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Comparison of coronary heart disease risk assessments in individuals with metabolic syndrome using three diagnostic definitions: cross sectional study

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ABSTRACT

Objective: Metabolic syndrome (MetS) is a notable risk factor for coronary heart disease (CHD). However, there are difference in methods for defining MetS. The purpose of this study was to explore which MetS definition more fully reflects the 10-year probability of CHD based on the Framingham risk algorithm.

Design: Cross- sectional study.

Setting: Date from the China Health and Nutrition Survey and the Influencing Factors of Chronic Diseases Survey conducted among residents of the Nanshan District in Shenzhen, China.

Participants: 1721 participators aged 20-80 years were included in this study.

Methods: MetS was diagnosed according to the criteria from the National Cholesterol Education Program's Adult Treatment Panel (revised NCEP-ATP III), the International Diabetes Federation (IDF), and the Chinese Diabetes Society (CDS). The NCEP-ATP III algorithm was used to calculate the Framingham risk score and the Framingham risk algorithm was used to define low (<6%), moderate (6-10%), moderately high (10-20%), and high (>20%) probability of CHD over 10 years. The chi-square test with or without the Bonferroni correction was used to compare differences in the distribution of the 10-year estimated risk for CHD among the three definitions.

Results: Compared to other definitions, the revised NCEP-ATP III identified more participators (30.96%) as having MetS, while the CDS showed the highest 10-year probability for CHD. The 10-year probability for CHD in participators with MetS was significantly higher than that of participators without MetS ($p<0.001$), and all definitions were more predictive of CHD risk in males than in females (all $p<0.001$).

Conclusion: This study demonstrated differences in the prevalence and distribution of the 10-year estimated risk for CHD depending on the definition of MetS. A significant finding of this study was that MetS definitions have better predictive performance in males than in females. Further studies in China, especially longitudinal studies, are needed to determine which definition of MetS is best suited to predict CHD risk.

Strengths and limitations of this study

1. This study investigate the discrepancy in the prevalence of MetS when using three different definitions (the revised NCEP-ATP III, the IDF, and the CDS criteria) in the Chinese population.

2. A key strength of this study is that we explore which MetS definition more fully reflects the 10-year probability of CHD based on the Framingham risk algorithm.

3. This is a cross-sectional study with associated limitations and further studies are needed to determine which MetS definition is the most predictive for the development of CHD.

INTRDUCTION

Metabolic syndrome (MetS) is typically diagnosed based upon abnormalities in a specific set of clinical measures and is consorted with an increased risk of coronary heart disease (CHD).[1-3] A meta-analysis by Mottillo et al. showed that MetS is accompanied with increased risk in cardiovascular outcomes and all-cause mortality.[4] Another meta-analysis including 43 cohorts reported that the relative risk for cardiovascular events and deaths is 1.78 times greater in individuals with MetS.[5] In addition, a matched cohort study found that participators with MetS have a 2.85-fold (2.27-3.57) and 1.80-fold (1.42-2.28) increase in CHD risk in the unadjusted and fully adjusted models, respectively.[6]

At present, diverse methods are used to define MetS, including the 2002 US Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III);[7] the 2005 International Diabetes Federation (IDF) criteria;[8] the 2004 Chinese Diabetes Society (CDS) criteria;[9] and the 2009 Joint Interim Statement (JIS) criteria.[10] Although these criteria have similar components, there are also variations. For example, the criteria of the revised NCEP-ATPIII and IDF are the same except that the IDF criteria include abdominal obesity as an obligatory component to define MetS. The CDS hold the opinion that the importance of each components is equal and use body mass index (BMI) rather than waist circumference (WC) as an index to define obesity. In addition, the cut-off values for specific components in the ATP III criteria are different from those in the revised NCEP-ATPIII and IDF criteria, except for the cut-off value for triglyceride levels. Furthermore, the JIS criteria were created from a collaboration of global expert groups and are similar to the revised NCEP-ATPIII criteria, with national or regional cut-off values for waist circumference.

The differences among these definitions of MetS have resulted in discrepancies in the reported prevalence of MetS among various populations and have led to difficulties identifying target populations for prevention and control of MetS. Most importantly, since MetS is known to be a risk factor for CHD, it is vital to know

which MetS definition is the best predictor of CHD development.

The present study aimed to investigate the discrepancy in the prevalence of MetS when using three different definitions (the revised NCEP-ATP III, the IDF, and the CDS criteria) in the Chinese population. The study also aimed to explore which MetS definition more fully reflects the 10-year probability of CHD based on the Framingham risk algorithm.

METHODS

Subjects

We combined the data from the parts of the China Health and Nutrition Survey with aim of examine the association between the status of health and the changes of economic and social, with the data from the Influencing Factors of Chronic Diseases Survey. Briefly, the study was composed of two cross sectional studies conducted among residents of the Nanshan District in Shenzhen, Guangdong Province in 2015. During the investigation, a complex, multistage probability sample design was used for both of the survey distribution. Besides, the participators admitted into the survey were required to be a eligible adults and had been living at the Nanshan District at least 6 month.

This study sample consisted of 1820 adults; however, 99 subjects were excluded because anthropometric or biochemical information for accurate diagnosis of MetS was lacking. In total, 1721 participators aged 20 to 80 years old were ultimately eligible for analysis. All participators were informed the specific details and provided informed consent before the surveys, both of them were approved by the Ethics Committee of the Shenzhen Nanshan Center for Chronic Disease Control.

Measurements

A face-to-face interview was conducted by the investigator who was trained to administer both of the surveys. A standardized questionnaire was used to collect information regarding the participators' demographic characteristics, smoking status, drinking status, physical activity, medical history, and medication use. Weight, height,

and waist circumference were measured by the investigator using standard measurement methods. Weight and height were measured while the participators were marginally clothed without shoes using the SK-X80 (Sonka Corporation, Shenzhen, China) and recorded to the nearest 0.1 kg. The BMI was calculated as weight in kilograms divided by the square of height in meters. WC was measured to the nearest 0.1 cm at the midpoint between the lower rib and the iliac crest at the end of normal expiration while the participators were standing. Blood pressure was measured using a standard mercury sphygmomanometer with the cuff on the right upper arm after 5 minutes of rest. Three blood pressure readings were recorded, and the mean of the three readings was calculated.

Laboratory tests

Participators were required to fast overnight (at least 10 hours) before blood collection by the nurse. Blood was drawn from the vein in the morning in the Community Health Service Center and was transferred to the Shenzhen Nanshan Center for Chronic Disease Control for further treatment within 2 hours of blood collection. Blood specimens were collected in a 5-ml EDTA vacuum tube for routine examination and 5-ml coagulation tubes for biochemical analysis and were stored in a cooler during transportation. When the specimens arrived at the Department of Laboratory Medicine, they were centrifuged at 3000×g for 10 minutes at room temperature instantaneously. Fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), low-density lipoprotein concentration (LDL-C), and high-density lipoprotein concentration (HDL-C) were analyzed by an automatic clinical chemistry analyzer (HITACH 7080, Tokyo, Japan). The FBG, TC, TG, HDL-C, and LDL-C were determined by enzymatic methods.

Definition of MetS and the Framingham risk algorithm

In this study, we used three different definitions of MetS as follows: the revised NCEP-ATPIII Criteria for Asians (revised by the American Heart Association and the National Heart, Lung, and Blood Institute (AHA/NHLBI) in 2005 [11] and are the same

criteria as the Joint Interim Statement in 2009[10]), IDF criteria for Asians,[8] and the CDS criteria.[9] The details of the three criteria are listed in Table 1. The Framingham risk score was calculated from the NCEP-ATP III algorithm,[7] and we defined the 10-year probability of CHD as low (<6%), moderate (6-10%), moderately high (10-20%), and high (>20%) [12] (based on the Framingham risk algorithm). Participators with preexisting diabetes or self-reported CVD (including heart attack, heart failure, or stroke) were distributed to the high risk group. Diabetes was defined as having a fasting glucose level of 7.0 mmol/L after a 12-hour fast, use of oral hypoglycemic agents or insulin, or self-reported diagnosis of diabetes.

Table 1 Defintion of the metabolic syndrome

MetS components	Revised NCEP-ATP III criteria (3 or more)	IDF criteria (central obesity and 2 or more)	CDS criteria (BMI and 2 or more)
WC (BMI)	WC≥90/80cm(M/W)	WC≥90/80cm(M/W)	BMI≥25kg/m2
SBP/DBP	≥130/85 mmHg or MP	≥130/85 mmHg or MP	≥140/90 mmHg or MP
FBG(mmol/L)	≥5.6mmol/L or MT	≥5.6mmol/L or MT	≥6.1mmol/L or MT
TG(mmol/L)	≥ 1.70mmol/L	≥ 1.70mmol/L	
HDL-C(mmol/L)	＜1.0/1.3mmol/L(M/W)	＜1.0/1.3mmol/L(M/W)	
TG(mmol/L) and HDL-C(mmol/L)			TG≥ 1.70mmol/L or (and) HDL-C＜0.9/1.0mmol/L(M/W)

BMI Body mass index; WC Waist circumference; M men; W women; MP medication for blood pressure; MT medication for blood glucose; FBG Fasting blood glucose; SBP systolic blood pressure; DBP diastolic blood pressure; HDL-C high-density lipoprotein cholesterol; LDL-C low-density lipoprotein cholesterol; TG total glycerides;

Statistical analysis

Continuous variables with normal and skewed distributions were expressed as the means (SD) and medians (interquartile range), respectively. Categorical variables were reported as percentages, and the difference was compared using the chi-square test with or without the Bonferroni correction. First, the prevalence of MetS was calculated based on the three definitions of MetS, and the differences were compared. Second, the distribution of the 10-year estimated risk for CHD, according to each of the three definitions of MetS, was compared to evaluate which definition is the best predictor of CHD development. A two-sided p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS software (version 20.0; SPSS Inc., Chicago, Illinois).

RESULTS

Prevalence of MetS

A total of 1721 participators aged 20 to 80 years were included in this study. The general characteristics of the participators are presented in Table 2. The prevalence of MetS based on the definitions from the revised NCEP-ATP III, IDF, and CDS criteria is presented in Table 3. The age- and sex-adjusted prevalence of MetS among participants aged 20 to 80 years according to the revised ATP III, IDF, and CDS criteria were 30.96%, 19.93%, and 10.88%, respectively. The age-standardized prevalence of MetS for males aged 20 to 80 years according to the revised NCEP-ATP III, IDF, and CDS criteria was 30.21%, 10.85%, and 13.12%, respectively, and that for females aged 20 to 80 years was 31.74%, 29.24%, and 8.58%, respectively. The difference in the prevalence of MetS based on the three definitions was large for both sexes. In particular, the prevalence of MetS based on the revised ATP III criteria in females was 3.7-fold greater than that based on the CDS criteria.

Table 2 Characteristics of the participators

	Total (n=1721)	Males (n=716, 41.6%)	Females (n=1005, 58.4%)
Age (years)	44.41±12.43	45.23±12.47	43.83±12.38
Body mass index (kg/m^2)	23.68±3.31	24.64±3.16	23.00±3.24
Waist circumference (cm)	82.08±9.84	86.91±9.03	78.63±8.90
Fasting blood glucose (mmol/L)	5.29±1.22	5.43±1.50	5.19±0.96
Triglycerides (mmol/L)	1.47±1.21	1.80±1.41	1.23±0.98
Total cholesterol (mmol/L)	4.28±0.96	4.31±0.96	4.26±0.96
HDL-C (mmol/L)	1.31±0.35	1.15±0.31	1.42±0.34
LDL-C (mmol/L)	2.59±0.80	2.70±0.82	2.50±0.78
SBP (mmHg)	118.46±16.19	122.69±14.77	115.45±16.49
DBP (mmHg)	75.99±10.31	79.58±9.72	73.42±9.93
Hypertension (%)	13.9	16.9	11.8
Diabetes (%)	5.3	6.8	4.2
Dyslipidemia (%)	10.2	14.5	7.2
Current smoker (%)	5.7	13.0	5.1
Central obesity (%)	24.2	13.3	31.9
Framingham risk score (%)	1(1,2)	2(0,8)	1(1,1)

Data are expressed as the means ± standard deviation, medians (P_{25}, P_{75}), or percentages.

Hypertension, diabetes, and dyslipidemia were diagnosed before the study; central obesity is defined as ≥80 cm for men and ≥90 cm for women.

The age- and sex-adjusted prevalence of MetS increased with age in those younger than 30 years to those older than 60 years from 17.78% to 36.1%, 9.26% to 35.93%, and 0.44% to 23.17% based on the revised ATP III, IDF, and CDS criteria, respectively. We find that the age-specific prevalence for females was higher than that of males according to the IDF criteria (females: 29.24% (95%CI: 26.4-32.1%); males: 10.85% (95%CI: 8.6-13.2%)), but the results were opposite using the CDS criteria (females: 8.58% (95%CI: 7.1-10.6%); males: 13.12% (95%CI: 10.6-15.6%)). An analysis stratified by age according to the revised ATP III criteria showed that the prevalence of MetS in males aged <40 years was higher than that in females in the same age group, while the reverse was true for those aged ≥50 years (Table 3, Figure 1).

Table 3 Prevalence of metabolic syndrome among the study population

Age groups (years)	Revised ATP III criteria			IDF criteria			CDS criteria		
	Men (n=716)	Women (n=1005)	Total (n=1721)	Men (n=716)	Women (n=1005)	Total (n=1721)	Men (n=716)	Women (n=1005)	Total (n=1721)
20~	20.90	14.50	17.78 #	7.50	11.10	9.26 #	0.00	0.90	0.44 #
30~	29.90	22.10	26.04 #	11.90	20.10	15.96 #	10.00	1.70	5.89 #
40~	36.70	30.70	33.74 #	8.20	27.30	17.61 #	13.30	5.20	9.31 #
50~	29.30	40.20	34.64 #	8.30	38.60	23.13 #	18.80	16.30	17.58 #
60~	36.10	54.30	45.30 #	19.30	52.20	35.93 #	26.10	20.30	23.17 #
Overall	35.5	28.3	31.6 #	25.2	25.4	25.3 #	27.9	10.9	18.7 #
	(32.0-39.0)	(25.5-31.0)	(29.4-33.8)	(22.0-28.3)	(22.7-28.1)	(23.2-27.3)	(24.6-31.2)	(9.0-12.9)	(16.9-20.6)
Overall (standardized)	30.21 *	31.74 *	30.96 +	10.85 *	29.24 *	19.93+	13.12 *	8.58 *	10.88 +
	(26.8-33.5)	(28.9-34.6)	(28.8-33.2)	(8.6-13.2)	(26.4-32.1)	(18.0-21.8)	(10.6-15.6)	(7.1-10.6)	(9.4-12.3)

*Age-adjusted percentages for men and women. # Sex-adjusted percentages for each age group. +Age-and sex- adjusted percentages.

