

Dynamic changes in metabolic health status in Chinese adults: Multiple population-based surveys in Shanghai, China

Yihui Yang^{1†}, Yanyun Li^{2†}, Jianfeng Pei¹, Minna Cheng², Wanghong Xu^{1*} , Yan Shi^{2*}

¹Department of Epidemiology, School of Public Health, Fudan University, Shanghai, China, and ²Department of NCDs Prevention and Control, Shanghai Municipal Center for Disease Control and Prevention, Shanghai, China

Keywords

Components, Metabolic syndrome, Prevalence trend

*Correspondence

Yan Shi
Tel.: +86-21-6209-3550
Fax: +86-21-6219-7682
E-mail address:
shiyang@scdc.sh.cn

Wang Hong Xu
Tel.: +86-21-5423-7679
Fax: +86-21-5423-7334
E-mail address:
wanghong.xu@fudan.edu.cn

J Diabetes Investig 2021; 12: 1784–1796

doi:10.1111/jdi.13556

ABSTRACT

Aims/introduction: Metabolic syndrome (MS) has been increasing worldwide. The secular change in MS components, however, remains unclear. This study aimed to examine the dynamic change in metabolic health status in Chinese adults.

Materials and methods: Three population-based surveys using multistage stratified sampling were performed in Chinese aged 35–74 years in Shanghai in 2002–2003 ($n = 12,302$), 2009 ($n = 7,400$), and 2017 ($n = 19,023$). MS was defined according to the Adult Treatment Panel III criteria for Asian-Americans. Generalized Estimating Equations and Cochran-Armitage Trend Test was used to assess the prevalence trend over the years.

Results: The prevalence of MS doubled in Chinese adults over the period (P for trend < 0.001). The largest increase occurred in younger men. Among MS components, the prevalence of high waist-circumference (HWC), high blood glucose (HBG) and high blood pressure (HBP) increased in all subjects, whereas the prevalence of high triglycerides (HTG) and low high-density lipoprotein cholesterol (LHC) increased in men but decreased in women. The increase in HBP contributed most to elevated MS, followed by HBG and HWC, resulting in the HBP-HBG-HWC the most common cluster of MS components. Metabolically unhealthy overweight also grew over the period.

Conclusions: Metabolic health status has been exacerbating in Chinese adults and may increase burden of non-communicable diseases.

INTRODUCTION

Metabolic syndrome (MS), a constellation of cardio-metabolic risk factors including abdominal obesity, hypertension, dyslipidemia and insulin resistance, is widely used to define individuals' metabolic health status. MS has been increasing around the world^{1,2}, including in China, a country experiencing a rapid nutritional transition characterized with sedentary lifestyle and high energy food intake over past decades³. Due to the significant associations of MS with the risk of type 2 diabetes mellitus and cardiovascular disease (CVD), as well as all-cause mortality^{4–6}, the global epidemic of MS may have imposed a heavy public health burden in both developed and developing countries¹.

Recent years, evidence is accumulating that the effect of metabolic health status, incorporating components of MS, is heterogeneous on the risk of CVD and all-cause mortality. In

the Framingham Heart Study, a specific cluster of MS components (e.g., central obesity, high blood pressure and hyperglycemia) was found to confer a 2.36-fold increase in incident cardiovascular events and a 3-fold increased risk of mortality⁷. Data also suggest that the metabolic health status predicts CVD risk better than body mass index (BMI), an indicator for overall overweight / obesity. The CVD risk was observed lower in overweight/obese people at an absence of MS components, but higher in normal weight people in the presence of one/more MS components^{8–10}. At the same time, the presentation of MS and MS components varied with race and ethnicity¹¹. For example, Asian Americans had a higher prevalence of MS than their non-Hispanic White counterparts at a same level of BMI¹², highlighting the more importance role of metabolic health status in Asian populations.

MS is a dynamic status that changes over time, which can be observed at both individual and population levels. A subject can switch from metabolically healthy to metabolically

[†]Yihui Yang and Yanyun Li contributed equally as co-first authors.
Received 8 November 2020; revised 17 March 2021; accepted 27 March 2021

unhealthy status and vice versa, while a population may vary in cluster of MS components over time due to the changes in risk exposure and in distribution of sex and age^{13–15}. So far, the upward trend in prevalence of MS over past decades has been well documented^{2,16,17}. The unbalanced change in components of MS was also observed. However, no previous study has specifically examined the shift of MS components and the potential impact on disease burden of non-communicable diseases (NCDs). Therefore, we hypothesized that the metabolic health status may change over time and shape the disease burden of CVD.

To test the hypothesis, we took advantage of the data from three population-based cross-sectional studies conducted in Shanghai, China, to describe the prevalence trend of MS and its components in the population by sex and age group. Our results may help to identify determinants of the trends, estimate the disease burden of CVD and develop more targeted interventions for specific high-risk individuals.

MATERIALS AND METHODS

Study population

Three population-based surveys were conducted in Chinese adults in Shanghai, China, in 2002–2003, 2009 and 2017, respectively, aimed to estimate prevalence of type 2 diabetes mellitus, detect undiagnosed type 2 diabetes mellitus and identify common modifiable risk factors for the disease.

The details of the three surveys using multistage stratified sampling procedure were described in our previous reports^{18–20}. Briefly, a representative sample of the general population was randomly selected through a multistage sampling process in the 2002–2003 survey. First, four districts and two counties were randomly selected from a total of 12 districts and seven counties in Shanghai, China. Next, 1–2 sub-districts or towns were randomly selected from each selected district or county. And then, 1–2 communities or villages were randomly selected from each selected sub-district or town. Finally, 1,000–2,000 eligible subjects (permanent residents of Shanghai, 15–74 years old and having been in the city for at least 5 years) were randomly selected from each selected community or village and invited to participate in the survey. Pregnant women, individuals with type I diabetes, and physically or mentally disabled persons were excluded from the participation. A total of 17,526 eligible subjects were recruited, and 14,401 (82.2%) participated the survey (Figure S1A).

The 2009 survey and the 2017 survey used a similar sampling method. Due to the rapid urbanization in Shanghai, the counties in rural areas were transferred into districts in urban areas gradually, which led to the changes of the sampling framework (Figure S1). The inclusion and exclusion criteria were also similar to those in the 2002–2003 survey, except that only those at age of 35–74 years old were eligible for the 2009 survey. Among 11,844 eligible adults contacted in the 2009 survey, 7,414 were interviewed, yielding a response rate of 62.6% (Figure S1B). In the 2017 survey, 21,625 of 23,993 eligible

subjects (90.1%) completed the interview, in which 1,789 subjects were the participants of the 2009 survey (Figure S1C).

To make the three surveys comparable, we excluded 2,099, 14 and 2,602 subjects younger than 35 years or older than 74 years from the 2002–2003, the 2009 and the 2017 surveys, respectively. Therefore, the final analysis included 12,302 subjects (5,023 men and 7,279 women) of the 2002–2003 survey, 7,400 subjects (3,454 men and 3,946 women) of the 2009 survey and 19,023 subjects (7,616 men and 11,407 women) of the 2017 survey.

The Institutional Review Board (IRB) in the Shanghai Municipal Center for Disease Control and Prevention approved the study. Informed consent was obtained from each participant before data collection.

