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Association of predicted fat mass, predicted lean mass and predicted percent fat with diabetes mellitus in Chinese population: a 15-year prospective cohort

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ABSTRACT

Objectives With body mass index (BMI) failing to distinguish the mass of fat from lean, several novel predicted equations for predicted fat mass (FM), predicted lean mass (LM) and predicted per cent fat (PF) were recently developed and validated. Our aim was to explore whether the three novel parameters could better predict diabetes mellitus (DM) than the commonly used obesity indicators, including BMI, waist circumference, hip circumference and waist-hip ratio.

Design A 15-year prospective cohort was used.

Setting It was a prospective cohort, consisting of a general Chinese population from 1992 to 2007.

Participants This cohort enrolled 711 people. People suffering from DM at baseline (n=24) were excluded, and 687 non-diabetics with complete data were included to the analysis.

Primary outcome New-onset DM.

Results After the follow-up, 74 (48 men and 26 women) incidences of DM were documented. For men, the adjusted HRs were 1, 5.19 (p=0.003) and 7.67 (p<0.001) across predicted PF tertiles; 1, 2.86 (p=0.029) and 5.60 (p<0.001) across predicted FM tertiles; 1, 1.21 (p=0.646) and 2.27 (p=0.025) across predicted LM tertiles. Predicted FM performed better than other commonly used obesity indicators in discrimination with the highest Harrell's C-statistic among all the body composition parameters. Whereas, for women, none of the three novel parameters was the independent predictor.

Conclusion Predicted PF, predicted LM and predicted FM could independently predict the risk of DM for men, with predicted FM performing better in discrimination than other commonly used obesity indicators. For women, larger samples were further needed.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study explored whether the three novel body composition parameters, including predicted fat mass, predicted lean mass and predicted per cent fat, could predict diabetes mellitus (DM) better than body mass index and other commonly used obesity indicators.
⇒ Cox's regression analysis was used to estimate HRs for DM, and Harrell's C-statistic was used to assess and compare the discriminatory ability of all the parameters in predicting new-onset DM.
⇒ The relatively small sample size might possibly lead to a statistical power decrease.

INTRODUCTION

Diabetes mellitus (DM) is a collection of chronic metabolic conditions, characterised by elevated blood glucose levels resulting from the body's inability to produce insulin or resistance to insulin action or both.[1] There are two primary forms of DM, insulin-dependent DM (type 1 diabetes mellitus, T1DM) and non-insulin-dependent DM (type 2 diabetes mellitus, T2DM). T2DM is the most common form, making up 90%–95% of all patients with diabetes.[1] DM and its complications can result in disability and premature death,[2] as well as enormous economic and social burdens.[3] There is no cure for DM; thus, prevention is the best intervention.

Among the well-known modifiable risk factors, obesity, defined as an excess accumulation of body fat, is regarded as a major risk factor.[4] Body mass index (BMI) has been mostly used as a simple and reasonable measure of general adiposity in clinical and public health settings. However, since it is defined as the result of weight in kilogram divided by height in metre squared, BMI is in poor discrimination of metabolically distinct components such as fat mass (FM) and lean mass (LM).[5] Direct measurement of FM and LM is impractical in large epidemiological studies for sophisticated and expensive technologies such as dual-energy X-ray absorptiometry (DXA) or imaging techniques (ie, MRI and CT).

Recently, Lee *et al* developed anthropometric prediction equations for FM, LM

and per cent fat (PF) from the large population samples of the non-institutionalized civilians in the USA from National Health and Nutrition Examination Survey.[6] In the original study, the validation tests showed robust and consistent results without evident substantial bias, and comparable abilities to predict obesity-related biomarkers with direct DXA measurements. Later, based on two large US prospective cohorts, predicted FM and predicted PF were both estimated to have a stronger association than BMI with T2DM.[7] However, body compositions differ across ethnic groups.[8 9] Healthy Chinese and South Asian individuals were measured to have a greater amount of visceral adipose tissue than Europeans with the same BMI or waist circumference (WC).[10] Therefore, we aimed to evaluate if these equations could better predict the risk of DM in comparison with BMI and other obesity indicators, including WC, hip circumference (HC) and waist-hip ratio (WHR), in a 15-year prospective cohort consisting of Chinese people.

MATERIALS AND METHODS

Study population

In 2007, supported by the Mega-projects of Science Research for China's 11th Five-Year Plan (Trends in the incidence of metabolic syndrome and integrated control in China), a group of 711 people, from an urban community situated in Chengdu, China, underwent a health examination. They also had a health examination in 1992 as part of the Chinese Multi-provincial Cohort Study approved by Beijing Institute of Heart, Lung, and Blood Vessel Disease that investigated cardiovascular risk factors across the country. Therefore, we picked up the data, and more details have been described elsewhere.[11 12] People suffering from DM at baseline (n=24) were excluded. No one had missing data. Finally, the remaining 687 people with complete data were included in the analysis. All of them provided written informed consent. The study was approved by the Ministry of Health of China, as well as the Ethics Committee of West China Hospital of Sichuan University.

Evaluation

Definition

DM was defined by self-reported history or fasting plasma glucose (FPG) ≥7.0 mmol/L.[13] Hypertension was a conventional blood pressure of ≥140 mm Hg systolic, ≥90 mm Hg diastolic or the use of antihypertensive drugs. DM family history was determined with a diagnosis of DM in the first-grade relatives. Smoking was defined as an average cigarette consumption of at least one per day. Frequent previous alcohol intake and present alcohol intake were both defined as alcohol consumption. Activity was defined as at least twice 20 min moderately intensive physical activity per week.

Data collection

Baseline data in 1992 included medical history, physical examination and biochemical tests. Questionnaires containing demographic information and cardiovascular disease risk factors were collected by well-trained investigators. WC was measured at the midpoint between the lower border of the rib cage and the iliac crest at the end of a normal exhalation. HC was measured at the maximum protrusion of the gluteal region. WHR was calculated by WC in centimetre divided by HC in centimetre. Height was measured without shoes. Weight was measured in light clothing. Blood pressure was measured in a sitting position after at least 15 min of rest, and the mean blood pressure of three measurements taken by a standardised mercury sphygmomanometer was used as a participant's blood pressure. Blood samples were drawn from participants in the morning after 12-hour overnight fasting. FPG, total cholesterol (TC) and triglyceride (TG) levels were determined in an enzymatic method, and high-density lipoprotein cholesterol (HDL-C) was measured by the phosphotungstic acid/$MgCl_2$ precipitation method. Low-density lipoprotein cholesterol (LDL-C) was measured using a standard kit.

