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BMI and waist circumference are associated with impaired glucose metabolism and type 2 diabetes in normal weight Chinese adults

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Abstract

Aims—To examine the associations of BMI and waist circumference with glucose metabolism and (pre)diabetes among adults with BMI < 25 kg/m².

Methods—We conducted a cross-sectional study in a nationally representative sample (10,098 men and 17,454 women) of Chinese adults aged ≥ 20 years with BMI < 25 kg/m². Glucose levels after at least 10 hours of overnight fasting, at 30 minutes and at 120 minutes after a standard 75-g oral glucose load were measured. Associations of BMI and waist circumference with outcomes

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were examined by general linear models for continuous outcomes and by logistic regression models for dichotomous outcomes.

Results—Among those with BMI < 25 kg/m², 18.8% of men and 17.1% of women had abnormal glucose metabolism, including 4.9% of men and 3.8% of women with undiagnosed type 2 diabetes. For each SD increase in BMI (2.1 kg/m²) and waist circumference (8.3 cm), fasting glucose levels increased by 0.128 and 0.170 mmol/L in men, and by 0.112 and 0.167 mmol/L in women, respectively; the corresponding increases for 2-hour post-load glucose levels were 0.121 and 0.217 mmol/L in men, and 0.241 and 0.362 mmol/L in women. When simultaneously included in the same model, these associations with waist circumference were stronger than with BMI.

Conclusion—Obesity measures are associated with abnormal glucose metabolism and diabetes, with central obesity playing a more prominent role than general obesity in Chinese population with BMI < 25 kg/m². Chinese diabetes prevention and treatment programs should incorporate targeting of normal weight adults with central obesity.

Keywords

glucose metabolism; type 2 diabetes; BMI; waist circumference; China

Introduction

Overweight and obesity contribute to abnormal glucose metabolism[1–3], which is mediated by its close association with increased insulin resistance[4, 5], and are a major determinant of type 2 diabetes[6–8]. Consequently, the rising obesity epidemic has contributed to the significantly increased prevalence of type 2 diabetes over the last three decades[9, 10].

Both central obesity, as measured by waist circumference, and general obesity, as measured by BMI, are strongly associated with risk of type 2 diabetes and impaired glucose metabolism[6, 11]. However, the relative contribution of general versus central obesity measures may vary in different populations[12–15]. Further, limited information is available about whether such relationships remain in people without excess body weight (BMI < 25 kg/m²)[2, 16]. Such information is important for prevention and intervention, because a significant proportion of the general population do not have excess body weight, more so in populations of developing countries, for example Chinese population[17].

Type 2 diabetes has become a major public health challenge in China with 9.7% of the adult population (20 years age or older) being diabetic and 15.5% prediabetic[18]. Increased BMI and waist circumference are major contributors to type 2 diabetes[17, 18]. However, limited information is available regarding to what extent such relationships persist in Chinese population without excess body weight. In the current study, we examined the associations of BMI and waist circumference with fasting glucose, 2-hour glucose, area under the curve (AUC) glucose during a glucose tolerance test, and (pre)diabetes by gender in a large, nationally representative sample of the Chinese population without excess body weight.

Research Design and Methods

Study Participants

The study participants have been previously described in detail[18]. In short, a nationally representative sample of persons 20 years of age or older in the general population was selected by a multistage, stratified sampling method. In total, 152 urban street districts and 112 rural villages were selected from 14 provinces. A total of 47,325 participants (87.3% of those invited to participate) completed the study. Of these, 1,086 participants (including 622 with BMI<25 kg/m²) were excluded due to missing data on demographic information or glucose levels during fasting or a 2 hour glucose tolerance test. Of the remaining 46,239 adults, 10,098 men and 17,454 women who had a BMI below 25 kg/m² and had not been previously diagnosed with type 2 diabetes were included in the final analysis. Characteristics of the study participants by sex are shown in Table 1.

The institutional review board or ethics committee at each participating institution approved the study protocol. Written informed consent was obtained from each participant before data collection.

