

# Prevalence, treatment patterns and control rates of metabolic syndrome in a Chinese diabetic population: China Cardiometabolic Registries 3B study

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## Keywords

Blood lipids, Diabetes mellitus, Metabolic syndrome

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## ABSTRACT

**Aims/Introduction:** To investigate the prevalence and risk factors of metabolic syndrome (MetS) in Chinese type 2 diabetes mellitus patients, and assess the effect of MetS on the treatment patterns and blood glucose, blood pressure and blood lipids goal achievements.

**Materials and Methods:** Data from 25,454 type 2 diabetes mellitus patients including demographic data, anthropometric measurements, treatment patterns, and blood glucose and lipid profiles were retrospectively analyzed.

**Results:** Using modified Adult Treatment Panel III MetS criteria, the prevalence of MetS was 57.4% in type 2 diabetes mellitus patients. Multivariable logistic regression analysis showed that type 2 diabetes mellitus patients, who also fulfilled the criteria for MetS, tended to be women, living in the northeast, with a diabetes duration  $\geq 5$  years and leading a sedentary lifestyle. Most MetS (53.4%) and non-MetS (57%) diabetes patients received oral hypoglycemic drugs. Insulin or insulin combination therapies were more applied in MetS (37.5%) than in non-MetS (33.1%) diabetes patients, and the percentages of MetS diabetes patients receiving antihypertensive and lipid-modulating drugs were 52.9% and 28.2% vs 38.3% and 19.3% of the non-MetS diabetes patients. Just 37.5%, 15.6% and 32.9% of the MetS diabetes patients vs 54.6%, 45.6% and 40.4% of the non-MetS diabetes patients achieved the individual target goals for control of blood glucose (glycosylated hemoglobin  $< 7\%$ ), blood pressure (systolic blood pressure  $< 130$  mmHg, diastolic blood pressure  $< 80$  mmHg) and blood lipids (total cholesterol  $< 4.5$  mmol/L), whereas just 2.1% achieved all three target goals.

**Conclusions:** MetS with a high prevalence in Chinese type 2 diabetes mellitus patients is associated with poor blood glucose, blood pressure and blood lipids control rate.

## INTRODUCTION

Metabolic syndrome (MetS), also called syndrome X or insulin resistance syndrome, is a clustering of hyperglycemia, dyslipidemia, central obesity and hypertension. Insulin resistance was suggested as the underlying cause when Reaven<sup>1</sup> introduced the concept in 1988. However, subsequently, several criteria are

now used for the definition of MetS worldwide<sup>2</sup>, with one of the overarching aims of defining MetS being to screen and prevent cardiovascular diseases. As the criteria for defining MetS can differ worldwide, several authors proposed that the Modified National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII) criteria, which adopted the cut-off value for waist circumference (WC) in Asians, is the most suitable MetS definition for cardiovascular risk factor screening<sup>3–6</sup>.

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A recent meta-analysis of 35 studies (including 22 Chinese articles and 13 English articles) comprising 226,653 participants reported that the pooled prevalence of MetS (using International Diabetes Federation [IDF] criteria) among these Chinese participants was 24.5% (95% confidence interval [CI] 22.0–26.9%), and the prevalence of MetS in China was increased from 23.8% between 2000 and 2005 to 27% between 2010 and 2015<sup>7</sup>. Another study reported an overall age-adjusted prevalence of MetS in China of 21.3% (NCEP ATP III) in 2009, and individuals who were women, aged  $\geq 40$  years, urban residents and overweight or obese had a higher risk of complicating MetS<sup>8</sup>. Both MetS and diabetes exerted a synergic effect in the pathogenesis of cardiovascular disease (CVD), resulting in a high prevalence of CVD<sup>9</sup>. Effective control of blood glucose, blood pressure (BP) and blood lipid levels (3B) have beneficial effects in reducing both short- and long-term CVD in patients with MetS<sup>10</sup>. However, no epidemiological study has been carried out to investigate the prevalence and treatment patterns of MetS in diabetes patients across major regions of China. Furthermore, there is no related research about blood glucose (or glycosylated hemoglobin [HbA1c]), BP and total cholesterol (TC) control in patients with combined type 2 diabetes and MetS, whereas very few reports exist about the present treatment patterns of MetS in China. The aim of the present study was to investigate the prevalence of MetS in Chinese diabetes patients, and to assess impact factors (lifestyle, demographics, urbanity) that influence the occurrence of MetS. In addition, the treatment patterns and control rates of blood glucose, BP and blood lipids in Chinese type 2 diabetes patients with MetS were assessed using data from the China Cardiometabolic Registries 3B (CCMR-3B) study.

## METHODS

### Patients

The study was carried out according to the Good Clinical Practice and the International Conference on Harmonization guidelines. Study protocol was approved by the ethics committee of Peking University People's Hospital and other hospitals where an individual committee review was required. All patients gave written informed consent. CCMR-3B is a cross-sectional, multicenter and multispecialty study of type 2 diabetes patients in China<sup>11</sup>. The CCMR-3B study was carried out on patients from a variety of hospitals including tier 1, tier 2 and tier 3 hospitals. The geographical regions were divided into northeast, northwest, north, southwest, central south and east China. The database, which covered the major populated provinces and cities in China, was representative of nationwide Chinese diabetes patients.