Equation profiles

Equations for predicted FM (kg)[6]

$$\begin{aligned}\textit{For men}\quad &= -18.592 \times age\,(year) - 0.080 \times height\,(cm) + 0.226 \times weight\,(kg)\\ &\quad + 0.387 \times WC\,(cm) + 0.080 \times Mexican - 0.188 \times Hispanic - 0.483\\ &\quad \times Black + 1.050 \times other\ ethnicity\\ \textit{For women}\quad &= 11.817 + 0.041 \times age\,(year) - 0.199 \times height\,(cm) + 0.610 \times weight\,(kg)\\ &\quad + 0.044 \times WC\,(cm) + 0.388 \times Mexican - 0.073 \times Hispanic - 1.187\\ &\quad \times Black + 0.325 \times other\ ethnicity\end{aligned}$$

Equations for predicted LM (kg)[6]

$$\begin{aligned}\textit{For men}\quad &= 19.363 + 0.001 \times age\,(year) + 0.064 \times height\,(cm) + 0.756 \times weight\,(kg)\\ &\quad - 0.366 \times WC\,(cm) - 0066 \times Mexican + 0.231 \times Hispanic + 0.432\\ &\quad \times Black - 1.007 \times other\ ethnicity\\ \textit{For women}\quad &= -10.683 - 0.039 \times age\,(year) + 0.186 \times height\,(cm) + 0.383 \times weight\,(kg)\\ &\quad - 0.043 \times WC\,(cm) - 0.359 \times Mexican - 0.059 \times Hispanic + 1.085\\ &\quad \times Black - 0.34 \times other\ ethnicity\end{aligned}$$

Equations for predicted PF (%)[6]

$$\begin{aligned}\textit{For men}\quad &= 0.02 + 0.00 \times age\,(year) - 0.07 \times height\,(cm) - 0.08 \times weight\,(kg)\\ &\quad + 0.48 \times WC\,(cm) + 0.32 \times Mexican + 0.02 \times Hispanic - 0.65\\ &\quad \times Black + 1.12 \times other\ ethnicity\\ \textit{For women}\quad &= 50.46 + 0.07 \times age\,(year) - 0.26 \times height\,(cm) + 0.27 \times weight\,(kg)\\ &\quad + 0.10 \times WC\,(cm) + 0.89 \times Mexican + 0.49 \times Hispanic - 1.57\\ &\quad \times Black + 0.43 \times other\ ethnicity\end{aligned}$$

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Statistical analyses

For descriptive results, variables were expressed as the mean±SD, median and IQR, or counts and percentages as appropriate. Smoking, alcohol intake, activity, hypertension and family history of DM were expressed as dummy variables (presence=1, absence=0). Differences

in baseline characteristics between participants with and without new-onset DM were tested by independent t-test for normally distributed variables and by the non-parametric Mann-Whitney U test for skewed variables. Interactions between categorical variables were evaluated with the Pearson's χ^2 test, and Fisher's exact probabilities were used if necessary. Correlations between different variables were determined using Pearson's or Spearman's analysis.

We treated all the parameters as sex-specific tertiles. The cumulative incidences of DM across tertiles were graphically displayed according to the method of Kaplan-Meier, with comparisons among groups by the log-rank test. Cox proportional hazards regression models were used to assess the impact of the variables on the incidence rate of DM. Furthermore, restricted cubic spline analysis was used to visualise the relations between variables and incident DM. To quantify and compare the discriminative ability of different parameters, Harrell's c-index was calculated. A generally accepted approach suggests that the C-index of less than 0.60 reflects poor discrimination; 0.60–0.75, possibly helpful discrimination, and more than 0.75, clearly useful discrimination.[14]

All statistical tests were two sided, and p value <0.05 was considered statistically significant. Statistical analyses were performed using R V.3.6.3.

RESULTS

Baseline characteristics

After excluding people suffering from DM at baseline (n=24), the remaining 687 (399 men and 288 women) people free of DM at baseline with complete data were included in the analysis.

Those who had subsequent DM were associated with higher baseline levels of FPG, weight, BMI, WC, HC, predicted FM, predicted LM and predicted PF for men; associated with higher baseline levels of TC, TG, height, BMI, WC, HC, predicted FM and predicted PF, and lower baseline level of HDL-C for women. At baseline, age was not of significance between the two groups both in men and women, but there was still a trend that people suffering incident DM were older. Other details of baseline information are shown in table 1.

As shown in online supplemental table S1, predicted FM was strongly correlated with WC (r_s=0.98), followed

Table 1 Basic characteristics of people with or without subsequent DM

	Men (N=399)			Women (N=288)		
Variables	Subsequent DM (n=48)	Subsequent non-DM (n=351)	P value	Subsequent DM (n=26)	Subsequent non-DM (n=262)	P value
Age (years)	50.6±5.0	49.0 (45.0–53.0)	0.079	48.4±6.8	46.0 (42.0–52.0)	0.127
Smoking (%)	32 (66.7)	213 (60.7)	0.425	0	2 (0.8)	1.000
Hypertension (%)	9 (18.8)	50 (14.2)	0.410	7 (26.9)	38 (14.5)	0.150
DM family history (%)	3 (6.3)	9 (2.6)	0.165	3 (11.5)	18 (6.9)	0.418
SBP (mm Hg)	118.1±14.5	110.0 (105.0–120.0)	0.061	119.0 (103.0–132.5)	110.0 (102.0–120.0)	0.240
DBP (mm Hg)	74.0 (70.0–80.0)	72.0 (70.0–80.0)	0.292	76.4±12.1	70.0 (71.0–80.0)	0.226
FPG (mmol/L)	4.6±0.8	4.0 (3.8–4.7)	<0.001	4.6±0.9	3.8 (4.0–4.7)	0.052
TC (mmol/l)	4.4 (4.1–4.8)	4.3 (3.9–4.8)	0.419	5.0±0.7	4.4 (3.9–5.0)	0.006
TG (mmol/L)	1.9 (1.7–3.0)	1.9 (1.5–2.4)	0.104	1.9 (1.5–2.3)	1.8 (1.4–2.2)	<0.001
HDL-C (mmol/L)	1.2 (1.0–1.4)	1.2 (1.1–1.4)	0.193	1.2±0.2	1.3 (1.1–1.5)	0.009
LDL-C (mmol/L)	2.2±0.8	2.1 (1.7–2.7)	0.556	2.4±1.0	2.3 (1.8–2.8)	0.460
Height (cm)	165.4±5.9	165.3±5.6	0.898	151.9±4.4	151.0 (155.0–159.0)	0.006
Weight (cm)	68.5 (61.3–74.8)	62.9±8.2	<0.001	58.6±9.0	56.4±7.5	0.168
BMI (kg/m^2)	24.8 (23.0–26.6)	23.0 (20.9–24.8)	<0.001	25.3±3.3	23.4±2.6	0.001
WC (cm)	83.6±8.2	78.0 (72.0–83.0)	<0.001	79.9±7.6	73.5±7.1	<0.001
HC (cm)	95.0 (90.0–97.0)	91.0 (87.0–95.0)	<0.001	95.4±7.4	92.6±5.8	0.021
WHR	0.89±0.05	0.85±0.06	0.001	0.84±0.04	0.79±0.05	<0.001
FM (kg)	16.4±5.2	13.3 (9.6–16.2)	<0.001	21.8±5.4	19.6±4.3	0.014
LM (kg)	50.2±5.0	48.1±4.5	0.004	34.3±3.5	34.4±3.4	0.894
PF (%)	24.0±3.4	21.8±3.1	<0.001	38.6±2.9	36.4±2.4	<0.001

BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; FM, fat mass; FPG, fasting plasma glucose; HC, hip circumference; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LM, lean mass; PF, per cent fat; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WHR, waist-hip ratio.

