin sensitivity. In addition, a meta-analysis including thirty-two randomised controlled trials also indicated that anthocyanins were beneficial for glycaemic control by reducing fasting blood glucose, 2-h postprandial glucose and HbA1c<sup>(15)</sup>. Second, anthocyanin-rich fruit also contains low sugar and moderate amounts of other nutrients that may help decrease GDM risk, such as fruit fibre<sup>(41)</sup>, vitamin C<sup>(42)</sup>,  $\beta$ -carotenoids<sup>(14)</sup> and other phytochemicals<sup>(43)</sup>.

Our study suggested that GI and GL differences in fruit may not be the key factors in determining fruit intake and GDM risk. Carbohydrates, a characteristic nutrient in fruits, have been considered to influence glucose levels. One study found that consumption of moderate- or high-GI fruit was positively associated with GDM risk<sup>(18)</sup>; however, the aforementioned study was conducted in tropical areas with a very different dietary habit from our study population. Another study suggested that both low- and high-GI fruit was associated with a lower GDM risk<sup>(19)</sup>, suggesting that fruit GI values may not have different impacts on GDM risk. One large prospective study conducted in Asian women and another meta-analysis involving three large cohort studies ( $n$  66 105 women) both found no association between GI-grouped or GL-grouped fruit intake and T2DM risk in women<sup>(12)</sup>. Fruits are naturally low-GI and low-GL foods. Among the fifty-nine individual fruits we collected that represent the most consumed fruits in Asia, only 17 % of fruits were high-GI fruits. In addition, the total fruit contribution to dietary GL was also small (approximately 15 %), and this contribution ratio was consistent with those of studies among other populations<sup>(12)</sup>. Although fruits contain natural sugar, their metabolism is different from that of starch and added free sugar. Fruits also contain dietary fibre, which affects the GI and GL. A recent study suggested that although GI and GL were not significantly associated with the risk of GDM, higher GI and GL were associated with lower fibre intake, which may be a risk factor for GDM<sup>(44)</sup>. Furthermore, previous studies have shown that pre-pregnancy fruit fibre intake may lower the risk of GDM<sup>(41,45)</sup>, and a recent study suggested that a dietary pattern characterised by high fibre may lower the GDM risk<sup>(46)</sup>; however, evidence regarding whether dietary fibre intake





during pregnancy influence the risk of GDM is still lacking. Therefore, we further adjusted the dietary fibre intake to examine whether the dietary fibre may change any association; however, further adjustment for dietary fibre intake did not alter the observed results. Several studies on fruit fibre and T2DM risk may explain this phenomenon. First, the association between soluble dietary fibre from fruit and T2DM risk is quite weak or absent<sup>(46)</sup>, and second, the amount of dietary fibre intake through fruits may not be sufficient to reduce the risk of diabetes<sup>(47)</sup>. Although the soluble fibre and beneficial antioxidants in fruits may also help delay sugar digestion and absorption and one RCT indicated that a moderate natural fructose (from fruits) diet can help reduce insulin resistance<sup>(48)</sup>, the carbohydrate present in fruit (including sugar and fibre) may not be a key factor in determining the association between fruit intake and GDM risk. Whether fruit carbohydrate has an impact on diabetes risk needs further investigation.

We also found that higher grape intake was inversely associated with GDM risk; however, after adjustment for anthocyanin intake, the association tended to be non-linear. To the best of our knowledge, no previous studies have investigated individual fruit intake and GDM risk. Previous studies suggested that apples, bananas, apples, pears and peaches were associated with the risk of T2DM<sup>(12,13,16)</sup>, considering GDM may share the similar pathophysiology with T2DM, we hypothesised that above-mentioned individual fruits would be associated with the risk of GDM. In accordance with our findings, some studies found that grape intake was inversely associated with T2DM risk<sup>(12,13)</sup>. Grapes are rich in anthocyanins; however, after adjustment for anthocyanin intake in further models, the inverse link remained significant but tended to be non-linear, which suggested that anthocyanins may interact with other nutrients to decrease GDM risk. In addition to anthocyanins, grapes contain resveratrol in the skin and multiple polyphenols in the seed. Resveratrol is a bioactive compound that has been used in diabetes management and reduces blood glucose levels in GDM rats<sup>(49)</sup>. In addition, some RCT indicated that grape product or grape seed extract may reduce insulin resistance and increase glucose metabolism<sup>(50–52)</sup>. We did not find associations between the intakes of other individual fruits and GDM risk in the current study. Considering that there is a paucity of information about individual fruit intake and GDM, further research is needed.

The current study has several strengths. First, it is the first prospective cohort study to investigate the association between anthocyanin-rich fruit intake and GDM risk. Second, information on fruit consumption was collected during early pregnancy ( $13.8 \pm 2.0$  weeks before GDM diagnosis) in our study, which can enable earlier preventive efforts for GDM. Third, the individual fruit types collected were quite detailed, and we examined individual fruit in our cohort, thereby providing a specific reference for recommendations. Our research also has some

limitations. First, we collected our dietary data over  $11.0 \pm 1.8$  gestational weeks, and early pregnancy reaction (such as vomiting) would influence the dietary intake; however, the rate of severe vomiting was only 6% in our study, and participants with severe vomiting were rescheduled. Furthermore, vomited foods were not counted during the dietary interview. Second, not all individual fruits were fully investigated; only five individual fruits (apples, bananas, grapes, pears and peaches) were examined separately because other individual fruits were consumed at too low of rate to have sufficient statistical power in our study population. Additionally, the five individual fruits we studied are commonly consumed in both Western and Asian populations. In addition, although trained interviewers used estimation tools to help participants minimise the recall bias, we cannot exclude all the measurement errors and residual confounding possibilities due to the observational nature of our study. Finally, our study population was composed of Chinese pregnant women; therefore, it may not be generalisable to other ethnic populations, and our results need to be confirmed by further larger prospective studies and randomised clinical trials.

In conclusion, anthocyanin-rich fruit and grape intake, but not total fruit intake, was inversely associated with GDM risk. Our findings suggest that higher specific fruit intake during early pregnancy may help prevent GDM.

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## Supplementary material

For supplementary material accompanying this paper visit <https://doi.org/10.1017/S1368980021001920>



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