

The associations of protein intake with body fat and glycaemic control in adult Chinese men and women

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Abstract

Aims/hypothesis: High protein diets were popular in weight control. However, the role of protein intake on adiposity and related metabolic conditions in free-living populations is not clear. We aimed to evaluate the associations of protein intake with adiposity and glycaemic control among adult Chinese in a nation-wide population-based survey.

Methods: The data were from China Health and Nutrition Survey 2009. A total of 9360 men and women aged 18 years or older were included. Body fat percentage was calculated using validated Chinese-specific equations. Fasting serum levels of glucose, insulin, and HbA_{1c} were measured. Dietary intake levels of macronutrients were evaluated by food weighing approach combined with a 3-day food intake recall.

Results: Averagely, our participants have 12.5% energy intake from dietary protein. With multivariate-adjustment including total energy intake, the odds ratios (OR) of over adiposity (body fat percentage $\geq 20/30$ % for men/women) and central obesity (waist circumference $\geq 90/80$ cm for men/women) were 1.51 (1.30, 1.75) and 1.40 (1.21, 1.62), respectively, comparing extreme quintiles of relative protein intake, while fat and carbohydrate were not associated with adiposity indices. Moreover, higher relative protein intake was associated with elevated concentration of blood glucose ($\beta \pm \text{SE}$: 1.233 ± 0.583), insulin (23.211 ± 9.191), HbA_{1c} (1.057 ± 0.369), and insulin resistance indicated by homeostasis model assessment of insulin resistance (7.558 ± 2.928) (all $P < 0.05$). Further adjusting for body mass index attenuated the associations.

Conclusion/Interpretation: In Chinese adults, higher habitual protein consumption was associated with higher adiposity and worse glycaemic control, independent of total energy intake.

Introduction

Over one third of the world population were threatened by obesity in 2016, according to the World Health Organization [1]. Although it is well accepted that obesity could be directly led by energy overconsumption which exceed the body requirement [2], different dietary compositions, particularly macronutrients, were linked to varied susceptibilities of adiposity accumulation [3]. Most of previous studies were focused on the potential effects of carbohydrate or fat intake, while relatively few evidences were available for the role of protein intake [4]. In the context of weight loss, high protein diets, such as Atkin's diet, were reported to be effective in reserving lean mass and intensifying fat loss [5]. On the contrary, in general population without intervention, high habitual protein intake was associated with elevated body adiposity levels among several western populations [6-10]. The precise reason was not clear for the inconsistency between experimental and observational studies. However, it would be helpful to know whether and to what degree the associations between macronutrients and adiposity are attributable to energy intake.

Both macronutrient metabolism and fat storage are closely regulated by insulin action [11]. In turn, insulin resistance could also be triggered by changes in macronutrient change [12]. Dietary modification hence was regarded as one of the most effective approaches to prevent diabetes, but the predominant emphasis of dietary guidelines was put on the quality and quantity of carbohydrate and fat intake [13]. While recommending food rich in protein, their content of fat or glycaemic index were of great concern [12]. Interestingly, emerging evidences suggested that total protein intake, per se, was positively associated with diabetes risks, both in cross-sectional and prospective studies [14, 15]. However, only limited studies reported the associations between protein intake and index of glycaemic control, with inconsistent results [16-18].

With rapid nutrition transition and upwards of sedentary lifestyles during the past a few decades in China, over 100 million Chinese are categorised as obesity nowadays, ranking the top among all countries [19]. Meanwhile, approximately one-fourth of the world diabetes patients live in China [20], and over 60% of those with diabetes were unaware of their

diagnosis, with no clear treatment of glycaemic control. The evidence was quite limited for the associations between macronutrient intake and adiposity or glycaemic control across the country, given a handful of regional studies [15, 21-23]. Therefore, the present study was aimed to evaluate the cross-sectional association of macronutrient intake, with an emphasize on protein, with adiposity and glycaemic control indices, among a nation-wide sample in China.

Methods

Participants

The data of the current study was from the China Health and Nutrition Survey (CHNS) 2009. The CHNS is a dynamic prospective cohort study across China, to evaluate the potential effects of social-economic changes in China on a wide range of nutrition-related health outcomes. Detailed study design has been described previously [24]. In brief, the first survey was carried out at 1989, and eight follow-up surveys were conducted up to 2011. Individuals of 228 communities from nine provinces were invited to participate the surveys. The study protocol was approved by the institutional review committees of National Institute of Nutrition and Food Safety, the Chinese Center for Disease Control and Prevention, the China–Japan Friendship Hospital, Ministry of Health, China, and the University of North Carolina at Chapel Hill. Informed consents were provided by all the participants. Among adult participants (aged 18 years or older), 10076 of them have available data of physical examination and dietary intakes in 2009. We further excluded those missing weight or height information ($n = 577$) and those with an estimated energy intake less than 500 kcal or above 5000 kcal ($n = 139$). Finally, 9360 participants were included in the current analyses.

Data collection

Questionnaires were applied to collect information on demography, education, smoking, drinking, and physical activity levels. Education level was grouped as low (uneducated, primary school, or junior middle school), medium (upper middle school, technical, or vocational degree), or high (university, college, or master/higher degree). Physical activity

was categorized into three levels (low, moderate, and heavy) based on a 5-category record. Smoking (current, or not) and alcohol drinking (current, or not) histories were also recorded. Anthropometric variables were measured by trained health workers. Height was measured to the nearest 0.1 cm with a portable stadiometer, with participant's shoes off, while weight was measured in light indoor clothing to the nearest 0.1 kg using a calibrated beam scale. Body mass index (BMI) was calculated as weight in kilogram divided by the squared height in meters. Waist circumference was measured at the midpoint between lowest rib and the iliac with a flexible tape, to the nearest 0.1 cm. Body fat percentage was calculated using validated gender-specific equations for Chinese population, with age, BMI and waist circumference as dependent variables [25].

Dietary measurement

Dietary information of CHNS was collected by a combination of 3-day dietary record at individual level and a food-weighing approach at household level during the same 3-day period [26]. With food models and pictures, categories and amount of food intake were recorded at individual level by trained health workers. Household food consumption was determined by a weighing method described previously. Any differences between data from two approaches were carefully compared and sorted by revising at both individual and household levels. Intakes of macronutrients (carbohydrate [g], protein [g], and fat [g]) and total energy (kcal) was calculated according to the Chinese Food Composition Table [27]. Percentage of total energy intake for each macronutrient was determined by multiplying the amount with energy value (4 kcal for each gram of carbohydrate or protein, 9 kcal for each gram of fat), then divided by total energy consumption.