The patients included in the study were aged  $\geq 18$  years and diagnosed with type 2 diabetes according to World Health Organization criteria, at least 6 months before screening. The CCMR-3B database (<http://www.ccmregistry.org/index.html>) enrolled 25,454 type 2 diabetes outpatients with an average age of 63 years, with male participants accounting for 47% of the total number.

### Study design

MetS was defined using modified NCEP-ATP III criteria with at least three of the following criteria being met: (i) WC  $\geq 90$  cm in men or  $\geq 80$  cm in women (defined as abdominal obesity); (ii) triglycerides  $\geq 1.7$  mmol/L; (iii) high-density lipoprotein cholesterol (HDL-C)  $< 1.04$  mmol/L in men or  $< 1.29$  mmol/L in women; (iv) systolic BP (SBP)  $\geq 130$  mmHg or diastolic BP (DBP)  $\geq 85$  mmHg; and (v) fasting plasma glucose  $\geq 6.1$  mmol/L. As all included patients were diagnosed with type 2 diabetes, they all met criterion<sup>5</sup>. The 3B achievement rate was defined as HbA1c  $< 7\%$ , SBP  $< 130$  mmHg, DBP  $< 80$  mmHg, TC  $< 4.5$  mmol/L).

The WC was determined between the midpoint of the superior border of the hip bone of the right axillary midline and the lower margin of the 12th rib at the end of expiration.

### Clinical data collection and standards

Data collected by self-reporting including demographics, socioeconomic status (education level, marital and employment status, individual and family incomes, and medical insurance), health behaviors (smoking, drinking and exercise patterns), individual and family medical history, previous diagnosis of hypertension or dyslipidemia, previous use of antihypertensive agents or lipid modulators, symptoms of hypoglycemia, and current medication<sup>12</sup>. In addition, pre-specified clinical and laboratory data including HbA1c, serum lipid profile, serum creatinine and physical examinations were collected. "Drinking" was defined as, on average,  $\geq 50$  g of alcohol per day for  $\geq 1$  year. "Smoking" was defined as smoking at least one cigarette per day for  $\geq 1$  year. The glycemic control rate was defined as the proportion of individuals with an HbA1c concentration of  $< 7.0\%$ , the BP control rate a SBP  $< 130$  mmHg and a DBP  $< 80$  mmHg, and the blood lipid control rate as TC  $< 4.5$  mmol/L<sup>12</sup>. The target goals were consistent with the Chinese guidance for diabetes prevention and treatment, which was used in the CCMB-3B study<sup>13</sup>.

### Statistical analysis

Continuous variables are reported as the mean  $\pm$  standard deviation. Categorical variables are reported as frequency, percentages and standard errors. Comparisons between groups were analyzed using a *t*-test or Mann–Whitney *U*-test for continuous variables, and a Pearson  $\chi^2$ -test for categorical variables. The statistical analyses were carried out using SAS 9.4 (SAS Institute, Cary, NC, USA). The prevalence was analyzed based on the 2010 China national census by using the direct PROC STD RATE method, which is a procedure in the SAS software. A multivariable logistic regression was carried out with MetS status as the dependent variable, and sex, region, residence, age groups, education level, physical activity, smoking and drinking status as independent variables. A  $\chi^2$ -test was used to test for differences between groups with different numbers of metabolic abnormalities (3/4/5) for each demographic factor or for "Metabolic syndrome (ATP III definition)". A *P*-value  $< 0.05$  was considered statistically significant.

**RESULTS**

Data from the CCMR-3B study, including a total of 25,454 patients diagnosed with type 2 diabetes, were analyzed. The overall percentage of MetS prevalence in diabetes patients was 57.4% (14,610/25,454), with men having a lower prevalence than women ( $P < 0.001$ ). The overall mean SBP (137.2 mmHg), DBP (80.6 mmHg), body mass index (BMI; 25.7 kg/m<sup>2</sup>) and WC (89.9 cm) were higher in MetS patients than in non-MetS patients. We also observed that type 2 diabetes patients with MetS had higher TC, LDL-C, triglycerides and fasting plasma glucose blood serum concentrations, and a lower HDL-C level compared with non-MetS patients. Macrovascular (CVD, cerebrovascular disease and peripheral vascular disease) and microvascular complications (nephropathy, retinopathy and neuropathy) occurred more commonly in patients with both type 2 diabetes and MetS (Table 1). Table S1 shows the prevalence of MetS components according to the number of components meeting the modified APTIII criteria. The prevalence of individual components of MetS in type 2 diabetes is shown in Table S2. Most diabetes patients had high BP (71.7%), followed by abdominal obesity (WC;

50.8%) and hypertriglyceridemia (43.9%), 42.8% of whom had low HDL-C serum levels. There were also some differences between men and women on the detailed components of MetS.

Furthermore, there were also prevalence differences of comorbidities regarding regions, residence and age, and smoking or drinking status, as well as the frequency of exercise.

Next, we carried out multiple logistic regression analyses with MetS status used to analyze the risk factors as predictors.