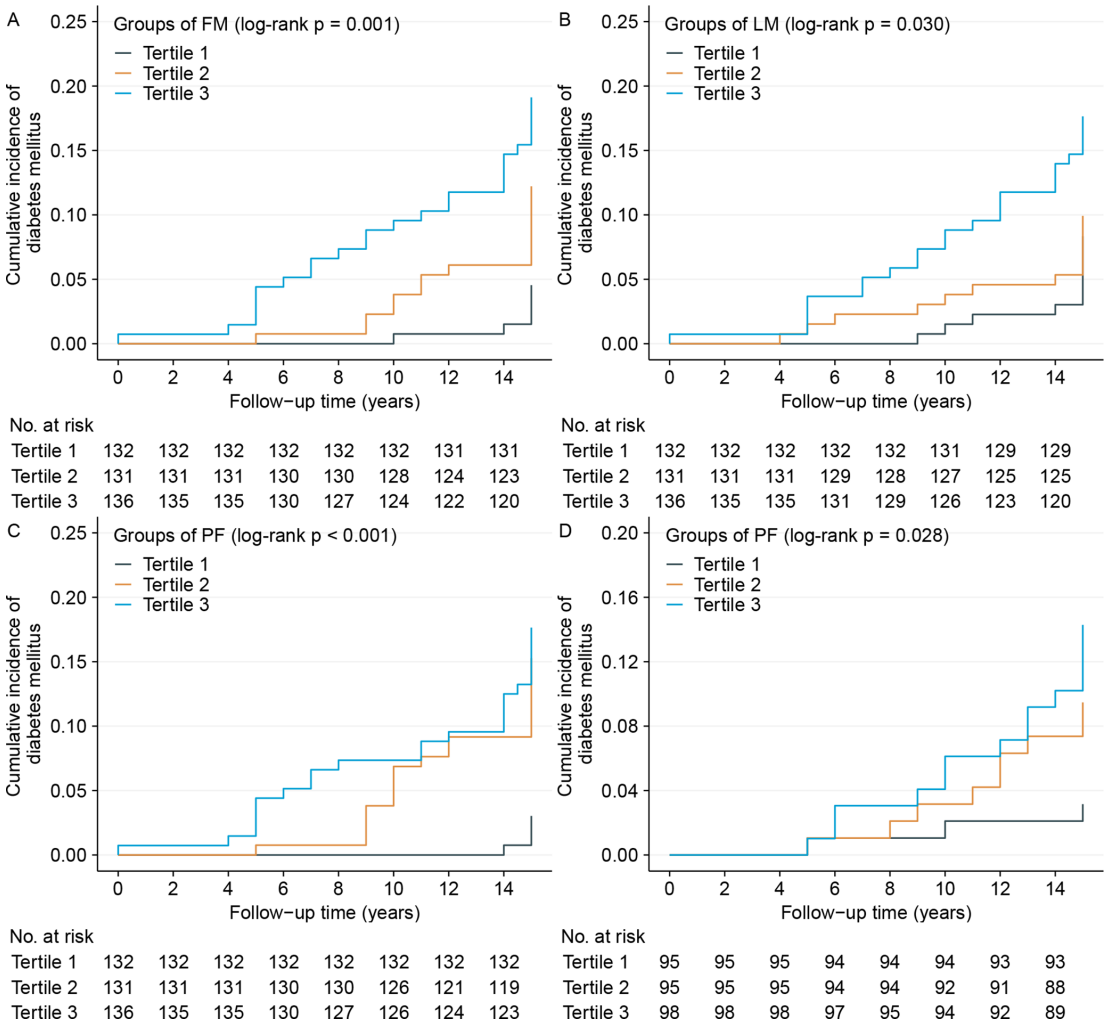

Figure 1 Cumulative incidence of DM across tertiles of novel predicted body composition during follow-up. Survival curves were presented as Kaplan-Meier curves, and the log-rank tests were used for comparison among tertiles. For men (n=399), the cumulative incidences of DM evaluated by Kaplan-Meier analysis were significantly different across the tertiles of predicted FM (A, log-rank p=0.001), predicted LM (B, log-rank p=0.030) and predicted PF (C, log-rank p<0.001). For women (n=288), the cumulative incidence of DM evaluated by Kaplan-Meier analysis was just significantly different across the tertiles of predicted PF (D, log-rank p=0.028). People in the top tertile had the highest cumulative incidence of DM. DM, diabetes mellitus; FM, fat mass; LM, lean mass; PF, per cent fat.

by BMI (r_s=0.88) and HC (r_s=0.82) in men; strongly correlated with BMI (r_s=0.94), followed by HC (r_s=0.87) and WC (r_s=0.83) in women. Predicted LM had a strong correlation with predicted FM (r_s=0.83) in women and a relatively strong correlation with HC (r_s=0.71) in men, but relatively weakly with WHR both in men (r_s=0.15) and women (r_s=0.29). Predicted PF was strongly correlated with WC (r_s=0.97) in men and BMI (r_s=0.95) in women, but relatively weakly with predicted LM both in men (r_s=0.35) and women (r_s=0.51).

Survival analysis

All the body composition parameters were divided into tertiles. Tertile 1 had the lowest estimated values, while tertile 3 had the highest. The category boundaries of all the parameters were displayed by gender in online supplemental table S2. After the follow-up of 15 years, 74 (48 men and 26 women) incidences of DM were documented (incidence rate: 0.74 per 100 person-years; 95% CI: 0.57 to 0.91). As figure 1A–C present, for men, the cumulative incidences of DM evaluated by Kaplan-Meier analysis were significantly different across the tertiles of predicted FM (log-rank p=0.001), predicted LM (log-rank p=0.030) and predicted PF (log-rank p<0.001), and people in tertile 3 had the highest cumulative incidence of DM. For women, however, only predicted PF (log-rank p=0.028) could help to distinguish the cumulative incidence across the tertiles (figure 1D).

For other obesity indicators, the cumulative incidences of DM evaluated by Kaplan-Meier analysis were significantly different across the tertiles of BMI (log-rank p<0.001), WC (log-rank p=0.001), HC (log-rank p=0.006) and WHR (log-rank p=0.001) in men; WC (log-rank p=0.002) and WHR (log-rank p<0.001) in women.

Relation to risk of DM

Univariable Cox regression analysis is shown in online supplemental table S3. Predicted FM, predicted PF, BMI, WC, HC and WHR were risk factors of DM both for men and women, and predicted LM was a risk factor for men only. Variables showing statistical significance in univariable analysis or clinical relevance (p<0.1) were entered into multivariable analysis.

In multivariable analysis, we adjusted potential confounders including hypertension (yes/no), DM family history (yes/no), smoking (yes/no), alcohol (yes/no), activity (yes/no), TG, TC, HDL-C, LDL-C and FPG in men; hypertension (yes/no), DM family history (yes/no), smoking (yes/no), alcohol (yes/no), activity (yes/no), SBP, TG, TC, HDL-C and FPG in women.

As table 2 shows, in men, predicted FM (p<0.001), predicted LM (p=0.043) and predicted PF (p<0.001) were all the significantly independent predictors with the top tertiles associated with the highest risk of DM. Compared with the other parameters we studied, predicted PF in higher level was more strongly associated with increased risk of DM, since it showed a positive association with the risk of DM with the adjusted HR for tertile 2 and tertile 3 estimated as 5.19 (95% CI: 1.77 to 15.20, p=0.003) and 7.67 (95% CI: 2.64 to 22.35, p<0.001), respectively. There was a positive association between predicted FM and the risk of DM (HR: 2.86, 95% CI: 1.12 to 7.33, p=0.029 for tertile 2; HR: 5.60, 95% CI: 2.27 to 13.80, p<0.001 for tertile 3, respectively) as well. Other commonly used parameters such as BMI (p<0.001), WC (p<0.001), HC (p=0.004) and WHR (p<0.001) were also significant predictors (online supplemental table S4), and WC and WHR showed a positive association across tertiles.

As for the women, however, none of the three novel parameters was significantly independent after adjustment (table 2), as well as other commonly used obesity indicators but WHR, which (p<0.001) remained stable and significant (online supplemental table S4).

Furthermore, as table 2 shows, we treated the predicted FM, predicted LM and predicted PF as continuous variables. In men, all of them were independent risk factors and it is true of the restricted cubic splines used to flexibly model and visualise the relations with risk of DM (online supplemental figure S1). With the medians as reference points, all the three novel parameters showed an overall positive association with DM in men (figure 1); while in women, only predicted PF was independently associated with DM (table 2; HR: 1.34 per 1-SD increase, 95% CI: 1.15 to 1.57, p<0.001), and the restricted cubic spline shows the similar relationship, especially after the median (online supplemental figure 2).