Measurement of clinical traits

At the 2009 survey of CHNS, overnight fasting blood were collected from the participants. The whole blood was centrifuged immediately after collection, and stored at -86 °C for future measurement. Serum glucose was measured using a glucose oxidase phenol 4-aminoantipyrine peroxidase kit (Randox) and a Hitachi 7600 analyzer (Hitachi, Tokyo,

Japan). Serum insulin was tested using a XH-6020 gamma counter (North Institute of Biological Technology, Beijing, China) with radioimmunity assay kit (North Institute of Biological Technology, Beijing, China). Whole blood HbA_{1c} was detected with high performance liquid chromatography (model HLC-723 G7; Tosoh Corporation, Tokyo, Japan). The homeostasis model assessment of insulin resistance (HOMA-IR) was estimated as: $\text{HOMA-IR} = \text{glucose (mmol/L)} \times \text{insulin (}\mu\text{U/mL)} / 22.5$.

Definition of outcomes

Obesity was defined as BMI ≥ 28 kg/m² according to the recommendation of Cooperative Meta-Analysis Group of the Working Group on Obesity in China [28], while over adiposity (overweight or obesity as defined body fat percentage) was defined as body fat percentage ≥ 20 % for men and ≥ 30 % for women, respectively [29]. Abdominal obesity was defined as waist circumference ≥ 90 cm for men and ≥ 80 cm for women. Type 2 diabetes was defined as fasting glucose ≥ 7.0 mmol/L, previous diagnosis, or use of anti-diabetic medications.

Statistical analysis

Characteristics were presented as means \pm SD or percentage as appropriate. Between-group differences were compared with general linear regression for continuous variables and Chi-square test for categorical variables. Adjusted means of adiposity indices by levels of macronutrient intake were estimated using general linear regression with adjustment of age, sex, residence (urban or rural), education (low, medium, or high), smoking (yes or no), drinking (yes or no), and physical activity (low, moderate, or high). Total energy intake was additionally adjusted in alternative models where appropriate. Odds ratios of obesity, over adiposity, and type 2 diabetes were estimated using the Logistic regression with adjustment of covariates aforementioned. BMI and waist circumference were additionally adjusted for in alternative models. A macronutrient substitution model was used to estimate the contribution of the relative macronutrient intake on adiposity and glycemic control[30]. Herein, we calculated the coefficient of 5% energy substituted by one macronutrient with another in the model. Two-sided $P < 0.05$ was considered as statistically significant. All the analyses were

conducted with SAS 9.3 (SAS Institute, Cary, NC, USA) or R (the R Foundation for Statistical Computing, Vienna, Austria).

Results

Characteristics of the participants are presented by quintiles of relative protein intake as percentage of total energy intake (E%) in Table 1. Accordingly, those with higher intake of protein reported lower levels of carbohydrate and fat intake, and tend to consume less total energy. Meanwhile, participants with higher protein intake were likely to be younger, to live in urban areas, and to have higher education attainment. Those in the highest group showed higher levels of plasma insulin and HOMA-IR, compared with those in the lowest group.

Total energy intake was associated with both body fat percentage and waist circumference (**Supplemental figure 1**). To better understand the associations between macronutrient intake and adiposity levels, we presented adjusted means of body fat percentage and waist circumference by both absolute intake (**Figure 1**) and relative intake levels as percentage of total energy (E%) (**Figure 2**). In **Figure 1**, significant associations with body fat percentage and waist circumferences were observed for absolute values of carbohydrate, protein, and fat, with adjustment for age, sex, residence, education, smoking, alcohol drinking, and physical activity levels. Interestingly, by further adjusting for total energy intake, the associations were largely eliminated for carbohydrate and fat, but sustained for protein intake. In **Figure 2**, significant associations were only observed between relative intake of protein (E%) with body fat percentage and waist circumference regardless of adjustment of total energy intake, while no associations were detected for relative intakes of carbohydrate and fat (E%).

With multi-variable adjustment, total energy intake was positively associated with risk of adiposity accumulation, especially at abdomen (**Table 2**). Compared with those in the first quintile, the Odds ratios (OR) (95% confidence interval [CI]) of over adiposity and abdominal obesity among subjects in the highest quintile were 1.51 (1.30, 1.75) and 1.40 (1.21, 1.62), respectively. Meanwhile, relative protein intake (E%) was also positively associated with

risks of over adiposity and abdominal obesity, with multivariable adjustment including total energy intake. The ORs (95%CI) for comparing extreme quintiles were 1.57 (1.35, 1.82) and 1.48 (1.28, 1.70), respectively. No obvious association was detected for carbohydrate and fat intake with adiposity indices.

As was shown in **Table 3**, relative protein intake (E%) was associated with increased levels of glucose, insulin, HOMA-IR, and HbA_{1c}. However, by further adjusting for BMI, the associations tended to fade off. Furthermore, fasting glucose was negatively associated with relative carbohydrate intake (E%), but showed a positive association with relative fat intake (E%), even after adjusting for BMI. A positive association was also detected between relative protein intake (E%) with type 2 diabetes (**Table 4**). However, the association tended to reduce by further adjusting for BMI and waist circumference. The ORs (95%CI) were 0.87 (0.66, 1.16), 1.10 (0.84, 1.43), 1.24 (0.95, 1.61), and 1.23 (0.94, 1.60) for each quintile respectively, in comparison of the lowest group of relative protein intake. The negative association for carbohydrate and the positive association for fat seemed not influenced by adjusting for adiposity indices (**Table 4**).

We also conducted stratified analyses for the associations between protein with adiposity/type 2 diabetes according to gender, age, and urban-rural residence (**Supplemental table 1**). Overall, stratified analyses showed consistent directions of the associations. No apparent interaction was detected for either age group effects or for the associations with type 2 diabetes. However, the associations between relative protein intake with over adiposity and abdominal obesity were likely to be stronger in men and rural areas, compared with their counterparts. Macronutrient substitution analyses showed largely consistent directions of the associations with indices of both adiposity and glycemic control (**Supplemental table 2**).

Discussion

In this nation-wide population-based study in China, habitual intake of protein was positively associated with excess adiposity levels at abdomen and whole body, independent of total energy intake, while the associations between carbohydrate and fat intake with body adiposity

could be largely explained by total energy intake. Moreover, higher relative protein intake was associated with worse glycemic control, partly explained by adiposity levels.