Table 2 shows that women had an almost 100% higher risk of having complicating MetS compared with men (odds ratio 1.99, 95% CI 1.88–2.11,  $P < 0.001$ ). In particular, female patients with a duration of diabetes >5 years were at a higher risk of contracting complicating MetS compared with those patients with <5 years diabetes history, whereas men did not show this trend. In comparison with the southwest regions, northeastern residents had a significantly higher risk of complicating MetS, and central southern residents had a lower risk of complicating MetS than participants in regions other than the southwest. Individuals who did not participate in frequent exercise (least three times per week) had a higher risk of complicating MetS ( $P < 0.001$ ). In addition, men who were currently

**Table 1** | Baseline characteristics of diabetes study participants according to their metabolic syndrome status

	MetS (n = 14,610)	Non-MetS (n = 10,844)	P-value
Mean age, years* (SD)	62.6 (11.81)	62.5 (11.86)	0.087
<50, n (%)	2,328 (15.9)	1,742 (16.1)	
51–64, n (%)	5,545 (38.0)	4,240 (39.1)	
≥65, n (%)	6,719 (46.0)	4,835 (44.6)	
Sex			
Male, n (%)	5,985 (41.0)	5,970 (55.1)	<0.001
Female, n (%)	8,625 (59.0)	4,874 (44.9)	
Mean SBP, mmHg (SD)	137.2 (16.28)	127.4 (14.48)	<0.001
Mean DBP, mmHg (SD)	80.6 (10.92)	76.4 (8.13)	<0.001
Mean waist circumference, cm (SD)	89.9 (10.22)	82.9 (9.02)	<0.001
Mean weight, kg (SD)	68.6 (12.00)	63.3 (10.87)	<0.001
Mean BMI, kg/m <sup>2</sup> (SD)	25.7 (3.52)	23.6 (3.26)	<0.001
Mean total cholesterol, mmol/L (SD)	5.1 (1.54)	4.8 (1.29)	<0.001
Mean LDL cholesterol, mmol/L (SD)	2.9 (0.94)	2.7 (0.87)	<0.001
Mean HDL cholesterol, mmol/L (SD)	1.2 (0.47)	1.4 (0.57)	<0.001
Mean triglycerides, mmol/L (SD)	2.4 (1.92)	1.4 (0.95)	<0.001
Mean FPG, mmol/L (SD)	9.0 (3.34)	7.6 (3.25)	<0.001
Complications (comorbidities)			
CVD, n (%)	2,370 (16.2)	1,419 (13.1)	<0.001
CBD, n (%)	1,574 (10.8)	1,001 (9.2)	<0.001
PVD, n (%)	242 (1.7)	149 (1.4)	0.070
Nephropathy, n (%)	2,391 (16.4)	1,282 (11.8)	<0.001
Retinopathy, n (%)	2,703 (18.5)	1,827 (16.8)	<0.001
Neuropathy, n (%)	2,355 (16.1)	1,506 (13.9)	<0.001

BMI, bodt mass index; CBD, cerebrovascular disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PVD, peripheral vascular disease; SBP, systolic blood pressure; SD, standard deviation. A  $\chi^2$ -test was used to test the differences between metabolic syndrome (MetS) and non-MetS for categorical variables. A *t*-test was used to test the differences between MetS and non-MetS for continous variables.

**Table 2** | Multivariable logistic regression analyses on risk factors for metabolic syndrome in female and male type 2 diabetes patients

	Total		Female		Male	
	Odds ratio (95% CI)	<i>P</i> -value	Adjusted odds ratio (95% CI)	<i>P</i> -value	Adjusted odds ratio (95% CI)	<i>P</i> -value
Sex						
Male	1					
Female	1.99 (1.88–2.11)	<0.001				
Region						
Northeast	1.97 (1.81–2.15)	<0.001	1.87 (1.65–2.11)	<0.001	2.10 (1.85–2.38)	<0.001
North	1.33 (1.23–1.45)	<0.001	1.27 (1.13–1.42)	<0.001	1.42 (1.26–1.60)	<0.001
East	1.37 (1.25–1.49)	<0.001	1.31 (1.16–1.47)	<0.001	1.43 (1.26–1.62)	<0.001
Northwest	1.62 (1.48–1.76)	<0.001	1.47 (1.30–1.67)	<0.001	1.72 (1.52–1.95)	<0.001
Southwest	1		1		1	
Central south	1.11 (1.02–1.20)	<0.001	1.08 (0.96–1.21)	0.190	1.12 (0.98–1.27)	0.093
Residence						
Urban	1.05 (0.97–1.15)	0.231	1.21 (1.08–1.35)	0.001	0.90 (0.79–1.02)	0.101
Rural	1		1		1	
Age (years)						
≤50	1		1		1	
51–64	0.92 (0.85–1.00)	0.041	1.16 (1.02–1.30)	0.019	0.85 (0.76–0.94)	0.001
≥65	0.98 (0.90–1.06)	0.551	1.42 (1.26–1.61)	<0.001	0.74 (0.67–0.82)	<0.001
Education						
≥high school	1		1		1	
<high school	1.04 (0.98–1.11)	0.194	1.25 (1.13–1.38)	<0.001	0.95 (0.88–1.03)	0.190
Diabetes history						
<1 year	1		1		1	
1–5 years	1.02 (0.93–1.12)	0.701	0.99 (0.86–1.14)	0.882	1.06 (0.93–1.21)	0.372
5–10 years	1.10 (0.99–1.21)	0.073	1.20 (1.04–1.39)	0.014	0.99 (0.87–1.14)	0.924
>10 years	1.12 (1.01–1.23)	0.027	1.22 (1.06–1.40)	0.006	1.01 (0.88–1.16)	0.856
Physical activity						
Frequent/PRN (3 times/week)	1		1		1	
No exercise	1.21 (1.14–1.28)	<0.001	1.16 (1.08–1.26)	<0.001	1.23 (1.14–1.33)	<0.001
Smoking						
Current	1.20 (1.11–1.30)	<0.001	1.14 (0.88–1.47)	0.337	1.15 (1.05–1.25)	0.002
None	1		1		1	
Drinking						
Current	1.35 (1.22–1.49)	<0.001	1.37 (0.81–2.35)	0.244	1.30 (1.17–1.44)	<0.001
None	1		1		1	

