



Associations of fat and carbohydrate intake with becoming overweight and obese: an 11-year longitudinal cohort study

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Abstract

The effects of macronutrient intake on obesity are controversial. This research aims to investigate the associations between macronutrient intake and new-onset overweight/obesity. The relationship between the consumption of carbohydrate and total fat and obesity was assessed by the multivariable Cox model in this 11-year cohort, which included 6612 adults (3291 men and 3321 women) who were free of overweight and obesity at baseline. The dietary intake was recorded using a 24-h recall method for three consecutive days. Moreover, substitution models were developed to distinguish the effects of macronutrient composition alteration from energy intake modification. During 7.5 person years (interquartile range 4.3, 10.8) of follow-up, 1807 participants became overweight or obese. After adjusting for risk factors, the hazard ratio (HR) of overweight/obesity in extreme quintiles of fat was 1.48 (quintile 5 *v.* quintile 1, 95% CI 1.16, 1.89; $P_{\text{trend}} = 0.02$) in women. Additionally, replacing 5% of energy from carbohydrate with equivalent energy from fat was associated with an estimated 4.3% (HR 1.043, 95% CI 1.007, 1.081) increase in overweight/obesity in women. Moreover, dietary carbohydrate was inversely associated with overweight/obesity (quintile 5 *v.* quintile 1, HR 0.70, 95% CI 0.55, 0.89; $P_{\text{trend}} = 0.02$) in women. Total fat was related to a higher risk of overweight/obesity, whereas high carbohydrate intake was related to a lower risk of overweight/obesity in women, which was not observed in men.

Key words: Fat intake: Carbohydrate intake: Overweight: Obesity: China Health and Nutrition Survey

The number of people with overweight and obesity in the world presents great public health issues in developing and developed countries^(1–3), and 57.8% of global adults will become overweight or obese by 2030⁽⁴⁾. In China, it has been estimated that 42.0% of adults were either overweight or obese⁽⁵⁾. Obesity is a major risk factor for CVD, diabetes, hypertension and all-cause mortality in China^(6–9).

The reasons leading to overweight include the intricate interaction between behavioural, environmental, genetic, physiological, economic and social factors⁽¹⁰⁾. What makes the obesity epidemic is the imbalance between energy expenditure and energy intake and sedentary lifestyle⁽¹¹⁾. There is evidence that dietary nutrients and food consumption are determinants of weight change⁽¹²⁾. Various sources and proportions of protein⁽¹³⁾, carbohydrate⁽¹⁴⁾ and fat⁽¹⁵⁾ are suggested to prevent or treat obesity. Epidemiological research suggests that protein and carbohydrate

intakes are inversely related to BMI, while intake of fat contributes to obesity^(16,17). Nevertheless, it is controversial.

Previous randomised controlled trials (RCT) have studied the effects of different quantities of macronutrients on body weight maintenance and loss over a short time. Hooper *et al.*⁽¹⁵⁾ conducted a meta-analysis of ten cohort studies and thirty-three clinical trials and summed up that lower relative body weight was related to a low-fat diet. However, another randomised controlled dietary modification trial reported that low-fat diets (with 20–30% of its energy content from fat) were not beneficial in the long term for clinically significant weight loss compared with normal diets in postmenopausal women⁽¹⁸⁾. Some RCT examining lower-carbohydrate diets (ketogenic diet) compared with low-fat diets showed a bigger reduction of body weight in the individuals who had lower-carbohydrate diets^(19,20), while meta-analyses of better quality reported no or little difference in loss of weight among the two

Abbreviations: CHNS, Chinese Health and Nutrition Survey; HR, hazard ratio; IQR, interquartile range; RCT, randomised controlled trial.

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diets^(21,22). Furthermore, randomised intervention research is only successful in evaluating weight-loss strategies, not for assessing the cause of long-term changes in weight in non-obese people, which happens slowly over decades.

Although the insidious pace of long-term weight change makes it hard to detect in studies, long-term prospective cohorts yield important evidence for essential contributors to weight gain. Of those, one long-term cohort study discovered a significant positive connection between energy percentage and total gain in weight and fat⁽²³⁾. The Nurses' Health Study, which included 41 518 women with an 8-year follow-up, proved that energy content acquired from fat is weakly correlated with gain in weight⁽²⁴⁾. However, these cohort findings were conducted in North America or Europe where it is common to have nutritional excess instead of nutritional inadequacy, which is the norm around other regions of the world.

Data on an individual's macronutrient intake and its relation to overweight or obesity in Asia are still lacking. The dietary patterns in China are also different from the West, where most studies were ever performed. Therefore, this research aimed to assess the association between total fat and carbohydrate intake and overweight or obesity by analysing data obtained from the China Health and Nutrition Survey (CHNS) cohort study in 2000–2011.

Methods

Study population

The study was based on CHNS data completed in 2000, 2004, 2006, 2009 and 2011. This survey covered nine provinces (Heilongjiang, Henan, Hubei, Hunan, Guangxi, Guizhou, Shandong, Jiangsu and Liaoning) out of thirty-one provinces in China, thereby accounting for about 42% of China's total population⁽²⁵⁾. A multi-stage stratified sampling method was employed in the survey to choose the sample. The counties of nine provinces were stratified according to income, and four counties are selected randomly in each province by using the weighted sampling scheme. Villages and towns in the counties and urban and suburban sites in the cities were randomly selected. In each survey, only adults aged ≥ 18 years and their data on sex, age, urban–rural status, educational level, lifestyle factors and physical examinations (height, weight, as well as waist circumference) were extracted. Pregnant or lactating women were excluded, along with incomplete data, implausible or extreme BMI (< 15.0 or > 40.0 kg/m²) or height (< 120.0 cm) or extreme or implausible energy intake (male $> 25\,104$ or < 3347 kJ; female $> 16\,736$ or < 2510 kJ). All participants were not overweight or obese at baseline. The study was approved by the ethics review committee of the Chinese Center for Disease Control and Prevention and the University of North Carolina at Chapel Hill.

Dietary assessment

Dietary assessment was based on a three consecutive 24-h diet review recalls and a household-level food inventory record during the same time. The dietary data of the CHNS were obtained

through a 3-d consecutive 24-h diet review method combined with a family food-weighing method. To reduce recall bias, self-report forms of dietary records were distributed to household units to help the participants record daily food intake and to serve as supplementary materials for formal dietary surveys. At the same time, the quantity of cooking oil and condiments was measured before and after 3 d of household investigation and the quantities of purchases and waste were noted when entering the household every day. The consumption amount of cooking oil and condiments was obtained by weighing the food and was divided according to the energy intake of other foods of each family member. The average daily dietary nutrient intake of each family member was calculated by using the 3-d consecutive 24-h diet-reviewed survey data and the proportionally distributed household cooking oil and condiments consumption data combined with the Chinese Food Composition Table (2002 and 2004 editions). Detailed dietary data collection was described in previous literature^(26,27).

Outcomes of variable body composition

Trained health workers measured body weight and height based on the WHO standard protocol^(28,29). Subjects wearing light-weight clothing were measured to a unit of 0.01 kg on a calibrated beam scale. The height was recorded with a portable stadiometer on a millimetre scale^(26,30). BMI was put into three categories according to the Working Group on Obesity in China: overweight, 24.0 kg/m² \leq BMI < 28.0 kg/m²; general obesity, BMI ≥ 28.0 kg/m²; normal, $18.0 \leq$ BMI < 24.0 kg/m²⁽³¹⁾.