Data collection

A similar protocol was followed in the three surveys. Information on demographic and socioeconomic factors, diagnoses of diabetes, hypertension, dyslipidemia, coronary heart disease and stroke, tobacco and alcohol use, physical activity and family history of diabetes was collected by trained interviewers in community healthcare centers located in the residential areas of the participants. Smoking was defined as more than 100 cigarettes in whole lifetime. Alcohol drinking referred to drinking at least once per month for at least 6 months. Information on occupation was collected in the 2002–2003 and the 2009 survey only while the data on mental disorders was obtained in the 2009 and the 2017 survey only.

At the interview, each participant was measured for his/her blood pressure (BP), body weight, standing height and waist circumference (WC) by trained staff. BP was measured on the right arm in the sitting position using standard mercury sphygmomanometer after at least 5 min of rest. The participants were advised to refrain from coffee, tea or alcohol intake, cigarette smoking and vigorous exercise for 30 min before their examination. The first and fifth Korotkoff sounds were recorded as systolic BP and diastolic BP, respectively. Body weight and standing height were recorded while the subject was in light clothing and without shoes. Body weight was measured with electronic scales to the nearest 0.1 kg. Body height was measured to the nearest 0.1 cm by using a stadiometer. WC, recorded to the nearest 0.1 cm, was taken with a cloth tape and was measured on bare skin at the midline between the lower border of the ribs and the iliac crest in the horizontal plane after a normal expiration. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2) using the direct measurements.

Two measurements were taken and the mean of the replicates was used in the following analyses. Between two measurements of blood pressure, there was a period of at least 2 min.

Laboratory measurements

Biochemical assays were conducted in the three surveys following a similar protocol. All subjects were asked to maintain their

usual physical activity and diet for at least 3 days before the measurements. After at least 10 h of overnight fasting, a 1–1.5 mL venous blood specimen was collected in a vacuum tube containing sodium fluoride for the measurement of plasma glucose and a 3–3.5 mL non-anticoagulated venous blood specimen was collected for the measurement of triglyceride (TG) and high-density lipoprotein cholesterol (HDL). Fasting plasma glucose (FPG) was measured with glucose oxidase-peroxidase (GOD-PAP) method and serum cholesterol and triglyceride levels were assessed enzymatically using commercial reagents. HDL was measured by PTA-Mg method. The subjects with any abnormal results in the assays and their family doctors were informed of the results for early treatment.

Definition of metabolic health and overweight status

Overweight (BMI ≥ 25 kg/m²) was defined using the criteria of the World Health Organization Western Pacific Regional Office²¹. MS was defined by the revised NCEP ATP III criteria for Asian-Americans as having three or more of the following components: (i) high WC (HWC): WC ≥ 90 cm in men and ≥ 85 cm in women; (ii) high BP (HBP): systolic/ diastolic BP $\geq 130/85$ mmHg or taking antihypertensive drugs; (iii) high blood glucose (HBG): FPG ≥ 5.6 mmol/L or taking antidiabetic drugs; (iv) high TG (HTG): TG ≥ 1.70 mmol/L; or (v) low HDL (LHC): HDL < 1.03 mmol/L in men and < 1.30 mmol/L in women^{22,23}.

Based on these criteria, all study participants were categorized into one of four groups based on BMI (non-overweight < 25 kg/m² vs overweight ≥ 25 kg/m²) and the presence or absence of MS: (i) metabolically healthy, normal weight (MHNW); (ii) metabolically unhealthy normal weight (MUNW); (iii) metabolically healthy overweight (MHO); and (iv) metabolically unhealthy overweight (MUO).

Statistical analyses

Data are presented as median (Interquartile range, IQR) for continuous variables or as percentages for categorical variables. We calculated the prevalence and 95% confidence interval (CI) of MS and each component according to sex and age group in each survey. Age-standardized prevalence was calculated using the direct method based on the World Standardized Population presented by Segi²⁴ and modified by Doll *et al.*²⁵. The distribution curve and LMS (lambda, mu, sigma) methods were used to profile the percentile curves of BMI and WC over the three surveys^{19,26}. Nightingale diagram was used to present the clusters of MS components in all subjects and in those with MS. Due to the overlapping in subjects in the 2009 and the 2017 surveys, we used the generalized estimating equations (GEE) to test the time trend of the prevalence. The time was used as independent and continuous variable in the GEE model with an exchangeable working correlation matrix²⁷. We also estimated increasing economic burden of CVD caused by upward trend of MS and its components in Chinese adults in Shanghai (Methods S1).

Sensitivity analysis was conducted based on the 2017 survey data by excluding those also participating in the 2009 survey. Cochran-Armitage Trend test was used to test the trend of prevalence. A two-sided *P* value < 0.05 indicated statistical significance. All data analyses were performed using R 4.0.0 (The R Foundation for Statistical Computing, Vienna, Austria) and SAS 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Participant characteristics

Table 1 shows the characteristics of the participants. The subjects of the three surveys significantly differed in age, educational level, income *per capita*, alcohol drinking, and diagnoses of hypertension, type 2 diabetes mellitus and dyslipidemia. The subjects were also significantly different in average levels of body measurements, biochemical assays like FPG and HDL, with all *P* values for trend < 0.001 . However, no significant difference was observed for TG level in men and women over the three surveys.

More men (26.0%) and women (20.2%) in the 2009 survey engaged professional job than those (17.3% in men and 10.3% in women) in the 2002–2003 survey (all *P* values < 0.001). The prevalence of depression, insomnia, anxiety and other mental disorders were higher in the 2017 survey than in the 2009 survey in both men (1.0, 33.2, 2.5 and 8.1% vs 0.1, 4.7, 1.2 and 4.6%, respectively) and women (1.8, 41.4, 4.8 and 10.0% vs 0.1, 9.9, 2.3 and 7.1%, respectively) (all *P* values < 0.001) (data not shown in tables).

Prevalence and trend of MS

As shown in Figure 1a, the prevalence of MS was significantly higher in men than in women in three surveys. In men, the crude and age-adjusted prevalence were 23.0% (95% CI: 21.9–24.2) and 21.5% (95% CI: 20.2–22.9) in 2002–2003, 29.6% (95% CI: 28.0–31.1) and 26.6% (95% CI: 24.8–28.5) in 2009, and 45.3% (95% CI: 44.2–46.4) and 44.2% (95% CI: 41.8–46.7) in 2017, respectively. In women, the age-adjusted prevalence of MS were much lower than the crude prevalence, with the values being 20.2% (95% CI: 19.1–21.2) vs 21.8% (95% CI: 20.8–22.7) in 2002–2003, 25.3% (95% CI: 23.7–27.1) vs 29.6% (95% CI: 28.2–31.0) in 2009, and 32.3% (95% CI: 30.8–33.9) vs 41.5% (95% CI: 40.6–42.4) in 2017.

Figure 1b shows the sex- and age-specific prevalence of MS at the three surveys. Generally, the prevalence of MS increased with age in both men and women at each survey (*P* for trend < 0.05). The increase over the three survey was also observed at each age group and appeared more pronounced in men than in women, particularly in younger age-groups.