CI, confidence interval; PRN, pro re nata.

smoking and drinking alcohol had a higher risk of complicating MetS (odds ratio 1.15, 95% CI 1.05–1.25,  $P = 0.002$  and odds ratio 1.30, 95% CI 1.17–1.44,  $P < 0.001$ ).

We investigated the pharmaceutical treatment patterns for diabetes, hypertension and dyslipidemia (Table 3). Most MetS and non-MetS diabetes patients received oral hypoglycemic drugs (53.4% and 57%), biguanides (30.6% and 29.1%), sulfonylureas (25.4% and 26.5%) and/or a  $\alpha$ -glucosidase inhibitor (16.5% and 18.6%). The percentage of patients receiving insulin or insulin combination therapy was higher in the MetS (37.5%) than the non-MetS (33.1%) group. The percentage of patients receiving antihypertensive and lipid-modulating drugs in the MetS group was 52.9% and 28.2%, whereas in the non-MetS group it was 38.3% and 19.3%, respectively. The treatment coverage of antihypertensive and lipid-modulating drugs was

inadequate in both MetS and non-MetS patients. There were large differences in the therapeutic drugs prescribed between urban and rural areas, with urban patients being more concerned about the treatment of hypertension and hyperlipidemia.

In addition, we analyzed and compared the control rates of HbA1c, BP and TC in diabetes patients with or without MetS after different hypoglycemic, antihypertension and lipid-lowering therapies (Figure 1; Table S3). Just 37.5%, 15.6% and 32.9% of type 2 diabetes patients with MetS achieved the individual target goals for control of blood glucose (HbA1c <7%), BP (SBP <130 mmHg, DBP <80 mmHg) and blood lipids (TC <4.5 mmol/L), and in type 2 diabetes patients without MetS the values were 54.6%, 45.6% and 40.4%, respectively. The overall 3B control rate in MetS diabetes patients was

**Table 3** | Comparison of the treatment patterns in different residence regions, and patients with different education and diabetes history in type 2 diabetes metabolic syndrome and non-metabolic syndrome patient groups