Discrimination

Table 3 shows discriminative abilities evaluated by Harrell's c-index of different body composition parameters. In the male group, predicted FM had the highest Harrell's c-index of 0.679 (95% CI: 0.606 to 0.752), and predicted LM had the lowest Harrell's c-index of 0.619

Table 2 Multivariable Cox regression models for DM

		Multivariable hazards regression*	
	Case (%)	HR (95% CI)	P value
For men			
FM			
Per 1-SD increase		1.18 (1.11 to 1.25)	<0.001
T1 (reference)	6 (4.54)	1	–
T2	16 (12.21)	2.86 (1.12 to 7.33)	0.029
T3	26 (19.12)	5.60 (2.27 to 13.80)	<0.001
P value for trend			<0.001
LM			
Per 1-SD increase		1.10 (1.03 to 1.17)	0.003
T1 (reference)	11 (8.33)	1	–
T2	13 (9.92)	1.21 (0.54 to 2.70)	0.646
T3	24 (17.65)	2.27 (1.11 to 4.63)	0.025
P value for trend			0.043
PF			
Per 1-SD increase		1.25 (1.14 to 1.36)	<0.001
T1 (reference)	4 (3.03)	1	–
T2	20 (15.27)	5.19 (1.77 to 15.20)	0.003
T3	24 (17.65)	7.67 (2.64 to 22.35)	<0.001
P value for trend			<0.001
Women			
FM			
Per 1-SD increase		1.04 (0.95 to 1.15)	0.375
T1 (reference)	5 (5.26)	1	–
T2	9 (9.47)	1.38 (0.45 to 4.23)	0.571
T3	12 (12.24)	1.08 (0.35 to 3.37)	0.900
P value for trend			0.811
LM			
Per 1-SD increase		0.92 (0.81 to 1.05)	0.205
T1 (reference)	6 (6.28)	1	–
T2	13 (13.54)	1.33 (0.49 to 3.61)	0.576
T3	7 (7.14)	0.62 (0.19 to 2. 05)	0.432
P value for trend			0.332

Continued

Table 2 Continued

	Case (%)	Multivariable hazards regression* HR (95% CI)	P value
PF			
Per 1-SD increase		1.34 (1.15 to 1.57)	<0.001
T1 (reference)	3 (3.16)	1	–
T2	9 (9.47)	1.95 (0.49 to 7.66)	0.341
T3	14 (14.29)	2.39 (0.63 to 9.10)	0.202
P value for trend			0.442

*Adjusted for hypertension (yes/no), DM family history (yes/no), smoking (yes/no), alcohol (yes/no), activity (yes/no), TG, TC, HDL-C, LDL-C and FPG in men; DM family history (yes/no), smoking (yes/no), alcohol (yes/no), activity (yes/no), SBP, TG, TC, HDL-C and FPG in women.
DM, diabetes mellitus; FM, fat mass; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholestero; LDL-C, low-density lipoprotein cholesterol; LM, lean mass; PF, per cent fat; SBP, systolic blood pressure; T, tertile; TC, total cholesterol; TG, triglyceride.

(95% CI: 0.537 to 0.701). All of the parameters we studied could provide possibly helpful discriminative information in the prediction of DM.[14]

In the female group, since WHR was the only significantly independent risk factor of DM both as continuous variable and categorical variable, we just estimated Harrell's c-index of WHR (0.768, 95% CI: 0.697 to 0.839), and it showed a clearly useful discriminative ability in predicting DM.[14]

DISCUSSION

In this study, we investigated the predictive abilities for the risk of DM of three novel body composition parameters including predicted FM, predicted LM and predicted PF, and compared them with other obesity indicators, in a Chinese prospective population during 15 years of follow-up. For men, our results showed predicted FM, predicted LM and predicted PF could independently predict the new onset of DM; in all the parameters we studied, predicted FM had the best discriminative ability, providing possibly helpful information in the prediction of DM. For women, none of the three novel parameters could be significantly independent in multivariable analysis; of all the parameters we estimated, WHR was the only independent predictor, with Harrell's c-index of 0.768, which suggested a clearly useful discrimination.

To our knowledge, this was the first study in a Chinese prospective cohort to evaluate the associations of three novel body composition parameters with the incidence of DM. BMI has been preferred as a measure indicating overall obesity for a long time to identify people at increased risk of DM.[15] However, BMI was not thought as a good indicator of obesity recently.[5 16] It fails to distinguish the mass of fat from lean and had no gender distinction as well. For example, in common sense, athletes or someone liking exercise always had heavier weight for the mass of lean, they have greater BMI but they are not obese. Besides, ageing is associated with an accumulation of visceral fat and a progressive loss of muscle mass.[16] With the same BMI, an old man has more mass of fat with less mass of muscle than a younger man.

Recently, Lee *et al*[6] developed equations predicting FM, LM and PF to better reflect body composition. The predicted equations had a simple calculation and just require the information of gender, age, height, weight, WC and ethnicity, which are easily measurable and accessible in clinical settings or even at home. Lee *et al* later investigated the association between predicted FM and risk of DM in two large prospective cohorts of US men and women.[7] They found predicted FM, as well as predicted PF, had a stronger association with DM than BMI both in men and women. Similarly, in our study consisting of Chinese population, in the male group, both predicted FM

Table 3 Discriminative abilities evaluated by Harrell's c-index of different body composition parameters

	Men		Women	
Variables	Harrell's c-index	95% CI	Harrell's c-index	95% CI
FM	0.679	0.606 to 0.752	–	–
LM	0.619	0.537 to 0.701	–	–
PF	0.670	0.598 to 0.742	–	–
BMI	0.675	0.599 to 0.751	–	–
WC	0.673	0.600 to 0.746	–	–
WHR	0.652	0.578 to 0.726	0.768	0.697 to 0.839
HC	0.636	0.560 to 0.712	–	–

BMI, body mass index; FM, fat mass; HC, hip circumference; LM, lean mass; PF, per cent fat; WC, waist circumference; WHR, waist-hip ratio.

and predicted PF could independently predict incident DM and predicted FM had the highest Harrell's value. Higher predicted PF was more strongly associated with increased risk of DM than other parameters.

Besides in prediction of DM, predicted FM and predicted PF were also explored in association with risk of heart failure and myocardial infarction in adults with T2DM.[17] The results showed a decline in predicted FM but not predicted LM, over 1 year was significantly associated with lower risk of overall heart failure (adjusted HR per 10% decrease in predicted FM: 0.80; 95% CI: 0.68 to 0.95); decline in predicted FM was significantly associated with lower risk of both heart failure subtypes (with preserved or reduced ejection fraction).

In a post hoc analysis of data from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study,[18] researchers modified the two parameters, FM index and lean BMI, calculated by predicted FM and predicted LM, respectively, in kilograms divided by the square of height in metres. They found that in patients with T2DM, FM index had a strong positive association with a higher risk of a major adverse cardiovascular event, while predicted lean BMI was not associated with major cardiovascular events (p=0.34).

In a large prospective US cohort study of men,[19] there was a strong positive association between predicted FM and mortality from all causes, cardiovascular disease and cancer. Compared with those in the lowest fifth of predicted FM, men in the highest fifth had an HR of 1.35 (95% CI: 1.26 to 1.46) for all-cause mortality. In contrast, predicted LM showed a U-shaped association with all-cause mortality that men in the second to fourth-fifths had 8%–10% lower risk. The U-shaped associations were also found with deaths from cardiovascular disease and cancer. However, there was a strong inverse association between predicted LM and mortality from respiratory disease.