Data Collection

The China National Diabetes and Metabolic Disorders Study was conducted from June 2007 through May 2008. Data collection details have been previously described[18]. Information on demographic characteristics, personal and family medical history, and lifestyle risk factors was obtained by using a standard questionnaire in an interview with trained staff[19]. Cigarette smoking was defined as having smoked at least 100 cigarettes in one's lifetime; alcohol drinking as the consumption of at least 30 g of alcohol per week for 1 year or more; and regular leisure-time physical activity as participation in moderate or vigorous activity for 30 minutes or more per day at least 3 days a week. Body weight, height, and waist circumference were measured by standard methods, as described previously[20]. In particular, waist circumference was measured at the middle point between the rib cage and iliac crests[20].

All study investigators and staff members successfully completed a training program which specified the aims of the study and the specific tools and methods to be used. Detailed instructions were given at training sessions to interviewers who administered the study questionnaire. Clinical staff members were trained to obtain anthropometric measurements and blood specimens according to a standard protocol[19].

Before the oral glucose tolerance test, participants were instructed to maintain their usual physical activity and diet for at least 3 days. After at least 10 hours of overnight fasting, a venous blood specimen was collected in a vacuum tube containing sodium fluoride for plasma glucose measurement. Participants were given a standard 75-g glucose solution. Blood samples were drawn at 0, 30, and 120 minutes after the glucose load to measure glucose concentrations. Plasma glucose was measured by using a hexokinase enzymatic method. All the study laboratories successfully completed a standardization and certification program.

Impaired fasting glucose was defined as fasting glucose level ≥ 6.1 mmol/L (110 mg/dL), impaired glucose tolerance as 2-hour glucose level ≥ 7.8 mmol/L (140 mg/dL), and undiagnosed diabetes as fasting glucose level ≥ 7.0 mmol/L (126 mg/dL), 2-hour glucose level ≥ 11.1 mmol/L (200 mg/dL), or both[21].

Statistical Analysis

Fasting glucose, 2-hour glucose levels, and AUC glucose were treated as continuous variables, and impaired fasting glucose, impaired glucose tolerance, and previously undiagnosed type 2 diabetes were treated as dichotomous variables in the current study. AUC glucose was calculated using the trapezoidal method[22, 23] as [(glucose at 0 minute + glucose at 30 minutes) $\times 0.5$ + (glucose at 30 minutes + glucose at 120 minutes) $\times 1.5$]/2.0. General linear models were used to examine the associations of BMI and waist circumference with continuous variables by sex, adjusted for age, leisure-time physical activity, alcohol drinking, college education, cigarette smoking, and family history of type 2 diabetes. Least square means adjusted for the same covariates as above were calculated by decile of BMI or waist circumference in each sex group. Logistic regression models were used to examine trends in the prevalence of impaired fasting glucose, impaired glucose tolerance, or previously undiagnosed type 2 diabetes across BMI or waist circumference deciles, adjusted for the same covariates as above.

In order to compare the strength of associations of BMI versus waist circumference with the outcome variables we calculated regression coefficients (for continuous variables) and odds ratios (for dichotomous variables) associated with a one standard deviation increase in BMI (2.1 kg/m²) and waist circumference (8.3 cm); associations with one unit increase in BMI (kg/m²) and waist circumference (cm) were also presented as supplementary data. We also performed sensitivity analyses in samples with BMI < 23 kg/m² to reflect the fact that the ideal cutoff point to define overweight in Chinese population may be lower, though there is no consensus in this regard[24–26].

All data, including percentages and mean values, were weighted to represent the total population of Chinese adults (20 years of age or older) based on Chinese population data from 2006[18]. All *P* values are two-tailed and have not been adjusted for multiple testing. All statistical analyses were conducted with the use of SUDAAN 10.0 (Research Triangle Institute).

Results

Among those with BMI < 25 kg/m², 7.5% of men and 25.2% of women had abdominal obesity (waist circumference ≥ 90 cm for men and ≥ 80 cm for women). In total, 18.8% of men and 17.1% of women without excess body weight had abnormal glucose metabolism (impaired fasting glucose, impaired glucose tolerance, or previously unknown type 2 diabetes), including 4.9% of men and 3.8% of women with undiagnosed type 2 diabetes (Table 1).

Both BMI and waist circumference were significantly and linearly associated with levels of fasting glucose, 2-hour glucose, and AUC glucose in men and women (*P*<0.01 in all cases).