Covariates

For this cohort study, we also assessed overweight/obesity-related factors: age, urban sites, education level, waist circumference, physical activity, smoking status, alcohol drinking status, personal income and total energy intake.

Urbanisation was categorised as urban and rural. Education level was categorised as low level (illiterate and primary school degree), middle level (lower middle school degree) and high level (upper-middle school degree, technical/vocational degree, university or college degree and master's degree or higher). Total energy intake was calculated from 3-d dietary recall food composition tables. The metabolic equivalent index codes and detailed questions of the physical activity survey were also described before⁽³²⁾. Smoking status was categorised as ever and never smoked. Alcohol drinking status was categorised as drinker and abstainer. Personal income questions summarised each part of the individual income listed in the questionnaire.

Statistical analysis

Continuous and categorical variables were described as mean values and 95% CI and percentages and 95% CI. P_{trend} of categorical variables was determined by the linear-by-linear trend test. P_{trend} of continuous variables was determined by the Spearman's correlation. Overall, participants were categorised into five groups according to the percentage of energy (%E) provided by nutrient intake (total fat and carbohydrate), which was the total daily energy intake divided by the nutrient's energy



(e.g. for fat, $\%E = ((\text{fat (g)} \times 37) / \text{total energy intake (kJ)}) \times 100$). The interval of follow-up was defined as the time between baseline and the earliest moment when participants were diagnosed as overweight or obese, lost to or unavailable for follow-up, or at the end of follow-up. Spearman's correlation was used to examine the associations between percentages of energy obtained from total fat and carbohydrate.

Hazard ratios (HR) and 95% CI of obesity and overweight were calculated in accordance with individual total fat and carbohydrate intake (divided into five groups) in a time-dependent Cox proportional hazards regression model with follow-up duration as the timescale. To quantify the trend, a median in each quintile was assigned and modelled constantly with statistical significance checked by the Wald test.

For multivariable analyses, isoenergetic substitution models were built, which included the percentages of energy obtained from protein, total fat, energy intake and other potentially confounding variables. The coefficients of these models can be explained as the expected effects of replacing a certain proportion of energy from total fat or protein for equivalent energy from carbohydrate. Energy and age were adjusted for all models. In this model, the proportion of energy consumption from total protein and fat was counted as exposure and the total energy was selected as a covariate. Changes of the outcomes by replacing carbohydrate (2 or 5% of the energy) into other components were indicated by the coefficients of this model. Substitution models were chosen to distinguish the effects between alteration of macronutrient composition and modification of energy intake.

Subgroup analyses with multiplicative interaction terms were performed to show whether the associations of total fat and carbohydrate intake levels with the risk of overweight or obesity varied by age (<50 or ≥ 50 years), urban sites (yes or no), educational levels (low or high), waist circumference (<80 or ≥ 80 cm in women; <85 or ≥ 85 cm in men), energy intake (<8786 or ≥ 8786 kJ in women; <10 042 or $\geq 10 042$ kJ in men), physical activity (<200 or ≥ 200 metabolic equivalents-h/week), smoking status (ever or never) and alcohol drinking status (drinker or abstainer). A sensitivity analysis by adjusting energy from protein as a continuous variable in the multivariable-adjusted model was conducted to test the robustness of the associations observed in our primary analyses. *P* value was determined by the Wald test. Two-tailed *P* value <0.05 indicated statistical significance. Statistical analyses of isoenergetic substitution models were conducted with SAS software, version 9.3. All other statistical analyses were done with SPSS, version 20.0.

Results

Following the initial screening process, a total of 6612 participants (BMI < 24 kg/m²) were involved, including 3291 men and 3321 women from the CHNS (2000–2011) (Tables 1 and 2). We summarised the procedures in a flow chart in Fig. 1.

Baseline characteristics of participants and data on the intake of macronutrients

The mean age of 44.8 (95% CI 44.2, 45.3) years old for men, and women was 44.5 (95% CI 44.0, 45.0) years old (Tables 1 and 2).

The mean baseline BMI (kg/m²) was 21.1 (95% CI 21.1, 21.2) for men and 21.1 (95% CI 21.0, 21.1) for women (Tables 1 and 2). At baseline, men had higher levels of total energy intake from carbohydrate, while women had higher levels of total energy intake from fat than women (*P* < 0.05). In this study, nearly half of the participants (43.6%) had a high-fat diet (at least 30% energy), 40.1% for men and 47.1 for women (*P* < 0.05), and 29.4% more than 65% of their energy came from carbohydrate at baseline, 30.9% for men and 27.8 for women (*P* < 0.05) (see online Supplementary Table S1). The results of Spearman's correlation showed that the correlations between the percentage of energy from total fat and the percentage of energy from carbohydrate were inverse both in men and women (*r* = -0.91, *P* = 0.00 in men; *r* = -0.96, *P* = 0.00 in women).

Incident cases and rates of individuals with overweight and obesity

During the mean follow-up of 7.5 (interquartile range (IQR) 4.3, 10.8) person years, a total of 1807 individuals became overweight or obese, including 936 (51.8%) men (901 overweight and thirty-five obese) and 871 (48.2%) women (835 overweight and thirty-six obese). In this cohort, the adjusted incident rate of overweight/obesity was 3.98 (95% CI 3.73, 4.22) per 100 person years in men and 3.58 (95% CI 3.34, 3.82) per 100 person years in women (Table 3). For both men and women, the proportion of energy from total carbohydrate and fat was divided into five quintiles, respectively. The incident rate of overweight/obesity was the highest in quintile 5 and the lowest in quintile 1 of energy from total fat intake both in men and women (*P*_{trend} < 0.05; Table 3). However, on the other hand, higher carbohydrate intake was related to a lower incidence of overweight/obesity in men and women (*P*_{trend} < 0.05; Table 3).

Associations between the intake of macronutrients and the risk of overweight/obesity (BMI ≥ 24.0 kg/m²)

Higher fat intake was related to a higher risk of overweight/obesity in the age-adjusted models of men (quintile 5 *v.* quintile 1, HR 1.24, 95% CI 1.01, 1.51; *P*_{trend} = 0.01) and women (quintile 5 *v.* quintile 1, HR 1.42, 95% CI 1.14, 1.76; *P*_{trend} = 0.03) (Figs. 2 and 3). The positive connection became stronger after adjusting due to other potential confounding variables in women (quintile 5 *v.* quintile 1, HR 1.48, 95% CI 1.16, 1.89; *P*_{trend} = 0.02), while this association was no longer apparent in men (Figs. 2 and 3). Comparisons of carbohydrate intake in the age-adjusted models indicated that more intake was related to a smaller risk of overweight/obesity in men (quintile 5 *v.* quintile 1, HR 0.76, 95% CI 0.62, 0.93; *P*_{trend} = 0.01) and women (quintile 5 *v.* quintile 1, HR 0.73, 95% CI 0.59, 0.90; *P*_{trend} = 0.02) (Figs. 2 and 3). In addition, higher carbohydrate intake was still related to a smaller risk of becoming overweight/obese (quintile 5 *v.* quintile 1, HR 0.70, 95% CI 0.55, 0.89; *P*_{trend} = 0.02) by multivariable adjustment for covariates in women, but not in men (Figs. 2 and 3).