Diets high in protein content have been proposed to be effective in body weight management, especially the context of weight loss, for its potential effects of appetite suppressing, satiety increasing, and eating related thermogenesis [31]. However, in free-living population, the role of habitual dietary protein intake and body adiposity was not clear. Similarly, several studies reported positive associations between dietary intake of protein as percentage of total energy and adiposity indices, while those studies only presented results with or without adjustment of total energy intake [6-10, 21]. So far as we know, there is no clear picture to what degree this positive association could be attributable to the energy contribution of protein intake. While our study presented mean adiposity values both with and without energy adjustment for macronutrient intake levels, which clearly illustrated positive associations of protein intake with central and overall adiposity. By contrast, the associations of carbohydrate and fat intake with adiposity was largely explained by energy intake. Interestingly, a study among 617 Canadians with multi-ethnic background showed inverse association between energy adjusted protein intake with central adiposity [32], however, with limited sample size, the study did not provide comprehensive results stratified by ethnic groups, therefore in their study, the potential confounding effect of ethnic background was not clear.

Without being attenuated by adjusting for energy intake, the mechanism underling the positive association of protein intake with adiposity seems difficult to interpret, given prior knowledge of the anti-obesity effects of high protein diets during weight control[31]. However, not all the studies supported a beneficial effects of high protein diet on adiposity. A meta-analysis of 15 randomized controlled trials with long-term duration (≥ 12 months) suggested no effects of high protein diets on weight, waist circumference, or fat mass, as compared with normal protein diets[33]. In spite of low energy contribution of dietary protein (usually less than 15%), human seems to have precise regulatory ability to optimize their protein intake[4]. Using an acute human experiment[34], Simpson and colleagues

demonstrated that, when provided with diets low in protein, participants tended to consume more to maintain an optimized protein intake, at the expense of overconsumption of fat and carbohydrate. Conversely, when provided diets high in protein, fewer food was consumed. This “protein leverage hypothesis” [4] may have well explained the “paradox” of weight loss effects of high-protein diets in trials and a detrimental associations of high protein intake and adiposity in observational studies, particularly in the context of habitual dietary intake with low protein proportion. Unfortunately, we were unable to test this hypothesis with available data in the current study. More mechanism studies in molecular levels are needed to reveal the precise reasons. Branched-chain amino acids in circulation were linked with insulin resistance, which in turn, may lead to adiposity accumulation[35].

In consistence with previous observational studies [15, 36, 37], we observed a positive association between protein intake as percentage of total energy and type 2 diabetes. However, in China, over 60% of persons with diabetes were unaware of their diagnosis, and over 50% of patients treated had no appropriate glycemic control [38]. It is therefore urgent to identify dietary factors contributing to glycemic control in general population regardless of diagnosis. Studies in this regard have been less abundant than those addressing dietary contribution on new cases of diabetes. Among 1284 American Indians with diabetes, Xu et. al. reported that higher fat intake and lower carbohydrate intake were associated with higher levels of HbA_{1c}, with no association for protein intake [17]. Similarly, in 3310 US Hispanics/Latinos, those with HbA_{1c} \geq 7.0% tended to consume more fat and less carbohydrate, with no difference for protein [18]. In our study with larger sample size, we not only observed comparable associations for fat and carbohydrate intake, but also reported that higher relative protein intake was associated with worse conditions of glycemic control, as indicated by their associations with circulating levels of glucose, insulin, HOMA-IR, and HbA_{1c}. It is noteworthy that our population had consumed lower habitual protein as energy percentage than the population in the above two studies (12%, vs. 16% to 18%). If the aforementioned protein leverage hypothesis is true, it is likely that human may act more sensitively when provided with low protein density food, just as in our study case. This would

also explain a stronger association among rural participants with lower energy contribution from protein [39], compared with urban participants (Supplementary Table 1). Meanwhile, the associations for both diabetes and indices of glycemic control was somewhat attenuated by further adjusting adiposity levels (Table 3 and Table 4), potentially suggesting a partial mediating effect of adiposity.

As far as we know, this is the largest study reporting habitual protein intake and adiposity in a free-living population. One of the major limitations of the current study is the cross-sectional feature, by which a temporal association could not be established. Without available data of food sources of macronutrients, the specific associations for animal protein and plant-based protein were not evaluated. However, with enhanced sample size, stratified analysis, multivariate adjustment models, and validated and population-specific approaches of measuring food intake and body fat content[24, 25], the current associations were unlikely captured by chance.

In summary, we observed a positive association between habitual protein intake and both overall and abdominal adiposity accumulation, independent of total energy intake in Chinese population, with relatively lower energy contribution from protein, compared western populations. Furthermore, higher relative protein intake was linked to worse glycemic control conditions, although adiposity adjustment slightly attenuated this association. Our results may highlight further studies to reveal potential mechanisms in protein-mediated obesity and related metabolic changes among free-living population.

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Table 1 Characteristics of the participants by quintiles of relative protein intake

	Q1	Q2	Q3	Q4	Q5
<i>n</i>	1,872	1,872	1,872	1,872	1,872
Male, % ¹	47.3	48.3	48.3	46.5	46.1
Age, years	53.2 ± 15.2	50.1 ± 15.1	50.3 ± 15.2	49.2 ± 15.1	49.6 ± 15.9
Protein intake, g	51.0 ± 15.7	58.9 ± 16.6	65.2 ± 19.4	71.4 ± 21.5	81.8 ± 27.0
Protein intake, E%	9.1 ± 1.0	10.9 ± 0.4	12.2 ± 0.4	13.7 ± 0.5	16.9 ± 2.0
Carbohydrate intake, g	308.4 ± 103.3	308.4 ± 97.5	307.1 ± 104.8	290.9 ± 98.3	251.8 ± 92.3
Carbohydrate intake, E%	55.3 ± 11.6	57.3 ± 10.2	57.4 ± 10.9	56.1 ± 10.3	52.0 ± 10.6
Fat intake, g	86.5 ± 43.8	75.4 ± 33.7	71.9 ± 34.4	69.4 ± 32.3	67.0 ± 31.7
Fat intake, E%	34.2 ± 11.9	31.0 ± 9.8	29.9 ± 10.5	29.7 ± 10.1	30.6 ± 10.1
Total calorie intake, kcal	2258.8 ± 676.8	2166.6 ± 605.0	2151.8 ± 636.3	2085.7 ± 621.1	1951.1 ± 624.1
Glucose, mmol/L	5.4 ± 1.5	5.3 ± 1.3	5.4 ± 1.5	5.4 ± 1.5	5.5 ± 1.5
Insulin, µU/ml	13.2 ± 27.7	14.5 ± 24.0	14.1 ± 14.9	14.4 ± 18.9	15.7 ± 24.1
HOMA-IR	3.4 ± 7.8	3.7 ± 7.5	3.7 ± 5.6	3.8 ± 6.3	4.2 ± 8.2
HbA _{1c} , %	5.6 ± 0.9	5.6 ± 0.8	5.6 ± 1.0	5.7 ± 0.9	5.6 ± 0.9
Current smoking, %	29.4	30.0	27.8	25.6	26.7
Current drinking, % ¹	30.5	33.3	32.3	33.7	34.6
Urban residence, %	21.4	23.81	32.4	38.3	52.2
Education level, %					
≤ 9 years	84.3	80.2	75.0	71.5	66.7
10-12 years	13.1	16.0	19.5	21.5	25.2
> 12 years	2.6	3.8	5.4	7.0	8.1
Physical activity level, %					
Light	43.7	47.4	53.1	55.8	67.2
Moderate	10.9	13.9	13.4	15.2	15.7
High	45.4	38.7	33.5	29.0	17.1

HbA_{1c}, hemoglobin A_{1c}; HOMA-IR, homeostasis model assessment of insulin resistance. Values are mean ± SD or percentage.