Similarly, both BMI and waist circumference were associated with the prevalence of impaired fasting glucose, impaired glucose tolerance, and previously undiagnosed type 2 diabetes ($P < 0.001$). In Figure 1, levels of fasting glucose, 2-hour glucose, AUC glucose increased linearly as BMI or waist circumference increased from the bottom decile to the top decile. The prevalence of impaired fasting glucose, impaired glucose tolerance, and previously undiagnosed type 2 diabetes also increased in a similar fashion (Figure 2), except that the prevalence of type 2 diabetes seemed to be lowest in the second and the third deciles of BMI and waist circumference. Of note, the associations of outcomes with BMI and waist circumference were somewhat stronger in women than in men; however the sex differences were not statistically significant after multiple comparison adjustment.

When both BMI and waist circumference were rescaled by their respective standard deviations (2.1 kg/m² for BMI and 8.3 cm for waist circumference), the strength of associations with outcome variables was overall stronger for waist circumference than for BMI (Tables 2 and 3). When simultaneously included in the same model, the associations for both BMI and waist circumference were attenuated substantially with waist circumference consistently and significantly ($P < 0.05$) associated with all outcome variables (Tables 2 and 3); for BMI, only associations with fasting glucose levels in both men and women and with 2-hour glucose and impaired glucose tolerance in women remained significant ($P < 0.01$) (Tables 2 and 3). Results for one unit increase in BMI and waist circumference are presented in Supplementary Tables 1 and 2. In logistic regression models, increases in c-statistics, a measure of overall model performance, ranged from 0.002 to 0.012 ($p < 0.01$ in all cases) when waist circumference was added to the models that included BMI and other covariates. When analyses were restricted to those with BMI < 23 kg/m², associations of all outcomes with BMI and waist circumference were overall weaker than among those with BMI < 25 kg/m²; however, associations with waist circumference remained largely statistically significant (Supplementary Tables 3 and 4).

Excluding those with BMI < 18.5 kg/m² ($n = 1,964$) did not materially change the results presented above.

Discussion

Compared to previous reports [17, 18], we examined in those who did not have excess body weight associations of BMI and waist circumference with fasting glucose, 2-hour glucose, AUC glucose, and (pre)diabetes by gender. We demonstrated that 18.8% of men and 17.1% of women aged 20 years or older with BMI < 25 kg/m² had impaired glucose metabolism, with 4.9% of men and 3.8% of women having undiagnosed diabetes. Both BMI and waist circumference were positively associated with glucose metabolism and risk of (pre)diabetes. These findings suggest that efforts to prevent and treat diabetes in the Chinese general population should include targeting of adults with a normal body weight. Waist circumference had a stronger association with glucose impairment and diabetes compared to BMI, and waist circumference remained significant for all the glucose impairment outcomes and diabetes when conditioned on BMI. These results underscore the importance of central obesity in the development of abnormal glucose metabolism and type 2 diabetes for adults in the Chinese general population.

Our findings are consistent with a previous report from cross-sectional analysis of a 4071 rural Chinese women with BMI < 23kg/m²[16]. The presence of these associations in people with normal weight strongly suggests that the associations of obesity measures with glucose metabolism and risk of type 2 diabetes are continuous across the full spectrum of body weight[6, 11, 27]. There may not be a cut-point beyond which risk of type 2 diabetes abruptly increases within the normal body weight range. It is known that body fatness varies substantially in people with similar levels of BMI[28]. Our findings are consistent with previously reported associations between body fat and (pre)diabetes in a cross-sectional analysis of 4828 Spanish adults attending a university clinic[2]. Given that a majority of the general population in China is not overweight or obese and that our findings suggest more than 17% of them are (pre)diabetic and 4–5% have undiagnosed diabetes, diabetes prevention and treatment intervention programs to control body weight should include targeting of adults with BMI < 25 kg/m².

The associations of central obesity with glucose metabolism and type 2 diabetes seemed to be stronger than for general obesity in people without excess body weight. Previous studies in the Chinese population[29–31] and other populations[13, 32, 33], which included participants with a full range of BMI, have shown similar findings. BMI, a measure of general obesity, does not differentiate fat mass from fat-free mass and cannot inform fat distribution, while waist circumference, a measure of central obesity, is more closely correlated to visceral fat. Visceral fat is associated with increased circulating inflammatory cytokines and adhesion molecules[4, 5, 34–37], which promotes the development of insulin resistance and type 2 diabetes[4, 5, 34, 38]. The fact that waist circumference was associated with glucose metabolism and type 2 diabetes even when conditioned on BMI strongly indicates that central obesity is more closely associated with risk of (pre)diabetes and suggests that waist circumference should be included in assessing risk of type 2 diabetes in clinical practice, even in patients with BMI less than 25 kg/m².