Isoenergetic (2 and 5% of energy) substitution of carbohydrate by total protein and fat

As there was no association between macronutrient intake and the risk of overweight/obesity in men (see online



Table 1. Characteristics of Chinese men by quintiles of macronutrients at the baseline (*n* 3291)
(Mean values and 95 % confidence intervals; percentages and 95 % confidence intervals)

Variable	Quintile of percentage energy from fat					Quintile of percentage energy from carbohydrate								
	Quintile 1	Quintile 3	Quintile 5	<i>P</i> _{trend}	Quintile 1	Quintile 3	Quintile 5	<i>P</i> _{trend}						
Age (years)*	44.3	42.2, 44.5	44.6	43.4, 45.7	47.5	46.2, 48.7	0.00	48.4	47.2, 49.6	44.4	43.3, 45.6	43.1	42.0, 44.2	0.00
Urban location (%)†	16.7	13.9, 19.6	31.7	28.1, 35.2	51.8	48.0, 55.7	0.00	53.9	50.1, 57.7	32.5	28.9, 36.1	15.3	12.5, 18.1	0.00
Waist circumference (cm)*	77.2	76.7, 77.8	76.9	76.3, 77.5	79.0	78.4, 79.6	0.00	79.1	78.5, 79.7	77.2	76.6, 77.7	76.9	76.4, 77.4	0.00
BMI (kg/m ²)*	21.2	21.0, 21.3	21.1	21.0, 21.2	21.3	21.1, 21.4	0.04	21.3	21.2, 21.4	21.0	20.9, 21.2	21.1	21.0, 21.2	0.02
Hypertension (%)†	18.3	15.3, 21.2	18.7	15.7, 21.7	22.3	19.1, 25.6	0.00	24.5	21.2, 27.8	16.5	13.6, 19.3	18.4	15.4, 21.4	0.00
Ever smoking (%)†	65.2	61.5, 68.8	64.4	60.7, 68.1	62.6	58.9, 66.3	0.65	66.0	62.4, 69.6	63.9	60.2, 67.6	63.7	60.0, 67.4	0.45
Alcohol intake (%)†	62.3	58.5, 66.0	63.3	59.6, 67.0	55.7	51.8, 59.6	0.04	66.7	63.0, 70.2	60.6	56.8, 64.4	58.6	54.7, 62.4	0.01
Education levels														
Primary/illiterate (%)†	46.3	42.5, 50.2	36.5	32.8, 40.2	32.9	29.2, 36.5	0.00	33.4	29.8, 37.1	37.2	33.5, 40.9	46.5	42.6, 50.4	0.00
Middle school (%)†	37.6	33.9, 41.3	41.1	37.3, 44.9	34.3	30.6, 38.0	0.10	34.2	30.5, 37.9	38.4	34.7, 42.2	37.8	34.0, 41.6	0.48
High/above (%)†	16.1	3.3, 18.9	22.4	19.2, 25.7	32.9	29.2, 36.5	0.00	32.4	28.7, 36.0	24.4	21.1, 27.7	15.7	12.9, 18.5	0.00
Physical activity (MET-h/week)*	387.4	370.5, 404.2	323.5	305.5, 341.4	222.3	206.1, 238.6	0.00	224.2	208.0, 240.3	299.3	282.5, 316.2	398.0	380.6, 415.5	0.00
Income (yuan/year)*	1582.0	1257.0, 1907.1	3118.8	2469.8, 3769.9	3845.3	3245.0, 4445.0	0.00	4444.0	3769.1, 5118.9	3161.1	2522.6, 3799.7	1392.9	1095.0, 1690.7	0.00
Energy intake (kJ/d)*	10 073.0	9848.7, 10 297.7	10 232.8	10 039.5, 10 426.5	10 382.6	10 160.4, 10 604.8	0.00	10 465.9	10 237.0, 10 694.7	10 133.2	9942.4, 10 324.0	10 051.6	9834.5, 10 268.8	0.00
Carbohydrate intake (g/d)*	436.4	426.1, 446.7	361.8	354.7, 368.9	274.4	267.7, 281.1	0.00	262.3	255.9, 268.7	360.9	354.1, 367.8	445.7	435.8, 455.5	0.00
Fat intake (g/d)*	37.8	36.7, 39.0	74.6	73.1, 76.1	119.2	116.1, 122.3	0.00	113.8	110.6, 117.1	75.6	74.0, 77.3	39.2	38.0, 40.4	0.00
Protein intake (g/d)*	69.7	67.8, 71.6	72.6	70.9, 74.3	72.5	70.6, 74.4	0.00	78.5	76.1, 80.8	70.8	69.2, 72.3	66.2	64.6, 67.8	0.00

MET, metabolic equivalents.
* Mean with 95 % CI.
† Percentage with 95 % CI.

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Table 2. Characteristics of Chinese women by quintiles of macronutrients at the baseline (*n* 3321)
(Mean values and 95 % confidence intervals; percentages and 95 % confidence intervals)

Variable	Quintile of percentage energy from fat					Quintile of percentage energy from carbohydrate								
	Quintile 1		Quintile 3		Quintile 5	<i>P</i> _{trend}	Quintile 1		Quintile 3		Quintile 5	<i>P</i> _{trend}		
Age (years)*	44.0	42.9, 45.1	44.7	43.5, 45.8	45.9	44.6, 47.1	0.04	45.6	44.3, 46.8	44.5	43.3, 45.6	44.0	42.9, 45.1	0.10
Urban location (%)†	16.1	13.3, 18.8	34.3	30.7, 38.0	52.0	48.2, 55.9	0.00	56.0	52.3, 59.8	34.6	31.0, 38.2	14.5	11.8, 17.2	0.00
Waist circumference (cm)*	74.5	74.0, 75.0	74.3	73.7, 74.8	75.0	74.4, 75.6	0.24	75.0	74.4, 75.6	74.1	73.5, 74.6	74.2	73.6, 74.7	0.08
BMI (kg/m ²)*	21.0	20.9, 21.1	21.0	20.8, 21.1	21.2	21.1, 21.3	0.11	21.2	21.1, 21.3	21.0	20.9, 21.2	21.0	20.8, 21.1	0.07
Hypertension (%)†	13.0	10.4, 15.5	13.8	11.1, 16.4	14.2	11.6, 16.9	0.02	14.7	12.1, 17.4	13.1	10.5, 15.7	12.4	9.9, 14.9	0.07
Ever smoking (%)†	5.2	3.5, 6.9	3.1	1.7, 4.4	4.4	2.8, 6.0	0.39	4.9	3.3, 6.5	2.3	1.1, 3.4	4.7	3.1, 6.3	0.03
Alcohol intake (%)†	8.5	6.3, 10.6	11.4	8.9, 13.9	12.4	9.8, 14.9	0.11	14.7	12.0, 17.4	8.4	6.3, 10.5	8.9	6.7, 11.1	0.00
Education levels														
Primary/illiterate (%)†	65.1	61.4, 68.8	45.8	41.9, 49.6	42.8	39.0, 46.7	0.00	39.3	35.5, 43.0	45.8	41.9, 49.6	66.4	62.7, 70.0	0.00
Middle school (%)†	25.2	21.8, 28.6	29.4	25.9, 33.0	26.5	23.1, 29.9	0.13	27.6	24.1, 31.0	29.8	26.3, 33.3	26.0	22.6, 29.4	0.51
High/above (%)†	9.7	7.5, 12.0	24.8	21.5, 28.2	30.7	27.1, 34.2	0.00	33.2	29.6, 36.8	24.4	21.1, 27.7	7.7	5.6, 9.7	0.00
Physical activity (MET-h/week)*	393.1	375.3, 410.8	295.1	276.6, 313.5	225.5	209.7, 241.4	0.00	210.0	195.6, 224.4	278.4	260.4, 296.4	409.6	392.2, 427.0	0.00
Income (yuan/year)*	626.9	450.1, 803.7	2281.4	1788.1, 2774.7	2781.7	2318.0, 3245.3	0.00	3146.0	2636.4, 3655.6	2066.2	1618.9, 2513.4	477.8	342.4, 613.2	0.00
Energy intake (kJ/d)*	8439.5	8259.2, 8619.9	8493.1	8323.2, 8663.0	8992.7	8804.8, 9180.5	0.00	8889.3	8700.2, 9078.4	8413.2	8245.4, 8581.0	8514.0	8336.2, 8691.8	0.00
Carbohydrate intake (g/d)*	369.3	361.0, 377.6	297.2	290.1, 302.3	232.0	226.3, 237.6	0.00	225.5	220.1, 230.9	294.5	288.6, 300.3	374.5	366.3, 382.6	0.00
Fat intake (g/d)*	34.0	33.1, 35.0	66.0	64.7, 67.4	107.4	104.8, 110.0	0.00	104.1	101.4, 106.8	65.8	64.4, 67.3	34.8	33.8, 35.8	0.00
Protein intake (g/d)*	58.2	56.6, 59.8	61.7	60.2, 63.3	63.5	61.8, 65.2	0.00	69.6	67.5, 71.8	59.6	58.2, 61.0	55.9	54.6, 57.1	0.00