¹ Values were all significantly different ($P < 0.05$) for group comparisons except for gender and alcohol drinking.

Table 2 Adjusted odds ratios (95% CI) of obesity phenotypes by relative macronutrient intake

	Obesity	Over adiposity	Abdominal obesity
Total energy intake, kcal ¹			
Q1	1.00	1.00	1.00
Q2	0.99 (0.79–1.23)	1.1 (0.95–1.26)	1.16 (1.01–1.33)
Q3	1.16 (0.93–1.44)	1.27 (1.1–1.47)	1.23 (1.07–1.41)
Q4	0.94 (0.75–1.19)	1.23 (1.06–1.43)	1.19 (1.03–1.37)
Q5	1.35 (1.08–1.69)	1.51 (1.3–1.75)	1.40 (1.21–1.62)
<i>P</i> for trend	<i>P</i> = 0.032	<i>P</i> < 0.001	<i>P</i> < 0.001
Carbohydrate intake, E% ²			
Q1	1.00	1.00	1.00
Q2	1.15 (0.93–1.43)	1.09 (0.94–1.25)	0.87 (0.76–1.00)
Q3	1.12 (0.90–1.40)	1.07 (0.92–1.23)	0.92 (0.80–1.05)
Q4	1.05 (0.83–1.32)	0.99 (0.85–1.15)	0.93 (0.81–1.07)
Q5	1.07 (0.85–1.36)	1.02 (0.87–1.18)	0.88 (0.76–1.02)
<i>P</i> for trend	<i>P</i> = 0.868	<i>P</i> = 0.716	<i>P</i> = 0.259
Fat intake, E% ²			
Q1	1.00	1.00	1.00
Q2	1.04 (0.83–1.30)	0.98 (0.85–1.13)	0.97 (0.84–1.11)
Q3	0.92 (0.73–1.15)	0.89 (0.77–1.03)	0.97 (0.84–1.12)
Q4	0.98 (0.78–1.23)	0.98 (0.85–1.13)	0.96 (0.84–1.11)
Q5	0.93 (0.74–1.17)	0.90 (0.77–1.04)	0.98 (0.85–1.13)
<i>P</i> for trend	<i>P</i> = 0.432	<i>P</i> = 0.210	<i>P</i> = 0.761
Protein intake, E% ²			
Q1	1.00	1.00	1.00
Q2	0.96 (0.77–1.21)	1.14 (0.99–1.31)	1.07 (0.93–1.23)
Q3	0.97 (0.78–1.22)	1.52 (1.31–1.75)	1.37 (1.19–1.57)
Q4	1.17 (0.93–1.45)	1.61 (1.39–1.86)	1.46 (1.27–1.68)
Q5	1.19 (0.95–1.49)	1.57 (1.35–1.82)	1.48 (1.28–1.70)
<i>P</i> for trend	<i>P</i> = 0.036	<i>P</i> < 0.001	<i>P</i> < 0.001

1 Adjusted for age, sex, residence, education, smoking, drinking, and physical activity.

2 Adjusted for age, sex, residence, education, smoking, drinking, physical activity, and total energy intake.

Table 3 Associations between macronutrient intakes with parameters of glycaemic control

Nutrien t	Glucose		Insulin		HOMA- IR		HbA1c	
	β	<i>P</i>	β	<i>P</i>	β	<i>P</i>	β	<i>P</i>
	coefficient	value	coefficient	value	coefficient	value	coefficient	value
	t \pm SE		t \pm SE		t \pm SE		t \pm SE	
Total energy intake, kcal								
Model 1	$2.4 \times 10^{-5} \pm 2.6 \times 10^{-5}$	0.357	$-2.2 \times 10^{-4} \pm 4.1 \times 10^{-4}$	0.59	$-7.6 \times 10^{-5} \pm 1.3 \times 10^{-4}$	0.56	$1.1 \times 10^{-5} \pm 1.7 \times 10^{-5}$	0.49
Model 2	$6.5 \times 10^{-7} \pm 2.6 \times 10^{-5}$	0.980	$-4.9 \times 10^{-4} \pm 4.1 \times 10^{-4}$	0.23	$-1.7 \times 10^{-4} \pm 1.3 \times 10^{-4}$	0.20	$5.5 \times 10^{-6} \pm 1.6 \times 10^{-5}$	0.73
Carbohydrate intake, E%								
Model 3	-0.769 ± 0.156	<0.00	0.179 ± 2.470	0.94	-0.549 ± 0.787	0.48	-0.061 ± 0.099	0.53
Model 4	-0.755 ± 0.154	<0.00	0.320 ± 2.449	0.89	-0.502 ± 0.780	0.52	-0.052 ± 0.097	0.59
Fat intake, E%								
Model 3	0.599 ± 0.157	<0.00	-2.572 ± 2.476	0.29	-0.174 ± 0.789	0.82	0.010 ± 0.099	0.91
Model 4	0.609 ± 0.154	<0.00	-2.443 ± 2.455	0.32	-0.130 ± 0.781	0.86	0.018 ± 0.097	0.85
Protein intake, E%								
Model 3	1.233 ± 0.583	0.035	23.211 ± 9.191	0.01	7.558 ± 2.928	0.01	1.057 ± 0.369	0.00
Model 4	0.749 ± 0.575	0.192	17.740 ± 9.127	0.05	5.724 ± 2.905	0.04	0.712 ± 0.362	0.04

HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model assessment of insulin resistance.

Model 1 Adjusted for age, sex, residence, education, smoking, drinking, and physical activity.

Model 2 Adjusted for age, sex, residence, education, smoking, drinking, physical activity, and BMI.

Model 3 Adjusted for age, sex, residence, education, smoking, drinking, physical activity, and total energy intake.

Model 4 Adjusted for age, sex, residence, education, smoking, drinking, physical activity, total energy intake, and BMI.

Table 4 Adjusted odds ratios (95% CI) of type 2 diabetes by relative macronutrient intakes.