Adjustment was conducted with sample survey data of 1% population in 2015 by the direct methods.

The 10-year probability of CHD according to MetS status

The Framingham risk algorithm was used to estimate the 10-year probability of CHD. The distributions of the 10-year estimated risk for CHD based on the three different definitions of MetS were compared (Table 4). Among those with MetS based on the CDS criteria, 39.4% had a 10-year risk for CHD of 6% (low), 6.7% had a 10-year CHD risk of 6-10% (moderate), 7.2% had a 10-year CHD risk of 10-20% (moderately

high), and 7.2% had a 10-year CHD risk of 20% (high). The remaining 39.4% of participators with MetS had diabetes and/or CVD. This is in contrast to those without MetS, of whom a considerably higher proportion had a low risk (85.0%), and lower proportions had a moderate (3.3%), moderately high (5.5%), or high risk (1.6%) or had diabetes and/or CVD (4.7%) ($p<0.001$). Similar heterogeneity in those with MetS and those without MetS was found based on the revised NCEP-ATP III criteria and the IDF criteria ($p<0.001$). Of those with MetS, based on the revised NCEP-ATP III criteria and the IDF criteria, 67.5% and 74.2% had a low risk, 3.5% and 3.0% had a moderate risk, 5.2% and 3.3% had a moderately high risk, and 23.8% and 19.5% had a high risk or had diabetes and/or CVD, respectively. There were no significant differences in CHD risk distributions of those with MetS based on the revised NCEP-ATP III criteria and the IDF criteria ($p=0.252$), while a significant difference was observed based on the CDS criteria ($p<0.001$, Figure 2).

We further compared the distribution of the 10-year estimated risk for CHD based on the three different MetS definitions in males and females (Figure 3). There were no significant differences in the distribution of the 10-year estimated risk for CHD in males with MetS among the three definitions, except between the revised NCEP-ATP III criteria and the CDS criteria ($p=0.001$). As shown in Figure 3, a significant difference was found in the 10-year risk in females with MetS based on the CDS definition and the remaining definitions ($p<0.001$), while no significant difference was found based on the revised NCEP-ATP III criteria and the IDF criteria. Compared to females, a higher risk of CHD was found in males for all three definitions ($p<0.001$, Figure 3).

Table 4 Distribution of the 10-year estimated risk for CHD based on the three definitions of MetS

		Revised ATP III criteria	IDF criteria	CDS criteria
MetS(+)	Low (<6%)	67.5	74.2	39.4
	Moderate (6-10%)	3.5	3	6.7
	Moderate High (10-20%)	5.2	3.3	7.2
	High (>20%)	3.7	3.5	7.2
	DM/CVD	20.1	16	39.4
MetS(-)	Low (<6%)	86.1	81.9	85
	Moderate (6-10%)	3.7	3.8	3.3

	Moderate High (10-20%)	5.9	6.3	5.5
	High (>20%)	1.4	1.8	1.6
	DM/CVD	2.9	6.2	4.7
P-value		<0.001	<0.001	<0.001

P-value: based on a comparison of the distributions of risk groups between those with versus those without metabolic syndrome

DISCUSSION

This study shows that the prevalence of MetS and the distribution of the 10-year estimated risk for CHD vary depending on how MetS is defined. In this study, the difference among the revised NCEP-ATP III, IDF, and CDS criteria was evaluated. The 10-year risk for CHD was significantly higher in participators with MetS than those without MetS, and all three definitions were more predictive of CHD risk in males than in females. Compared to the other criteria, participants with MetS based on the CDS criteria had a higher 10-year risk for CHD; however, the CDS criteria also led to the lowest prevalence of MetS.

This is not the first study to investigate the extent to which three current definitions of MetS can estimate the 10-year probability for CHD in individuals with MetS based on the Framingham risk algorithm. Suzuki et al. [13] used the Framingham risk score, not the 10-year probability for CHD, to compare the differences among four different MetS definitions. Their results showed that the risk score in males with MetS was significantly higher, by three-fold, than that in females with MetS based on all four diagnostic criteria. However, the results failed to accurately compare the difference between males and females because females are required to have a higher score for each risk category. Therefore, in the present study, we compared the distribution of the 10-year estimated risk for CHD between males and females. Our study revealed that all three definitions of MetS that we evaluated were more predictive for the 10-year CHD risk in males than in females. Simultaneously, there were significant differences in the prevalence of MetS between males and females. A greater number of females met the diagnostic criteria of MetS using the IDF criteria, while the CDS criteria led to a greater number of males having MetS. There was no significant difference in the prevalence of MetS in females and males based on the

revised NCEP-ATP III criteria. The finding that the 10-year probability for CHD in males differed based on the definition of MetS is consistent with the findings of previous studies. Mak et al. [14] suggested that the adverse impact of MetS was greater among males than females, which is in line with another study.[15] Therefore, it appears that the impacts of various risk factors on cardiovascular diseases and their outcomes differ according to sex in patients with MetS.[16] Notably, different forms of obesity have different impacts on cardiovascular disease risk. In particular, android obesity, which is more common in males and postmenopausal females,[17] is associated with future cardiovascular events.[18] This sex difference may also be due to other characteristics of the subjects, such as age and smoking status. In contrast, some studies [5 19 20] have suggested that all definitions of MetS (NCEP-ATP III, IDF, AHA/NHLBL, and JIS) are more predictive of CHD risk in females than in males.

Among the definitions of MetS evaluated in the current study, the IDF criteria identified fewer participants (19.93%) as having MetS than the revised NCEP-ATP III criteria (30.96%), but this underestimated prevalence did not translate into better predictive performance; There was no significant difference in the distribution of the 10-year risk for CHD between the revised NCEP-ATP III and the IDF criteria. This finding is consistent with the results of previous studies, in which similar risks for cardiovascular diseases were reported with different levels of sensitivity depending on the definition of MetS.[19 21 22] The lower prevalence based on the IDF criteria may be due to the requirement of central obesity for the diagnosis of MetS, even though they share the same components and the same cu-off values. This demand decreases the number of individuals satisfying the criteria for MetS under the IDF criteria compared to the revised ATP III. However, a recent cohort study conducted by Keihani [23] showed that abdominal obesity and the presence of metabolic derangements are both relevant risk factors for future CVD. Similar results were found in another study by Zhao et al.,[24] which compared the long-term risk of cardiovascular diseases between patients with MetS with or without central obesity. They found that most patients with MetS (78%) had central obesity, with no significant difference in the 10-year absolute and relative risk of coronary heart disease and ischemic CVD events between the two

MetS groups. This highlights that focusing on abdominal obesity while ignoring the other components of metabolic syndrome may not be a benign suggestion. Another study [25] using ROC curve and Cox regression analyses showed that the ATP III criteria better predicted CVD than the IDF criteria.

Compared to the other criteria, the CDS criteria led to the lowest prevalence of MetS and the highest 10-year probability for CHD in the current study. Subjects diagnosed with obesity (BMI ≥25 kg/m^2) were more common than those diagnosed with central obesity (32.31% *vs* 24.17%). Therefore, the lowest prevalence and the highest risk for CHD are mainly caused by the thresholds of high blood pressure and elevated blood glucose of the CDS criteria, which are higher than those of the other criteria. Our findings are partially in accordance with the results of previous studies, in which CDS had the highest specificity to identify MetS in the Chinese population based on a 6.3-year cohort study.[25] However, despite the high specificity, the study also found that the CDS criteria had the lowest sensitivity among the three definitions, and more than 50% of patients may be misdiagnosed.

There are several limitations to our study. First, although the original Framingham coronary heart disease risk assessment has been validated in previous studies,[26] the algorithm does not include obesity or TG levels, which could potentially influence the risk estimation. Furthermore, a previous report found that the Framingham algorithm overestimates the risk of CHD in the Chinese population.[27] Second, our analysis was based on cross-sectional data; therefore, we were unable to calculate positive and negative predictive values for CHD or determine which MetS definition is the most predictive for the development of CHD. Therefore, further studies conducted in China, especially longitudinal studies, are needed to determine which MetS definition is best suited to predict CHD.

This study contributes to the body of evidence that differences exist in the prevalence and distribution of the 10-year estimated risk for CHD depending on the definition of MetS. Among the definitions evaluated (the revised NCEP-ATP III, IDF, and CDS), the CDS criteria led to the highest 10-year probability for CHD and the lowest prevalence of MetS. A significant finding of this study was that all three

definitions of MetS had better predictive performance in males compared to females.

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Contributors The authors' contributions were as follows: Xiaolin Peng and Liping Hao conceived and designed the study, and critically revised the manuscript; Juan Zhou analyzed the data and wrote the paper; Qin Gao and Jun Wang participated in the laboratory assay. Ming Zhang, Jianping Ma, Changyi Wang and Hongen Chen collected the data and revised the manuscript. All the authors read and approved the final version of the manuscript.

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REFERENCE

1. Sattar N, Gaw A, Scherbakova O, et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation* 2003;108(4):414-9.
2. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes care* 2005;28(7):1769-78.
3. Noda H, Iso H, Saito I, et al. The impact of the metabolic syndrome and its components on the incidence of ischemic heart disease and stroke: the Japan public health center-based study. *Hypertens Res* 2009;32(4):289-98.
4. Mottillo S, Filion KB, Genest J, et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. *J Am Coll Cardiol* 2010;56(14):1113-32.
5. Gami AS, Witt BJ, Howard DE, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol* 2007;49(4):403-14.
6. Esteghamati A, Hafezi-Nejad N, Sheikhbahaei S, et al. Risk of coronary heart disease associated with metabolic syndrome and its individual components in Iranian subjects: a matched cohort study.

J Clin Lipidol 2014;8(3):279-86.

7. National Cholesterol Education Program Expert Panel on Detection E, Treatment of High Blood Cholesterol in A. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;106(25):3143-421.
8. Alberti KG, Zimmet P, Shaw J, et al. The metabolic syndrome--a new worldwide definition. *Lancet* 2005;366(9491):1059-62.
9. Metabolic syndrome study cooperation group of Chinese diabetes society. *Chinese Journal of Diabetes Mellitus* 2004;12(3):156-61.
10. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120(16):1640-5.
11. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement: Executive Summary. *Crit Pathw Cardiol* 2005;4(4):198-203.
12. Hoang KC, Ghandehari H, Lopez VA, et al. Global coronary heart disease risk assessment of individuals with the metabolic syndrome in the U.S. *Diabetes care* 2008;31(7):1405-9.
13. Suzuki T, Zeng Z, Zhao B, et al. Comparison of coronary heart disease risk among four diagnostic definitions of metabolic syndrome. *J Endocrinol Invest* 2016;39(11):1337-46.
14. Mak KH, Ma S, Heng D, et al. Impact of sex, metabolic syndrome, and diabetes mellitus on cardiovascular events. *J Am Coll Cardiol* 2007;100(2):227-33.
15. Qiao Q, Group DS. Comparison of different definitions of the metabolic syndrome in relation to cardiovascular mortality in European men and women. *Diabetologia* 2006;49(12):2837-46.
16. Regitz-Zagrosek V, Lehmkuhl E, Weickert MO. Gender differences in the metabolic syndrome and their role for cardiovascular disease. *Clin Res Cardiol* 2006;95(3):136-47.
17. Williams CM. Lipid metabolism in women. Proc Nutr Soc 2004;63(1):153-60.
18. Ibrahim MM. Subcutaneous and visceral adipose tissue: structural and functional differences. *Obes Rev* 2010;11(1):11-8.
19. Hosseinpanah F, Asghari G, Barzin M, et al. Prognostic impact of different definitions of metabolic syndrome in predicting cardiovascular events in a cohort of non-diabetic Tehranian adults. *Int J Cardiol* 2013;168(1):369-74.
20. Wang C, Hou X, Bao Y, et al. The metabolic syndrome increased risk of cardiovascular events in Chinese--a community based study. *Int J Cardiol* 2010;139(2):159-65.
21. Mancia G, Bombelli M, Facchetti R, et al. Impact of different definitions of the metabolic syndrome on the prevalence of organ damage, cardiometabolic risk and cardiovascular events. *J hypertens* 2010;28(5):999-1006.
22. Nilsson PM, Engstrom G, Hedblad B. The metabolic syndrome and incidence of cardiovascular disease in non-diabetic subjects--a population-based study comparing three different definitions. *Diabet Med* 2007;24(5):464-72.
23. Keihani S, Hosseinpanah F, Barzin M, et al. Abdominal obesity phenotypes and risk of cardiovascular disease in a decade of follow-up: the Tehran Lipid and Glucose Study. *Atherosclerosis* 2015;238(2):256-63.

24. Zhao D, Grundy SM, Wang W, et al. Ten-year cardiovascular disease risk of metabolic syndrome without central obesity in middle-aged chinese. *J Am Coll Cardiol* 2007;100(5):835-9.
25. Zhou H, Guo ZR, Yu LG, et al. Evidence on the applicability of the ATPIII, IDF and CDS metabolic syndrome diagnostic criteria to identify CVD and T2DM in the Chinese population from a 6.3-year cohort study in mid-eastern China. *Diabetes Res Clin Pract* 2010;90(3):319-25.
26. D'Agostino RB, Sr., Grundy S, Sullivan LM, et al. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. *JAMA* 2001;286(2):180-7.
27. Liu J, Hong Y, D'Agostino RB, Sr., et al. Predictive value for the Chinese population of the Framingham CHD risk assessment tool compared with the Chinese Multi-Provincial Cohort Study. *JAMA* 2004;291(21):2591-9.

Figure legends:

Figure 1 Prevalence of MetS among adults aged 20 to 80 years in this study area.

Figure 2 The distribution of the 10-year estimated risk for CHD in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (<6%), moderate (6 to 10%),moderately high (10 to 20%), and high (>20% or history of diabetes or CVD).

Figure 3 The distribution of the 10-year estimated risk for CHD by sex in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (<6%), moderate (6 to 10%),moderately high (10 to 20%), and high (>20% or history of diabetes or CVD).