MET, metabolic equivalents.
* Mean with 95 % CI.
† Percentage with 95 % CI.

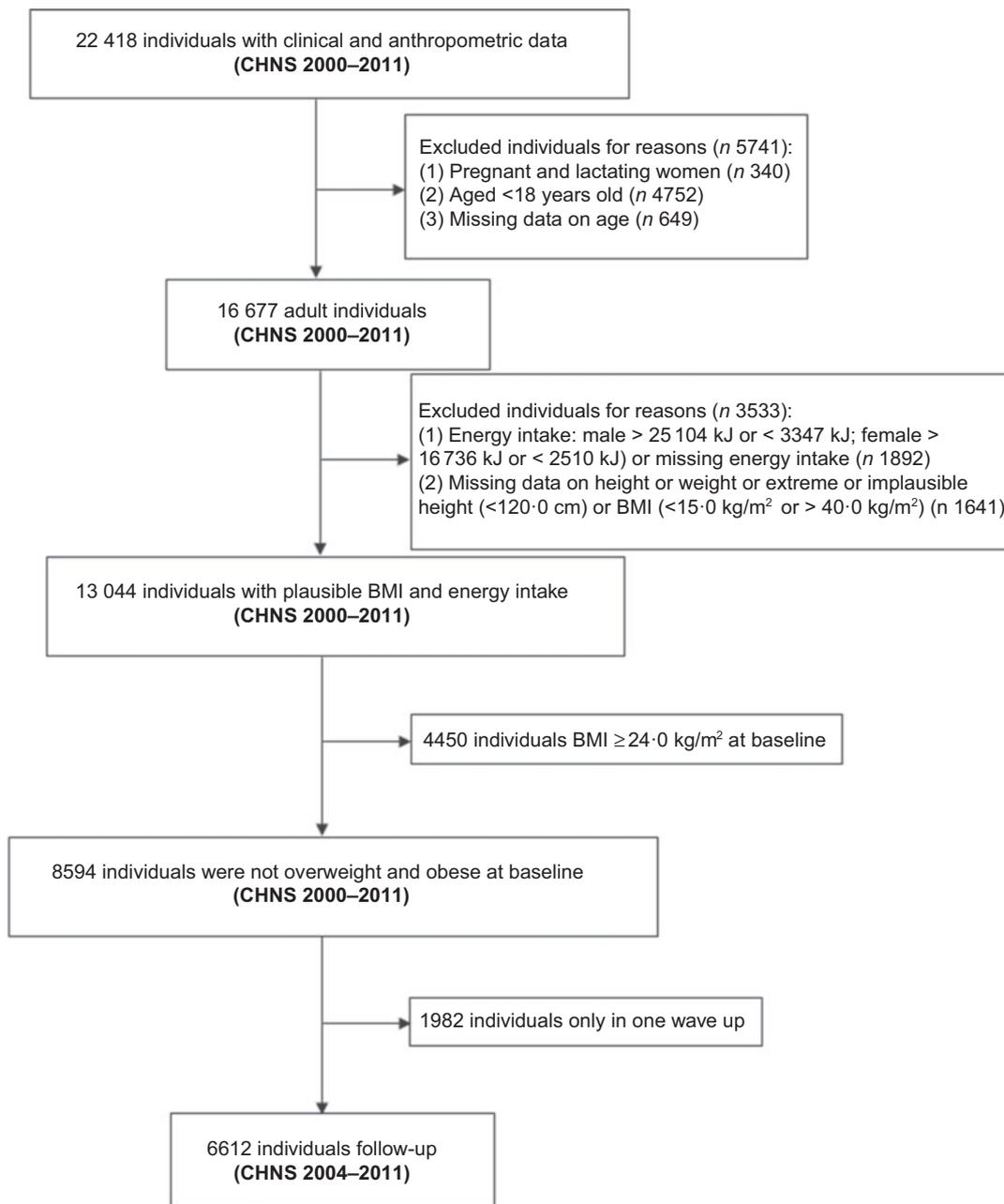


Fig. 1. Flow chart illustrating the sample selection for the present study. CHNS, Chinese Health and Nutrition Survey.

Supplementary Table S2), the isoenergetic (2 and 5 % of energy) replacement of carbohydrate by total fat and protein was only conducted in women (Table 4). In the multivariable-adjusted model, replacing 5 % energy of carbohydrate into equal energy of total fat was associated with an estimated 4.3 % increase in overweight/obesity (HR 1.043, 95 % CI 1.007, 1.081; Table 4); additionally, isoenergetic substitution of carbohydrate by total fat was associated with a 4.9 % higher risk of overweight (HR 1.049, 95 % CI 1.012, 1.088; Table 4). However, it was not associated with obesity. Substituting 5 % of energy from carbohydrate with similar energy from protein was not related to getting

either overweight or obese in the multivariable-adjusted model (Table 4).