A unique feature of our study is that we were able to show the positive associations of BMI and waist circumference with 2-hour post-load glucose levels in a large (n=27,452), nationally representative sample of the Chinese population without excess body weight. It is known that among prediabetic Chinese individuals, more than two-thirds (68% in men and 74% in women) have normal fasting glucose[18]. These numbers were even higher in the current study: 72% of prediabetic men and 75% of prediabetic women with BMI below 25 kg/m² had normal fasting glucose. Given the high risk of developing type 2 diabetes in individuals with impaired glucose tolerance[39], an oral glucose test may be necessary in people with normal fasting glucose if other risk characteristics, such as older age, positive family history of type 2 diabetes, and cigarette smoking, are present[40].

Despite its strengths, our study was based on a cross-sectional rather than a prospective analysis. However, we excluded participants with known type 2 diabetes to reduce the potential for bias caused by lifestyle changes or use of diabetes medications. Another limitation was that we lacked the data to adjust for other dietary factors.

In conclusion, our results suggest that obesity measures, particularly waist circumference, are significantly associated with glucose metabolism and risk of (pre)diabetes even in

Chinese adults classified as having normal body weight. This association underscores the importance of adiposity in the development of impaired glucose metabolism and type 2 diabetes. Our findings also suggest that diabetes treatment and prevention programs in the Chinese general population should incorporate targeting of normal weight adults with central obesity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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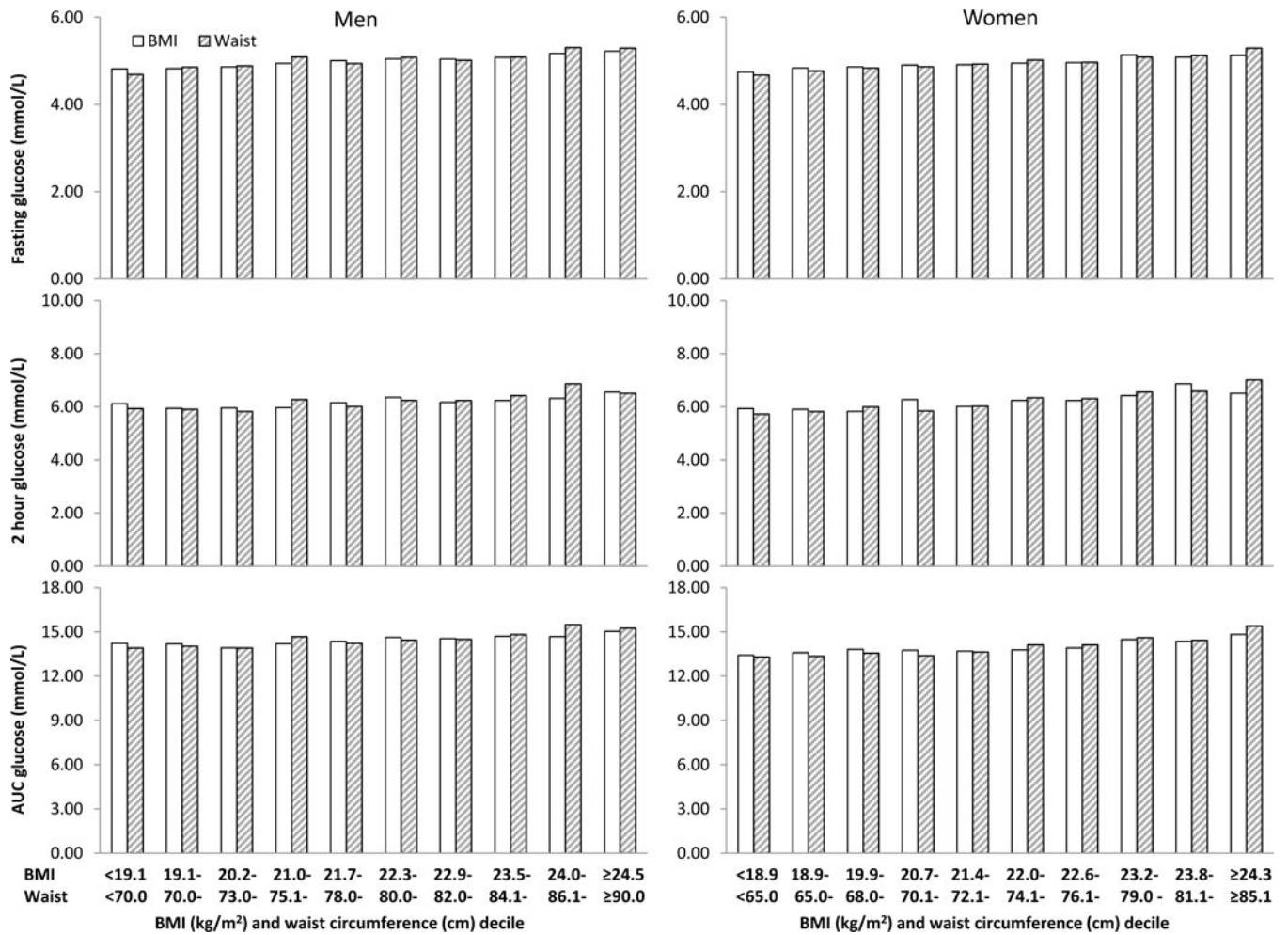