Prevalence and trend of MS components

The prevalence of HBP was the dominant component of MS in both men and women in all the three surveys (Figure 2a). The prevalence of HBP, HBG and HWC, both crude and age-adjusted, increased over the three surveys in men and women

Table 1 | Characteristics of participants in the 2002–2003, 2009 and 2017 surveys

	Men			Women			P for trend	P for trend
	The 2002–2003 survey (n = 5,023)	The 2009 survey (n = 3,454)	The 2017 survey (n = 7,616)	The 2002–2003 survey (n = 7,279)	The 2009 Survey (n = 3,946)	The 2017 survey (n = 11,407)		
Age (years) (median, IQR)	54.0 (46.0, 64.0)	55.0 (48.0, 61.0)	63.0 (56.0, 68.0)	51.0 (45.0, 61.0)	55.0 (49.0, 61.0)	62.0 (55.0, 66.0)	<0.001	<0.001
Education (n, %)								
Primary school and below	1,112 (22.3)	619 (17.9)	1,539 (20.2)	2,996 (41.4)	1,066 (27.0)	3,261 (28.6)	<0.001	<0.001
Middle school	1,768 (35.4)	1,576 (45.6)	3,687 (48.4)	2,254 (31.1)	1,784 (45.2)	4,935 (43.3)		
High school	1,376 (27.5)	955 (27.7)	1,684 (22.1)	1,633 (22.6)	940 (23.8)	2,558 (22.4)		
College or above	739 (14.8)	303 (8.8)	706 (9.3)	357 (4.9)	154 (3.9)	653 (5.7)		
Monthly income per capita (USD) (n, %)								
<154	1,838 (37.0)	170 (4.9)	53 (0.7)	3,088 (42.4)	159 (4.0)	76 (0.7)	<0.001	<0.001
154–461	1,911 (38.5)	1,445 (41.9)	2,935 (38.6)	2,793 (38.4)	1,845 (46.8)	4,404 (38.6)		
462–769	1,110 (22.3)	1,146 (33.2)	3,923 (51.5)	1,302 (17.9)	1,312 (33.3)	5,978 (52.4)		
>769	109 (2.2)	691 (20.0)	701 (9.2)	92 (1.3)	629 (15.9)	944 (8.3)		
Alcohol drinking (n, %)								
Former	291 (5.9)	122 (3.5)	375 (4.9)	8 (0.1)	7 (0.2)	20 (0.2)	0.039	0.039
Current	1,540 (31.0)	1,416 (41.0)	1,640 (21.6)	112 (1.5)	122 (3.1)	122 (1.1)		
Cigarette smoking (n, %)								
Former	444 (8.9)	256 (7.4)	1,340 (17.6)	18 (0.2)	11 (0.3)	28 (0.2)	0.110	0.110
Current	2,645 (52.8)	2,039 (59.1)	3,847 (50.5)	109 (1.5)	64 (1.6)	100 (0.9)		
Measurements (median, IQR)								
BMI (kg/m ²)	24.3 (22.1, 26.3)	24.2 (22.2, 26.3)	25.1 (23.1, 27.2)	24.0 (21.9, 26.5)	24.0 (21.9, 26.3)	24.5 (22.5, 26.7)	<0.001	<0.001
WC, cm	84.0 (77.0, 90.0)	85.0 (79.0, 91.0)	89.0 (83.0, 94.2)	78.0 (72.0, 84.0)	80.0 (74.0, 87.0)	83.0 (77.5, 89.0)	<0.001	<0.001
Systolic BP, mmHg	126 (116, 138)	125 (115, 137)	139 (128, 151)	119 (109, 138)	122 (111, 135)	136 (125, 150)	<0.001	<0.001
Diastolic BP, mmHg	78 (73, 88)	80 (73, 87)	84 (78, 91)	78 (70, 86)	79 (71, 83)	82 (75, 88)	<0.001	<0.001
FPG, mmol/L	5.0 (4.5, 5.6)	5.0 (4.6, 5.6)	5.7 (5.2, 6.6)	5.0 (4.5, 5.5)	5.0 (4.7, 5.5)	5.5 (5.2, 6.2)	<0.001	<0.001
TG, mmol/L	1.4 (1.0, 2.0)	1.4 (0.9, 2.2)	1.4 (1.0, 2.0)	1.3 (0.9, 1.8)	1.4 (0.9, 2.0)	1.3 (1.0, 1.8)	0.906	0.511
HDLc, mmol/L	1.3 (1.1, 1.6)	1.2 (1.0, 1.5)	1.3 (1.1, 1.5)	1.4 (1.2, 1.7)	1.4 (1.2, 1.6)	1.5 (1.3, 1.8)	<0.001	<0.001
Previous metabolic disorders (n, %)								
Hypertension [†]	952 (19.0)	1,101 (31.9)	3,490 (45.8)	1,161 (15.9)	1,115 (28.3)	4,647 (40.7)	<0.001	<0.001
Type 2 diabetes [†]	368 (7.3)	362 (10.5)	1,266 (16.6)	418 (5.7)	334 (8.5)	1,445 (12.7)	<0.001	<0.001
Dyslipidemia [†]	337 (6.7)	358 (10.4)	1,432 (18.8)	422 (5.8)	395 (10.0)	2,291 (20.1)	<0.001	<0.001
Overweight (BMI ≥ 25 kg/m ²)	2,034 (40.6)	1,365 (39.6)	3,922 (51.5)	2,795 (38.4)	1,510 (38.3)	4,873 (42.7)	<0.001	<0.001

Continuous variables presented as the median (IQR), while categorical variables as number (%). Generalized estimating equation was used to test the trend. Missing values excluded from the analysis for men in the 2002–2003, the 2009 and the 2017 surveys: Education (n = 28,10), Monthly income per capita (n = 55,24), Alcohol drinking (n = 54,222), Cigarette smoking (n = 9,35), BMI and overweight (n = 9,30), WC (n = 21,30), BP (n = 10,02), FPG (n = 0,06), TG (n = 7,06), HDLC (n = 3,06) and diagnosis of dyslipidemia (n = 8,20); for women: Education (n = 39,20), Monthly income per capita (n = 4,15), Alcohol drinking (n = 2,110), Cigarette smoking (n = 0,49), BMI and overweight (n = 3,10), WC (n = 17,10), BP (n = 1,0,7), FPG (n = 0,0,12), TG (n = 4,0,9), HDLC (n = 3,0,8), and diagnosis of dyslipidemia (n = 10,0,0). P values shown in bold indicated a negative trend. † Diagnosed by physicians according to the 1999 WHO criteria. ‡ Diagnosed by physicians according to the Chinese guideline of dyslipidemia. BMI, body mass index; BP, blood pressure; FPG, fasting plasma glucose; HDLC, high-density lipoprotein cholesterol; TG, Triglycerides; WC, waist circumference.