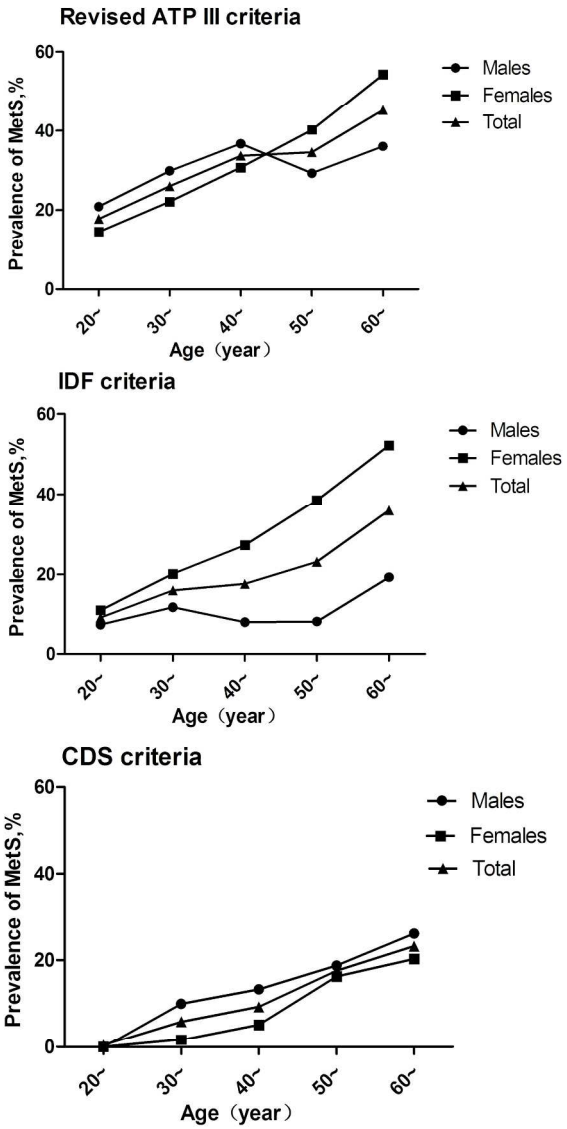

Figure 1 Prevalence of MetS among adults aged 20 to 80 years in the study area

Figure 1

187x293mm (300 x 300 DPI)

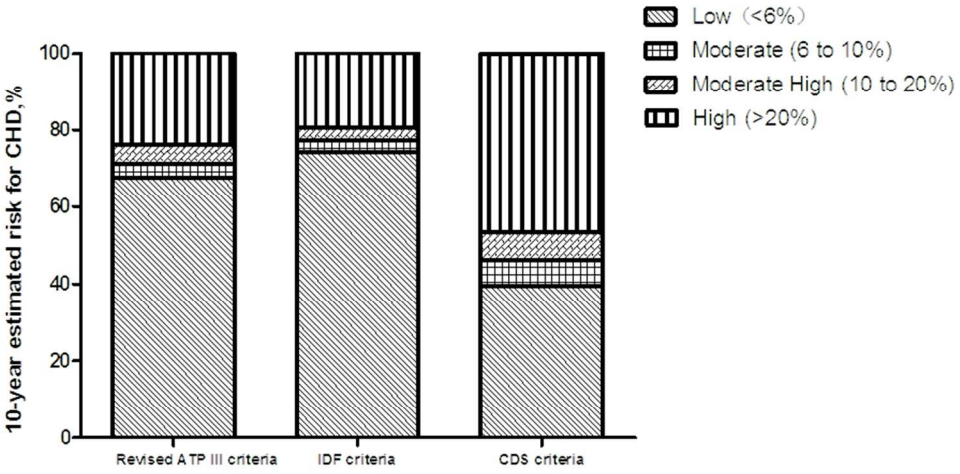

Figure 2 The distribution of the 10-year estimated risk for CHD in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (<6%), moderate (6 to 10%), moderately high (10-20%), and high (>20% or history of diabetes or CVD).

Figure 2

79x50mm (300 x 300 DPI)

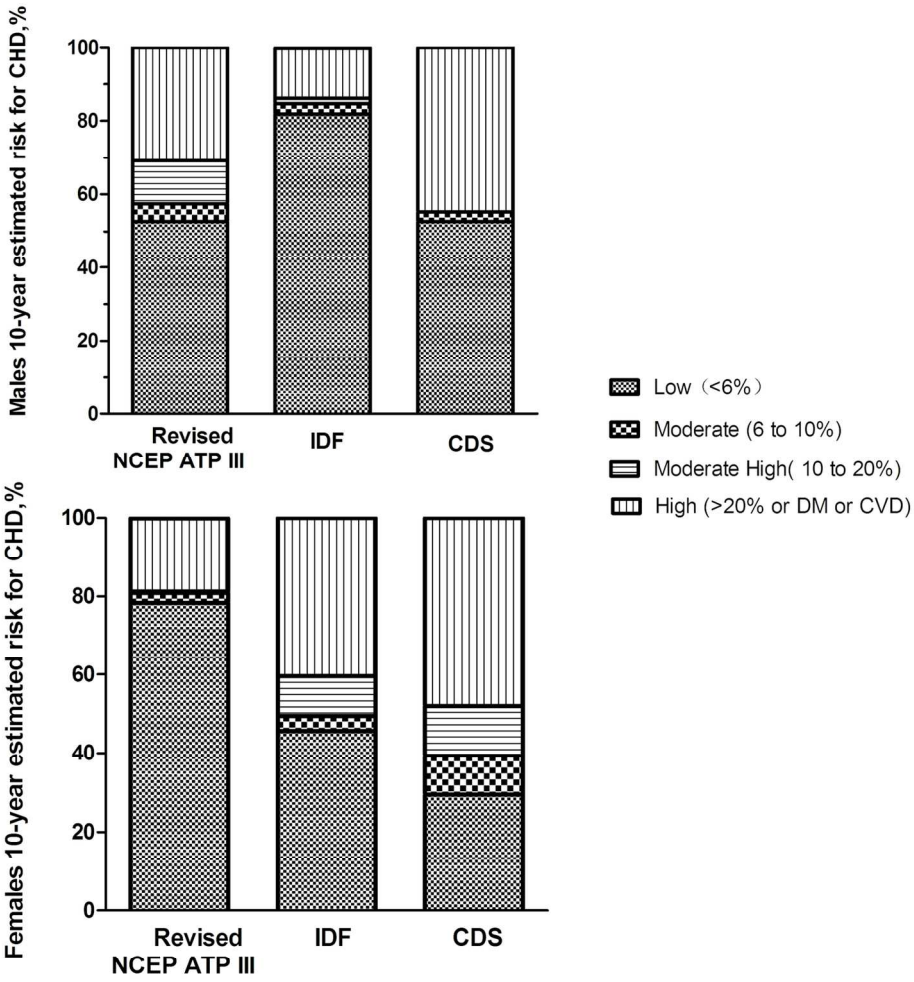

Figure 3 The distribution of the 10-year estimated risk for CHD by sex in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (>6%), moderate (6 to 10 %),moderately high (10 to 20%), and high (?20% or history of diabetes or CVD).

Figure 3

143x172mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	*6*
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			7

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Comparison of coronary heart disease risk assessments in individuals with metabolic syndrome using three diagnostic definitions: cross sectional study

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Comparison of coronary heart disease risk assessments among individuals with metabolic syndrome using three diagnostic definitions: A cross-sectional study

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ABSTRACT

Objective: Metabolic syndrome (MetS) is a notable risk factor of coronary heart disease (CHD). However, there are difference in the methods used to define MetS. The purpose of this study was to determine which MetS definition most fully reflects the 10-year probability of CHD based on the Framingham risk algorithm.

Design: Cross-sectional study.

Setting: Data were obtained from the China Health and Nutrition Survey and the Influencing Factors of Chronic Diseases Survey conducted among residents of Nanshan District in Shenzhen, China.

Participants: In total, 1721 participants aged 20-80 years were included in this study.

Methods: MetS was diagnosed according to the criteria of the National Cholesterol Education Program's Adult Treatment Panel (revised NCEP-ATP III), the International Diabetes Federation (IDF), and the Chinese Diabetes Society (CDS). The NCEP-ATP III algorithm was used to calculate the Framingham risk score, and the Framingham risk score was used to define the probability of developing CHD within 10 years either as low (<6%), moderate (6-10%), moderately high (10-20%), or high (>20%). Chi-square tests with or without the Bonferroni correction were used to compare the differences in the distribution of the 10-year estimated risk of developing CHD among the three definitions.

Results: Compared to the other definitions, the revised NCEP-ATP III criteria identified more participants (30.96%, 95% CI: 28.8%-33.2%) as having MetS, while the CDS criteria showed the highest 10-year probability of developing CHD. The 10-year probability of developing CHD in the participants with MetS was significantly higher than that in the participants without MetS (CDS: $\chi2=157.65$, revised ATP III: $\chi2=45.17$, IDF: $\chi2=306.15$, all $p<0.001$), and all definitions more fully reflect the CHD risk in males than in females (revised NCEP-ATP III: $\chi2=72.83$; IDF: $\chi2=63.60$; CDS: $\chi2=23.84$; all $p<0.001$).

Conclusions: This study demonstrates the differences in the prevalence and distribution of the 10-year estimated risk of developing CHD based on the definition of MetS. A significant finding of this study is that the MetS definitions have better

performance for males than for females. Further studies in China, especially longitudinal studies, are needed to determine which definition of MetS is best suited for predicting CHD risk.

Strengths and limitations of this study

1. We combined data from parts of the China Health and Nutrition Survey and the Influencing Factors of Chronic Diseases Survey. The complex, multistage probability sample design is fairly representative of the Chinese population in Shenzhen.
2. There was a low percentage of missing data in general.
3. Three definitions of MetS were used to compare the discrepancy in the prevalence of MetS and the 10-year probability of developing CHD based on the Framingham risk score.
4. This study adopted a cross-sectional design, and the Framingham algorithm may overestimate the risk of developing CHD in a Chinese population. Therefore, cohort studies investigating CHD events are needed to further prove the predictive value and determine which MetS definition is the most predictive of the development of CHD.

INTRODUCTION

Metabolic syndrome (MetS) is typically diagnosed based on abnormalities in a specific set of clinical measures and is associated with an increased risk of developing coronary heart disease (CHD). [1-3] A meta-analysis conducted by Mottillo et al. showed that MetS is associated with an increased risk of cardiovascular outcomes and all-cause mortality. [4] Another meta-analysis including 43 cohorts reported that the relative risk of cardiovascular events and deaths is 1.78 times greater in individuals with MetS. [5] In addition, a matched cohort study found that participants with MetS have a 2.85-fold (2.27-3.57) and 1.80-fold (1.42-2.28) increase in CHD risk in the unadjusted and fully adjusted models, respectively. [6]

Currently, diverse methods are used to define MetS, including the 2002 US Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III); [7] the 2005 International Diabetes Federation (IDF) criteria; [8] the 2004 Chinese Diabetes Society (CDS) criteria; [9] and the 2009 Joint Interim Statement (JIS) criteria. [10] Although these criteria have similar components, there are also variations. For example, the criteria of the revised NCEP-ATPIII and IDF are the same, but the IDF criteria include abdominal obesity as an obligatory component defining MetS. The CDS criteria consider the importance of each component equal and use the body mass index (BMI) rather than waist circumference (WC) as an index to define obesity. In addition, the cut-off values for specific components in the ATP III criteria differ from those in the revised NCEP-ATPIII and IDF criteria, except for the cut-off value for triglyceride levels. Furthermore, the JIS criteria were created in a collaboration among global expert groups and are similar to the revised NCEP-ATPIII criteria, including the national and regional cut-off values for WC.

The differences among these definitions of MetS have resulted in discrepancies in the reported prevalence of MetS among various populations and difficulties in identifying target populations for the prevention and control of MetS. Most importantly, since MetS is known to be a risk factor for developing CHD, knowledge regarding which MetS definition better reflects the risk of developing CHD is critical.

The present study aimed to investigate the discrepancy in the prevalence of MetS using three different definitions (the revised NCEP-ATP III, the IDF, and the CDS criteria) in the Chinese population. This study also aimed to determine which MetS definition most fully reflects the 10-year probability of developing CHD based on the Framingham risk algorithm.

METHODS

Subjects

We combined data from parts of the China Health and Nutrition Survey to examine the association between health status and changes in economic and social conditions with data from the Influencing Factors of Chronic Diseases Survey. Briefly, this study comprised two cross-sectional studies conducted among residents of Nanshan District in Shenzhen, Guangdong Province in 2015. During the investigation, a complex, multistage probability sample design was used for the distribution of both surveys. In addition, the participants included in the survey were required to be eligible adults who had been living in Nanshan District for at least 6 months.

This study sample consisted of 1820 adults; however, 99 subjects were excluded because anthropometric or biochemical information needed for an accurate diagnosis of MetS was lacking. In total, 1721 participants aged 20 to 80 years old were ultimately eligible for analysis. All participants were informed of the specific details and provided informed consent before the surveys, both of which were approved by the Ethics Committee of the Shenzhen Nanshan Center for Chronic Disease Control.

Patients and public involvement

The patients were not directly involved in the design of the study nor in the recruitment and carrying out of the study. The results of this study will be disseminated to the study participants through different channels. First, we directly communicate with the Community Health Service Center, which will provide the related results to the residents, especially patients with MetS. Second, the work will be published in an open-access peer-reviewed journal to provide everyone with the

opportunity to obtain the information.

Measurements

A face-to-face interview was conducted by an investigator who was trained to administer both surveys. A standardized questionnaire was used to collect information regarding the participants' demographic characteristics, smoking status, drinking status, physical activity, medical history, and medication use. Weight, height, and WC were measured by an investigator using standard measurement methods. Weight and height were measured while the participants were marginally clothed without shoes using an SK-X80 (Sonka Corporation, Shenzhen, China) and recorded to the nearest 0.1 kg. The BMI was calculated as weight in kilograms divided by the square of height in metres. The WC was measured to the nearest 0.1 cm at the midpoint between the lower rib and the iliac crest at the end of normal expiration while the participants were standing. Blood pressure was measured using a standard mercury sphygmomanometer with the cuff on the right upper arm after 5 minutes of rest. Three blood pressure readings were recorded, and the mean of the three readings was calculated.

Laboratory tests

The participants were required to fast overnight (at least 10 hours) before blood collection was conducted by the nurse. Blood was drawn from the vein in the morning at the Community Health Service Center and transferred to the Shenzhen Nanshan Center for Chronic Disease Control for further treatment within 2 hours of blood collection. The blood specimens were collected in a 5-ml EDTA vacuum tube for routine examination and 5-ml coagulation tubes for the biochemical analysis and stored in a cooler during transportation. Once the specimens arrived at the Department of Laboratory Medicine, they were centrifuged at 3000×g for 10 minutes at room temperature instantaneously. The fasting blood glucose (FBG) level, total cholesterol (TC) level, triglycerides (TG) level, low-density lipoprotein concentration (LDL-C), and high-density lipoprotein concentration (HDL-C) were analysed by an automatic

clinical chemistry analyser (HITACH 7080, Tokyo, Japan). FBG, TC, TG, HDL-C, and LDL-C were determined by enzymatic methods.