Figure 1. Least square mean levels of fasting glucose, 2 hour glucose, and area under the curve (AUC) glucose adjusted for age, education, leisure-time physical activity, alcohol drinking, family history of type 2 diabetes by BMI or waist circumference decile and sex. *P* for trend <0.01 in all cases.

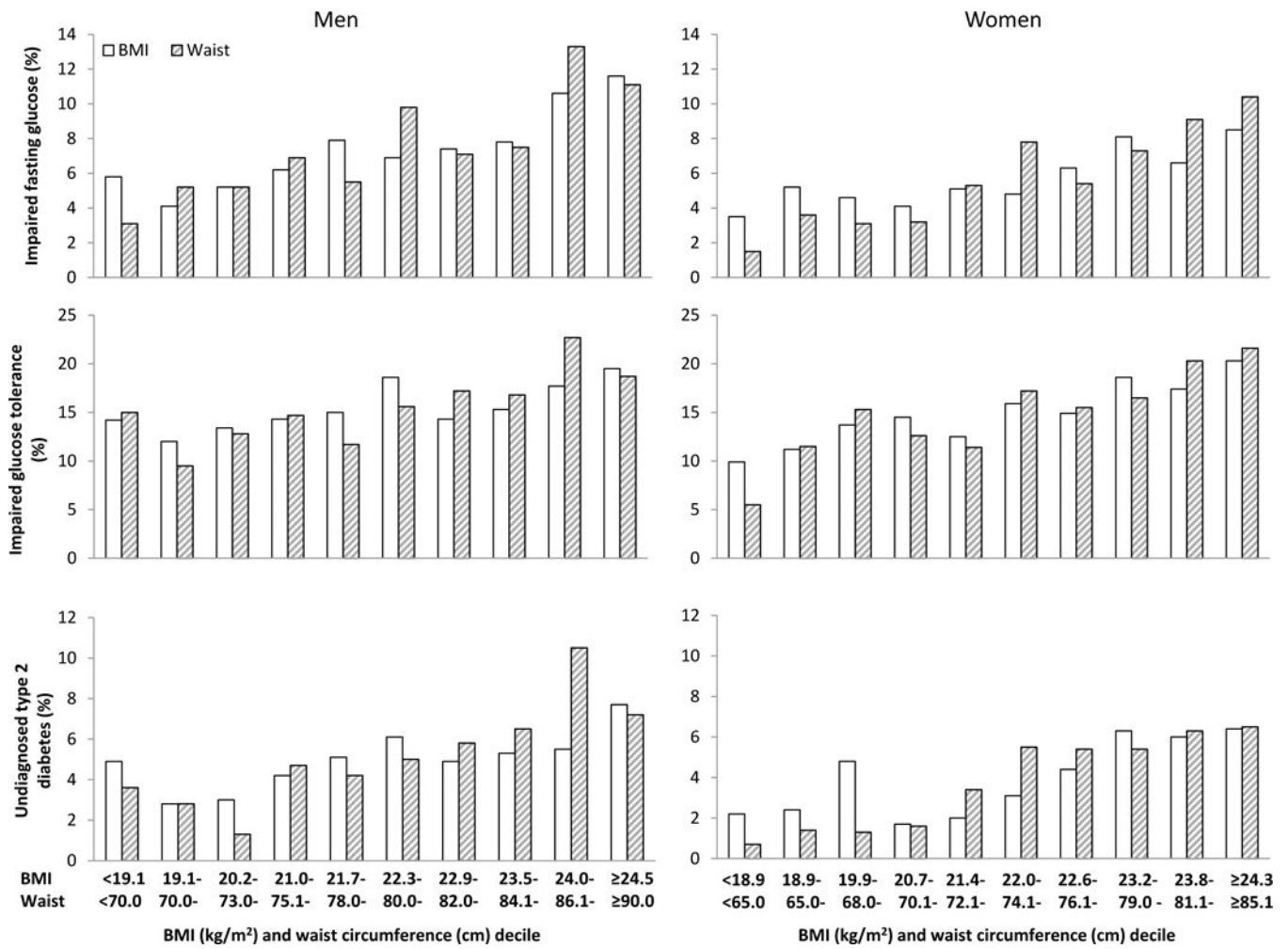


Figure 2. Prevalence of impaired fasting glucose, impaired glucose tolerance, and previously undiagnosed type 2 diabetes by BMI or waist circumference decile and sex. *P* for trend <0.001 in all cases.

Table 1

Characteristics of Study Participants by Sex, China, 2007–2008

Variable	Men (n=10,098)	Women (n=17,454)	p for sex difference
Age (years)	45.1 (45.0, 45.2)	45.0 (44.9, 45.1)	0.08
BMI (kg/m ²)	21.8 (21.7, 21.9)	21.6 (21.5, 21.7)	<0.001
Waist (cm)	78.1 (77.9, 78.4)	74.4 (74.1, 74.6)	<0.0001
Fasting Glucose (mmol/L)	5.0 (5.0, 5.0)	5.0 (4.9, 5.0)	0.13
2 hour Glucose (mmol/L)	6.2 (6.1, 6.3)	6.3 (6.2, 6.4)	0.12
AUC Glucose (mmol/L)	14.5 (14.4, 14.6)	14.1 (14.0, 14.2)	<0.0001
Glucose category (%)			0.004
Normal	81.2 (79.8, 82.4)	82.9 (81.6, 84.1)	
Isolated impaired fasting glucose	2.9 (2.4, 3.5)	2.1 (1.8, 2.4)	
Isolated impaired 2 hour glucose	10.1 (9.0, 11.2)	10.1 (8.9, 11.3)	