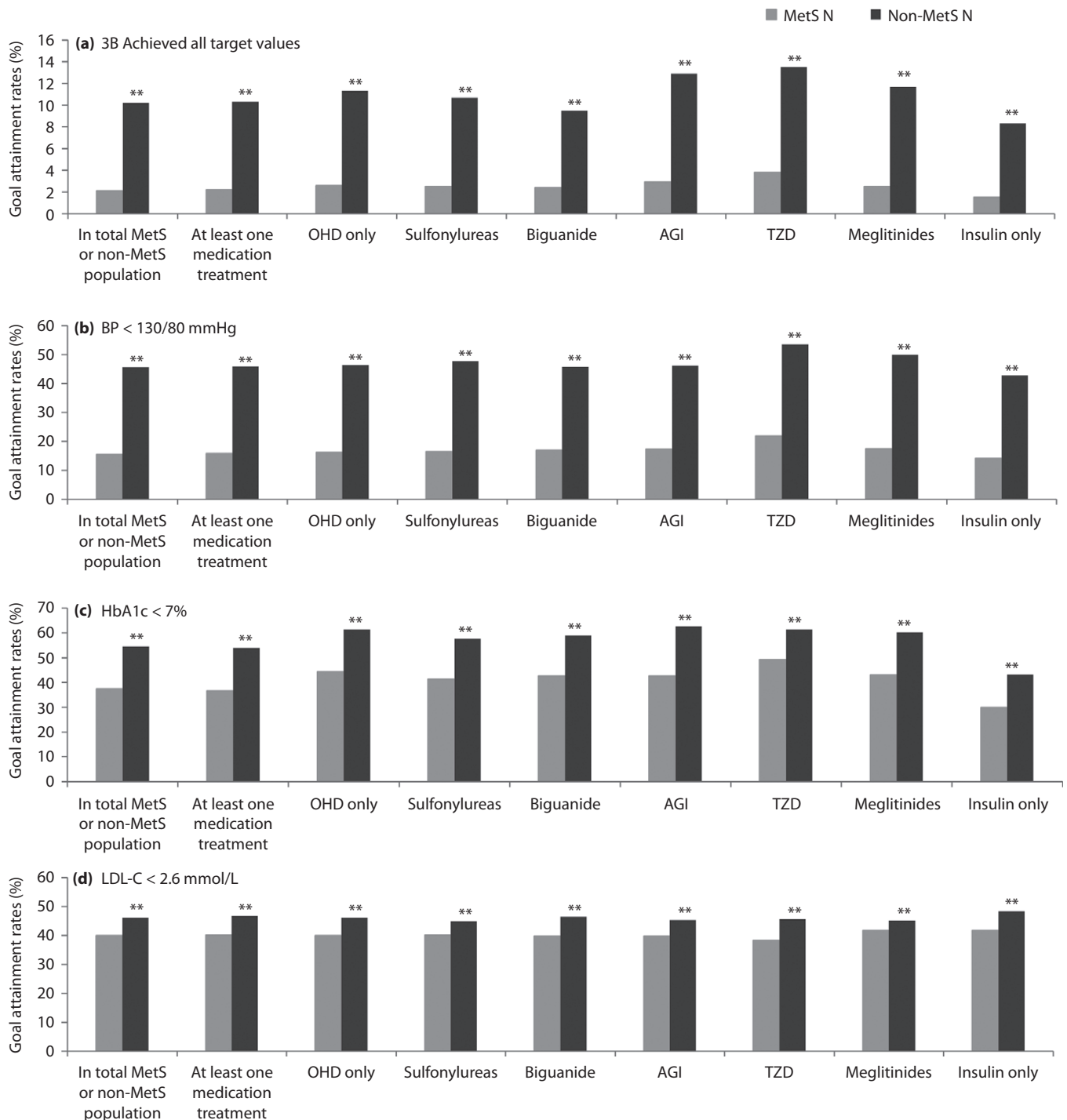
Treatment of coverage information of different drugs between T2DM with MetS or non-MetS, n (%)										
	OHD only	Sulfonylureas	Biguanide	AGI	TZD	Meglitinides	Insulin only	OHD + insulin	Antihypertensive drugs	Lipid-modulating drugs
MetS (n = 14,610)	7,804 (53.4)	3,706 (25.4)	4,471 (30.6)	2,411 (16.5)	712 (4.9)	636 (4.4)	2,556 (17.5)	2,920 (20.0)	7,730 (52.9)	4,122 (28.2)
Sex										
Male	3,077 (39.4)**	1,363 (36.8)**	1,805 (40.4)**	964 (40.0)**	294 (41.3)**	276 (43.4)**	1,102 (43.1)**	1,237 (42.4)**	3,014 (39.0)**	1,826 (44.3)**
Female	4,727 (60.6)	2,343 (63.2)	2,666 (59.6)	1,447 (60.0)	418 (58.7)	360 (56.6)	1,454 (56.9)	1,683 (57.6)	4,716 (61.0)	2,296 (55.7)
Region										
Northeast	1,031 (13.2)**	250 (6.7)**	575 (12.9)**	362 (15.0)**	12 (1.7)**	83 (13.1)**	641 (25.1)**	622 (21.3)**	1,430 (18.5)**	921 (22.3)**
North	1,530 (19.6)	633 (17.1)	859 (19.2)	768 (31.9)	67 (9.4)	115 (18.1)	314 (12.3)	506 (17.3)	1,538 (19.9)	911 (22.1)
East	1,324 (17.0)	837 (22.6)	656 (14.7)	362 (15.0)	146 (20.5)	72 (11.3)	439 (17.2)	525 (18.0)	1,515 (19.6)	587 (14.2)
Northwest	1,099 (14.1)	404 (10.9)	602 (13.5)	239 (9.9)	42 (5.9)	81 (12.7)	439 (17.2)	423 (14.5)	965 (12.5)	591 (14.3)
Southwest	1,404 (18.0)	820 (22.1)	855 (19.1)	306 (12.7)	167 (23.5)	141 (22.2)	468 (18.3)	550 (18.8)	1,286 (16.6)	578 (14.0)
Central south	1,416 (18.1)	762 (20.6)	924 (20.7)	374 (15.5)	278 (39.0)	144 (22.6)	255 (10.0)	294 (10.1)	996 (12.9)	534 (13.0)
Residence										
Urban	6,885 (88.2)	3,151 (85.0)	3,893 (87.1)	2,252 (93.4)	626 (87.9)	586 (92.1)	2,257 (88.3)	2,703 (92.6)	7,049 (91.2)	3,791 (92.0)**
Rural	919 (11.8)	555 (15.0)	578 (12.9)	159 (6.6)	86 (12.1)	50 (7.9)	299 (11.7)	217 (7.4)	681 (8.8)	331 (8.0)
Age (years)										
50	1,217 (15.6)	509 (13.7)	839 (18.8)	307 (12.7)	164 (23.0)	104 (16.4)	395 (15.5)**	469 (16.1)	734 (9.5)**	651 (15.8)**
51–64	2,978 (38.2)	1,481 (40.0)	1,879 (42.0)	868 (36.0)	288 (40.4)	225 (35.4)	937 (36.7)	1,162 (39.8)	2,721 (35.2)	1,588 (38.5)