Subgroup and sensitivity analyses

To gain a deeper understanding of the connection between the risk of obesity and intake of macronutrients, a subgroup analysis was conducted. In women, positive associations between fat intake and overweight/obesity were more pronounced in the younger individuals (<50 years) who lived in rural areas, had a lower educational level, lower energy intake and a smaller

Table 3. Incident rates of overweight and obesity among Chinese men and women by quintiles of macronutrients (Mean values and 95 % confidence intervals; median values and interquartile ranges)

Types of macronutrients	Incidence (per 100 person-years)*										Total	
	Quintile 1		Quintile 2		Quintile 3		Quintile 4		Quintile 5		Mean	95 % CI
	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI		
Percentage energy from carbohydrate												
Men												
Median	43.7		53.0		59.7		65.3		73.4		59.6	
IQR	39.3, 46.7		51.3, 54.8		58.1, 61.2		64.0, 67.2		71.1, 76.7		51.3, 67.1	
Overweight	4.35	3.74, 4.96	3.84	3.29, 4.40	3.89	3.34, 4.45	3.63	3.10, 4.15	3.47†	2.96, 3.97	3.81	3.57, 4.06
Obese	0.33	0.16, 0.51	0.09	0.00, 0.17	0.11	0.01, 0.20	0.12	0.02, 0.22	0.19	0.07, 0.31	0.16	0.11, 0.21
Overweight/obese	4.68	4.06, 5.31	3.93	3.37, 4.49	4.00	3.44, 4.57	3.75	3.22, 4.28	3.66†	3.14, 4.18	3.98	3.73, 4.22
Women												
Median	44.1		52.7		58.7		64.4		72.9		58.6	
IQR	39.6, 46.8		50.9, 54.1		57.1, 60.1		62.9, 66.1		70.4, 76.1		50.8, 66.1	
Overweight	4.00	3.42, 4.59	3.36	2.83, 3.89	3.38	2.86, 3.91	3.92	3.37, 4.47	2.62†	2.18, 3.05	3.42	3.18, 3.65
Obese	0.23	0.09, 0.37	0.22	0.08, 0.36	0.10	0.01, 0.19	0.08	0.00, 0.16	0.16	0.05, 0.26	0.16	0.11, 0.22
Overweight/obese	4.23	3.63, 4.84	3.58	3.03, 4.12	3.48	2.95, 4.01	3.99	3.44, 4.55	2.77†	2.33, 3.22	3.58	3.34, 3.82
Percentage energy from fat												
Men												
Median	14.9		22.1		27.4		33.0		41.5		27.4	
IQR	11.9, 17.1		20.4, 23.4		26.0, 28.8		31.5, 34.8		38.7, 45.8		20.4, 34.8	
Overweight	3.66	3.15, 4.18	3.29	2.79, 3.79	3.90	3.35, 4.45	3.94	3.37, 4.50	4.36†	3.75, 4.98	NA	NA
Obese	0.23	0.10, 0.36	0.09	0.01, 0.18	0.10	0.01, 0.19	0.14	0.03, 0.25	0.25	0.10, 0.40	NA	NA
Overweight/obese	3.90	3.36, 4.43	3.38	2.88, 3.89	4.01	3.45, 4.56	4.08	3.51, 4.65	4.61†	3.99, 5.24	NA	NA
Women												
Median	15.8		23.9		29.3		34.8		43.1		29.2	
IQR	12.8, 18.2		22.2, 25.4		27.8, 30.6		33.3, 36.7		40.6, 47.5		22.1, 36.6	
Overweight	2.60	2.17, 3.03	4.01	3.45, 4.56	3.31	2.79, 3.83	3.26	2.75, 3.78	4.03†	3.43, 4.62	NA	NA
Obese	0.15	0.05, 0.26	0.10	0.01, 0.19	0.12	0.02, 0.22	0.22	0.08, 0.35	0.18	0.05, 0.30	NA	NA
Overweight/obese	2.75	2.31, 3.20	4.11	3.54, 4.67	3.43	2.90, 3.96	3.48	2.95, 4.02	4.20†	3.59, 4.81	NA	NA

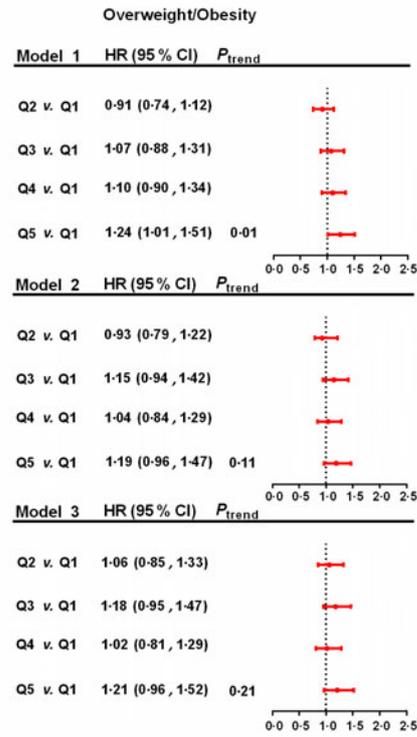
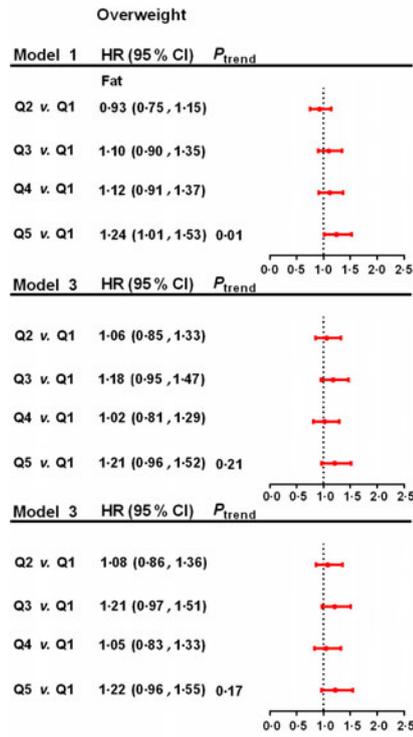
IQR, interquartile range; NA, not applicable.

* Age adjusted using the direct method to the year 2010 census population.

† $P_{trend} < 0.05$.