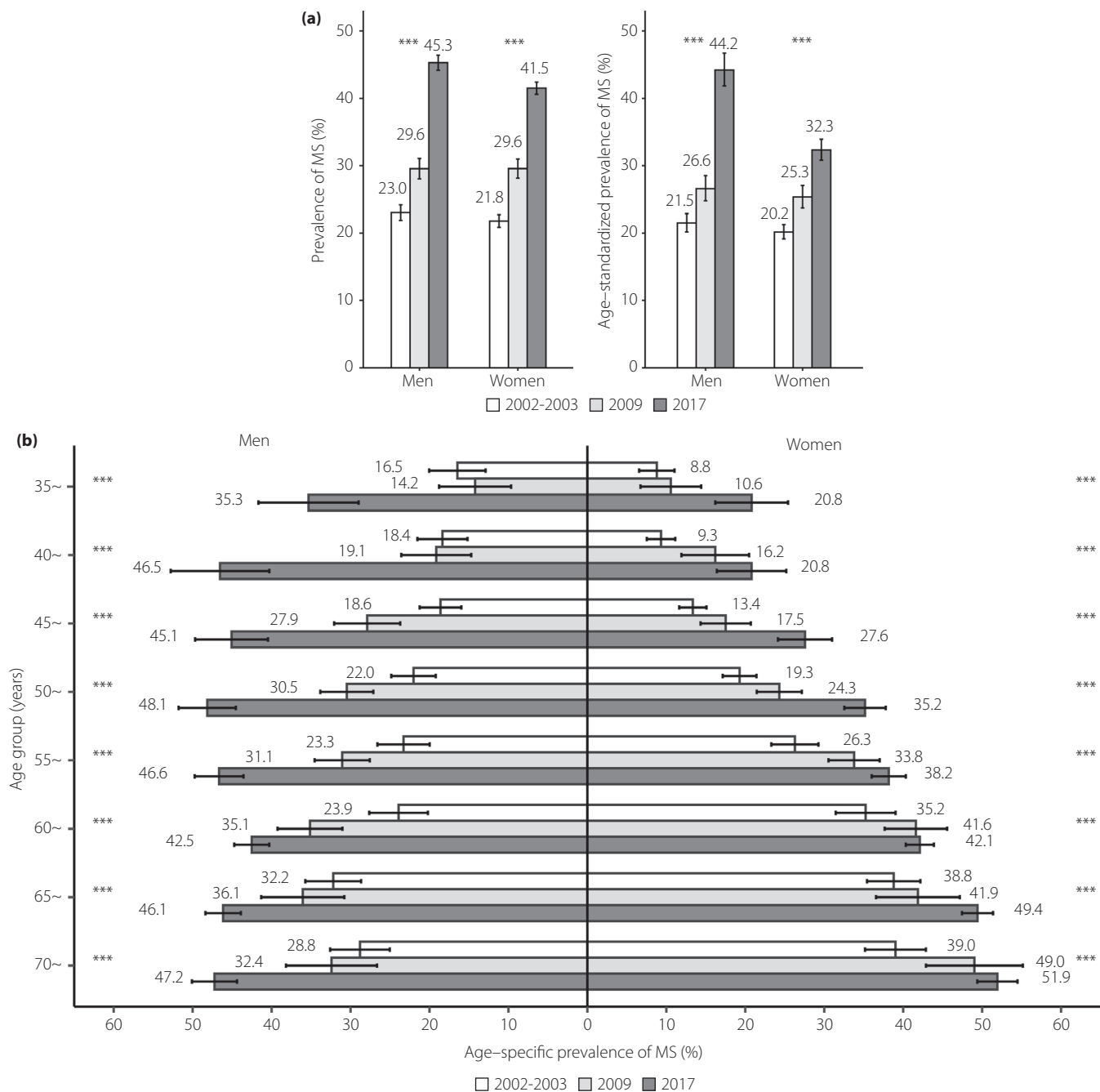


Figure 1 | Prevalence of metabolic syndrome in Chinese men and women in the 2002–2003, 2009 and 2017 population-based surveys. (a) Crude and age-standardized prevalence; (b) Age-specific prevalence. Generalized estimating equations were used to test the prevalence trend. Bars indicate 95% CIs. ****P* for trend <0.001; ***P* for trend <0.01; **P* for trend <0.05.

(*P* for trend <0.001), and the increases appeared more pronounced from 2009 to 2017 than those from 2002–2003 to 2009. The changes in prevalence of dyslipidemia, on the other hand, varied by sex, with the age-adjusted prevalence of HTG increasing in men but decreasing in women. The crude prevalence of LHC was the highest in the 2009 survey in both men and women.

The prevalence of HWC, HBG and HBP were observed to increase with age in both men and women in each survey (*P* for trend <0.05), as presented in Figure 2b. Regarding the dyslipidemia, the prevalence of HTG increased with age in women, but was observed to increase and then decrease with age in men. The prevalence of LHC decreased with age in men and remained stable in women.