≥65	3,596 (46.1)	1,708 (46.1)	1,748 (39.1)	1,231 (51.1)	260 (36.5)	307 (48.3)	1,222 (47.8)	1,287 (44.1)	4,265 (55.2)	1,881 (45.6)
Education										
High school	1,685 (21.6)**	646 (17.4)**	975 (21.8)**	644 (26.7)**	169 (23.7)	164 (25.8)**	570 (22.3)**	796 (27.3)	1,710 (22.1)**	1,160 (28.1)**
<High school	6,119 (78.4)	3,060 (82.6)	3,496 (78.2)	1,767 (73.3)	543 (76.3)	472 (74.2)	1,986 (77.7)	2,124 (72.7)	6,020 (77.9)	2,962 (71.9)
Diabetes duration										
<1 year	761 (9.8)	272 (7.3)	443 (9.9)	209 (8.7)	52 (7.3)**	69 (10.8)	140 (5.5)	132 (4.5)	558 (7.2)**	370 (9.0)
1–5 years	3,073 (39.4)	1,366 (36.9)	1,776 (39.7)	861 (35.7)	293 (41.2)	239 (37.6)	548 (21.4)	512 (17.5)	2,203 (28.5)	1,222 (29.6)
5–10 years	1,995 (25.6)	1,018 (27.5)	1,176 (26.3)	608 (25.2)	190 (26.7)	172 (27.0)	580 (22.7)	716 (24.5)	1,851 (23.9)	967 (23.5)
≥10 years	1,975 (25.3)	1,050 (28.3)	1,076 (24.1)	733 (30.4)	177 (24.9)	156 (24.5)	1,288 (50.4)	1,560 (53.4)	3,118 (40.3)	1,563 (37.9)
Non-MetS (n = 10,844)	6,184 (57.0)	2,872 (26.5)	3,152 (29.1)	2,021 (18.6)	666 (6.1)	510 (4.7)	1,890 (17.4)	1,700 (15.7)	4,149 (38.3)	2,088 (19.3)
Sex										
Male	3,282 (53.1)	1,522 (53.0)	1,651 (52.4)	1,112 (55.0)	360 (54.1)	297 (58.2)	1,138 (60.2)	982 (57.8)	2,293 (55.3)	1,224 (58.6)
Female	2,902 (46.9)	1,350 (47.0)	1,501 (47.6)	909 (45.0)	306 (45.9)	213 (41.8)	752 (39.8)	718 (42.2)	1,856 (44.7)	864 (41.4)
Region										
Northeast	534 (8.6)	133 (4.6)	264 (8.4)	181 (9.0)	7 (1.1)	39 (7.6)	329 (17.4)	203 (11.9)	472 (11.4)	296 (14.2)
North	1,212 (19.6)	474 (16.5)	554 (17.6)	666 (33.0)	86 (12.9)	99 (19.4)	209 (11.1)	315 (18.5)	938 (22.6)	564 (27.0)
East	968 (15.7)	590 (20.5)	392 (12.4)	280 (13.9)	101 (15.2)	65 (12.7)	308 (16.3)	277 (16.3)	816 (19.7)	303 (14.5)
Northwest	813 (13.1)	288 (10.0)	394 (12.5)	167 (8.3)	43 (6.5)	57 (11.2)	289 (15.3)	209 (12.3)	419 (10.1)	211 (10.1)
Southwest	1,363 (22.0)	748 (26.0)	774 (24.6)	334 (16.5)	209 (31.4)	149 (29.2)	526 (27.8)	489 (28.8)	924 (22.3)	412 (19.7)
Central south	1,294 (20.9)	639 (22.2)	774 (24.6)	393 (19.4)	220 (33.0)	101 (19.8)	229 (12.1)	207 (12.2)	580 (14.0)	302 (14.5)