Lean body mass accounts for most of the human body mass, and it is essential not only in the stress response but also in metabolism.[20] Muscle loss may have negative effects.[20–22] Son *et al* previously conducted a 2-yearly prospective assessment in middle-aged and older Korean adults, and reported that low muscle mass was associated with an increased risk of T2DM, independent of general obesity.[23] In contrast, in our research, for the development of DM, the protective role of predicted LM could not be concluded. Instead, the top tertile of predicted LM had an increased risk in the male group. Since there is a lack of randomised clinical trial studies that directly assess the role of increased muscle mass in the prevention of new onset DM,[24] the association between predicted LM and risk of DM needs further explorations. After all, increased LM was not always simply reported as the protective factor of diseases or mortality.[17–19]

There are certainly some limitations in our study. First, 687 was a relatively small sample size, possibly leading to a statistical power decrease, for example, the results in women. Nevertheless, we still observed that as a continuous variable, predicted PF could independently predict the risk of incident DM in women. Maybe in a larger population, the relationships and comparisons would be more accurate. Second, due to the absence of oral glucose tolerance tests and haemoglobin A1c data in our study, some people might not be adequately diagnosed. Third, only one follow-up examination was carried out, so that there was no guarantee whether some 'interval censoring' might have occurred.

In conclusion, in the general Chinese population, predicted FM, predicted LM and predicted PF could independently predict the risk of DM in men, and predicted FM performed better in discrimination than other commonly used obesity indicators including BMI, WC, HC and WHR. For women, however, predicted FM, predicted LM, predicted PF, as well as other obesity indicators, but WHR, could not remain stable and independent in multivariable analysis, which might be attributed to the relatively small sample size with the corresponding few endpoints. Therefore, the conclusion of these findings should be extrapolated with caution, and larger samples from different races are needed to explore the predictive abilities of the three novel equations reflecting body composition on incident DM and other diseases.

Correction notice This article has been corrected since published online. The affiliations of last three authors are corrected along with the equal contribution statement.

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Contributors LL and SJ: Participated in the conception and design of the study, performed data collection and statistical analysis and wrote the draft of the manuscript. CB: Participated in the conception and design of the study, performed statistical analysis and wrote the revision version. SH and XC: Guarantors and participated in the design of the study, performed the statistical analysis and revised subsequent drafts. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Obtained.

Ethics approval This study involves human participants and was approved by Ministry of Health of China and the Ethics Committee of West China Hospital of Sichuan University. We inquired the source of the original data, and the literature (Chin J Cardiol 1999;27:5–8) did not give the reference number of the ethical units. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Table S1 Spearman correlations among different predicted body composition parameters

	WC	HC	WHR	BMI	FM	LM	PF
Men							
WC	1.00	0.77	0.80	0.79	0.98	0.52	0.97
HC		1.00	0.28	0.76	0.82	0.71	0.69
WHR			1.00	0.51	0.72	0.15	0.84
BMI				1.00	0.88	0.69	0.75
FM					1.00	0.66	0.92
LM						1.00	0.35
PF							1.00
Women							
WC	1.00	0.83	0.74	0.76	0.83	0.62	0.84
HC		1.00	0.28	0.79	0.87	0.74	0.78
WHR			1.00	0.39	0.42	0.29	0.53
BMI				1.00	0.94	0.63	0.95
FM					1.00	0.83	0.89
LM						1.00	0.51
PF							1.00

BMI, body mass index; FM, fat mass; HC, hip circumference; LM, lean mass; PF: percent fat; WC, waist circumference; WHR, waist-hip ratio

All correlations were significant with $p < 0.05$.

Table S2 Category boundaries of all the body composition parameters

	Men (n = 399)			Women (n = 288)		
	Tertile 1 (n = 132)	Tertile 2 (n = 131)	Tertile 3 (n = 136)	Tertile 1 (n = 95)	Tertile 2 (n = 95)	Tertile 3 (n = 98)
FM (kg)	< 11.088	11.088 - 15.650	> 15.650	< 17.478	17.478 - 21.573	> 21.573
LM (kg)	< 46.377	46.377 - 50.377	> 50.377	< 32.867	32.867 - 35.735	> 35.735
PF (%)	< 20.622	20.622 - 23.304	> 23.304	< 35.402	35.402 - 37.630	> 37.630
BMI (kg/m^2)	< 21.800	21.800 - 24.500	> 24.500	<22.200	22.200 - 24.700	> 24.700
WC (cm)	< 75.000	75.000 - 82.000	> 82.000	< 71.000	71.000 -76.000	> 76.000
HC (cm)	< 90.000	90.000 - 94.000	> 94.000	< 90.000	90.000 - 95.000	> 95.000
WHR	< 0.841	0.841 - 0.879	> 0.879	< 0.773	0.773 - 0.814	> 0.814

BMI, body mass index; FM, fat mass; HC, hip circumference; LM, lean mass; PF: percent fat; WC, waist circumference; WHR, waist-hip ratio

Table S3 Univariable Cox regression analysis for DM

Variable	Change	HR	95% CI	p
Men				
Age (years)	1-SD increment	1.05	0.996-1.10	0.072
Smoking (%)	Yes vs no	0.79	0.44-1.45	0.448
Hypertension (%)	Yes vs no	1.36	0.66-2.81	0.406
DM family history (%)	Yes vs no	0.44	0.14-1.40	0.163
SBP (mm Hg)	1-SD increment	1.02	0.998-1.036	0.076
DBP (mm Hg)	1-SD increment	1.02	0.998-1.052	0.234
FPG (mmol/L)	1-SD increment	1.78	1.26-2.52	0.001
TC (mmol/l)	1-SD increment	1.15	0.79-1.66	0.476
TG (mmol/L)	1-SD increment	1.16	0.91-1.47	0.248
HDL-C (mmol/L)	1-SD increment	0.57	1.16-2.00	0.376
LDL-C (mmol/L)	1-SD increment	1.04	0.73-1.48	0.818
Height (cm)	1-SD increment	1.01	0.96-1.06	0.834
Weight (cm)	1-SD increment	1.07	1.04-1.11	< 0.001
BMI (kg/m^2)	1-SD increment	1.23	1.13-1.33	< 0.001
WC (cm)	1-SD increment	1.09	1.05-1.13	< 0.001
HC (cm)	1-SD increment	1.09	1.05-1.14	< 0.001
WHR	0.01-SD increment	1.09	1.04-1.15	< 0.001
FM (kg)	1-SD increment	1.16	1.09-1.22	< 0.001
LM (kg)	1-SD increment	1.10	1.04-1.17	0.002
PF (%)	1-SD increment	1.23	1.13-1.34	< 0.001
Women				
Age (years)	1-SD increment	1.04	0.98-1.11	0.161
Smoking (%)	Yes vs no	20.306	--	0.771

Hypertension (%)	Yes vs no	2.00	0.84-4.76	0.116
DM family history (%)	Yes vs no	0.57	0.17-1.88	0.353
SBP (mm Hg)	1-SD increment	1.02	0.999-1.04	0.062
DBP (mm Hg)	1-SD increment	1.03	0.99-1.07	0.111
FPG (mmol/L)	1-SD increment	1.86	1.14-3.03	0.013
TC (mmol/l)	1-SD increment	1.67	1.12-2.50	0.012
TG (mmol/L)	1-SD increment	1.46	1.26-1.69	< 0.001
HDL-C (mmol/L)	1-SD increment	0.081	0.01-0.54	0.009
LDL-C (mmol/L)	1-SD increment	1.05	0.67-1.65	0.824
Height (cm)	1-SD increment	0.91	0.84-0.98	0.009
Weight (cm)	1-SD increment	1.04	0.986-1.09	0.156
BMI (kg/m^2)	1-SD increment	1.27	1.10-1.46	0.001
WC (cm)	1-SD increment	1.11	1.06-1.17	< 0.001
HC (cm)	1-SD increment	1.08	1.01-1.16	0.019
WHR	0.01-SD increment	1.17	1.09-1.25	< 0.001
FM (kg)	1-SD increment	1.11	1.02-1.21	0.013
LM (kg)	1-SD increment	0.99	0.89-1.12	0.912
PF (%)	1-SD increment	1.38	1.19-1.60	< 0.001

BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; FPG, fasting plasma glucose; FM, fat mass; HC, hip circumference; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LM, lean mass; SBP, systolic blood pressure; PF, percent fat; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WHR, waist-hip ratio.