Combined impaired glucose	1.0 (0.8, 1.3)	1.2 (0.9, 1.6)	
Previously undiagnosed diabetes	4.9 (4.3, 5.7)	3.8 (3.2, 4.4)	
College or higher level of education (%)	20.9 (19.7, 22.2)	18.3 (17.4, 19.2)	0.001
Regular leisure-time physical activity (%)	32.3 (30.7, 33.9)	32.1 (30.7, 33.6)	0.89
Cigarette smoking (%)	53.5 (51.8, 55.2)	3.5 (3.0, 4.1)	<0.0001
Alcohol drinking (%)	40.4 (38.7, 42.0)	3.7 (3.2, 4.2)	<0.0001
Family history of type 2 diabetes (%)	8.2 (7.3, 9.2)	10.3 (9.3, 11.3)	0.001

Mean (95% CI) or percentage (95% CI) is shown.

AUC: area under the curve

Isolated impaired fasting glucose was defined as fasting glucose level ≥ 6.1 mmol/L (110 mg/dL) and <7.0 mmol/L (126 mg/dL), and 2-hour glucose level in the glucose-tolerance test <7.8 mmol/L (140 mg/dL); isolated impaired glucose tolerance as fasting glucose level <6.1 mmol/L and 2-hour glucose level ≥ 7.8 mmol/L and <11.1 mmol/L (200 mg/dL); combined impaired fasting glucose and impaired glucose tolerance as fasting glucose level ≥ 6.1 mmol/L and <7.0 mmol/L and 2-hour glucose level ≥ 7.8 mmol/L and <11.1 mmol/L; and previously undiagnosed diabetes as fasting glucose level ≥ 7.0 mmol/L, 2-hour glucose level ≥ 11.1 mmol/L, or both.