**Table 3** (Continued)

Treatment of coverage information of different drugs between T2DM with MetS or non-MetS, <i>n</i> (%)										
	OHD only	Sulfonylureas	Biguanide	AGI	TZD	Meglitinides	Insulin only	OHD + insulin	Antihypertensive drugs	Lipid-modulating drugs
Residence										
Urban	5,517 (89.2)	2,461 (85.7)	2,777 (88.1)	1,911 (94.6)	600 (90.1)	466 (91.4)	1,664 (88.0)	1,571 (92.4)	3,826 (92.2)	1,977 (94.7)
Rural	667 (10.8)	411 (14.3)	375 (11.9)	110 (5.4)	66 (9.9)	44 (8.6)	226 (12.0)	129 (7.6)	323 (7.8)	111 (5.3)
Age (years)										
50	919 (14.9)	385 (13.4)	576 (18.3)	220 (10.9)	141 (21.2)	77 (15.1)	342 (18.1)	281 (16.5)	274 (6.6)	242 (11.6)
51–64	2,470 (39.9)	1,165 (40.6)	1,382 (43.8)	726 (35.9)	295 (44.3)	205 (40.2)	707 (37.4)	690 (40.6)	1,466 (35.3)	840 (40.2)
≥65	2,780 (45.0)	1,314 (45.8)	1,189 (37.7)	1,067 (52.8)	229 (34.4)	228 (44.7)	835 (44.2)	726 (42.7)	2,397 (57.8)	1,003 (48.0)
Education										
High school	1,570 (25.4)	604 (21.0)	793 (25.2)	607 (30.0)	187 (28.1)	165 (32.4)	475 (25.1)	508 (29.9)	1,027 (24.8)	673 (32.2)
<High school	4,614 (74.6)	2,268 (79.0)	2,359 (74.8)	1,414 (70.0)	479 (71.9)	345 (67.6)	1,415 (74.9)	1,192 (70.1)	3,122 (75.2)	1,415 (67.8)
Diabetes history										
<1 year	607 (9.8)	213 (7.4)	316 (10.0)	166 (8.2)	87 (13.1)	56 (11.0)	115 (6.1)	90 (5.3)	263 (6.3)	196 (9.4)
1–5 years	2,498 (40.4)	1,087 (37.8)	1,285 (40.8)	769 (38.1)	283 (42.5)	196 (38.4)	438 (23.2)	328 (19.3)	1,268 (30.6)	677 (32.4)
5–10 years	1,567 (25.3)	784 (27.3)	790 (25.1)	502 (24.8)	161 (24.2)	126 (24.7)	419 (22.2)	395 (23.2)	945 (22.8)	472 (22.6)
≥10 years	1,512 (24.5)	788 (27.4)	761 (24.1)	584 (28.9)	135 (20.3)	132 (25.9)	918 (48.6)	887 (52.2)	1,673 (40.3)	743 (35.6)

A  $\chi^2$ -test was used to test the difference between metabolic syndrome (MetS) and non-MetS. \* $P < 0.05$ ; \*\* $P < 0.01$ . AGI,  $\alpha$ -glucosidase inhibitor; OHD, oral hypoglycemic drugs; TZD, thiazolidinedione.



**Figure 1** | Analysis of the blood pressure (BP), glycosylated hemoglobin (HbA1c), low-density lipoprotein cholesterol (LDL-C) and total blood glucose, BP and blood lipid levels (3B) goal attainment rates of metabolic syndrome (MetS) and non-MetS type 2 diabetes patients after hyperglycemic treatments. AGI,  $\alpha$ -glucosidase inhibitor; OHD, oral hypoglycemic drugs; TZD, thiazolidinedione.

significantly lower than in non-MetS patients (2.1% vs 10.2%,  $P < 0.01$ ). The control rates of 3Bs were all lower in patients with MetS compared with patients without MetS, during all

types of antihyperglycemia, antihypertension and lipid-lowering treatments (1.5–3.8%, 1.6%, 2.2% vs 9.5–13.5%, 9.2%, 12.0%, respectively). The control rates of WC, BMI, LDL, TC, BP and

HbA1c separately were also significantly higher in patients without MetS compared with patients with MetS.

Finally, we analyzed the effects of BP, lipid or both goal attainments on glycemic control rates in diabetes patients with or without MetS, and found that the blood lipid control rates, but not the BP control rates influenced glycemic control rates in both diabetes patients with and without MetS (Table S4).

## DISCUSSION

The present study showed a prevalence of MetS in the Chinese type 2 diabetes (CCMR-3B) population of 57.4%. In general, MetS as a cluster of criteria is supposed to be more indicative as a risk factor indicator for CVD than single factors alone<sup>14</sup>. According to our data, most diabetes patients had high BP (71.7%), followed by abdominal obesity (WC; 50.8%) and hypertriglyceridemia (43.9%). With fasting blood glucose already enhanced in the diabetes population, additional high BP and hypertriglyceridemia already led to the diagnosis of MetS, even with normal WC. In contrast, though the modified NCEP-ATPIII and IDF definitions are the same for Asian people, in contrast to NCEP-ATPIII criteria, obesity is mandatory for IDF diagnosis of MetS. Therefore, IDF categorization would have led to a somewhat lower MetS incidence rate in the present study<sup>3</sup>. However, as the percentage of women in the abdominal obesity group was essentially higher (63.3% women vs 37.8% men), other risk factors, though significantly more enhanced in men, were less pronounced in women (Table S2), the higher MetS prevalence in female type 2 diabetes patients can be attributed mainly to a higher incidence of overweight women (Table 1). In addition, the duration of diabetes was an increased risk for complicating MetS, but only in women. Taken together, patients with diabetes who also fit the definition of MetS tended to be women, had a longer duration of diabetes and failed to carry out significant physical activity, which is consistent with other studies, in which the incidence of MetS was higher in women than in men, even if different definitions of MetS were used<sup>8,15</sup>.

Compared with a cross-sectional study in the USA with a harmonious definition of MetS<sup>16,17</sup>, the present findings showed that Chinese type 2 diabetes patients with MetS had a higher SBP, and lower DBP, WC and BMI than USA patients. The TC and low-density cholesterol levels in the present study were lower than those measured in USA diabetes patients with MetS, but HDL-C levels in type 2 diabetes patients with MetS in our study were similar to those in the USA. All these findings indicated that the population characteristics are different between Chinese and USA individuals. Interestingly, when the individual component prevalence between the 3B study and the Ford study were compared, we found a similar pattern that men had a lower prevalence of abdominal obesity and lower HDL-C, but a higher prevalence of elevated BP than women<sup>18</sup>.