Table S4 Multivariable Cox regression models of commonly used obesity indicators for DM

	Case (%)	Multivariable hazards regression *	
		HR (95% CI)	p
For men			
BMI			
per 1-SD increase		1.27 (1.16-1.380	< 0.001
T1 (reference)	9 (6.87%)	1	-
T2	10 (7.75%)	1.09 (0.44-2.69)	0.856
T3	29 (20.86%)	3.90 (1.81-8.37)	< 0.001
p for trend			< 0.001
WC			
per 1-SD increase		1.10 (1.07-1.14)	< 0.001
T1 (reference)	5 (4.03%)	1	-
T2	17 (12.78%)	3.24 (1.19-8.78)	0.021
T3	26 (18.31%)	5.97 (2.27-15.71)	< 0.001
p for trend			< 0.001
HC			
per 1-SD increase		1.11 (1.06-1.16)	< 0.001
T1 (reference)	9 (7.03%)	1	-
T2	11 (9.40%)	1.19 (0.49-2.88)	0.701
T3	28 (18.18%)	2.87 (1.35-6.08)	0.006
p for trend			0.004
WHR			
per 0.01-SD increase		1.09 (1.04-1.15)	< 0.001
T1 (reference)	5 (3.82%)	1	-

T2	18 (13.85%)	3.65 (1.35-9.83)	0.011
T3	25 (18.12%)	5.42 (2.07-14.18)	0.001
p for trend			< 0.001
Women			
BMI			
per 1-SD increase		1.23 (1.07-1.42)	0.005
T1 (reference)	4 (4.40%)	1	-
T2	8 (8.33%)	1.50 (0.44-5.07)	0.515
T3	14 (13.86%)	1.64 (0.50-5.36)	0.413
p for trend			0.712
WC			
per 1-SD increase		1.10 (1.04-1.16)	0.001
T1 (reference)	4 (4.26%)	1	-
T2	4 (4.60%)	0.77 (0.18-3.18)	0.712
T3	18 (16.82%)	2.54 (0.83-7.78)	0.104
p for trend			0.051
HC			
per 1-SD increase		1.06 (0.99-1.14)	0.114
T1 (reference)	4 (5.06%)	1	-
T2	8 (8.33%)	1.26 (0.37-4.33)	0.718
T3	14 (12.39%)	1.52 (0.47-4.92)	0.481
p for trend			0.768
WHR			
per 0.01-SD increase		1.16 (1.07-1.25)	< 0.001
T1 (reference)	1 (1.06%)	1	-
T2	5 (5.21%)	4.54 (0.53-38.91)	0.168

T3	20 (20.41%)	15.91 (2.10-120.52)	0.007
p for trend			< 0.001

*, adjusted for hypertension (yes/no), DM family history (yes/no), smoking (yes/no), alcohol (yes/no), activity (yes/no), TG, TC, HDL-C, LDL-C, and FPG in men; DM family history (yes/no), smoking (yes/no), alcohol (yes/no), activity (yes/no), SBP, TG, TC, HDL-C, and FPG in women

BMI, body mass index; DM, diabetes mellitus; FPG, fasting plasma glucose; HC, hip circumference; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SD, standard deviation; T, tertile; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WHR, waist-hip ratio

Figure S1 Associations of three novel predicted body composition with risk of DM for men

Restricted cubic splines were used to flexibly models and visualize the relations of different parameters with risk of DM. Hazard ratios are indicated by solid lines and 95% CIs by shaded areas. Reference points were the medians for FM (A; 13.61 kg), LM (B; 48.27 kg), and PF (C; 22.04%), respectively. The dotted line represents HR = 1. Confounders in Table 2 were adjusted.