Definition of MetS and the Framingham risk algorithm

In this study, we used the following three different definitions of MetS: the revised NCEP-ATPIII Criteria for Asians (revised by the American Heart Association and the National Heart, Lung, and Blood Institute (AHA/NHLBI) in 2005 [11] and are the same criteria as those used by the JIS in 2009 [10]), IDF criteria for Asians,[8] and CDS criteria. [9] The details of the three criteria are provided in Table 1. The Framingham risk score was calculated by utilizing the NCEP-ATP III algorithm, [7] which uses the following variables: sex, age, TC, smoking status, HDL-C, and SBP (treatment for hypertension and SBP value). The 10-year probability of developing CHD was calculated based on the risk score by gender. In addition, we defined the 10-year probability of developing CHD as low (<6%), moderate (6-10%), moderately high (10-20%), and high (>20%) [12]. Participants with pre-existing diabetes or self-reported CVD (including heart attack, heart failure, or stroke) were distributed to the high-risk group. Diabetes was defined as having a fasting glucose level of 7.0 mmol/L after a 12-hour fast, use of oral hypoglycaemic agents or insulin, or self-reported diagnosis of diabetes.

Table 1 Definitions of metabolic syndrome

MetS components	Revised NCEP-ATP III criteria (3 or more)	IDF criteria (central obesity and 2 or more)	CDS criteria (BMI and 2 or more)
WC (BMI)	WC≥90/80 cm (M/W)	WC≥90/80 cm (M/W)	BMI≥25 kg/m^2
SBP/DBP	≥130/85 mmHg or MP	≥130/85 mmHg or MP	≥140/90 mmHg or MP
FBG (mmol/L)	≥5.6 mmol/L or MT	≥5.6 mmol/L or MT	≥6.1 mmol/L or MT
TG (mmol/L)	≥1.70 mmol/L	≥1.70 mmol/L	
HDL-C (mmol/L)	<1.0/1.3 mmol/L (M/W)	<1.0/1.3 mmol/L (M/W)	
TG (mmol/L) and HDL-C (mmol/L)			TG≥1.70 mmol/L or (and) HDL-C<0.9/1.0 mmol/L (M/W)

BMI body mass index; WC waist circumference; M men; W women; MP medication for blood pressure; MT medication for blood glucose; FBG fasting blood glucose; SBP systolic blood pressure; DBP diastolic blood pressure; HDL-C high-density lipoprotein cholesterol; LDL-C low-density lipoprotein cholesterol; TG total glycerides;

Statistical analysis

Continuous variables with normal and skewed distributions are expressed as the

means (SD) and medians (interquartile range), respectively. Categorical variables are reported as percentages, and the differences were compared using chi-squares test with or without Bonferroni correction. First, the prevalence of MetS was calculated based on the three definitions of MetS, and the differences were compared. Second, the distribution of the 10-year estimated risk of developing CHD according to each of the three definitions of MetS was compared to determine which definition is the best predictor of CHD development. A two-sided p-value less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS software (version 20.0; SPSS Inc., Chicago, Illinois).

RESULTS

Prevalence of MetS

In total, 1721 participants aged 20 to 80 years were included in this study. The general characteristics of the participants are presented in Table 2. The prevalence of MetS based on the definitions by the revised NCEP-ATP III, IDF, and CDS criteria is presented in Table 3. The age- and sex-adjusted prevalence of MetS among participants aged 20 to 80 years according to the revised ATP III, IDF, and CDS criteria was 30.96%, 19.93%, and 10.88%, respectively. The age-standardized prevalence of MetS among males aged 20 to 80 years according to the revised NCEP-ATP III, IDF, and CDS criteria was 30.21%, 10.85%, and 13.12%, respectively, and that for females aged 20 to 80 years was 31.74%, 29.24%, and 8.58%, respectively. The difference in the prevalence of MetS based on the three definitions was large in both sexes. In particular, the prevalence of MetS based on the revised ATP III criteria in the females was 3.7-fold greater than that based on the CDS criteria.

Table 2 Characteristics of the participants

	Total (n=1721)	Males (n=716, 41.6%)	Females (n=1005, 58.4%)
Age (years)	44.41±12.43	45.23±12.47	43.83±12.38
Body mass index (kg/m^2)	23.68±3.31	24.64±3.16	23.00±3.24
Waist circumference (cm)	82.08±9.84	86.91±9.03	78.63±8.90
Fasting blood glucose (mmol/L)	5.29±1.22	5.43±1.50	5.19±0.96

Triglycerides (mmol/L)	1.47±1.21	1.80±1.41	1.23±0.98
Total cholesterol (mmol/L)	4.28±0.96	4.31±0.96	4.26±0.96
HDL-C (mmol/L)	1.31±0.35	1.15±0.31	1.42±0.34
LDL-C (mmol/L)	2.59±0.80	2.70±0.82	2.50±0.78
SBP (mmHg)	118.46±16.19	122.69±14.77	115.45±16.49
DBP (mmHg)	75.99±10.31	79.58±9.72	73.42±9.93
Hypertension (%)	13.9	16.9	11.8
Diabetes (%)	5.3	6.8	4.2
Dyslipidaemia (%)	10.2	14.5	7.2
Current smoker (%)	5.7	13.0	5.1
Central obesity (%)	24.2	13.3	31.9
10-year probability of developing CHD (%)	1 (1, 2)	2 (0, 8)	1 (1, 1)

Data are expressed as the means±standard deviation, medians (P_{25}, P_{75}), or percentages.

Hypertension, diabetes, and dyslipidaemia were diagnosed before the study; central obesity is defined as ≥80 cm for men and ≥90 cm for women.

The age- and sex-adjusted prevalence of MetS increased with age in those younger than 30 years to those older than 60 years from 17.78% to 36.1%, 9.26% to 35.93%, and 0.44% to 23.17% based on the revised ATP III, IDF, and CDS criteria, respectively. The age-specific prevalence in the females was found to be higher than that in the males according to the IDF criteria (females: 29.24% (95% CI: 26.4-32.1%); males: 10.85% (95% CI: 8.6-13.2%)), but the results were opposite using the CDS criteria (females: 8.58% (95% CI: 7.1-10.6%); males: 13.12% (95% CI: 10.6-15.6%)). An analysis stratified by age according to the revised ATP III criteria showed that the prevalence of MetS in males aged <40 years was higher than that in females in the same age group, while the reverse was true for those aged ≥50 years (Table 3, Figure 1).

Table 3 Prevalence of metabolic syndrome among the study population

Age groups (years)	Revised ATP III criteria			IDF criteria			CDS criteria		
	Men (n=716)	Women (n=1005)	Total (n=1721)	Men (n=716)	Women (n=1005)	Total (n=1721)	Men (n=716)	Women (n=1005)	Total (n=1721)
20~	20.90	14.50	17.78 #	7.50	11.10	9.26 #	0.00	0.90	0.44 #
30~	29.90	22.10	26.04 #	11.90	20.10	15.96 #	10.00	1.70	5.89 #
40~	36.70	30.70	33.74 #	8.20	27.30	17.61 #	13.30	5.20	9.31 #
50~	29.30	40.20	34.64 #	8.30	38.60	23.13 #	18.80	16.30	17.58 #
60~	36.10	54.30	45.30 #	19.30	52.20	35.93 #	26.10	20.30	23.17 #

Overall	35.5 (32.0-39.0)	28.3 (25.5-31.0)	31.6 # (29.4-33.8)	25.2 (22.0-28.3)	25.4 (22.7-28.1)	25.3 # (23.2-27.3)	27.9 (24.6-31.2)	10.9 (9.0-12.9)	18.7 # (16.9-20.6)
Overall (standardized)	30.21 * (26.8-33.5)	31.74 * (28.9-34.6)	30.96 + (28.8-33.2)	10.85 * (8.6-13.2)	29.24 * (26.4-32.1)	19.93+ (18.0-21.8)	13.12 * (10.6-15.6)	8.58 * (7.1-10.6)	10.88 + (9.4-12.3)

*Age-adjusted percentages for men and women. # Sex-adjusted percentages for each age group. +Age- and sex-adjusted percentages.

Adjustment was conducted using sample survey data from 1% of the population in 2015 by direct methods.

Ten-year probability of developing CHD according to the MetS status

The Framingham risk algorithm was used to estimate the 10-year probability of developing CHD. The distributions of the 10-year estimated risk of developing CHD based on the three different definitions of MetS were compared (Table 4). Among those with MetS, based on the CDS criteria, 39.4% had a 10-year CHD risk of 6% (low), 6.7% had a 10-year CHD risk of 6-10% (moderate), 7.2% had a 10-year CHD risk of 10-20% (moderately high), and 7.2% had a 10-year CHD risk of 20% (high). The remaining 39.4% of participants with MetS had diabetes and/or CVD. In contrast, among those without MetS, a considerably higher proportion had a low risk (85.0%), and lower proportions had a moderate (3.3%), moderately high (5.5%), or high risk (1.6%) or had diabetes and/or CVD (4.7%) (χ^2=157.65, p<0.001). Similar heterogeneity in those with MetS and those without MetS was found based on the revised NCEP-ATP III criteria (χ^2=45.17, p<0.001) and the IDF criteria (χ^2=306.15, p<0.001). Of those with MetS, based on the revised NCEP-ATP III criteria and the IDF criteria, 67.5% and 74.2% had a low risk, 3.5% and 3.0% had a moderate risk, 5.2% and 3.3% had a moderately high risk, and 23.8% and 19.5% had a high risk or had diabetes and/or CVD, respectively. There were no significant differences in the CHD risk distributions of those with MetS based on the revised NCEP-ATP III criteria and the IDF criteria (χ^2=5.36, p=0.252), while a significant difference was observed based on the CDS criteria (with the revised NCEP-ATP III criteria: χ^2=45.71, with IDF: χ^2=62.69, all p<0.001, Figure 2).

We further compared the distribution of the 10-year estimated risk of developing CHD based on the three different MetS definitions in the males and females (Figure 3). There were no significant differences in the distribution of the 10-year estimated

risk of developing CHD in males with MetS among the three definitions, except for between the revised NCEP-ATP III criteria and the CDS criteria (χ^2=17.41, p=0.002). As shown in Figure 3, a significant difference was found in the 10-year risk in females with MetS based on the CDS definition and the remaining definitions (with revised NCEP-ATP III criteria: χ^2=25.33, with IDF: χ^2=37.09, all p<0.001), while no significant difference was found based on the revised NCEP-ATP III criteria and the IDF criteria (χ^2=37.09, p=0.245). Compared to the females, a higher CHD risk was found in the males using all three definitions (revised NCEP-ATP III: χ^2=72.83; IDF: χ^2=63.60; CDS: χ^2=23.84; all p<0.001, Figure 3).

Table 4 Distribution of the 10-year estimated risk of developing CHD based on the three definitions of MetS

		Revised ATP III criteria	IDF criteria	CDS criteria
MetS(+)	Low (<6%)	67.5	74.2	39.4
	Moderate (6-10%)	3.5	3	6.7
	Moderate High (10-20%)	5.2	3.3	7.2
	High (>20%)	3.7	3.5	7.2
	DM/CVD	20.1	16	39.4
MetS(-)	Low (<6%)	86.1	81.9	85
	Moderate (6-10%)	3.7	3.8	3.3
	Moderate High (10-20%)	5.9	6.3	5.5
	High (>20%)	1.4	1.8	1.6
	DM/CVD	2.9	6.2	4.7
p-value		<0.001	<0.001	<0.001

p-value: based on a comparison of the distributions of risk groups between those with and those without metabolic syndrome

DISCUSSION

This study shows that the prevalence of MetS and the distribution of the 10-year estimated risk of developing CHD vary depending on how MetS is defined. In this study, the difference among the revised NCEP-ATP III, IDF, and CDS criteria was evaluated. The 10-year risk of developing CHD was significantly higher in the participants with MetS than that in the participants without MetS, and all three definitions demonstrated better performance in reflecting the risk of developing CHD in males than in females. Compared to the other criteria, the participants with MetS based on the CDS criteria had a higher 10-year CHD risk; however, the CDS criteria

also led to the lowest prevalence of MetS.

The previous study have examined the ability of different MetS definitions in predicting cardiovascular diseases. [13-17] However, to the best of our knowledge, the findings were inconsistent. Similarly, this study was not the first to estimate the 10-year probability in individuals with MetS based on the Framingham risk algorithm. [12 18] Suzuki et al. [18] used the Framingham risk score rather than the 10-year probability of developing CHD to compare the differences among four different MetS definitions. Their results showed that the risk score in males with MetS was significantly higher by three-fold than that in females with MetS based on all four diagnostic criteria. However, the results failed to accurately compare the difference between males and females because females are required to have a higher score in each risk category. Therefore, in the present study, we compared the distribution of the 10-year estimated risk of developing CHD between males and females. Our study revealed that all three evaluated definitions of MetS had better performance in reflecting the 10-year CHD risk in males than in females. Furthermore, similar to studies conducted in other populations [19 20], there were significant differences in the prevalence of MetS between the males and females. A greater number of females met the diagnostic criteria of MetS using the IDF criteria, while the CDS criteria led to a greater number of males having MetS. There was no significant difference in the prevalence of MetS between the females and males based on the revised NCEP-ATP III criteria. The finding that the 10-year probability of developing CHD in males differed based on the definition of MetS is consistent with the findings of previous studies. Mak et al. [21] suggested that the adverse impact of MetS was greater among males than females, which is consistent with another study. [15] Therefore, the impacts of various risk factors on cardiovascular diseases and their outcomes appear to differ according to sex in patients with MetS. [22] Notably, different forms of obesity have different impacts on cardiovascular disease risk. In particular, android obesity, which is more common in males and postmenopausal females, [23] is associated with future cardiovascular events. [24] This sex difference may also be due to other characteristics of the subjects, such as age and smoking status. In contrast, some studies [5 13 25] have

suggested that all definitions of MetS (NCEP-ATP III, IDF, AHA/NHLBL, and JIS) are more predictive of the CHD risk in females than in males.

Among the definitions of MetS evaluated in the current study, the IDF criteria identified fewer participants (19.93%) as having MetS than the revised NCEP-ATP III criteria (30.96%), but this lower prevalence did not translate into better performance. There was no significant difference in the distribution of the 10-year risk of developing CHD between the revised NCEP-ATP III and the IDF criteria. This finding is consistent with the results of previous studies in which similar risks of cardiovascular diseases were reported with different levels of sensitivity depending on the definition of MetS. [13 26 27] The lower prevalence based on the IDF criteria may be due to the requirement of central obesity for the diagnosis of MetS, even though these criteria share the same components and same cut-off values. Compared to the revised ATP III criteria, this demand decreases the number of individuals satisfying the criteria for MetS under the IDF criteria. In addition, if the threshold value of abdominal obesity differs among different MetS definitions, the discrepancy in prevalence may be reversed. For instance, Scuteri et al. [19] reported that the prevalence of MetS based on the IDF criteria was higher than that based on the ATP criteria, which may result from the lower waist circumstance threshold values applied to the European population by the IDF. Notably, a recent cohort study conducted by Keihani [28] showed that abdominal obesity and the presence of metabolic derangements are both relevant risk factors for future CVD. Similar results were found in another study by Zhao et al., [29] who compared the long-term risk of cardiovascular diseases between patients with MetS with or without central obesity. These authors found that most patients with MetS (78%) had central obesity, and no significant difference was observed in the 10-year absolute and relative risk of CHD and ischaemic CVD events between the two MetS groups. This finding highlights the fact that focusing on abdominal obesity while ignoring the other components of MetS may not be ideal. Another study [16] using an ROC curve and Cox regression analyses showed that the ATP III criteria better predicted CVD than the IDF criteria.