Previous studies noted that the rise of obesity was more pronounced in rural than in urban regions<sup>19,20</sup>, which has also been observed particularly in the north of China, and is

reflected in the incidence of impaired fasting glucose<sup>21,22</sup>. In addition, in agreement with previous studies, tobacco and alcohol consumption, as well as a lack of physical exercise, are significant risk factors for complicating MetS<sup>8,23,24</sup>, but tobacco and alcohol consumption only in men, which might be explained by the low percentages of smoking (3.44%) and alcohol consumption (4.5%) amongst Chinese women<sup>25,26</sup>.

The higher MetS prevalence in the northern regions (north, northeast and northwest) of China, especially in the northeast, might be explained by these factors, as several studies have shown a difference in the dietary and physical activity of populations in northern and southern regions of China, which could have contributed to these regional disparities<sup>24,27–29</sup>. This showed that when treating patients from these regions, a great deal of diabetes health education is required to enhance their understanding of diabetes and metabolic disorder, and much effort should be devoted to diet control and exercise therapy.

In the present study, the most frequently used oral antidiabetic agents were metformin, sulfonylureas and  $\alpha$ -glucosidase inhibitors in MetS and non-MetS patients. The percentage of patients receiving insulin or insulin combination therapy, antihypertensive drugs and lipid-modulating drugs was higher in MetS compared with non-MetS patients. An observational study<sup>30</sup> reported a similar reduction of glycemia in patients with different BMIs after insulin was added to treatment regimens that included oral glucose lowering drugs. In the present study, MetS patients had higher average levels of fasting plasma glucose, BP, TC and triglycerides than non-MetS patients, meanwhile insulin, antihypertensive and lipid-lowering drugs were used more frequently in MetS than in non-MetS patients. In contrast, the control rate of individual targets for blood glucose, BP and blood lipids were significantly lower in MetS compared with non-MetS type 2 diabetes patients, suggesting that these patients might require lifestyle interventions, tighter weight loss and control, as well as a strengthened control of 3B.

As for the 3B control rate, according to previous research, combined HbA1c, blood lipids and BP goal achievement rates for drug-treated type 2 diabetes patients have been reported to be as low as 4.5%<sup>31</sup>. In the present study, the overall 3B goal attainment rates were significantly lower in MetS (2.1%) compared with non-MetS (10.2%) type 2 diabetes patients, even with higher medical coverage rates in MetS patients. As 50.8% of the MetS patients in the present study were diagnosed with abdominal obesity, these data are partly in agreement with recent publications, in which obesity was a factor for poor 3B control in Chinese type 2 diabetes patients<sup>32,33</sup>. Furthermore, our additional findings illustrate that blood lipid attainment might influence blood glucose attainment; patients who achieved their lipid control targets were more likely to achieve their target glucose level. Our findings confirm the negative impact of metabolic disorders on achieving 3B treatment goals, which emphasizes the importance of metabolic control in type 2 diabetes with MetS.



There were several strengths to the present study. A major strength was the large, nationally representative cohort of patients studied in China, which is the first to report the prevalence and risk factors for MetS in Chinese diabetes patients. In addition, the study is the first to show the control rates of 3B in Chinese diabetes patients who also have MetS. Therefore, the present study provides critical information for policy makers and primary physicians to improve the health of Chinese diabetes patients with MetS.

Several limitations of the present study should be addressed. First, a selection bias might exist because the results of this study were obtained from Chinese diabetes patients and a large number of individuals likely remain undiagnosed. Therefore, the prevalence and treatment patterns might not accurately reflect the actual situation in China. Second, this was an observational and cross-sectional study that did not assess long-term outcomes. Finally, because the parameters (blood lipids, HbA1c, etc.) were not measured in a central laboratory, systematic bias due to lack of standardized assessments might exist.

In conclusion, MetS is highly prevalent and associated with poor 3B control rate in Chinese type 2 diabetes patients. A strategy for controlling multiple risk factors and modifying the metabolic disorder should be considered in order to reduce the high prevalence of MetS in Chinese type 2 diabetes patients.

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## DISCLOSURE

GC, JL, YZ and RZ are employees of MSD China Holding Co., Ltd. The authors declare no other conflict of interest.

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## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Table S1** | Prevalence of metabolic syndrome individual components in type 2 diabetes patients based on abnormality parity.

**Table S2** | Prevalence of metabolic syndrome individual components in type 2 diabetes patients based on abnormality numbers.

**Table S3** | Analysis of the effects of blood pressure, lipid or both goal attainments on glycemic control rates in metabolic syndrome or non-metabolic syndrome type 2 diabetes patients.

**Table S4** | Comparison of the goal attainment rates of metabolic syndrome and non-metabolic syndrome type 2 diabetes patients after hyperglycemic, antihypertensive or lipid modulation therapies.

**Appendix S1** | The Appendix for a complete list of investigators.