Men

Fat



Carbohydrate

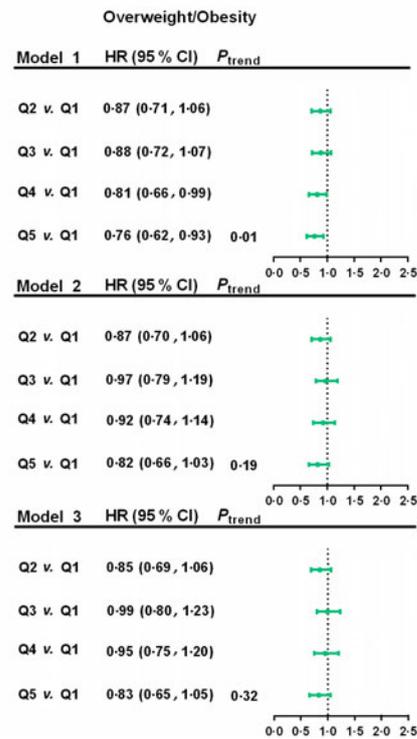
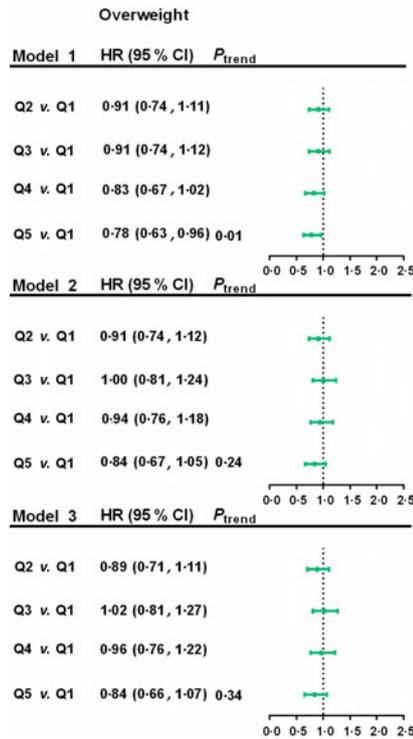
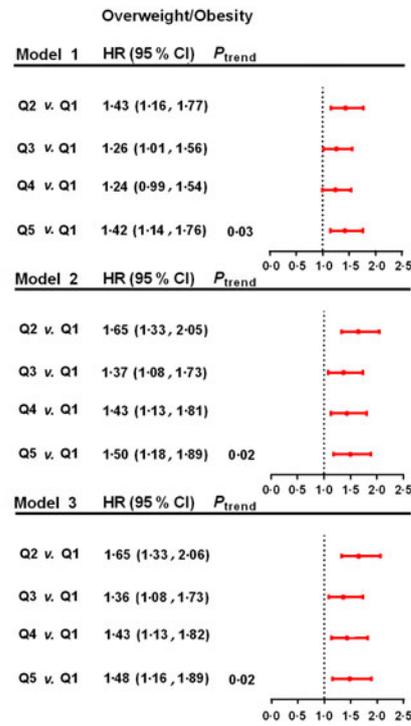
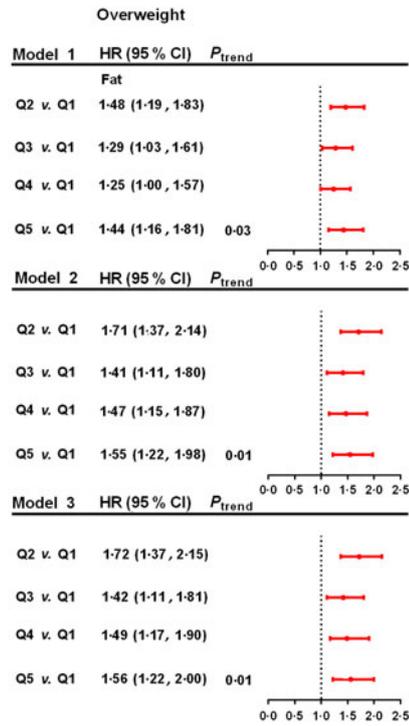


Fig. 2. Associations between percentage energy from fat and carbohydrate by quintiles and overweight and overweight/obesity among men. Model 1: hazard ratios (HR) and 95 % CI are adjusted for age, urban or rural location, education level, waist circumference, ever smoking (never, ever), alcohol drinking (abstainer or drinker) and personal income. Model 2: HR and 95 % CI are adjusted for age, urban or rural location, education level, waist circumference, ever smoking (never, ever), alcohol drinking (abstainer or drinker), personal income, physical activity and energy intake.

Women

Fat



Carbohydrate

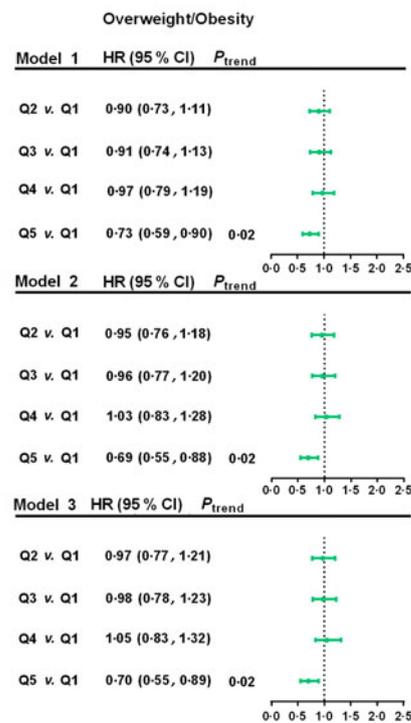
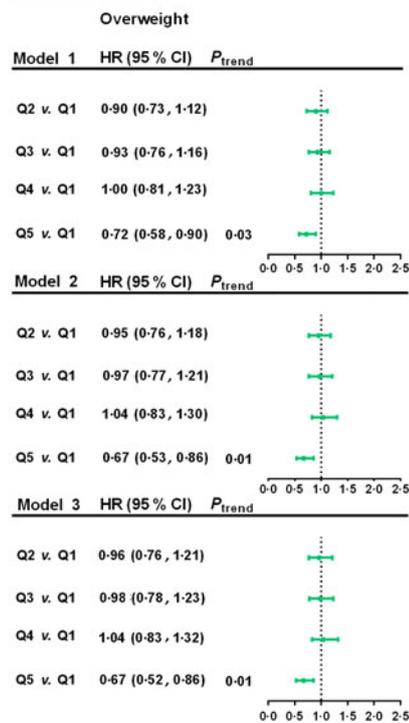


Fig. 3. Associations between percentage energy from fat and carbohydrate by quintiles and overweight and overweight/obesity among women. Model 1: hazard ratios (HR) and 95 % CI are adjusted for age. Model 2: HR and 95 % CI are adjusted for age, urban or rural location, education level, waist circumference, ever smoking (never, ever), alcohol drinking (abstainer or drinker) and personal income. Model 3: HR and 95 % CI are adjusted for age, urban or rural location, education level, waist circumference, ever smoking (never, ever), alcohol drinking (abstainer or drinker), personal income, physical activity and energy intake.

Table 4. Risk of overweight/obesity associated with isoenergetic (2 and 5% of energy) replacement of carbohydrate with fat or protein among women (Hazard ratios (HR) and 95% confidence intervals)

Clinical outcomes	Carbohydrate replaced by fat				Carbohydrate replaced by protein			
	2% of energy		5% of energy		2% of energy		5% of energy	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Overweight								
Model 1*	1.015	1.003, 1.028	1.039	1.007, 1.073	1.011	0.964, 1.061	1.028	0.911, 1.160
Model 2†	1.019	1.005, 1.034	1.049	1.013, 1.087	1.008	0.959, 1.061	1.021	0.900, 1.158
Model 3‡	1.019	1.005, 1.034	1.049	1.012, 1.088	1.012	0.961, 1.065	1.030	0.906, 1.171
Obesity								
Model 1*	1.003	0.942, 1.068	1.008	0.862, 1.179	1.186	1.006, 1.399	1.533	1.014, 2.316
Model 2†	0.981	0.914, 1.053	0.954	0.799, 1.139	1.092	0.900, 1.325	1.246	0.769, 2.019
Model 3‡	0.957	0.887, 1.031	0.895	0.742, 1.081	1.038	0.823, 1.308	1.097	0.615, 1.957
Overweight/obesity								
Model 1*	1.015	1.002, 1.028	1.038	1.006, 1.071	1.020	0.974, 1.069	1.051	0.935, 1.181
Model 2†	1.018	1.004, 1.032	1.046	1.010, 1.082	1.012	0.964, 1.063	1.032	0.913, 1.166
Model 3‡	1.017	1.003, 1.031	1.043	1.007, 1.081	1.013	0.963, 1.065	1.032	0.911, 1.170

* Model 1. HR and 95% CI are adjusted for age and energy intake.