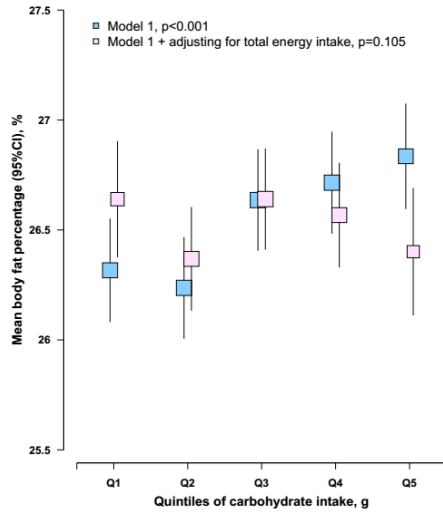
	Model 1	Model 2	Model 3
Carbohydrate intake, E%			
Q1	1.00	1.00	1.00
Q2	0.82 (0.64–1.03)	0.82 (0.64–1.04)	0.83 (0.65–1.06)
Q3	0.77 (0.61–0.99)	0.78 (0.61–1.00)	0.78 (0.60–1.00)
Q4	0.80 (0.62–1.02)	0.82 (0.64–1.06)	0.81 (0.63–1.05)
Q5	0.61 (0.46–0.81)	0.62 (0.47–0.82)	0.60 (0.45–0.80)
<i>P</i> for trend	<i>P</i> = 0.001	<i>P</i> = 0.003	<i>P</i> = 0.002
Fat intake, E%			
Q1	1.00	1.00	1.00
Q2	1.30 (0.98–1.71)	1.33 (1.01–1.76)	1.34 (1.01–1.78)
Q3	1.25 (0.95–1.65)	1.28 (0.97–1.69)	1.29 (0.97–1.71)
Q4	1.22 (0.93–1.62)	1.25 (0.94–1.65)	1.26 (0.95–1.68)
Q5	1.47 (1.12–1.93)	1.48 (1.12–1.94)	1.51 (1.14–1.99)
<i>P</i> for trend	<i>P</i> = 0.023	<i>P</i> = 0.024	<i>P</i> = 0.018
Protein intake, E%			
Q1	1.00	1.00	1.00
Q2	0.91 (0.69–1.20)	0.89 (0.67–1.17)	0.87 (0.66–1.16)
Q3	1.18 (0.91–1.52)	1.12 (0.86–1.45)	1.10 (0.84–1.43)
Q4	1.34 (1.03–1.73)	1.24 (0.95–1.61)	1.24 (0.95–1.61)
Q5	1.33 (1.02–1.72)	1.26 (0.97–1.64)	1.23 (0.94–1.60)
<i>P</i> for trend	<i>P</i> = 0.002	<i>P</i> = 0.011	<i>P</i> = 0.015

Model 1 Adjusted for age, sex, residence, education, smoking, drinking, physical activity, and total energy intake.

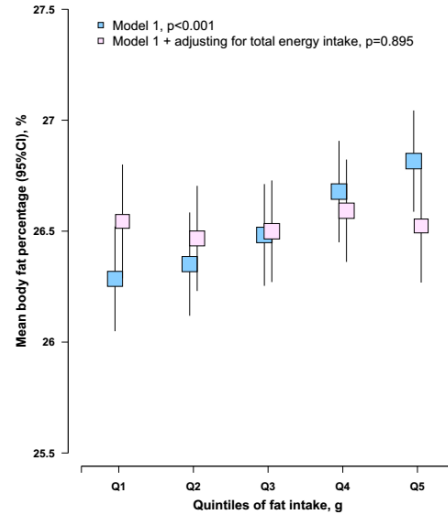
Model 2 Adjusted for age, sex, residence, education, smoking, drinking, physical activity, total energy intake, and BMI.

Model 3 Adjusted for age, sex, residence, education, smoking, drinking, physical activity, total energy intake, BMI, and waist circumference.