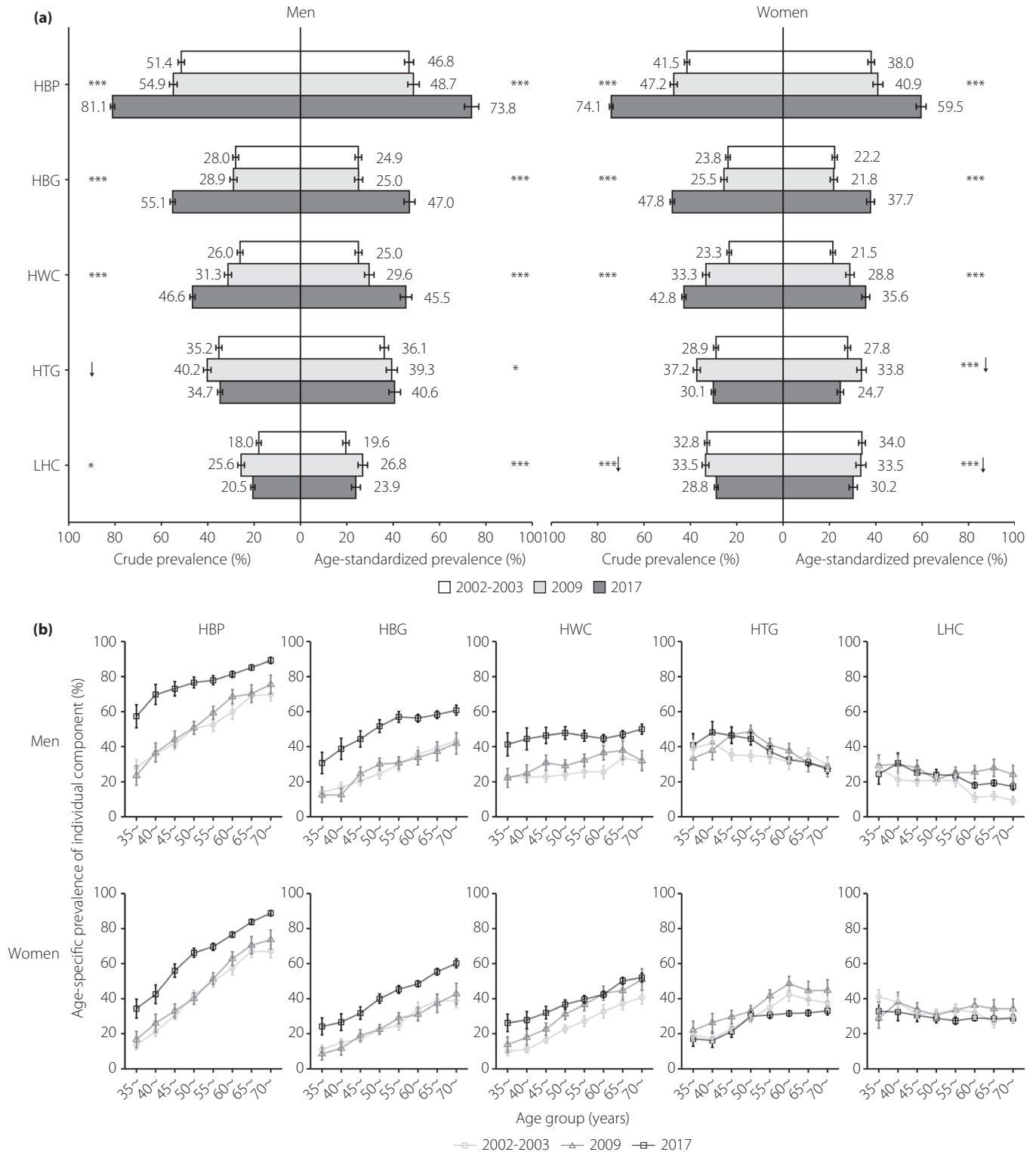


Figure 2 | Prevalence of metabolic syndrome components in Chinese men and women in the 2002–2003, 2009 and 2017 population-based surveys. (a) Crude and age-standardized prevalence; (b) Age-specific prevalence. Generalized estimating equations were used to test the prevalence trend. Bars indicate 95% CIs. **P* for trend <0.05; ***P* for trend <0.01; ****P* for trend <0.001. HBG, high blood glucose; HBP, high blood pressure; HTG, high triglyceride; HWC, high waist circumference; LHC, low high-density lipoprotein cholesterol.

Figure 3 shows the distribution curves of BMI and WC in men and women. The curves of BMI were almost overlapped in the three surveys, particularly in women, and the BMI level remained relevant stable along with age in both men and women (Figure 3a). On the other hand, the curves of WC in both sexes were shifted to the

right from 2002–2003 to 2009 and 2017, with the mean WC increasing from 83.0 to 84.8 and 88.2 cm for men and from 77.7 to 80.3 and 83.1 cm for women. Stratified analysis by age groups observed a similar change pattern and an increasing trend of WC along with age in women (Figure 3b).

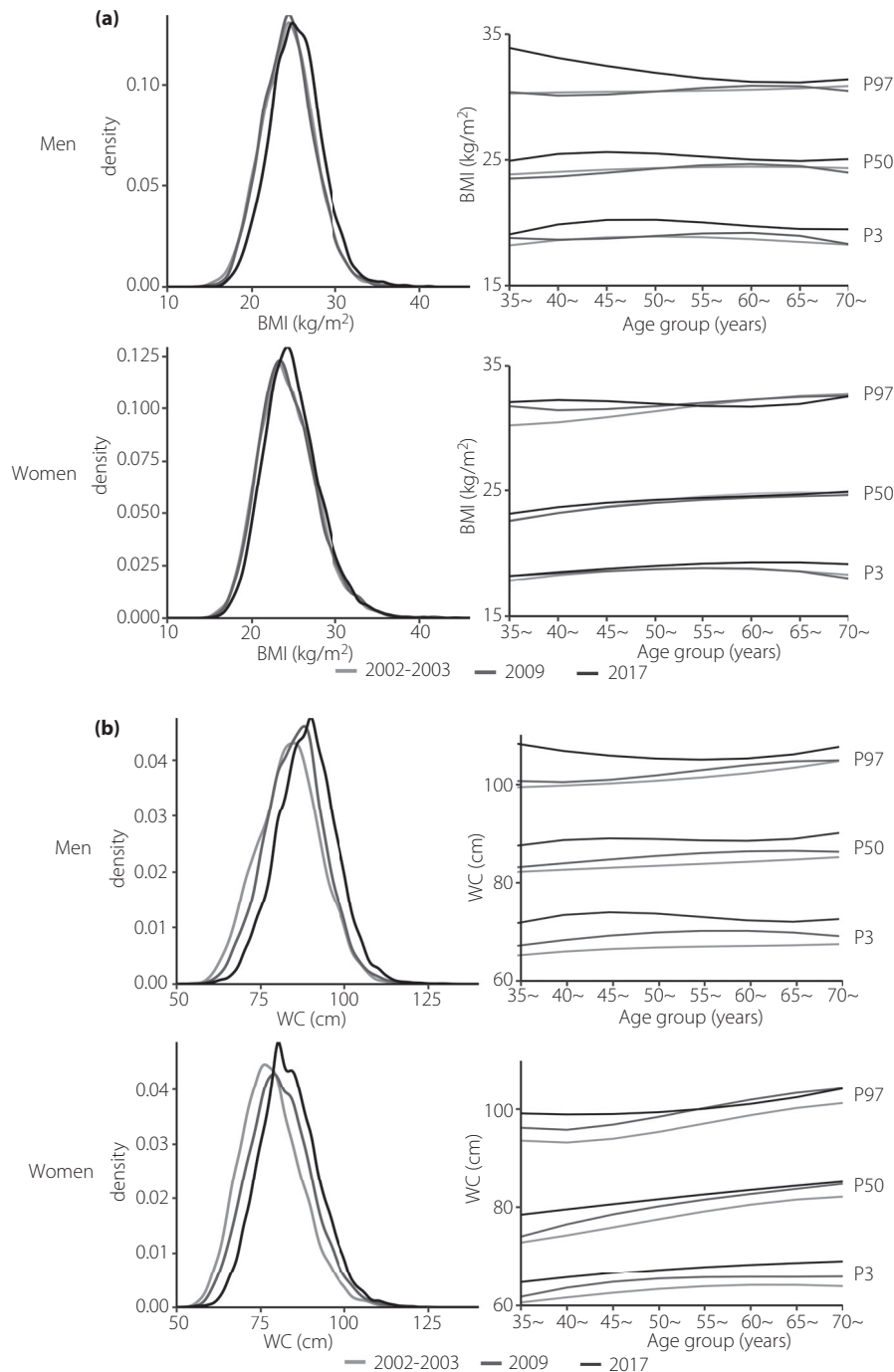


Figure 3 | Shifts in body mass index (a) and waist circumference (b) in Chinese men and women over the 2002–2003, 2009 and 2017 population-based surveys. BMI, body mass index; WC, waist circumference.

Changes in clusters of MS components

As presented in Figure 4a, most subjects had one or two components of MS. The proportions of subjects with 0 or 1 components decreased over the three surveys while those with 2 or more components increased in both men and women.

The details of the changed clusters of the components over the three surveys in all subjects and in subjects with MS were presented in Figure S2A,B. Overall, the clusters of MS components differed between men and women and changed over

time, but with HBP and related clusters remaining the most common abnormalities. In subjects with MS, the cluster HBP-HBG-HWC was the dominant one in the 2002–2003 [15.0% (95%CI: 13.0–17.1) in men and 11.0% (95%CI: 9.4–12.5) in women] and the 2017 surveys [26.0% (95%CI: 24.6–27.5) in men and 21.5% (95%CI: 20.3–22.7) in women] (Figure S2B). The simultaneous alteration in all the five MS components had a considerably lower prevalence in the 2002–2003 survey [5.0% (95%CI: 3.7–6.2) in men and 7.0% (95%CI: 5.7–8.2) in