† Model 2. HR and 95% CI are adjusted for age, urban or rural location, education level, waist circumference, ever smoking (never, ever), alcohol drinking (abstainer or drinker), personal income and energy intake.

‡ Model 3. HR and 95% CI are adjusted for age, urban or rural location, education level, waist circumference, ever smoking (never, ever), alcohol drinking (abstainer or drinker), personal income, physical activity and energy intake.

Table 5. Overweight/obesity risk for percentage energy from fat in subgroups among women* (Hazard ratios (HR) and 95% confidence intervals)

Subgroups	Percentage energy from fat										P_{trend}	$P_{\text{interaction}}$
	Quintile 1		Quintile 2		Quintile 3		Quintile 4		Quintile 5			
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI		
Region												
Urban	1 (Reference)		0.97	0.66, 1.44	0.88	0.59, 1.32	1.15	0.77, 1.70	1.09	0.74, 1.60	0.47	0.70
Rural	1 (Reference)		1.57	1.19, 2.05	1.44	1.09, 1.92	1.71	1.29, 2.26	1.35	1.01, 1.81	0.04	
Age												
<50 years	1 (Reference)		1.67	1.28, 2.17	1.32	0.99, 1.77	1.59	1.19, 2.11	1.63	1.21, 2.20	0.01	0.78
≥50 years	1 (Reference)		1.78	1.20, 2.66	1.34	0.88, 2.04	1.21	0.78, 1.87	1.50	0.98, 2.30	0.43	
Education levels												
Low	1 (Reference)		1.42	1.04, 1.92	1.36	0.99, 1.86	1.55	1.14, 2.11	1.51	1.09, 2.09	0.01	0.64
High	1 (Reference)		1.30	0.94, 1.80	0.92	0.65, 1.31	1.21	0.86, 1.69	1.15	0.80, 1.64	0.63	
Energy intake												
<8786 kJ	1 (Reference)		1.65	1.33, 2.06	1.36	1.08, 1.73	1.43	1.13, 1.81	1.48	1.16, 1.88	0.03	0.54
≥8786 kJ	1 (Reference)		1.55	1.12, 2.15	1.38	0.98, 1.94	1.69	1.21, 2.36	1.57	1.10, 2.26	0.01	
Waist circumference												
<80 cm	1 (Reference)		1.72	1.30, 2.27	1.34	0.99, 1.80	1.69	1.27, 2.26	1.55	1.14, 2.12	0.01	0.25
≥80 cm	1 (Reference)		1.45	1.01, 2.09	1.27	0.86, 1.88	1.14	0.76, 1.72	1.60	1.08, 2.39	0.14	
Physical activity												
<200 (MET-h/week)	1 (Reference)		1.31	0.90, 1.90	1.50	1.03, 2.17	1.19	0.81, 1.75	1.50	1.03, 2.19	0.10	0.42
≥200 (MET-h/week)	1 (Reference)		1.61	1.21, 2.14	1.32	0.98, 1.77	1.42	1.06, 1.92	1.46	1.07, 1.99	0.08	
Smoking status												
Never	1 (Reference)		1.61	1.29, 2.01	1.34	1.05, 1.70	1.37	1.08, 1.75	1.45	1.13, 1.85	0.047	0.76
Ever	1 (Reference)		2.00	0.59, 6.87	1.75	0.52, 5.88	3.06	0.92, 10.23	2.36	0.66, 8.46	0.13	
Alcohol drinking status												
Abstainer	1 (Reference)		1.64	1.30, 2.08	1.40	1.09, 1.79	1.40	1.08, 1.81	1.43	1.10, 1.85	0.06	0.47
Drinker	1 (Reference)		1.63	0.86, 3.09	1.29	0.62, 2.65	1.62	0.82, 3.20	2.00	1.03, 3.88	0.07	

MET, metabolic equivalents.

* HR and 95% CI are adjusted for age, urban or rural location, education level, waist circumference, ever smoking (never, ever), alcohol drinking (abstainer or drinker), personal income, physical activity and energy intake.

waist circumference (all $P_{\text{trend}} < 0.05$, $P_{\text{interaction}} > 0.05$; Table 5). On the other hand, stronger inverse associations between carbohydrate intake and overweight/obesity were found in all those subgroups (all $P_{\text{trend}} < 0.05$, $P_{\text{interaction}} > 0.05$; online Supplementary Fig. S1). In men, positive associations between

fat intake and overweight/obesity were pronounced in the quartile 2 of lower educational levels and in the quartile 5 of higher physical activity. Inverse association between carbohydrate intake and overweight/obesity was found in younger (<50 years) individuals who lived in rural areas, had a lower

educational level and higher physical activity (see online Supplementary Tables S3 and S4).

Sensitivity analyses showed that adjusting energy from protein intake strengthened our findings that the higher level of total fat intake and lower level of carbohydrate intake were related to the higher risk of overweight/obesity in women (quintile 5 *v.* quintile 1, HR 1.48, 95% CI 1.16, 1.89; $P_{\text{trend}} = 0.02$; see online Supplementary Table S5). The higher level of carbohydrate intake and lower level of total fat intake were related to the lower risk of overweight/obesity in women (quintile 5 *v.* quintile 1, HR 0.70, 95% CI 0.54, 0.90; $P_{\text{trend}} = 0.02$; see online Supplementary Table S6).

Discussion

In this large prospective cohort, divergent associations were observed between dietary fat and carbohydrate intake and overweight/obesity; moreover, the patterns of those connections were gender specific in China. Higher fat intake was related to a greater risk of overweight/obesity in women, but not in men. By contrast, high carbohydrate intake was inversely associated with becoming overweight/obese, especially in women. In this study, 43.6% of the population consumed a high-fat diet (>30% of energy intake) and 29.4% had more than 65% of their energy from carbohydrate at baseline.

It has been reported that lower fat intake at baseline and larger fat reduction were both related to greater drops in weight⁽¹⁵⁾. A previous systematic review of RCT also found that a small reduction in weight (1.5 kg, 95% CI -2.0, -1.1 kg) could be reflected in a reduction of BMI (-0.50 kg/m², 95% CI -0.74, -0.26 kg/m²) in adults by consuming less fat⁽³³⁾. This study revealed that higher fat intake could lead to a larger risk of obesity, which is in accordance with some previous cohort research^(24,34,35). Additionally, one cohort research found that greater total fat intake was related to greater gain in weight more strongly in females than in males⁽¹⁸⁾. However, Cundiff & Raghuvanshi⁽³⁶⁾ found no relationship between the proportion of intake energy from total fat and changes in BMI per year for diabetes patients. As most of those studies were conducted in North America and Europe, it might be difficult to transfer these findings to non-obese people in developing countries. In addition, compared with previous studies, the overall fat intake (27.9% of energy intake in men, 29.6% of energy intake in women) in our study was lower than that in the West (32.1% of energy intake in men, 32.6% of energy intake in women)⁽³⁷⁾. The gene-diet interactions might be another interpretation.