Compared to the other criteria, the CDS criteria led to the lowest prevalence of

MetS and the highest 10-year probability of developing CHD in the current study. Our findings are partially consistent with the results of previous studies in which CDS had the highest specificity in identifying MetS in a Chinese population based on a 6.3-year cohort study. [16] However, despite the high specificity, the study also found that the CDS criteria had the lowest sensitivity among the three definitions, and more than 50% of patients may be misdiagnosed. More subjects were diagnosed with obesity (BMI ≥25 kg/m^2) than central obesity (32.31% *vs* 24.17%). Therefore, the lowest prevalence and the highest risk of developing CHD are mainly caused by the thresholds of high blood pressure and elevated blood glucose in the CDS criteria, which are higher than those in the other criteria. However, discussing the superiority of the MetS definition that adopts BMI or waist circumference as an index of adiposity is necessary. Some studies posit that WC is a more advantageous index of adiposity. According to Scuteri et al., [30] WC is a significant predictor of new onset MetS. In addition, Scuteri et al.[31] indicated that WC correlated with arterial properties better than BMI and that as the WC increased, the arterial structure and function significantly changed within each BMI quartile, even though the cluster of MetS including abdominal adiposity has been consistently associated with arterial damage. [32 33]

The strength of our study should be mentioned. The complex, multistage probability sample design is fairly representative of the Chinese population in Shenzhen. In addition, the percentage of missing data is generally low. However, there are several limitations to our study. First, although the original Framingham CHD risk assessment has been validated in previous studies, [34] the algorithm does not include obesity and cardiorespiratory fitness,[35-37] which could have potentially influenced the risk estimation. Furthermore, a previous report found that the Framingham algorithm overestimates the risk of CHD in the Chinese population. [38] Second, our analysis was based on cross-sectional data; therefore, we were unable to calculate positive and negative predictive values for CHD or determine which MetS definition is the most predictive of the development of CHD. Thus, the results should be interpreted with caution. Further studies conducted in China, especially longitudinal studies, are needed to determine which MetS definition is best suited for predicting CHD.

This study contributes to the body of evidence showing that differences exist in the prevalence and distribution of the 10-year estimated risk of developing CHD depending on the definition of MetS. Among the definitions evaluated (the revised NCEP-ATP III, IDF, and CDS criteria), the CDS criteria led to the highest 10-year probability of developing CHD and the lowest prevalence of MetS. A significant finding of this study was that all three definitions of MetS had better performance in males compared to females.

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Contributors The author contributions were as follows: Xiaolin Peng and Liping Hao conceived and designed the study and critically revised the manuscript; Juan Zhou analysed the data and wrote the paper; Qin Gao and Jun Wang participated in the laboratory assay; and Ming Zhang, Jianping Ma, Changyi Wang and Hongen Chen collected the data and revised the manuscript. All authors read and approved the final version of the manuscript.

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Competing interests None.

Ethical approval The study was approved by the Ethics Committee of the Shenzhen Nanshan Center for Chronic Disease Control.

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REFERENCES

1. Sattar N, Gaw A, Scherbakova O, et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation* 2003;108(4):414-9.
2. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes care* 2005;28(7):1769-78.

3. Noda H, Iso H, Saito I, et al. The impact of the metabolic syndrome and its components on the incidence of ischemic heart disease and stroke: the Japan public health center-based study. *Hypertens Res* 2009;32(4):289-98.
4. Mottillo S, Filion KB, Genest J, et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. *J Am Coll Cardiol* 2010;56(14):1113-32.
5. Gami AS, Witt BJ, Howard DE, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol* 2007;49(4):403-14.
6. Esteghamati A, Hafezi-Nejad N, Sheikhbahaei S, et al. Risk of coronary heart disease associated with metabolic syndrome and its individual components in Iranian subjects: a matched cohort study. *J Clin Lipidol* 2014;8(3):279-86.
7. National Cholesterol Education Program Expert Panel on Detection E, Treatment of High Blood Cholesterol in A. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;106(25):3143-421.
8. Alberti KG, Zimmet P, Shaw J, et al. The metabolic syndrome--a new worldwide definition. *Lancet* 2005;366(9491):1059-62.
9. Metabolic syndrome study cooperation group of Chinese diabetes society. *Chinese Journal of Diabetes Mellitus* 2004;12(3):156-61.
10. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120(16):1640-5.
11. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement: Executive Summary. *Crit Pathw Cardiol* 2005;4(4):198-203.
12. Hoang KC, Ghandehari H, Lopez VA, et al. Global coronary heart disease risk assessment of individuals with the metabolic syndrome in the U.S. *Diabetes care* 2008;31(7):1405-9.
13. Hosseinpanah F, Asghari G, Barzin M, et al. Prognostic impact of different definitions of metabolic syndrome in predicting cardiovascular events in a cohort of non-diabetic Tehranian adults. International journal of cardiology 2013;168(1):369-74.
14. Kastorini CM, Panagiotakos DB, Georgousopoulou EN, et al. Metabolic syndrome and 10-year cardiovascular disease incidence: The ATTICA study. Nutrition, metabolism, and cardiovascular diseases : NMCD 2016;26(3):223-31.
15. Qiao Q, Group DS. Comparison of different definitions of the metabolic syndrome in relation to cardiovascular mortality in European men and women. Diabetologia 2006;49(12):2837-46.
16. Zhou H, Guo ZR, Yu LG, et al. Evidence on the applicability of the ATPIII, IDF and CDS metabolic syndrome diagnostic criteria to identify CVD and T2DM in the Chinese population from a 6.3-year cohort study in mid-eastern China. Diabetes research and clinical practice 2010;90(3):319-25.
17. Scuteri A, Najjar SS, Morrell CH, et al. The metabolic syndrome in older individuals: prevalence and prediction of cardiovascular events: the Cardiovascular Health Study. Diabetes care 2005;28(4):882-7.

18. Suzuki T, Zeng Z, Zhao B, et al. Comparison of coronary heart disease risk among four diagnostic definitions of metabolic syndrome. Journal of endocrinological investigation 2016;39(11):1337-46.
19. Scuteri A, Najjar SS, Orru M, et al. Age- and gender-specific awareness, treatment, and control of cardiovascular risk factors and subclinical vascular lesions in a founder population: the SardiNIA Study. Nutrition, metabolism, and cardiovascular diseases : NMCD 2009;19(8):532-41.
20. Scuteri A, Laurent S, Cucca F, et al. Metabolic syndrome across Europe: different clusters of risk factors. European journal of preventive cardiology 2015;22(4):486-91.
21. Mak KH, Ma S, Heng D, et al. Impact of sex, metabolic syndrome, and diabetes mellitus on cardiovascular events. The American journal of cardiology 2007;100(2):227-33.
22. Regitz-Zagrosek V, Lehmkuhl E, Weickert MO. Gender differences in the metabolic syndrome and their role for cardiovascular disease. Clinical research in cardiology : official journal of the German Cardiac Society 2006;95(3):136-47.
23. Williams CM. Lipid metabolism in women. The Proceedings of the Nutrition Society 2004;63(1):153-60.
24. Ibrahim MM. Subcutaneous and visceral adipose tissue: structural and functional differences. Obesity reviews : an official journal of the International Association for the Study of Obesity 2010;11(1):11-8.
25. Wang C, Hou X, Bao Y, et al. The metabolic syndrome increased risk of cardiovascular events in Chinese--a community based study. International journal of cardiology 2010;139(2):159-65.
26. Mancia G, Bombelli M, Facchetti R, et al. Impact of different definitions of the metabolic syndrome on the prevalence of organ damage, cardiometabolic risk and cardiovascular events. Journal of hypertension 2010;28(5):999-1006.
27. Nilsson PM, Engstrom G, Hedblad B. The metabolic syndrome and incidence of cardiovascular disease in non-diabetic subjects--a population-based study comparing three different definitions. Diabetic medicine : a journal of the British Diabetic Association 2007;24(5):464-72.
28. Keihani S, Hosseinpanah F, Barzin M, et al. Abdominal obesity phenotypes and risk of cardiovascular disease in a decade of follow-up: the Tehran Lipid and Glucose Study. Atherosclerosis 2015;238(2):256-63.
29. Zhao D, Grundy SM, Wang W, et al. Ten-year cardiovascular disease risk of metabolic syndrome without central obesity in middle-aged chinese. The American journal of cardiology 2007;100(5):835-9.
30. Scuteri A, Morrell CH, Najjar SS, et al. Longitudinal paths to the metabolic syndrome: can the incidence of the metabolic syndrome be predicted? The Baltimore Longitudinal Study of Aging. The journals of gerontology Series A, Biological sciences and medical sciences 2009;64(5):590-8.
31. Scuteri A, Orru M, Morrell CH, et al. Associations of large artery structure and function with adiposity: effects of age, gender, and hypertension. The SardiNIA Study. Atherosclerosis 2012;221(1):189-97.
32. Scuteri A, Cunha PG, Rosei EA, et al. Arterial stiffness and influences of the metabolic syndrome: a cross-countries study. Atherosclerosis 2014;233(2):654-60.
33. Scuteri A, Najjar SS, Orru M, et al. The central arterial burden of the metabolic syndrome is similar in men and women: the SardiNIA Study. European heart journal 2010;31(5):602-13.
34. D'Agostino RB, Sr., Grundy S, Sullivan LM, et al. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. Jama 2001;286(2):180-7.

35. Lavie CJ, Deedwania P, Ortega FB. Obesity is rarely healthy. The Lancet Diabetes & Endocrinology 2018
36. Kennedy AB, Lavie CJ, Blair SN. Fitness or Fatness: Which Is More Important? Jama 2018;319(3):231-32.
37. Deedwania P, Lavie CJ. Dangers and Long-Term Outcomes in Metabolically Healthy Obesity: The Impact of the Missing Fitness Component. Journal of the American College of Cardiology 2018;71(17):1866-68.
38. Liu J, Hong Y, D'Agostino RB, Sr., et al. Predictive value for the Chinese population of the Framingham CHD risk assessment tool compared with the Chinese Multi-Provincial Cohort Study. Jama 2004;291(21):2591-9.

Figure legends:

Figure 1 Prevalence of MetS among adults aged 20 to 80 years in this study area.

Figure 2 The distribution of the 10-year estimated risk for CHD in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (<6%), moderate (6 to 10%),moderately high (10 to 20%), and high (>20% or history of diabetes or CVD).

Figure 3 The distribution of the 10-year estimated risk for CHD by sex in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (<6%), moderate (6 to 10%),moderately high (10 to 20%), and high (>20% or history of diabetes or CVD).

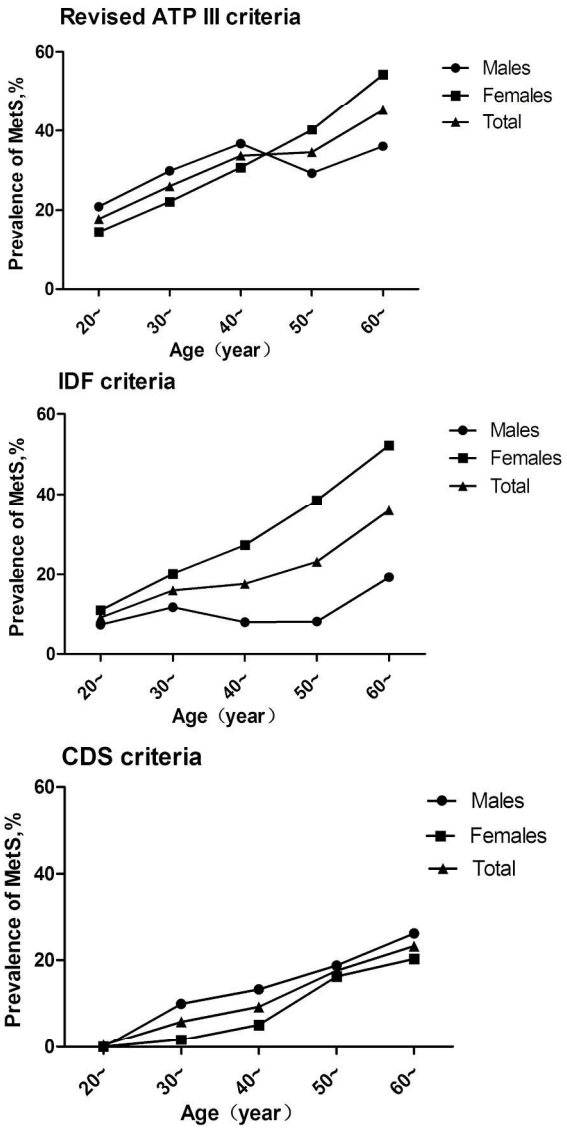

Figure 1 Prevalence of MetS among adults aged 20 to 80 years in the study area

Figure 1

187x293mm (300 x 300 DPI)

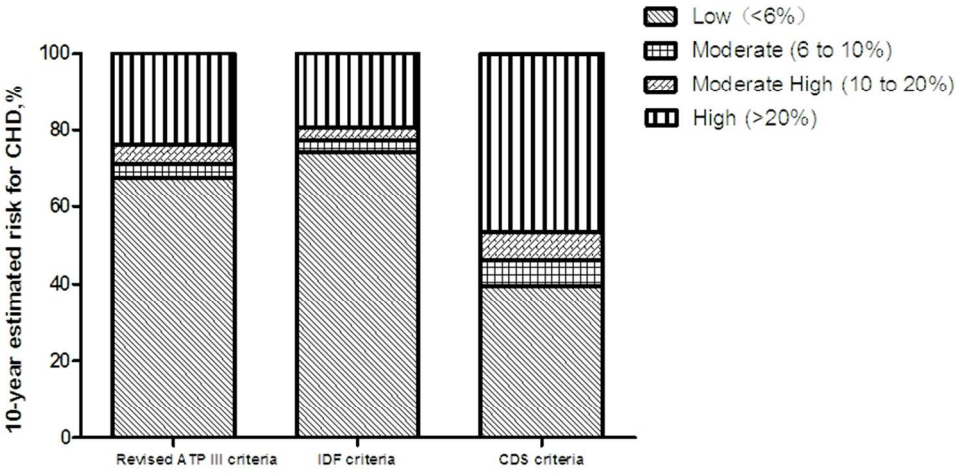

Figure 2 The distribution of the 10-year estimated risk for CHD in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (<6%), moderate (6 to 10%), moderately high (10-20%), and high (>20% or history of diabetes or CVD).