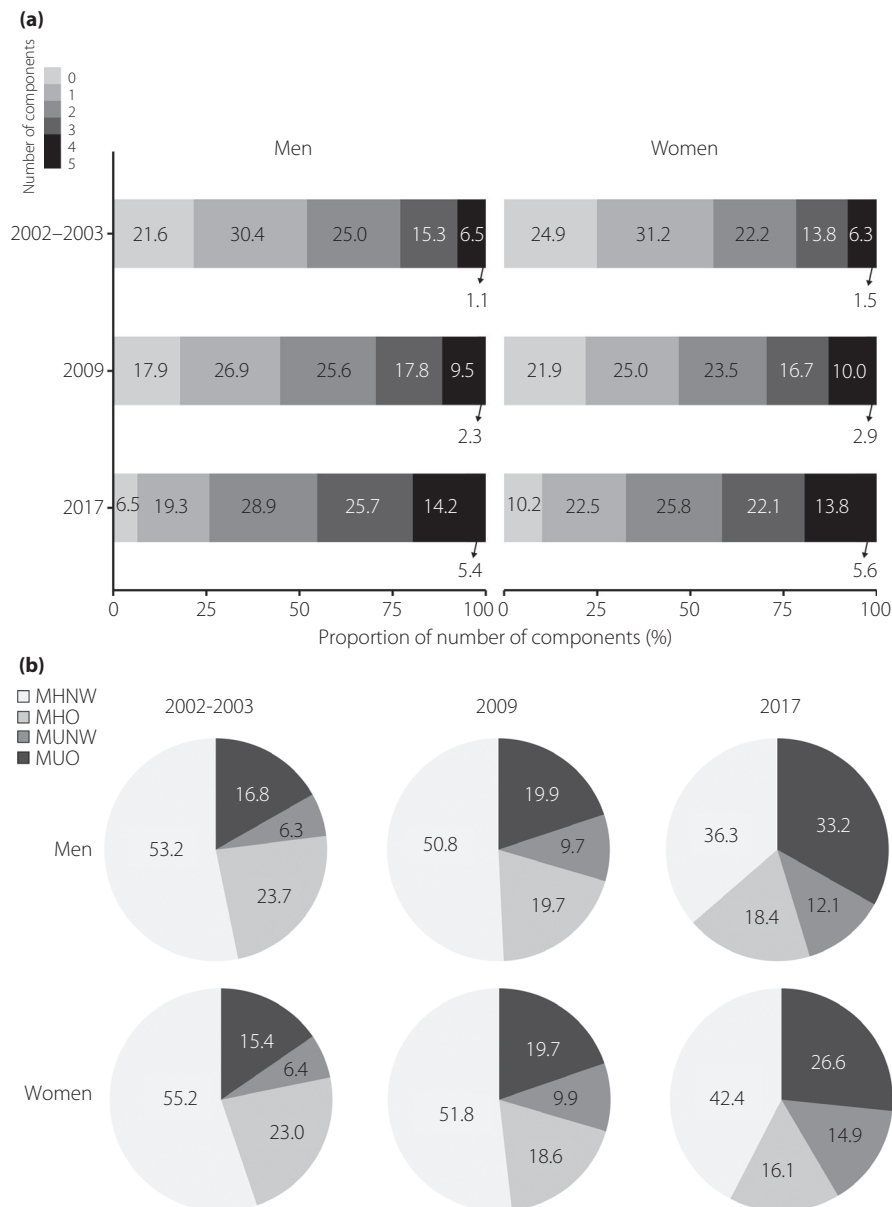


Figure 4 | Percentage of the number of metabolic syndrome components (a) and the metabolic type of overweight (b) among Chinese men and women in the 2002–2003, 2009 and 2017 population-based surveys. MHNW, metabolically healthy normal weight; MHO, metabolically healthy overweight; MUNW, metabolically unhealthy normal weight; MUO, metabolically unhealthy overweight.

women], but was higher in the 2009 [7.6% (95%CI: 6.0–9.3) in men and 9.9% (95%CI: 8.1–11.6) in women] and the 2017 surveys [(11.9% (95%CI: 10.8–13.0) in men and 13.6% (95%CI: 12.6–14.6) in women].

Prevalence and trends of metabolically unhealthy overweight

Figure 4b presents the prevalence of MHNW, MUNW, MHO and MUO in the three surveys. The prevalence of MUO were 16.8% (95%CI: 15.7–17.8), 19.9% (95%CI: 18.5–21.2) and 33.2% (95% CI: 32.1–34.2), respectively, in 2002–2003, 2009 and 2017 in men (*P* for trend <0.05) and increased from 15.4% (95% CI: 14.6–16.2), 19.7% (95% CI: 18.5–20.9) to 26.6% (95% CI: 25.8–27.5) in women over the three periods (*P* for trend <0.05). The prevalence of MUNW also increased in both men (6.3% (95% CI: 5.6–6.9), 9.7% (95% CI: 8.7–10.7) and 12.1% (95% CI: 11.4–12.9)) and women (6.4% (95% CI: 5.8–6.9), 9.9% (95% CI: 9.0–10.8) and 14.9% (95% CI: 14.2–15.5), respectively) over the three surveys.

Analysis of increases in medical costs for CVD

Using previously reported sex- and age-adjusted relative risk (RR) and calculated population attributable fraction (Table S1), we estimated the direct medical costs of CVD in the whole population of Shanghai based on the changes in prevalence of MS, MS components and metabolic type of overweight, respectively. As shown in Table 2, MS contributed to 24.9, 30.6 and 39.1% of incident CVD in 2002–2003, 2009 and 2017 in

Chinese adults of Shanghai, respectively, equivalent to about \$216 million increases in direct medical costs. The contribution of individual component to direct medical cost ranged from \$36 million (HDL-C) to \$320 million (hypertension). The increases in prevalence of HBP-HBG cluster and MUO accounted for approximately \$170 and \$69 million increases in direct medical expenditure, respectively.

Sensitivity analysis

Although 1,789 subjects of the 2017 survey who also participated in the 2009 survey had lower levels of education and income, and were more likely to smoke and drink (in men only), excluding these subjects from analysis did not change the estimates of prevalence of MS and MS components in 2017. The crude and age-standardized prevalence of MS were 45.7% (44.5–46.9%) and 44.8% (42.3–47.4%) in men, and 41.7% (40.8–42.7%) and 32.5% (30.9–34.1%) in women, respectively, in sensitivity analysis, very close to those in the main analyses. The estimates for prevalence of each MS component, clusters of components and metabolic type of overweight did not change substantially, either (data not shown). The crude and age-standardized prevalence of MS, HWC, HBG and HBP significantly increased along the three surveys.

DISCUSSION

Consecutive population-based surveys are usually conducted to observe the secular trend of prevalence of NCDs and related

Table 2 | Estimated direct medical cost for cardiovascular diseases related to upward trend of prevalent metabolic syndrome, metabolic syndrome components and metabolic type of overweight in the whole population in Shanghai

	Direct medical cost each year (USD)			Changes in direct medical cost (USD)		
	In 2002	In 2009	In 2017	From 2002 to 2009	From 2009 to 2017	From 2002 to 2017
MS	24,303,428	71,913,068	240,308,866	47,609,640	168,395,798	216,005,438
Individual components						
HBP	45,288,315	115,389,923	365,072,804	70,101,608	249,682,881	319,784,489
HBG	12,981,349	32,901,404	143,201,958	19,920,055	110,300,555	130,220,609
HWC	8,686,767	27,026,153	92,804,703	18,339,386	65,778,550	84,117,935
HTG	19,618,430	55,462,366	124,763,938	35,843,937	69,301,572	105,145,508
LHC	7,222,705	19,270,822	43,636,648	12,048,117	24,365,826	36,413,943
Main clusters of MS components						
HBP-HWC	12,102,912	38,541,644	156,108,573	26,438,733	117,566,928	144,005,661
HBP-HBG	13,762,182	36,191,544	183,765,603	22,429,362	147,574,059	170,003,421
HBG-HWC	12,786,141	37,601,604	180,692,600	24,815,464	143,090,996	167,906,459
Metabolic type of overweight						
MUO	6,515,356	19,459,777	75,272,511	12,944,422	55,812,734	68,757,156
MUNW	1,314,457	4,890,892	17,997,374	3,576,436	13,106,482	16,682,918
MHO	7,580,646	14,955,569	34,782,210	7,374,923	19,826,641	27,201,564