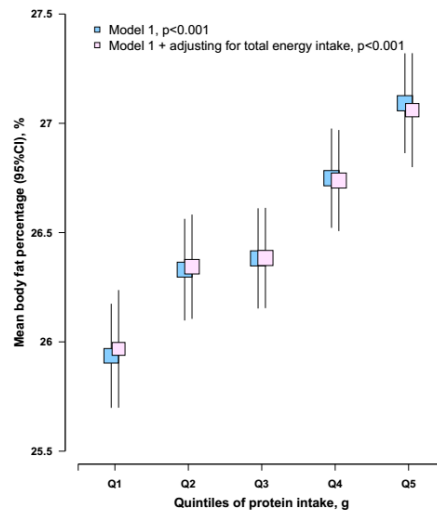
Body fat percentage



Body fat percentage



Body fat percentage



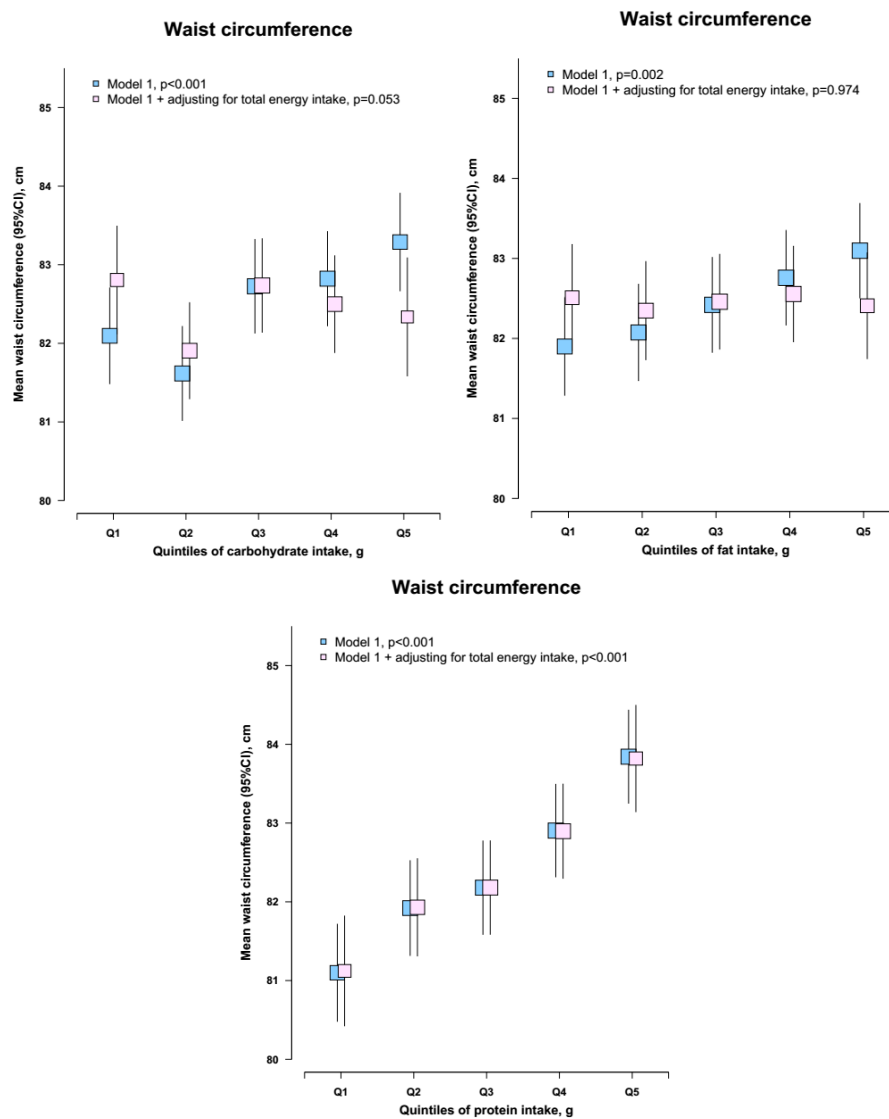
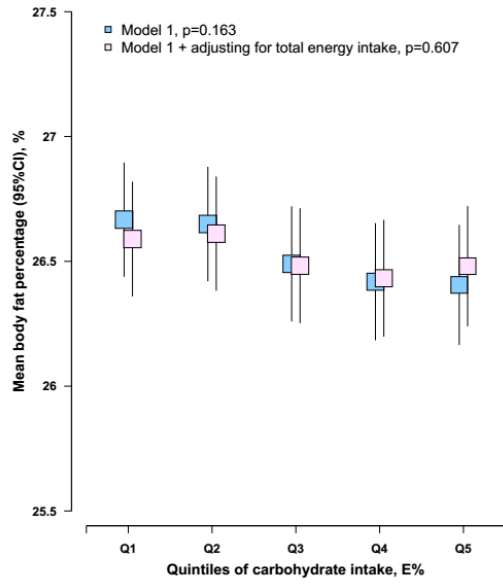


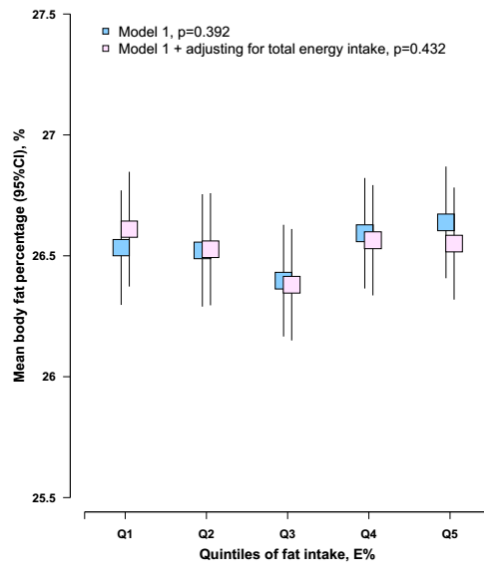
Figure 1 Adjusted means of body fat percentage and waist circumference by absolute macronutrient intake levels

Model1: adjusted for age, sex, residence, education, smoking, drinking, and physical activity.