Table 2

Regression Coefficients of Fasting and 2-Hour Postload Glucose Levels Associated with One Standard Deviation Increase in BMI and Waist Circumference in Chinese Adults with BMI < 25 kg/m² by Sex, 2007–2008

Dependent variable	Regression coefficient							
	Model 1			Model 2				
	BMI (2.1 kg/m ²)	Waist (8.3 cm)		BMI (2.1 kg/m ²)	Waist (8.3 cm)			
Estimate (95% CI)	P	Estimate (95% CI)	P	Estimate (95% CI)	P	Estimate (95% CI)	P	
Fasting glucose (mmol/L)								
Men	0.128 (0.097, 0.159)	<0.0001	0.170 (0.139, 0.202)	<0.0001	0.047 (0.005, 0.089)	0.03	0.139 (0.095, 0.182)	<0.0001
Women	0.112 (0.091, 0.132)	<0.0001	0.167 (0.139, 0.196)	<0.0001	0.043 (0.019, 0.068)	0.0005	0.138 (0.105, 0.171)	<0.0001
2 hour glucose (mmol/L)								
Men	0.121 (0.041, 0.200)	0.003	0.217 (0.132, 0.301)	<0.0001	-0.009 (-0.116, 0.098)	0.87	0.222 (0.109, 0.336)	<0.0001
Women	0.241 (0.182, 0.301)	<0.0001	0.362 (0.296, 0.428)	<0.0001	0.093 (0.022, 0.164)	0.01	0.299 (0.222, 0.377)	<0.0001
AUC glucose (mmol/L)								
Men	0.233 (0.115, 0.351)	0.0001	0.408 (0.286, 0.531)	<0.0001	-0.008 (-0.166, 0.150)	0.92	0.414 (0.250, 0.577)	<0.0001
Women	0.351 (0.262, 0.441)	<0.0001	0.581 (0.484, 0.678)	<0.0001	0.095 (-0.014, 0.205)	0.09	0.517 (0.399, 0.634)	<0.0001

AUC: area under the curve

Model 1 included age, education, leisure-time physical activity, alcohol drinking, family history of type 2 diabetes, and either BMI or waist circumference, but not both; Model 2 included both BMI and waist circumference and other covariates in model 1.

Table 3

Odds Ratios of Impaired Fasting Glucose, Impaired Glucose Tolerance, and Previously Undiagnosed Type 2 Diabetes Associated with One Standard Deviation Increase in BMI and Waist Circumference in Chinese Adults with BMI < 25 kg/m² by Sex, 2007–2008.

Dependent variable	Odds ratio							
	Model 1			Model 2				
	BMI (2.1 kg/m ²) Estimate (95% CI)	P	Waist (8.3 cm) Estimate (95% CI)	P	BMI (2.1 kg/m ²) Estimate (95% CI)	P	Waist (8.3 cm) Estimate (95% CI)	P
Impaired fasting glucose								
Men	1.371 (1.182, 1.590)	<0.0001	1.486 (1.318, 1.675)	<0.0001	1.131 (0.950, 1.345)	0.17	1.399 (1.216, 1.609)	<0.0001
Women	1.352 (1.193, 1.533)	<0.0001	1.517 (1.332, 1.728)	<0.0001	1.129 (0.982, 1.299)	0.09	1.422 (1.233, 1.641)	<0.0001
Impaired glucose tolerance								
Men	1.140 (1.009, 1.287)	0.04	1.191 (1.057, 1.342)	0.004	1.045 (0.923, 1.183)	0.49	1.161 (1.027, 1.313)	0.02
Women	1.275 (1.150, 1.413)	<0.0001	1.328 (1.139, 1.547)	0.0003	1.147 (1.035, 1.271)	0.009	1.224 (1.034, 1.448)	0.02
Diabetes								
Men	1.208 (1.011, 1.443)	0.04	1.361 (1.178, 1.572)	<0.0001	1.017 (0.839, 1.234)	0.86	1.351 (1.156, 1.578)	0.0002
Women	1.405 (1.126, 1.753)	0.003	1.554 (1.331, 1.815)	<0.0001	1.146 (0.900, 1.460)	0.27	1.455 (1.234, 1.714)	<0.0001

Model 1 included age, education, leisure-time physical activity, alcohol drinking, family history of type 2 diabetes, and either BMI or waist circumference; Model 2 included both BMI and waist circumference and other covariates in model 1.