CVD, cardiovascular disease; HBG, high blood glucose; HBP, high blood pressure; HTG, high triglyceride; HWC, high waist circumference; LHC, low high-density lipoprotein cholesterol; MHO, metabolically healthy overweight; MS, metabolic syndrome; MUNW, metabolically unhealthy, normal weight; MUO, metabolically unhealthy overweight; PAF, population attributable fraction.

factors. This approach also helps to recognize the drives behind the trend and predict the disease burden in the populations. In this study, the prevalence of MS defined by the revised NCEP ATP III criteria continues to exceed 20% in most sex- and age-specific groups of Chinese adults and increased significantly over the 15-year period from 2002 through 2017. These estimates are based on a large sample size from representative surveys that included metabolic measurements following standardized procedures.

MS has been epidemic globally over the past decades. Based on the NCEP ATP III criteria, the crude prevalence reported in other populations varied greatly, ranging from 9.0 to 52.6% in 2002–2003, from 10.0 to 36.3% in 2009, and from 35.1 to 44.4% in 2017 in men; and from 10.3 to 46.9% in 2002–2003, from 14.6 to 62.6% in 2009 and from 34.3 to 37.1% in 2017 in women (Table S2). MS has been climbing rapidly in low- and middle-income countries^{28,29}, but increasing slowly or even decreasing in high-income countries^{14,30}, suggesting the role of economic development, rapid urbanization and epidemic of sedentary lifestyle^{13,14}. In our population, the prevalence of MS was at a moderate level in 2002–2003 and 2009, but was at a high level in 2017 in global view, showing a speeding-up upward trend.

The observed discrepancy between the crude and age-standardized prevalence of the MS indicates the contribution of population ageing. MS is considered as an ageing-related disease, for risk exposure may be accumulated in individual as one gets older. In this study, however, the increase in the prevalence of MS was more pronounced in men below 60 years old. This was consistent with the findings in a Japanese cohort, where the MS prevalence in men increased until 60 years old and kept stable in the older generation³¹. The situation may be shaped by both global drives and local environments involving cultural, economic, and social factors. One possible reason is that this population were more likely to expose to high-stress jobs, which may disturb their neuroendocrine system and increase the risk of MS³².

The fact that the MS components did not change at a same speed may provide clues for potential drives for the trend. The prevalence of HWC, HBG and HBP substantially increased in both sexes, whereas the prevalence of HTG and LHC did not change much. This change pattern was also observed in the Framingham Heart Study³³ and Tehran lipid and glucose study³⁴. In other studies, however, parallel changes in dyslipidemia and other components were observed^{35,36}. Of the five components of MS, LHC was the one increasing the most in Korean population¹⁴. These findings indicate different risk exposures across populations.

There are several possible explanations for the unbalanced changes in cardio-metabolic risk factors in our population. First, the different trajectories of the metabolic factors with age may explain the discrepancy. Distinct from the WC which increases with age in humans³⁷, the TG level peaks at middle age^{38,39} and the HDLC level tends to decrease along with age or remains stable^{40,41}. The nature of biological phenomena involves age-related changes in inflammation and hormones³⁹,

as well as the differences in consumption, absorption and metabolisms of dietary fat^{39,40}. Therefore, due to the rapid population ageing in China, the average level of WC would be observed to increase along with the calendar year of the surveys, whereas those of TG and HDLC might not. Second, China has been experiencing a significant nutritional transition, resulting in the epidemic of western lifestyles characterized with reduced carbohydrates and increased protein and fat intake, decreased but still high level of sodium consumption, and sedentary behaviors^{42,43}. These factors were associated with elevated risk of obesity, hyperglycemic, dyslipidemia or hypertension, but in greatly varied magnitudes⁴⁴. Moreover, it has been reported that fat intake from animals has been decreasing in nine provinces of China since 2009, whereas fat intake from plants was observed to increase⁴⁵, which may have resulted in increased formation of HDLC⁴⁶. Tobacco and alcohol use may also contribute to the prevalent metabolic phenotypes⁴⁷ and explained the sex difference in prevalence trend of MS due to much higher consumptions in men than in women. Finally, awareness, treatment and control rates of each component of MS were greatly improved, but the improvements differed by the type of metabolic abnormalities^{48–50}.

Since we know little about the drives underlying the trends in prevalence of MS and its components, we could not make a reasonable prediction by establishing predictive models. The projection of prevalence using time series analysis needs to be based on a hypothesis that MS and its components would remain a certain climbing rate over time^{51,52}. However, the apparent speeding up trends and unbalanced changes in MS components observed in this study cast doubt on the assumption and accuracy of the forecasting. Therefore, we could not forecast the prevalence of MS using time series analysis, either. Future studies are warranted to extend the time frame to make a prediction.

The upward trends in prevalence of MS and its components may lead to an increasing burden of NCDs in this population. The increases in prevalence of MS and its components were estimated to cause additional millions of annual direct medical cost for CVD. The rising prevalence of MS was associated with additional 216,005,438 USD in direct medical cost for CVD, equivalent to 0.05% increases in GDP in Shanghai at the same period. The growth in disease burden was much higher from 2009 to 2017 than from 2002 to 2009. The estimated change in direct medical cost for MUO (\$69 million) was the largest one among the metabolic types of overweight, but much lower than that contributed by elevated BP alone. A multicomponent strategy has been supposed to manage MS risk factors⁵³. The evidence-based measures such as structured lifestyle interventions, introduction of sugar-sweetened beverage taxes, provision of increasing space for physical activity and design of more health-related curriculum in communities and schools are expected highly effective in our population to lower disease burden of CVD, particularly through control of HBP.

There are several strengths in this study. First, the three cross-sectional studies followed a similar multistage stratified

sampling procedure, ensuring the representation of the subjects. Second, the vigorous personnel training, data collection process and standard laboratory assays guarantee the high quality of the data. Moreover, the trend analyses were conducted in subgroups classified by sex and age group, and illustrated in various styles, allowing us to describe the trends comprehensively. Finally, the extensive inter-population comparisons of prevalence and trends of MS and its components make it possible to estimate and predict the disease burden of CVD, the main NCDs caused by metabolic abnormalities.

This study has several limitations. First, the three surveys were incomparable in sampling framework, sample size and response rate of investigation, which may have introduced selection bias. For example, due to the changed sampling framework in 2009, less subjects with educational level of college or above were selected in the 2009 survey. Considering the sex heterogeneity in relations of metabolic disorder with socioeconomic status (SES)^{54,55}, the prevalence of MS in the year may have been underestimated in men but overestimated in women. Second, although we used a standardized protocol for body measurement and biochemistry assays in the three surveys, we could not exclude the possible bias of batch. Moreover, lack of information on lifestyles and treatment limited our ability to evaluate the contributions of these factors to the upward trend of MS and its components. The differences in response rates of the three survey may also have biased the estimated upward trend of MS and its components. Finally, due to the cross-sectional design, we did not follow-up the subjects for incident CVD and other NCDs, and thus were unable to directly evaluate the associations of MS and its components with these outcomes for disease burden estimation and projection.