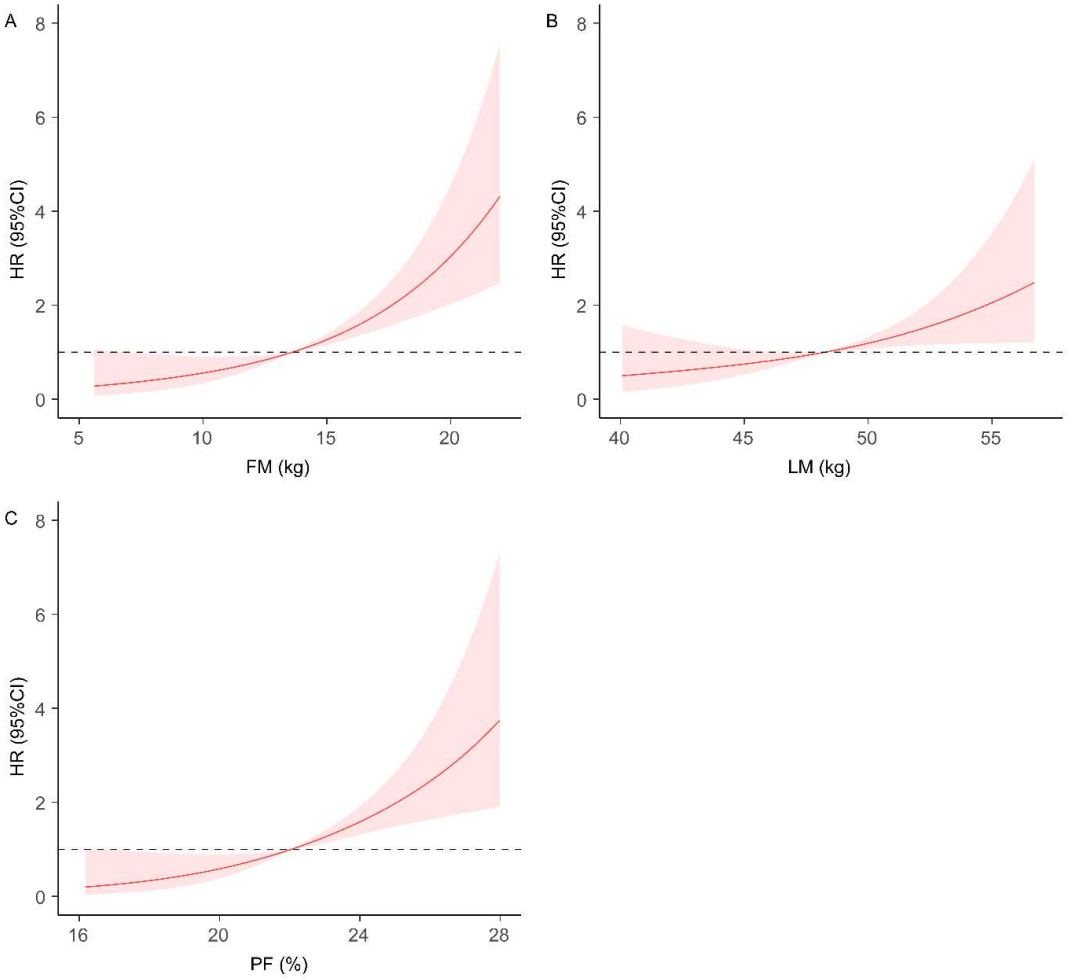
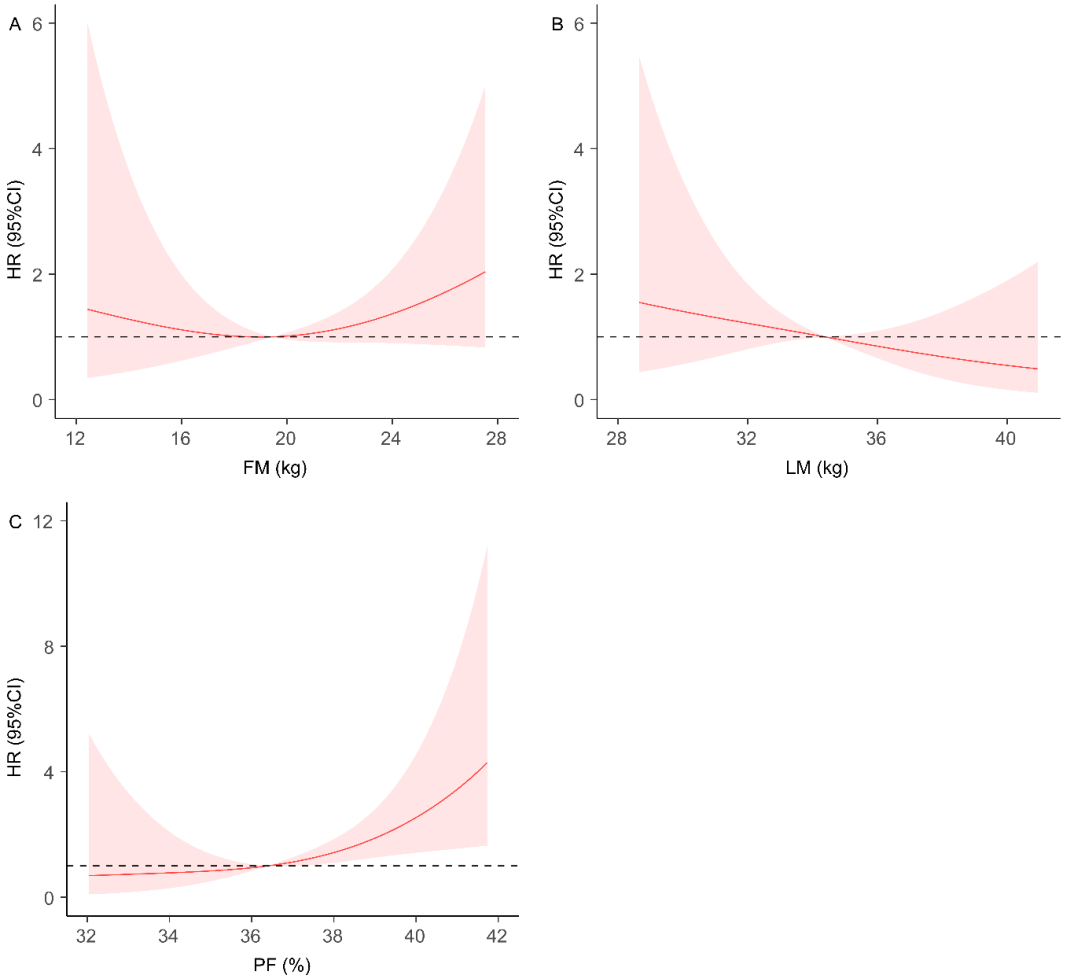


Figure S2 Associations of three novel predicted body composition with risk of DM for women

Restricted cubic splines were used to flexibly models and visualize the relations of different parameters with risk of DM. Hazard ratios are indicated by solid lines and 95% CIs by shaded areas. Reference points were the medians for FM (A; 19.45 kg), LM (B; 34.38 kg), and PF (C; 36.39%), respectively. The dotted line represents HR = 1. Confounders in Table 2 were adjusted.



Supplemental Materials

Table S1 Spearman correlations among different predicted body composition parameters

	WC	HC	WHR	BMI	FM	LM	PF
Men							
WC	1.00	0.77	0.80	0.79	0.98	0.52	0.97
HC		1.00	0.28	0.76	0.82	0.71	0.69
WHR			1.00	0.51	0.72	0.15	0.84
BMI				1.00	0.88	0.69	0.75
FM					1.00	0.66	0.92
LM						1.00	0.35
PF							1.00
Women							
WC	1.00	0.83	0.74	0.76	0.83	0.62	0.84
HC		1.00	0.28	0.79	0.87	0.74	0.78
WHR			1.00	0.39	0.42	0.29	0.53
BMI				1.00	0.94	0.63	0.95
FM					1.00	0.83	0.89
LM						1.00	0.51
PF							1.00

BMI, body mass index; FM, fat mass; HC, hip circumference; LM, lean mass; PF: percent fat; WC, waist circumference; WHR, waist-hip ratio

All correlations were significant with $p < 0.05$.

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PF (%)	< 20.622	20.622 - 23.304	> 23.304	< 35.402	35.402 - 37.630	> 37.630
BMI (kg/m^2)	< 21.800	21.800 - 24.500	> 24.500	<22.200	22.200 - 24.700	> 24.700
WC (cm)	< 75.000	75.000 - 82.000	> 82.000	< 71.000	71.000 -76.000	> 76.000
HC (cm)	< 90.000	90.000 - 94.000	> 94.000	< 90.000	90.000 - 95.000	> 95.000
WHR	< 0.841	0.841 - 0.879	> 0.879	< 0.773	0.773 - 0.814	> 0.814

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HC (cm)	1-SD increment	1.09	1.05-1.14	< 0.001
WHR	0.01-SD increment	1.09	1.04-1.15	< 0.001
FM (kg)	1-SD increment	1.16	1.09-1.22	< 0.001
LM (kg)	1-SD increment	1.10	1.04-1.17	0.002
PF (%)	1-SD increment	1.23	1.13-1.34	< 0.001
Women				
Age (years)	1-SD increment	1.04	0.98-1.11	0.161
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DM family history (%)	Yes vs no	0.57	0.17-1.88	0.353
SBP (mm Hg)	1-SD increment	1.02	0.999-1.04	0.062
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FPG (mmol/L)	1-SD increment	1.86	1.14-3.03	0.013
TC (mmol/l)	1-SD increment	1.67	1.12-2.50	0.012
TG (mmol/L)	1-SD increment	1.46	1.26-1.69	< 0.001
HDL-C (mmol/L)	1-SD increment	0.081	0.01-0.54	0.009
LDL-C (mmol/L)	1-SD increment	1.05	0.67-1.65	0.824
Height (cm)	1-SD increment	0.91	0.84-0.98	0.009
Weight (cm)	1-SD increment	1.04	0.986-1.09	0.156
BMI (kg/m^2)	1-SD increment	1.27	1.10-1.46	0.001
WC (cm)	1-SD increment	1.11	1.06-1.17	< 0.001
HC (cm)	1-SD increment	1.08	1.01-1.16	0.019
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FM (kg)	1-SD increment	1.11	1.02-1.21	0.013
LM (kg)	1-SD increment	0.99	0.89-1.12	0.912
PF (%)	1-SD increment	1.38	1.19-1.60	< 0.001

BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; FPG, fasting plasma glucose; FM, fat mass; HC, hip circumference; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LM, lean mass; SBP, systolic blood pressure; PF, percent fat; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WHR, waist-hip ratio.