Figure 2

79x50mm (300 x 300 DPI)

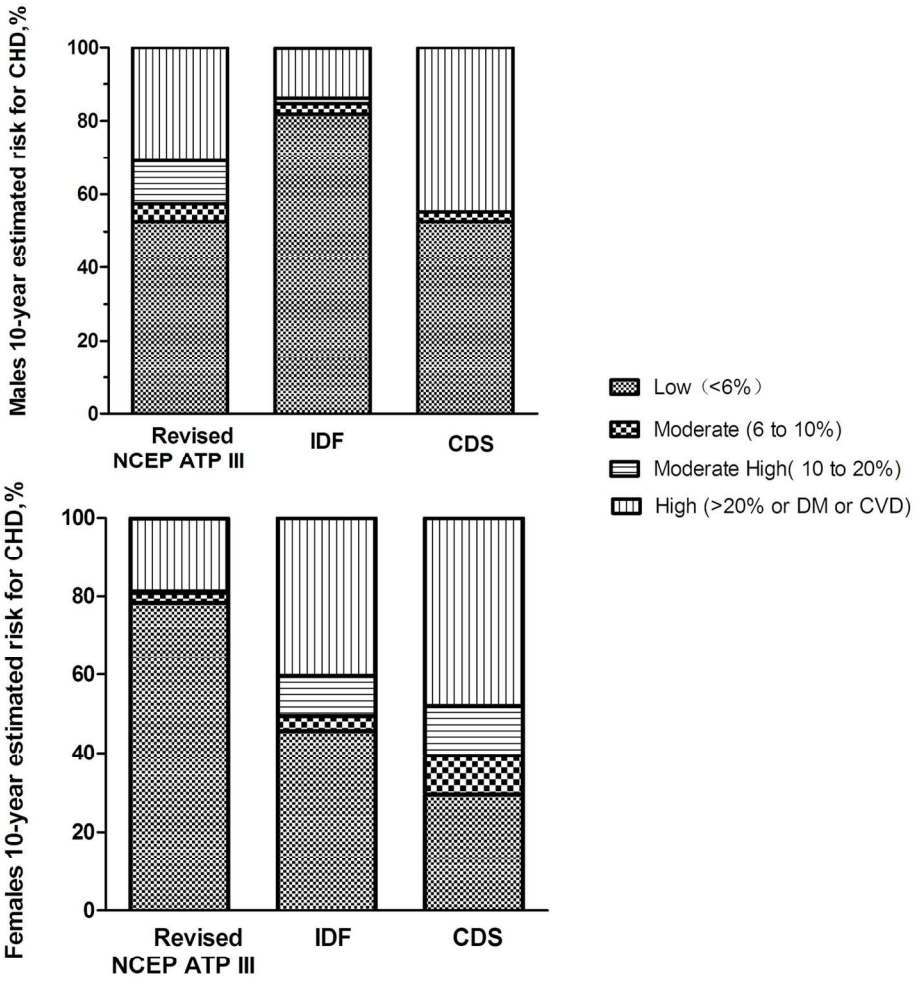

Figure 3 The distribution of the 10-year estimated risk for CHD by sex in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (>6%), moderate (6 to 10 %),moderately high (10 to 20%), and high (?20% or history of diabetes or CVD).

Figure 3

143x172mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	*6*
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			7

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Comparison of coronary heart disease risk assessments among individuals with metabolic syndrome using three diagnostic definitions: A cross-sectional study from China

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Comparison of coronary heart disease risk assessments among individuals with metabolic syndrome using three diagnostic definitions: A cross-sectional study from China

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ABSTRACT

Objective: Metabolic syndrome (MetS) is a notable risk factor of coronary heart disease (CHD). However, there are difference in the methods used to define MetS. The purpose of this study was to determine which MetS definition most fully reflects the 10-year probability of CHD based on the Framingham risk algorithm.

Design: Cross-sectional study.

Setting: Data were obtained from the China Health and Nutrition Survey and the Influencing Factors of Chronic Diseases Survey conducted among residents of Nanshan District in Shenzhen, China.

Participants: In total, 1721 participants aged 20-80 years were included in this study.

Methods: MetS was diagnosed according to the criteria of the National Cholesterol Education Program's Adult Treatment Panel (revised NCEP-ATP III), the International Diabetes Federation (IDF), and the Chinese Diabetes Society (CDS). The NCEP-ATP III algorithm was used to calculate the Framingham risk score, and the Framingham risk score was used to define the probability of developing CHD within 10 years either as low (<6%), moderate (6-10%), moderately high (10-20%), or high (>20%). Chi-square tests with or without the Bonferroni correction were used to compare the differences in the distribution of the 10-year estimated risk of developing CHD among the three definitions.

Results: Compared to the other definitions, the revised NCEP-ATP III criteria identified more participants (30.96%, 95% CI: 28.8%-33.2%) as having MetS, while the CDS criteria showed the highest 10-year probability of developing CHD. The 10-year probability of developing CHD in the participants with MetS was significantly higher than that in the participants without MetS (CDS: $\chi2=157.65$, revised ATP III: $\chi2=45.17$, IDF: $\chi2=306.15$, all $p<0.001$), and all definitions more fully reflect the CHD risk in males than in females (revised NCEP-ATP III: $\chi2=72.83$; IDF: $\chi2=63.60$; CDS: $\chi2=23.84$; all $p<0.001$).

Conclusions: This study demonstrates the differences in the prevalence and distribution of the 10-year estimated risk of developing CHD based on the definition of MetS. A significant finding of this study is that the MetS definitions have better

performance for males than for females. Further studies in China, especially longitudinal studies, are needed to determine which definition of MetS is best suited for predicting CHD risk.

Strengths and limitations of this study

1. The complex, multistage probability sample design is fairly representative of the Chinese population in Shenzhen.
2. There was a low percentage of missing data in general.
3. Three definitions of MetS were used to compare the discrepancy in the prevalence of MetS and the 10-year probability of developing CHD based on the Framingham risk score.
4. The Framingham algorithm may overestimate the risk of developing CHD in a Chinese population.
5. This study adopted a cross-sectional design, and cohort studies are needed to further prove the predictive value and determine which MetS definition is the most predictive of the development of CHD.

INTRODUCTION

Metabolic syndrome (MetS) is typically diagnosed based on abnormalities in a specific set of clinical measures and is associated with an increased risk of developing coronary heart disease (CHD). [1-3] A meta-analysis conducted by Mottillo et al. showed that MetS is associated with an increased risk of cardiovascular outcomes and all-cause mortality.[4] Another meta-analysis including 43 cohorts reported that the relative risk of cardiovascular events and deaths is 1.78 times greater in individuals with MetS. [5] In addition, a matched cohort study found that participants with MetS have a 2.85-fold (2.27-3.57) and 1.80-fold (1.42-2.28) increase in CHD risk in the unadjusted and fully adjusted models, respectively. [6]

Currently, diverse methods are used to define MetS, including the 2002 US Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III); [7] the 2005 International Diabetes Federation (IDF) criteria; [8] the 2004 Chinese Diabetes Society (CDS) criteria; [9] and the 2009 Joint Interim Statement (JIS) criteria. [10] Although these criteria have similar components, there are also variations. For example, the criteria of the revised NCEP-ATPIII and IDF are the same, but the IDF criteria include abdominal obesity as an obligatory component defining MetS. The CDS criteria consider the importance of each component equal and use the body mass index (BMI) rather than waist circumference (WC) as an index to define obesity. In addition, the cut-off values for specific components in the ATP III criteria differ from those in the revised NCEP-ATPIII and IDF criteria, except for the cut-off value for triglyceride levels. Furthermore, the JIS criteria were created in a collaboration among global expert groups and are similar to the revised NCEP-ATPIII criteria, including the national and regional cut-off values for WC.

The differences among these definitions of MetS have resulted in discrepancies in the reported prevalence of MetS among various populations and difficulties in identifying target populations for the prevention and control of MetS. Most importantly, since MetS is known to be a risk factor for developing CHD, knowledge regarding which MetS definition better reflects the risk of developing CHD is critical.

The present study aimed to investigate the discrepancy in the prevalence of MetS using three different definitions (the revised NCEP-ATP III, the IDF, and the CDS criteria) in the Chinese population. This study also aimed to determine which MetS definition most fully reflects the 10-year probability of developing CHD based on the Framingham risk algorithm.

METHODS

Subjects

We combined data from parts of the China Health and Nutrition Survey to examine the association between health status and changes in economic and social conditions with data from the Influencing Factors of Chronic Diseases Survey. Briefly, this study comprised two cross-sectional studies conducted among residents of Nanshan District in Shenzhen, Guangdong Province in 2015. During the investigation, a complex, multistage probability sample design was used for the distribution of both surveys. In addition, the participants included in the survey were required to be eligible adults who had been living in Nanshan District for at least 6 months.

This study sample consisted of 1820 adults; however, 99 subjects were excluded because anthropometric or biochemical information needed for an accurate diagnosis of MetS was lacking. In total, 1721 participants aged 20 to 80 years old were ultimately eligible for analysis. All participants were informed of the specific details and provided informed consent before the surveys, both of which were approved by the Ethics Committee of the Shenzhen Nanshan Center for Chronic Disease Control.

Patients and public involvement

The patients were not directly involved in the design of the study nor in the recruitment and carrying out of the study. The results of this study will be disseminated to the study participants through different channels. First, we directly communicate with the Community Health Service Center, which will provide the related results to the residents, especially patients with MetS. Second, the work will be published in an open-access peer-reviewed journal to provide everyone with the

opportunity to obtain the information.

Measurements

A face-to-face interview was conducted by an investigator who was trained to administer both surveys. A standardized questionnaire was used to collect information regarding the participants' demographic characteristics, smoking status, drinking status, physical activity, medical history, and medication use. Weight, height, and WC were measured by an investigator using standard measurement methods. Weight and height were measured while the participants were marginally clothed without shoes using an SK-X80 (Sonka Corporation, Shenzhen, China) and recorded to the nearest 0.1 kg. The BMI was calculated as weight in kilograms divided by the square of height in metres. The WC was measured to the nearest 0.1 cm at the midpoint between the lower rib and the iliac crest at the end of normal expiration while the participants were standing. Blood pressure was measured using a standard mercury sphygmomanometer with the cuff on the right upper arm after 5 minutes of rest. Three blood pressure readings were recorded, and the mean of the three readings was calculated.

Laboratory tests

The participants were required to fast overnight (at least 10 hours) before blood collection was conducted by the nurse. Blood was drawn from the vein in the morning at the Community Health Service Center and transferred to the Shenzhen Nanshan Center for Chronic Disease Control for further treatment within 2 hours of blood collection. The blood specimens were collected in a 5-ml EDTA vacuum tube for routine examination and 5-ml coagulation tubes for the biochemical analysis and stored in a cooler during transportation. Once the specimens arrived at the Department of Laboratory Medicine, they were centrifuged at 3000×g for 10 minutes at room temperature instantaneously. The fasting blood glucose (FBG) level, total cholesterol (TC) level, triglycerides (TG) level, low-density lipoprotein concentration (LDL-C), and high-density lipoprotein concentration (HDL-C) were analysed by an automatic

clinical chemistry analyser (HITACH 7080, Tokyo, Japan). FBG, TC, TG, HDL-C, and LDL-C were determined by enzymatic methods.

Definition of MetS and the Framingham risk algorithm

In this study, we used the following three different definitions of MetS: the revised NCEP-ATPIII Criteria for Asians (revised by the American Heart Association and the National Heart, Lung, and Blood Institute (AHA/NHLBI) in 2005 [11] and are the same criteria as those used by the JIS in 2009 [10]), IDF criteria for Asians,[8] and CDS criteria. [9] The details of the three criteria are provided in Table 1. The Framingham risk score was calculated by utilizing the NCEP-ATP III algorithm, [7] which uses the following variables: sex, age, TC, smoking status, HDL-C, and SBP (treatment for hypertension and SBP value). The 10-year probability of developing CHD was calculated based on the risk score by gender. In addition, we defined the 10-year probability of developing CHD as low (<6%), moderate (6-10%), moderately high (10-20%), and high (>20%) [12]. Participants with pre-existing diabetes or self-reported CVD (including heart attack, heart failure, or stroke) were distributed to the high-risk group. Diabetes was defined as having a fasting glucose level of 7.0 mmol/L after a 12-hour fast, use of oral hypoglycaemic agents or insulin, or self-reported diagnosis of diabetes.

Table 1 Definitions of metabolic syndrome

MetS components	Revised NCEP-ATP III criteria (3 or more)	IDF criteria (central obesity and 2 or more)	CDS criteria (BMI and 2 or more)
WC (BMI)	WC≥90/80 cm (M/W)	WC≥90/80 cm (M/W)	BMI≥25 kg/m^2
SBP/DBP	≥130/85 mmHg or MP	≥130/85 mmHg or MP	≥140/90 mmHg or MP
FBG (mmol/L)	≥5.6 mmol/L or MT	≥5.6 mmol/L or MT	≥6.1 mmol/L or MT
TG (mmol/L)	≥1.70 mmol/L	≥1.70 mmol/L	
HDL-C (mmol/L)	<1.0/1.3 mmol/L (M/W)	<1.0/1.3 mmol/L (M/W)	
TG (mmol/L) and HDL-C (mmol/L)			TG≥1.70 mmol/L or (and) HDL-C<0.9/1.0 mmol/L (M/W)

BMI body mass index; WC waist circumference; M men; W women; MP medication for blood pressure; MT medication for blood glucose; FBG fasting blood glucose; SBP systolic blood pressure; DBP diastolic blood pressure; HDL-C high-density lipoprotein cholesterol; LDL-C low-density lipoprotein cholesterol; TG total glycerides;

Statistical analysis

Continuous variables with normal and skewed distributions are expressed as the

means (SD) and medians (interquartile range), respectively. Categorical variables are reported as percentages, and the differences were compared using chi-squares test with or without Bonferroni correction. First, the prevalence of MetS was calculated based on the three definitions of MetS, and the differences were compared. Second, the distribution of the 10-year estimated risk of developing CHD according to each of the three definitions of MetS was compared to determine which definition is the best predictor of CHD development. A two-sided p-value less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS software (version 20.0; SPSS Inc., Chicago, Illinois).