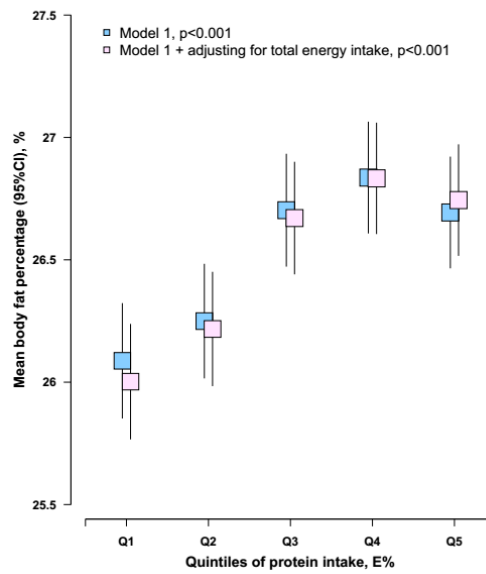
Body fat percentage



Body fat percentage



Body fat percentage



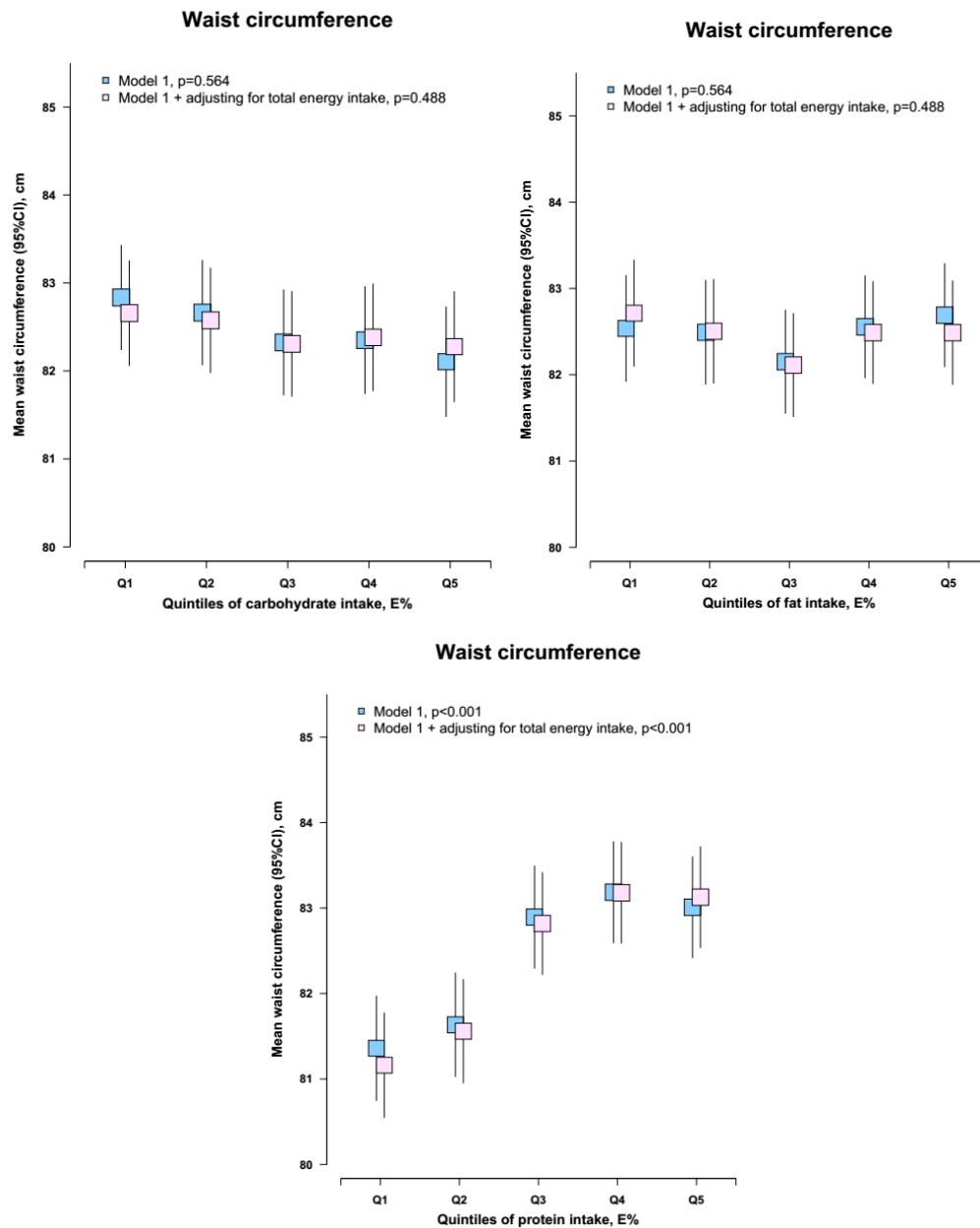


Figure 2 Adjusted means of body fat percentage and waist circumference by relative macronutrient intake levels (as percentage of total energy)

Model1: adjusted for age, sex, residence, education, smoking, drinking, and physical activity.

Supplemental Table 1 Adjusted odds ratios (95% CI) of adiposity and type 2 diabetes by relative protein intake according to gender, age, and residence.

	Obesity	Over adiposity	Abdominal obesity	Type 2 diabetes
Stratified by Gender				
Men				
Q1	1.00	1.00	1.00	1.00
Q2	1.06 (0.74–1.53)	1.19 (0.98–1.44)	1.19 (0.96–1.49)	0.72 (0.49–1.08)
Q3	1.02 (0.71–1.47)	1.68 (1.38–2.04)	1.62 (1.31–2.01)	1.24 (0.87–1.76)
Q4	1.24 (0.87–1.77)	1.64 (1.34–2.00)	1.56 (1.26–1.95)	1.39 (0.98–1.98)
Q5	1.45 (1.02–2.07)	1.81 (1.47–2.22)	1.76 (1.41–2.20)	1.41 (0.99–2.02)
<i>P</i> for trend	<i>P</i> = 0.020	<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> = 0.002
Women				
Q1	1.00	1.00	1.00	1.00
Q2	0.90 (0.67–1.21)	1.06 (0.85–1.31)	0.98 (0.82–1.18)	1.14 (0.78–1.67)
Q3	0.94 (0.70–1.27)	1.33 (1.07–1.66)	1.21 (1.00–1.45)	1.10 (0.75–1.62)
Q4	1.13 (0.85–1.51)	1.60 (1.28–2.00)	1.40 (1.16–1.69)	1.26 (0.86–1.83)
Q5	1.03 (0.77–1.39)	1.39 (1.11–1.75)	1.32 (1.09–1.60)	1.25 (0.85–1.83)
<i>P</i> for trend	<i>P</i> = 0.388	<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> = 0.217
<i>P</i> for interaction	<i>P</i> = 0.079	<i>P</i> < 0.001	<i>P</i> = 0.002	<i>P</i> = 0.130
Stratified by age groups				
< 50.8 years (Median)				
Q1	1.00	1.00	1.00	1.00

Q2	0.86 (0.61–1.22)	1.13 (0.92–1.38)	1.01 (0.82–1.25)	0.99 (0.58–1.68)
Q3	1.01 (0.72–1.41)	1.60 (1.31–1.96)	1.35 (1.10–1.65)	0.99 (0.58–1.67)
Q4	1.14 (0.82–1.58)	1.50 (1.23–1.84)	1.38 (1.12–1.69)	1.19 (0.72–1.99)
Q5	1.28 (0.91–1.78)	1.70 (1.38–2.10)	1.59 (1.28–1.96)	1.25 (0.74–2.10)
<i>P</i> for trend	<i>P</i> = 0.039	<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> = 0.261
≥ 50.8 years (Median)				
Q1	1.00	1.00	1.00	1.00
Q2	1.03 (0.76–1.40)	1.09 (0.88–1.34)	1.08 (0.90–1.31)	0.85 (0.62–1.17)
Q3	0.91 (0.66–1.24)	1.35 (1.09–1.67)	1.35 (1.12–1.64)	1.22 (0.91–1.65)
Q4	1.14 (0.84–1.54)	1.71 (1.36–2.15)	1.49 (1.22–1.81)	1.34 (0.99–1.80)
Q5	1.10 (0.81–1.50)	1.44 (1.15–1.80)	1.36 (1.12–1.66)	1.33 (0.98–1.79)
<i>P</i> for trend	<i>P</i> = 0.416	<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> = 0.005
<i>P</i> for interaction	<i>P</i> = 0.697	<i>P</i> = 0.0934	<i>P</i> = 0.489	<i>P</i> = 0.791
Stratified by residence				
Urban areas				
Q1	1.00	1.00	1.00	1.00
Q2	0.68 (0.44–1.04)	1.11 (0.82–1.51)	0.79 (0.59–1.05)	0.97 (0.56–1.66)
Q3	0.69 (0.46–1.03)	1.10 (0.83–1.46)	0.98 (0.75–1.28)	1.32 (0.81–2.15)
Q4	0.77 (0.53–1.13)	1.17 (0.88–1.55)	0.98 (0.75–1.27)	1.42 (0.89–2.29)
Q5	0.82 (0.57–1.17)	1.27 (0.97–1.67)	1.02 (0.79–1.31)	1.56 (1.00–2.45)
<i>P</i> for trend	<i>P</i> = 0.718	<i>P</i> = 0.069	<i>P</i> = 0.290	<i>P</i> = 0.012

Rural areas				
Q1	1.00	1.00	1.00	1.00
Q2	1.10 (0.84–1.44)	1.12 (0.96–1.31)	1.15 (0.98–1.35)	0.90 (0.65–1.23)
Q3	1.12 (0.85–1.47)	1.66 (1.40–1.96)	1.49 (1.26–1.75)	1.12 (0.82–1.54)
Q4	1.40 (1.07–1.84)	1.80 (1.51–2.14)	1.66 (1.41–1.96)	1.33 (0.97–1.81)
Q5	1.46 (1.09–1.95)	1.67 (1.38–2.02)	1.71 (1.43–2.05)	1.15 (0.81–1.62)
<i>P</i> for trend	<i>P</i> = 0.002	<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> = 0.069
<i>P</i> for interaction	<i>P</i> = 0.052	<i>P</i> = 0.005	<i>P</i> = 0.002	<i>P</i> = 0.772

Adjusted for age, sex, residence, education, smoking, drinking, physical activity, and total energy intake.