Table S4 Multivariable Cox regression models of commonly used obesity indicators for DM

	Case (%)	Multivariable hazards regression *	
		HR (95% CI)	p
For men			
BMI			
per 1-SD increase		1.27 (1.16-1.380	< 0.001
T1 (reference)	9 (6.87%)	1	-
T2	10 (7.75%)	1.09 (0.44-2.69)	0.856
T3	29 (20.86%)	3.90 (1.81-8.37)	< 0.001
p for trend			< 0.001
WC			
per 1-SD increase		1.10 (1.07-1.14)	< 0.001
T1 (reference)	5 (4.03%)	1	-
T2	17 (12.78%)	3.24 (1.19-8.78)	0.021
T3	26 (18.31%)	5.97 (2.27-15.71)	< 0.001
p for trend			< 0.001
HC			
per 1-SD increase		1.11 (1.06-1.16)	< 0.001
T1 (reference)	9 (7.03%)	1	-
T2	11 (9.40%)	1.19 (0.49-2.88)	0.701
T3	28 (18.18%)	2.87 (1.35-6.08)	0.006
p for trend			0.004
WHR			
per 0.01-SD increase		1.09 (1.04-1.15)	< 0.001
T1 (reference)	5 (3.82%)	1	-

T2	18 (13.85%)	3.65 (1.35-9.83)	0.011
T3	25 (18.12%)	5.42 (2.07-14.18)	0.001
p for trend			< 0.001
Women			
BMI			
per 1-SD increase		1.23 (1.07-1.42)	0.005
T1 (reference)	4 (4.40%)	1	-
T2	8 (8.33%)	1.50 (0.44-5.07)	0.515
T3	14 (13.86%)	1.64 (0.50-5.36)	0.413
p for trend			0.712
WC			
per 1-SD increase		1.10 (1.04-1.16)	0.001
T1 (reference)	4 (4.26%)	1	-
T2	4 (4.60%)	0.77 (0.18-3.18)	0.712
T3	18 (16.82%)	2.54 (0.83-7.78)	0.104
p for trend			0.051
HC			
per 1-SD increase		1.06 (0.99-1.14)	0.114
T1 (reference)	4 (5.06%)	1	-
T2	8 (8.33%)	1.26 (0.37-4.33)	0.718
T3	14 (12.39%)	1.52 (0.47-4.92)	0.481
p for trend			0.768
WHR			
per 0.01-SD increase		1.16 (1.07-1.25)	< 0.001
T1 (reference)	1 (1.06%)	1	-
T2	5 (5.21%)	4.54 (0.53-38.91)	0.168

T3	20 (20.41%)	15.91 (2.10-120.52)	0.007
p for trend			< 0.001

*, adjusted for hypertension (yes/no), DM family history (yes/no), smoking (yes/no), alcohol (yes/no), activity (yes/no), TG, TC, HDL-C, LDL-C, and FPG in men; DM family history (yes/no), smoking (yes/no), alcohol (yes/no), activity (yes/no), SBP, TG, TC, HDL-C, and FPG in women

BMI, body mass index; DM, diabetes mellitus; FPG, fasting plasma glucose; HC, hip circumference; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SD, standard deviation; T, tertile; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WHR, waist-hip ratio

Figure S1 Associations of three novel predicted body composition with risk of DM for men

Restricted cubic splines were used to flexibly models and visualize the relations of different parameters with risk of DM. Hazard ratios are indicated by solid lines and 95% CIs by shaded areas. Reference points were the medians for FM (A; 13.61 kg), LM (B; 48.27 kg), and PF (C; 22.04%), respectively. The dotted line represents HR = 1. Confounders in Table 2 were adjusted.

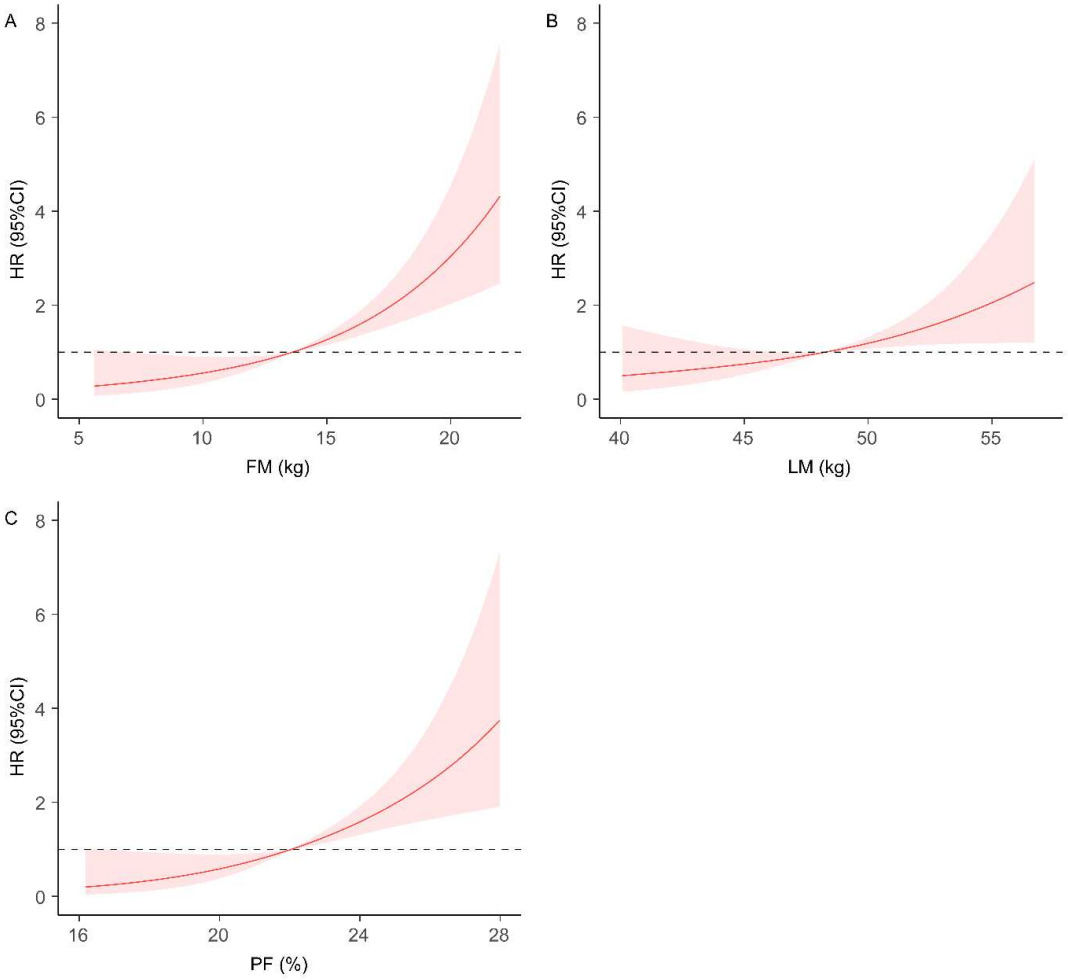

Figure S2 Associations of three novel predicted body composition with risk of DM for women

Restricted cubic splines were used to flexibly models and visualize the relations of different parameters with risk of DM. Hazard ratios are indicated by solid lines and 95% CIs by shaded areas. Reference points were the medians for FM (A; 19.45 kg), LM (B; 34.38 kg), and PF (C; 36.39%), respectively. The dotted line represents HR = 1. Confounders in Table 2 were adjusted.