RESULTS

Prevalence of MetS

In total, 1721 participants aged 20 to 80 years were included in this study. The general characteristics of the participants are presented in Table 2. The prevalence of MetS based on the definitions by the revised NCEP-ATP III, IDF, and CDS criteria is presented in Table 3. The age- and sex-adjusted prevalence of MetS among participants aged 20 to 80 years according to the revised ATP III, IDF, and CDS criteria was 30.96%, 19.93%, and 10.88%, respectively. The age-standardized prevalence of MetS among males aged 20 to 80 years according to the revised NCEP-ATP III, IDF, and CDS criteria was 30.21%, 10.85%, and 13.12%, respectively, and that for females aged 20 to 80 years was 31.74%, 29.24%, and 8.58%, respectively. The difference in the prevalence of MetS based on the three definitions was large in both sexes. In particular, the prevalence of MetS based on the revised ATP III criteria in the females was 3.7-fold greater than that based on the CDS criteria.

Table 2 Characteristics of the participants

	Total (n=1721)	Males (n=716, 41.6%)	Females (n=1005, 58.4%)
Age (years)	44.41±12.43	45.23±12.47	43.83±12.38
Body mass index (kg/m^2)	23.68±3.31	24.64±3.16	23.00±3.24
Waist circumference (cm)	82.08±9.84	86.91±9.03	78.63±8.90
Fasting blood glucose (mmol/L)	5.29±1.22	5.43±1.50	5.19±0.96

Triglycerides (mmol/L)	1.47±1.21	1.80±1.41	1.23±0.98
Total cholesterol (mmol/L)	4.28±0.96	4.31±0.96	4.26±0.96
HDL-C (mmol/L)	1.31±0.35	1.15±0.31	1.42±0.34
LDL-C (mmol/L)	2.59±0.80	2.70±0.82	2.50±0.78
SBP (mmHg)	118.46±16.19	122.69±14.77	115.45±16.49
DBP (mmHg)	75.99±10.31	79.58±9.72	73.42±9.93
Hypertension (%)	13.9	16.9	11.8
Diabetes (%)	5.3	6.8	4.2
Dyslipidaemia (%)	10.2	14.5	7.2
Current smoker (%)	5.7	13.0	5.1
Central obesity (%)	24.2	13.3	31.9
10-year probability of developing CHD (%)	1 (1, 2)	2 (0, 8)	1 (1, 1)

Data are expressed as the means±standard deviation, medians (P_{25}, P_{75}), or percentages.

Hypertension, diabetes, and dyslipidaemia were diagnosed before the study; central obesity is defined as ≥80 cm for men and ≥90 cm for women.

The age- and sex-adjusted prevalence of MetS increased with age in those younger than 30 years to those older than 60 years from 17.78% to 36.1%, 9.26% to 35.93%, and 0.44% to 23.17% based on the revised ATP III, IDF, and CDS criteria, respectively. The age-specific prevalence in the females was found to be higher than that in the males according to the IDF criteria (females: 29.24% (95% CI: 26.4-32.1%); males: 10.85% (95% CI: 8.6-13.2%)), but the results were opposite using the CDS criteria (females: 8.58% (95% CI: 7.1-10.6%); males: 13.12% (95% CI: 10.6-15.6%)). An analysis stratified by age according to the revised ATP III criteria showed that the prevalence of MetS in males aged <40 years was higher than that in females in the same age group, while the reverse was true for those aged ≥50 years (Table 3, Figure 1).

Table 3 Prevalence of metabolic syndrome among the study population

Age groups (years)	Revised ATP III criteria			IDF criteria			CDS criteria		
	Men (n=716)	Women (n=1005)	Total (n=1721)	Men (n=716)	Women (n=1005)	Total (n=1721)	Men (n=716)	Women (n=1005)	Total (n=1721)
20~	20.90	14.50	17.78 #	7.50	11.10	9.26 #	0.00	0.90	0.44 #
30~	29.90	22.10	26.04 #	11.90	20.10	15.96 #	10.00	1.70	5.89 #
40~	36.70	30.70	33.74 #	8.20	27.30	17.61 #	13.30	5.20	9.31 #
50~	29.30	40.20	34.64 #	8.30	38.60	23.13 #	18.80	16.30	17.58 #
60~	36.10	54.30	45.30 #	19.30	52.20	35.93 #	26.10	20.30	23.17 #

Overall	35.5 (32.0-39.0)	28.3 (25.5-31.0)	31.6 # (29.4-33.8)	25.2 (22.0-28.3)	25.4 (22.7-28.1)	25.3 # (23.2-27.3)	27.9 (24.6-31.2)	10.9 (9.0-12.9)	18.7 # (16.9-20.6)
Overall (standardized)	30.21 * (26.8-33.5)	31.74 * (28.9-34.6)	30.96 + (28.8-33.2)	10.85 * (8.6-13.2)	29.24 * (26.4-32.1)	19.93+ (18.0-21.8)	13.12 * (10.6-15.6)	8.58 * (7.1-10.6)	10.88 + (9.4-12.3)

*Age-adjusted percentages for men and women. # Sex-adjusted percentages for each age group. +Age- and sex-adjusted percentages.

Adjustment was conducted using sample survey data from 1% of the population in 2015 by direct methods.

Ten-year probability of developing CHD according to the MetS status

The Framingham risk algorithm was used to estimate the 10-year probability of developing CHD. The distributions of the 10-year estimated risk of developing CHD based on the three different definitions of MetS were compared (Table 4). Among those with MetS, based on the CDS criteria, 39.4% had a 10-year CHD risk of 6% (low), 6.7% had a 10-year CHD risk of 6-10% (moderate), 7.2% had a 10-year CHD risk of 10-20% (moderately high), and 7.2% had a 10-year CHD risk of 20% (high). The remaining 39.4% of participants with MetS had diabetes and/or CVD. In contrast, among those without MetS, a considerably higher proportion had a low risk (85.0%), and lower proportions had a moderate (3.3%), moderately high (5.5%), or high risk (1.6%) or had diabetes and/or CVD (4.7%) (χ^2=157.65, p<0.001). Similar heterogeneity in those with MetS and those without MetS was found based on the revised NCEP-ATP III criteria (χ^2=45.17, p<0.001) and the IDF criteria (χ^2=306.15, p<0.001). Of those with MetS, based on the revised NCEP-ATP III criteria and the IDF criteria, 67.5% and 74.2% had a low risk, 3.5% and 3.0% had a moderate risk, 5.2% and 3.3% had a moderately high risk, and 23.8% and 19.5% had a high risk or had diabetes and/or CVD, respectively. There were no significant differences in the CHD risk distributions of those with MetS based on the revised NCEP-ATP III criteria and the IDF criteria (χ^2=5.36, p=0.252), while a significant difference was observed based on the CDS criteria (with the revised NCEP-ATP III criteria: χ^2=45.71, with IDF: χ^2=62.69, all p<0.001, Figure 2).

We further compared the distribution of the 10-year estimated risk of developing CHD based on the three different MetS definitions in the males and females (Figure 3). There were no significant differences in the distribution of the 10-year estimated

risk of developing CHD in males with MetS among the three definitions, except for between the revised NCEP-ATP III criteria and the CDS criteria (χ^2=17.41, p=0.002). As shown in Figure 3, a significant difference was found in the 10-year risk in females with MetS based on the CDS definition and the remaining definitions (with revised NCEP-ATP III criteria: χ^2=25.33, with IDF: χ^2=37.09, all p<0.001), while no significant difference was found based on the revised NCEP-ATP III criteria and the IDF criteria (χ^2=37.09, p=0.245). Compared to the females, a higher CHD risk was found in the males using all three definitions (revised NCEP-ATP III: χ^2=72.83; IDF: χ^2=63.60; CDS: χ^2=23.84; all p<0.001, Figure 3).

Table 4 Distribution of the 10-year estimated risk of developing CHD based on the three definitions of MetS

		Revised ATP III criteria	IDF criteria	CDS criteria
MetS(+)	Low (<6%)	67.5	74.2	39.4
	Moderate (6-10%)	3.5	3	6.7
	Moderate High (10-20%)	5.2	3.3	7.2
	High (>20%)	3.7	3.5	7.2
	DM/CVD	20.1	16	39.4
MetS(-)	Low (<6%)	86.1	81.9	85
	Moderate (6-10%)	3.7	3.8	3.3
	Moderate High (10-20%)	5.9	6.3	5.5
	High (>20%)	1.4	1.8	1.6
	DM/CVD	2.9	6.2	4.7
p-value		<0.001	<0.001	<0.001

p-value: based on a comparison of the distributions of risk groups between those with and those without metabolic syndrome

DISCUSSION

This study shows that the prevalence of MetS and the distribution of the 10-year estimated risk of developing CHD vary depending on how MetS is defined. In this study, the difference among the revised NCEP-ATP III, IDF, and CDS criteria was evaluated. The 10-year risk of developing CHD was significantly higher in the participants with MetS than that in the participants without MetS, and all three definitions demonstrated better performance in reflecting the risk of developing CHD in males than in females. Compared to the other criteria, the participants with MetS based on the CDS criteria had a higher 10-year CHD risk; however, the CDS criteria

also led to the lowest prevalence of MetS.

The previous study have examined the ability of different MetS definitions in predicting cardiovascular diseases. [13-17] However, to the best of our knowledge, the findings were inconsistent. Similarly, this study was not the first to estimate the 10-year probability in individuals with MetS based on the Framingham risk algorithm. [12 18] Suzuki et al. [18] used the Framingham risk score rather than the 10-year probability of developing CHD to compare the differences among four different MetS definitions. Their results showed that the risk score in males with MetS was significantly higher by three-fold than that in females with MetS based on all four diagnostic criteria. However, the results failed to accurately compare the difference between males and females because females are required to have a higher score in each risk category. Therefore, in the present study, we compared the distribution of the 10-year estimated risk of developing CHD between males and females. Our study revealed that all three evaluated definitions of MetS had better performance in reflecting the 10-year CHD risk in males than in females. Furthermore, similar to studies conducted in other populations [19 20], there were significant differences in the prevalence of MetS between the males and females. A greater number of females met the diagnostic criteria of MetS using the IDF criteria, while the CDS criteria led to a greater number of males having MetS. There was no significant difference in the prevalence of MetS between the females and males based on the revised NCEP-ATP III criteria. The finding that the 10-year probability of developing CHD in males differed based on the definition of MetS is consistent with the findings of previous studies. Mak et al. [21] suggested that the adverse impact of MetS was greater among males than females, which is consistent with another study. [15] Therefore, the impacts of various risk factors on cardiovascular diseases and their outcomes appear to differ according to sex in patients with MetS. [22] Notably, different forms of obesity have different impacts on cardiovascular disease risk. In particular, android obesity, which is more common in males and postmenopausal females, [23] is associated with future cardiovascular events. [24] This sex difference may also be due to other characteristics of the subjects, such as age and smoking status. In contrast, some studies [5 13 25] have

suggested that all definitions of MetS (NCEP-ATP III, IDF, AHA/NHLBL, and JIS) are more predictive of the CHD risk in females than in males.

Among the definitions of MetS evaluated in the current study, the IDF criteria identified fewer participants (19.93%) as having MetS than the revised NCEP-ATP III criteria (30.96%), but this lower prevalence did not translate into better performance. There was no significant difference in the distribution of the 10-year risk of developing CHD between the revised NCEP-ATP III and the IDF criteria. This finding is consistent with the results of previous studies in which similar risks of cardiovascular diseases were reported with different levels of sensitivity depending on the definition of MetS. [13 26 27] The lower prevalence based on the IDF criteria may be due to the requirement of central obesity for the diagnosis of MetS, even though these criteria share the same components and same cut-off values. Compared to the revised ATP III criteria, this demand decreases the number of individuals satisfying the criteria for MetS under the IDF criteria. In addition, if the threshold value of abdominal obesity differs among different MetS definitions, the discrepancy in prevalence may be reversed. For instance, Scuteri et al. [19] reported that the prevalence of MetS based on the IDF criteria was higher than that based on the ATP criteria, which may result from the lower waist circumstance threshold values applied to the European population by the IDF. Notably, a recent cohort study conducted by Keihani [28] showed that abdominal obesity and the presence of metabolic derangements are both relevant risk factors for future CVD. Similar results were found in another study by Zhao et al., [29] who compared the long-term risk of cardiovascular diseases between patients with MetS with or without central obesity. These authors found that most patients with MetS (78%) had central obesity, and no significant difference was observed in the 10-year absolute and relative risk of CHD and ischaemic CVD events between the two MetS groups. This finding highlights the fact that focusing on abdominal obesity while ignoring the other components of MetS may not be ideal. Another study [16] using an ROC curve and Cox regression analyses showed that the ATP III criteria better predicted CVD than the IDF criteria.

Compared to the other criteria, the CDS criteria led to the lowest prevalence of

MetS and the highest 10-year probability of developing CHD in the current study. Our findings are partially consistent with the results of previous studies in which CDS had the highest specificity in identifying MetS in a Chinese population based on a 6.3-year cohort study. [16] However, despite the high specificity, the study also found that the CDS criteria had the lowest sensitivity among the three definitions, and more than 50% of patients may be misdiagnosed. More subjects were diagnosed with obesity (BMI ≥25 kg/m^2) than central obesity (32.31% *vs* 24.17%). Therefore, the lowest prevalence and the highest risk of developing CHD are mainly caused by the thresholds of high blood pressure and elevated blood glucose in the CDS criteria, which are higher than those in the other criteria. However, discussing the superiority of the MetS definition that adopts BMI or waist circumference as an index of adiposity is necessary. Some studies posit that WC is a more advantageous index of adiposity. According to Scuteri et al., [30] WC is a significant predictor of new onset MetS. In addition, Scuteri et al.[31] indicated that WC correlated with arterial properties better than BMI and that as the WC increased, the arterial structure and function significantly changed within each BMI quartile, even though the cluster of MetS including abdominal adiposity has been consistently associated with arterial damage. [32 33]

The strength of our study should be mentioned. The complex, multistage probability sample design is fairly representative of the Chinese population in Shenzhen. In addition, the percentage of missing data is generally low. However, there are several limitations to our study. First, although the original Framingham CHD risk assessment has been validated in previous studies, [34] the algorithm does not include obesity and cardiorespiratory fitness,[35-37] which could have potentially influenced the risk estimation. Furthermore, a previous report found that the Framingham algorithm overestimates the risk of CHD in the Chinese population. [38] Second, our analysis was based on cross-sectional data; therefore, we were unable to calculate positive and negative predictive values for CHD or determine which MetS definition is the most predictive of the development of CHD. Thus, the results should be interpreted with caution. Further studies conducted in China, especially longitudinal studies, are needed to determine which MetS definition is best suited for predicting CHD.

This study contributes to the body of evidence showing that differences exist in the prevalence and distribution of the 10-year estimated risk of developing CHD depending on the definition of MetS. Among the definitions evaluated (the revised NCEP-ATP III, IDF, and CDS criteria), the CDS criteria led to the highest 10-year probability of developing CHD and the lowest prevalence of MetS. A significant finding of this study was that all three definitions of MetS had better performance in males compared to females.