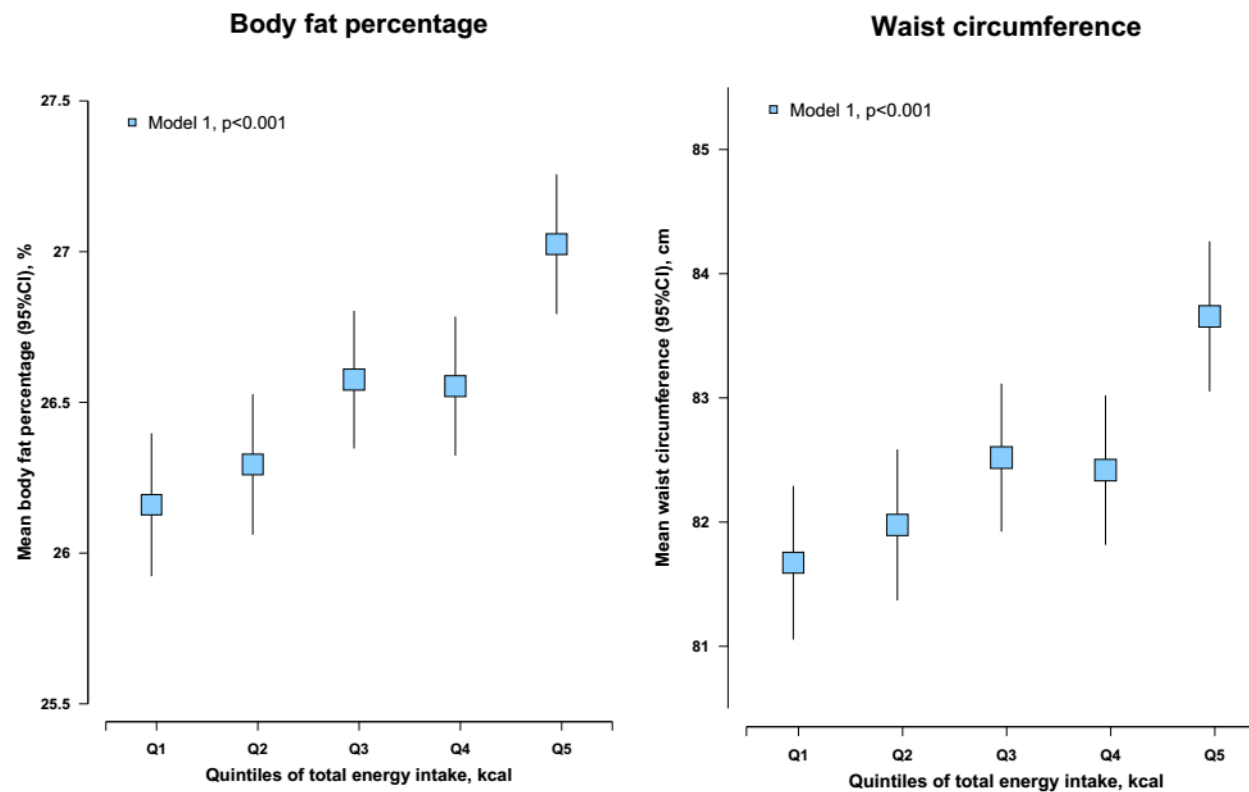
Supplemental Table 2 Associations between macronutrient substitution with adiposity and glycaemic indices.¹

Macronutrients intake, per 5% total energy	BF%, %	WC, cm	Glucose, mmol/L	Insulin, μ U/ml	HOMA-IR	HbA _{1c} , %
Substituting carbohydrate by fat						
β coefficient	0.010	0.023	0.034	-0.071	0.011	0.003
95%CI	(-0.030, 0.050)	(-0.081, 0.126)	(0.019, 0.050)	(-0.318, 0.176)	(-0.067, 0.090)	(-0.007, 0.013)
<i>P</i> value	0.623	0.665	<0.001	0.573	0.779	0.505
Substituting carbohydrate by protein						
β coefficient	0.478	1.263	0.086	1.110	0.386	0.055
95%CI	(0.331, 0.625)	(0.880, 1.647)	(0.028, 0.144)	(0.192, 2.028)	(0.094, 0.678)	(0.018, 0.092)
<i>P</i> value	<0.001	<0.001	0.004	0.018	0.010	0.003
Substituting fat by carbohydrate						
β coefficient	0.001	-0.002	-0.038	0.027	-0.022	-0.002
95%CI	(-0.039, 0.040)	(-0.104, 0.100)	(-0.053, -0.022)	(-0.216, 0.289)	(-0.099, 0.055)	(-0.012, 0.007)
<i>P</i> value	0.973	0.970	<0.001	0.830	0.580	0.646
Substituting fat by protein						
β coefficient	0.461	1.247	0.054	1.166	0.373	0.052
95%CI	(0.316, 0.606)	(0.869, 1.625)	(-0.003, 0.111)	(0.264, 2.068)	(0.086, 0.661)	(0.016, 0.089)
<i>P</i> value	<0.001	<0.001	0.065	0.011	0.0011	0.005
Substituting protein by carbohydrate						

β coefficient	-0.125	-0.373	-0.069	-0.674	-0.220	-0.016
95%CI	(-0.222, -0.028)	(-0.620, -0.120)	(-0.107, -0.031)	(-1.277, -0.071)	(-0.412, -0.028)	(-0.040, 0.008)
<i>P</i> value	0.012	0.004	< 0.001	0.029	0.025	0.192
Substituting protein by fat						
β coefficient	-0.129	-0.383	-0.033	-0.748	-0.210	-0.014
95%CI	(-0.226, -0.031)	(-0.637, -0.129)	(-0.072, 0.005)	(-1.352, -0.143)	(-0.403, -0.018)	(-0.038, 0.010)
<i>P</i> value	0.011	0.003	0.088	0.015	0.032	0.249

HbA_{1c}, hemoglobin A_{1c}; HOMA-IR, Homeostasis model assessment of insulin resistance.

¹Regression was adjusted for age, sex, residence, education, smoking, drinking, physical activity, and total energy intake.



Supplemental Figure 1 Adjusted means of body fat percentage and waist circumference by total energy intake levels.

Model 1: adjusted for age, sex, residence, education, smoking, drinking, and physical activity.