Carbohydrate plays an important role in the traditional Chinese diet. Evidence for the relationship between the main prevention of overweight/obesity and carbohydrate intake is scarce^(37,38) and needs further clarification. Our findings show a smaller risk of obesity or overweight with a higher carbohydrate intake, especially in women. Several randomised trials showed that a higher-carbohydrate diet leads to more or equivalent weight loss than a lower-carbohydrate diet in the follow-up beyond 6 months^(39,40). In addition, the results of a systematic review or meta-analysis suggested that a diet high in carbohydrate, or more energy intake through carbohydrate, did not

increase the odds of obesity⁽⁴¹⁾. In a Mediterranean cohort, the carbohydrate quality index indicated an inverse correlation with the risk of overweight/obesity⁽⁴²⁾. It was reported by Howard *et al.*⁽¹⁸⁾ that in women, higher consumption of total carbohydrate reduced weight gain. But in recent years, lower-carbohydrate diets have been increasingly used for weight reduction in many RCT and have been heavily promoted in the media and scientific publications^(43,44). However, most of these RCT were short term, did not take time into account and were conducted in small and highly selected populations such as severely obese adults or patients with type 2 diabetes that do not allow generalisation.

In the replacement analysis, when carbohydrate was substituted by total fat in women, the positive association with overweight/obesity was observed. This is similar to the pooled analyses by the Health Professionals Follow-Up, the Nurses' Health Study and the Nurses' Health Study II⁽³⁴⁾. This cohort study found that a 5% increase of energy from total fat instead of carbohydrate was related to a 0.19 kg (95% CI 0.15, 0.22 kg) gain in weight during a 4-year period, while another cohort study showed no such changes in ten European countries⁽⁴⁵⁾. Our study found a positive association with overweight/obesity only in Chinese women, but not in Chinese men. One of the reasons might be that the intake of macronutrients and energy is different in women and men, who consume more energy. Results from the recent research suggested that adult Chinese females have a dramatic nutrition transition towards a high-fat and low-carbohydrate diet⁽⁴⁶⁾. In our study, the total fat intake (IQR 22.1, 36.6% of energy) in women was higher than that in men (IQR 20.4, 34.8% of energy), while carbohydrate (IQR 50.8, 66.1% of energy) intake was lower than that in men (IQR 51.3, 67.1% of energy).

Furthermore, the intake of fat was positively related to the risk of overweight/obesity in women, living in rural areas, being younger, having a lower waist circumference and lower educational levels among women, while inverse associations of the above factors were observed in the carbohydrate intake in the same population. Grain is one of the main sources of our traditional diets in China, especially in rural areas. A prospective study in the USA showed an inverse relationship between increased grain consumption and weight gain⁽⁴⁷⁾. Some cohort studies stated that weight gain was related to younger women only and not older female or male with fat^(35,48), which was similar to our findings. In addition, several studies have demonstrated stronger associations between dietary carbohydrate intake and metabolic diseases in women than in men⁽⁴⁹⁾. Obesity prevalence is generally higher in women than in men, and there is also a sex difference in body fat distribution. Sex differences in obesity can be explained in part by the influence of gonadal steroids on body composition and appetite; however, behavioural, socio-cultural and chromosomal factors may also play an important role. As a vulnerable group, the impact of nutrition intake on women's health may be much greater⁽⁵⁰⁾. Macronutrient intake was associated with reproductive hormone concentrations and menstrual cycle phase⁽⁵¹⁾. Astrup *et al.*⁽⁵²⁾ observed that, among post-obese women, consuming a high-fat diet (50% of energy content derived from fat) resulted in preferential fat storage. A cross-sectional study suggested that

the increase of percentage energy from fat may be one of the important reasons for the increasing prevalence of overweight and obesity of women in China⁽⁵³⁾. Although the dietary status of women in developing countries like China is improving, the potential problems of rapid nutritional transition still existed. Further nutritional education and policy interventions still needed to improve nutrition status for Chinese females.

A high-fat diet is usually accompanied by a low carbohydrate intake. Since the percentage of energy from total fat and from carbohydrate is highly correlated, it is hard to distinguish the effect of fat *v.* carbohydrate. In the sensitivity analyses, total fat was related to a higher risk of overweight/obesity, whereas high carbohydrate intake was related to a lower risk of overweight/obesity in women, meaning that the higher level of total fat intake and lower level of carbohydrate intake were related to the higher risk of overweight/obesity in women. A prospective cohort study indicated that encouraging a low-fat, high-carbohydrate diet could be a promising approach for obesity prevention⁽³⁵⁾, which was consistent with our findings. Further research is needed to evaluate how subdivisions of energy, fat, carbohydrate and protein intakes are associated with obesity.

Over the last two decades in China, energy consumed from carbohydrate has reduced from 61.0 to 55.0% and energy obtained from fat has gone up from 28.0 to 32.9% from 2002 to 2012, which is unlike those in American findings^(16,54). A normal Chinese adult should have less than 30% of total energy from fat, less than 10–15% from protein and less than 55–65% from carbohydrate according to the Chinese Dietary Guideline of 2016. The relationship between macronutrient intake and overweight/obesity has been investigated in this study, which may provide a reference for dietary guidance in the intervention of excessive weight gain and obesity in China. It might not be the sole effect of macronutrients, but inequality and urbanisation, which were related to the risk of overweight and/or obesity. Urbanisation changed the Chinese diet and resulted in more fat and less carbohydrate consumption. These transitions have contributed to stark increases in the prevalence of conditions such as overweight and obesity, especially in urban areas and within high-income groups^(55,56). Health inequalities are mainly related to demographic and socio-economic determinants, including age, gender, income and education. Further studies will be required to investigate the relationship between these factors and the incidence of overweight and obesity in the future.

The highlights of the present research included a large sample size, a prospective design and potential confounders control. The use of an individual, consecutive 3-d recall method strengthened the accuracy of dietary recall and therefore the results and analysis. Furthermore, our study is the first large cohort study to explore the connection between the percentage energy consumed from total fat and carbohydrate and the risk of overweight/obesity in normal weight men and women in China. Certain limitations also existed in this study. Primarily, dietary consumptions were evaluated only at baseline, and it is likely that dietary alterations happen during the follow-up. Major diet changes could affect our observations, although the changes appeared after the baseline assessment. In addition, the research did not carry out further analyses according to the different categories of carbohydrate and fat due to lack of

data, which could have yielded more information on human weight changes. Lastly, only about 63% of the people in the 2000 survey were included in the 2011 survey. Thus, a potential selection bias due to loss of follow-up should be considered.

Conclusions

To sum up, high fat consumption was related to a positive impact on overweight/obesity, whereas more carbohydrate consumption was associated with a lower risk of obesity in female Chinese adults but not in males. The study highlights the essential role of macronutrients in the overweight/obesity risk among females. It remains to further investigate the effects of dietary fat and carbohydrate on the risks of overweight/obesity in men.

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Q.-B. T. and Y.-J. C. designed the study. Y.-J. C. contributed to the analysis and interpretation of data and the drafting of the article. H.-J. W. and B. Z. contributed to collecting the data. S.-F. Q., Y.-J. M., X.-B. P. and C. W. assisted in the analysis and review of the article. All authors read and approved the final manuscript.

The authors declared no conflicts of interest.

Supplementary material

For supplementary material referred to in this article, please visit <https://doi.org/10.1017/S0007114520001579>

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