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REFERENCES

1. Sattar N, Gaw A, Scherbakova O, et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation* 2003;108(4):414-9.
2. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the

metabolic syndrome: a summary of the evidence. *Diabetes care* 2005;28(7):1769-78.

3. Noda H, Iso H, Saito I, et al. The impact of the metabolic syndrome and its components on the incidence of ischemic heart disease and stroke: the Japan public health center-based study. *Hypertens Res* 2009;32(4):289-98.
4. Mottillo S, Filion KB, Genest J, et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. *J Am Coll Cardiol* 2010;56(14):1113-32.
5. Gami AS, Witt BJ, Howard DE, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol* 2007;49(4):403-14.
6. Esteghamati A, Hafezi-Nejad N, Sheikhbahaei S, et al. Risk of coronary heart disease associated with metabolic syndrome and its individual components in Iranian subjects: a matched cohort study. *J Clin Lipidol* 2014;8(3):279-86.
7. National Cholesterol Education Program Expert Panel on Detection E, Treatment of High Blood Cholesterol in A. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;106(25):3143-421.
8. Alberti KG, Zimmet P, Shaw J, et al. The metabolic syndrome--a new worldwide definition. *Lancet* 2005;366(9491):1059-62.
9. Metabolic syndrome study cooperation group of Chinese diabetes society. *Chinese Journal of Diabetes Mellitus* 2004;12(3):156-61.
10. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120(16):1640-5.
11. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement: Executive Summary. *Crit Pathw Cardiol* 2005;4(4):198-203.
12. Hoang KC, Ghandehari H, Lopez VA, et al. Global coronary heart disease risk assessment of individuals with the metabolic syndrome in the U.S. *Diabetes care* 2008;31(7):1405-9.
13. Hosseinpanah F, Asghari G, Barzin M, et al. Prognostic impact of different definitions of metabolic syndrome in predicting cardiovascular events in a cohort of non-diabetic Tehranian adults. International journal of cardiology 2013;168(1):369-74.
14. Kastorini CM, Panagiotakos DB, Georgousopoulou EN, et al. Metabolic syndrome and 10-year cardiovascular disease incidence: The ATTICA study. Nutrition, metabolism, and cardiovascular diseases : NMCD 2016;26(3):223-31.
15. Qiao Q, Group DS. Comparison of different definitions of the metabolic syndrome in relation to cardiovascular mortality in European men and women. Diabetologia 2006;49(12):2837-46.
16. Zhou H, Guo ZR, Yu LG, et al. Evidence on the applicability of the ATPIII, IDF and CDS metabolic syndrome diagnostic criteria to identify CVD and T2DM in the Chinese population from a 6.3-year cohort study in mid-eastern China. Diabetes research and clinical practice 2010;90(3):319-25.
17. Scuteri A, Najjar SS, Morrell CH, et al. The metabolic syndrome in older individuals: prevalence and prediction of cardiovascular events: the Cardiovascular Health Study. Diabetes care

2005;28(4):882-7.
18. Suzuki T, Zeng Z, Zhao B, et al. Comparison of coronary heart disease risk among four diagnostic definitions of metabolic syndrome. Journal of endocrinological investigation 2016;39(11):1337-46.
19. Scuteri A, Najjar SS, Orru M, et al. Age- and gender-specific awareness, treatment, and control of cardiovascular risk factors and subclinical vascular lesions in a founder population: the SardiNIA Study. Nutrition, metabolism, and cardiovascular diseases : NMCD 2009;19(8):532-41.
20. Scuteri A, Laurent S, Cucca F, et al. Metabolic syndrome across Europe: different clusters of risk factors. European journal of preventive cardiology 2015;22(4):486-91.
21. Mak KH, Ma S, Heng D, et al. Impact of sex, metabolic syndrome, and diabetes mellitus on cardiovascular events. The American journal of cardiology 2007;100(2):227-33.
22. Regitz-Zagrosek V, Lehmkuhl E, Weickert MO. Gender differences in the metabolic syndrome and their role for cardiovascular disease. Clinical research in cardiology : official journal of the German Cardiac Society 2006;95(3):136-47.
23. Williams CM. Lipid metabolism in women. The Proceedings of the Nutrition Society 2004;63(1):153-60.
24. Ibrahim MM. Subcutaneous and visceral adipose tissue: structural and functional differences. Obesity reviews : an official journal of the International Association for the Study of Obesity 2010;11(1):11-8.
25. Wang C, Hou X, Bao Y, et al. The metabolic syndrome increased risk of cardiovascular events in Chinese--a community based study. International journal of cardiology 2010;139(2):159-65.
26. Mancia G, Bombelli M, Facchetti R, et al. Impact of different definitions of the metabolic syndrome on the prevalence of organ damage, cardiometabolic risk and cardiovascular events. Journal of hypertension 2010;28(5):999-1006.
27. Nilsson PM, Engstrom G, Hedblad B. The metabolic syndrome and incidence of cardiovascular disease in non-diabetic subjects--a population-based study comparing three different definitions. Diabetic medicine : a journal of the British Diabetic Association 2007;24(5):464-72.
28. Keihani S, Hosseinpanah F, Barzin M, et al. Abdominal obesity phenotypes and risk of cardiovascular disease in a decade of follow-up: the Tehran Lipid and Glucose Study. Atherosclerosis 2015;238(2):256-63.
29. Zhao D, Grundy SM, Wang W, et al. Ten-year cardiovascular disease risk of metabolic syndrome without central obesity in middle-aged chinese. The American journal of cardiology 2007;100(5):835-9.
30. Scuteri A, Morrell CH, Najjar SS, et al. Longitudinal paths to the metabolic syndrome: can the incidence of the metabolic syndrome be predicted? The Baltimore Longitudinal Study of Aging. The journals of gerontology Series A, Biological sciences and medical sciences 2009;64(5):590-8.
31. Scuteri A, Orru M, Morrell CH, et al. Associations of large artery structure and function with adiposity: effects of age, gender, and hypertension. The SardiNIA Study. Atherosclerosis 2012;221(1):189-97.
32. Scuteri A, Cunha PG, Rosei EA, et al. Arterial stiffness and influences of the metabolic syndrome: a cross-countries study. Atherosclerosis 2014;233(2):654-60.
33. Scuteri A, Najjar SS, Orru M, et al. The central arterial burden of the metabolic syndrome is similar in men and women: the SardiNIA Study. European heart journal 2010;31(5):602-13.
34. D'Agostino RB, Sr., Grundy S, Sullivan LM, et al. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. Jama

2001;286(2):180-7.
35. Lavie CJ, Deedwania P, Ortega FB. Obesity is rarely healthy. The Lancet Diabetes & Endocrinology 2018
36. Kennedy AB, Lavie CJ, Blair SN. Fitness or Fatness: Which Is More Important? Jama 2018;319(3):231-32.
37. Deedwania P, Lavie CJ. Dangers and Long-Term Outcomes in Metabolically Healthy Obesity: The Impact of the Missing Fitness Component. Journal of the American College of Cardiology 2018;71(17):1866-68.
38. Liu J, Hong Y, D'Agostino RB, Sr., et al. Predictive value for the Chinese population of the Framingham CHD risk assessment tool compared with the Chinese Multi-Provincial Cohort Study. Jama 2004;291(21):2591-9.

Figure legends:

Figure 1 Prevalence of MetS among adults aged 20 to 80 years in this study area.

Figure 2 The distribution of the 10-year estimated risk for CHD in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (<6%), moderate (6 to 10%),moderately high (10 to 20%), and high (>20% or history of diabetes or CVD).

Figure 3 The distribution of the 10-year estimated risk for CHD by sex in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (<6%), moderate (6 to 10%),moderately high (10 to 20%), and high (>20% or history of diabetes or CVD).

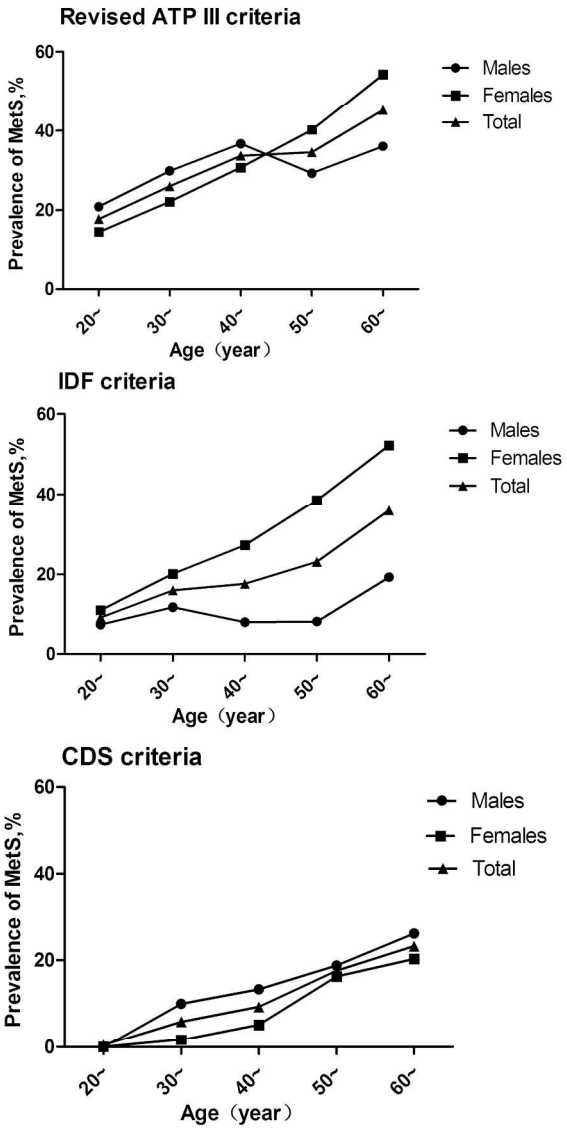

Figure 1 Prevalence of MetS among adults aged 20 to 80 years in the study area

Figure 1

187x293mm (300 x 300 DPI)

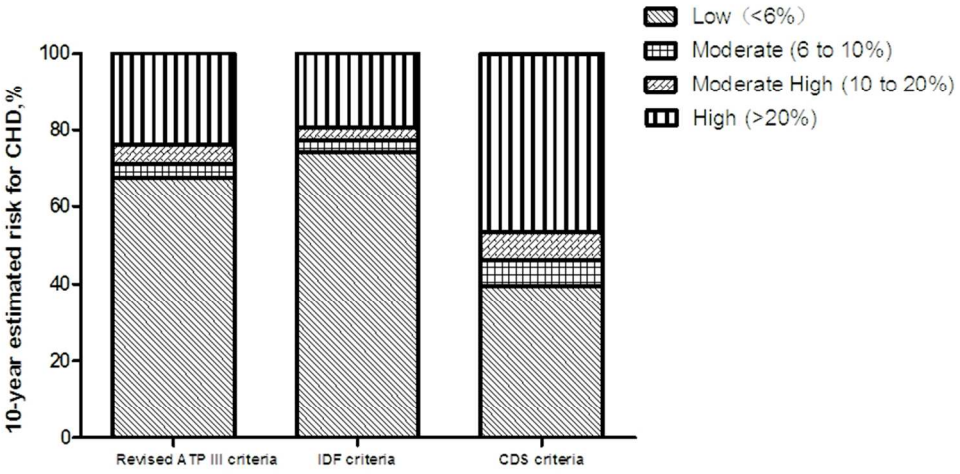

Figure 2 The distribution of the 10-year estimated risk for CHD in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (<6%), moderate (6 to 10%), moderately high (10-20%), and high (>20% or history of diabetes or CVD).

Figure 2

79x50mm (300 x 300 DPI)

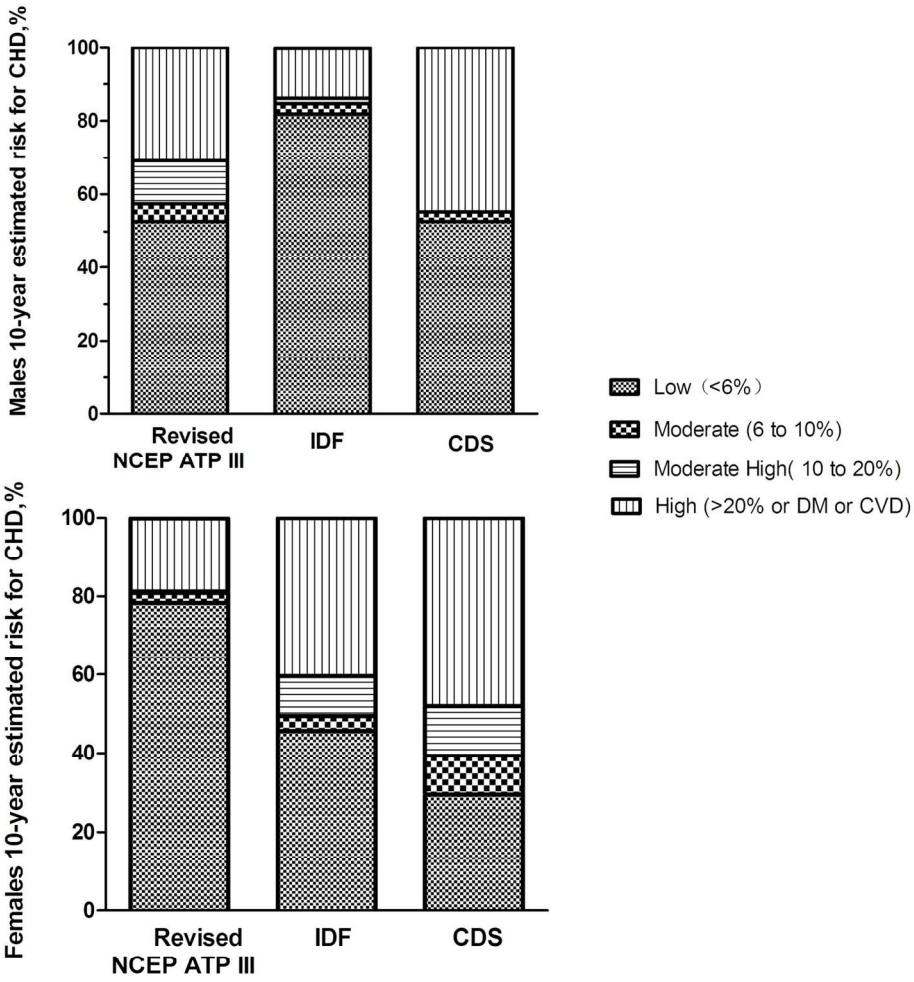

Figure 3 The distribution of the 10-year estimated risk for CHD by sex in individuals with metabolic syndrome based on the three different definitions of MetS. The risk categories are as follows: low (>6%), moderate (6 to 10 %),moderately high (10 to 20%), and high (?20% or history of diabetes or CVD).

Figure 3

143x172mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	*6*
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			7

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.