In conclusion, the prevalence of MS was at a high level and shows a speeding-up upward trend over past decades in Chinese adults. The increasing trend of MS, changed clusters of MS components and elevated metabolically unhealthy overweight, as well as the population ageing, predict a huge burden of CVD in the population and suggest the importance to address the accumulating metabolic disorders in the population.

ACKNOWLEDGMENTS

We thank the study participants of the three cross-sectional surveys and healthcare workers in each community involved. This work was supported by the National Nature Science Foundation of China (81573221 and 81773504), the Three-year Action Plan on Public Health, Phase IV, Shanghai, China (15GWZK0801) and Shanghai Science and Technology Achievement Transformation and Industrialization Project (18401933403). The funders play no role in study design, in the collection, analysis and interpretation of data, in the writing of the report, and in the decision to submit the article for publication.

DISCLOSURE

The authors declare that they have no conflicting interest.

REFERENCES

1. Saklayen MG. The global epidemic of the metabolic syndrome. *Curr Hypertens Rep* 2018; 20: 12.
2. Wang ZW, Wang X, Li X, *et al.* [Prevalence and trend of metabolic syndrome in middle-aged Chinese population]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2009; 30: 596–600.
3. Xu WH, Ruan XN, Fu XJ, *et al.* Prevalence of the metabolic syndrome in Pudong New Area of Shanghai using three proposed definitions among Chinese adults. *BMC Public Health* 2010; 10: 246.
4. Ju SY, Lee JY, Kim DH. Association of metabolic syndrome and its components with all-cause and cardiovascular mortality in the elderly: a meta-analysis of prospective cohort studies. *Medicine* 2017; 96: e8491.
5. Isomaa B, Almgren P, Tuomi T, *et al.* Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001; 24: 683–689.
6. Wilson PW, D'Agostino RB, Parise H, *et al.* Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. *Circulation* 2005; 112: 3066–3072.
7. Franco OH, Massaro JM, Civil J, *et al.* Trajectories of entering the metabolic syndrome: the framingham heart study. *Circulation* 2009; 120: 1943–1950.
8. Cho YK, Kang YM, Yoo JH, *et al.* Implications of the dynamic nature of metabolic health status and obesity on risk of incident cardiovascular events and mortality: a nationwide population-based cohort study. *Metabolism* 2019; 97: 50–56.
9. Caleyachetty R, Thomas GN, Toulis KA, *et al.* Metabolically healthy obese and incident cardiovascular disease events among 3.5 million men and women. *J Am Coll Cardiol* 2017; 70: 1429–1437.
10. Appleton SL, Seaborn CJ, Visvanathan R, *et al.* Diabetes and cardiovascular disease outcomes in the metabolically healthy obese phenotype: a cohort study. *Diabetes Care* 2013; 36: 2388–2394.
11. Moore JX, Chaudhary N, Akinyemiju T. Metabolic syndrome prevalence by race/ethnicity and sex in the United States, National Health and Nutrition Examination Survey, 1988–2012. *Prev Chronic Dis* 2017; 14: 1988–2012.
12. Palaniappan LP, Wong EC, Shin JJ, *et al.* Asian Americans have greater prevalence of metabolic syndrome despite lower body mass index. *Int J Obes* 2011; 35: 393–400.
13. Khosravi-Boroujeni H, Sarrafzadegan N, Sadeghi M, *et al.* Secular trend of metabolic syndrome and its components in a cohort of Iranian Adults from 2001 to 2013. *Metab Syndr Relat Disord* 2017; 15: 137–144.
14. Lim S, Shin H, Song JH, *et al.* Increasing prevalence of metabolic syndrome in Korea: the Korean National Health and Nutrition Examination Survey for 1998–2007. *Diabetes Care* 2011; 34: 1323–1328.
15. Hamer M, Bell JA, Sabia S, *et al.* Stability of metabolically healthy obesity over 8 years: the English Longitudinal Study of Ageing. *Eur J Endocrinol* 2015; 173: 703–708.

16. Huang J, Huang JLW, Withers M, *et al.* Prevalence of metabolic syndrome in Chinese women and men: a systematic review and meta-analysis of data from 734 511 individuals. *Lancet* 2018; 392(Supplement 1): S14.
17. Li R, Li W, Lun Z, *et al.* Prevalence of metabolic syndrome in Mainland China: a meta-analysis of published studies. *BMC Public Health* 2016; 16: 296.
18. Li R, Lu W, Jiang QW, *et al.* Increasing prevalence of type 2 diabetes in Chinese adults in Shanghai. *Diabetes Care* 2012; 35: 1028–1030.
19. Ruan Y, Mo M, Joss-Moore L, *et al.* Increased waist circumference and prevalence of type 2 diabetes and hypertension in Chinese adults: two population-based cross-sectional surveys in Shanghai, China. *BMJ Open* 2013; 3: e003408.
20. Li Y, Jiang H, Cheng M, *et al.* Performance and costs of multiple screening strategies for type 2 diabetes: two population-based studies in Shanghai, China. *BMJ Open Diabetes Res Care* 2020; 8, e001569.
21. World Health Organization International Association for the Study of Obesity, International Obesity Task Force. *The Asia-Pacific Perspective: Redefining Obesity and its Treatment*. Sydney: Health Communications Australia, 2000.
22. 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. *Circulation* 2005; 112: 2735–2752.
23. Aguilar M, Bhuket T, Torres S, *et al.* Prevalence of the metabolic syndrome in the United States, 2003–2012. *JAMA* 2015; 313: 1973–1974.
24. Segi M. *Cancer mortality for selected sites in 24 countries (1950–57)*. Sendai: Department of Public Health, Tohoku University of Medicine, 1960.
25. Doll R, Payne P, Waterhouse J. *Cancer Incidence in Five Continents, Vol. I*. Geneva: Union Internationale Contre le Cancer, 1966.
26. Cole TJ, Green PJ. Smoothing reference centile curves: the LMS method and penalized likelihood. *Stat Med* 1992; 11: 1305–1319.
27. Liang KY, Zeger AL. Longitudinal data analysis using generalized linear models. *Biometrika* 1986; 73: 13–22.
28. Ajlouni K, Khader Y, Alyousfi M, *et al.* Metabolic syndrome amongst adults in Jordan: prevalence, trend, and its association with socio-demographic characteristics. *Diabetol Metab Syndr* 2020; 12: 100.
29. Ostrihoňová T, Rimárová K, Bérešová J, *et al.* Prevalence and Trends of Metabolic Syndrome in Slovakia during the Period of 2003–2012. *Cent Eur J Public Health* 2017; 25: 313–320.
30. Shin D, Kongpakpaisarn K, Bohra C. Trends in the prevalence of metabolic syndrome and its components in the United States 2007–2014. *Int J Cardiol* 2018; 259: 216–219.
31. Kuzuya M, Ando F, Iguchi A, *et al.* Age-specific change of prevalence of metabolic syndrome: longitudinal observation of large Japanese cohort. *Atherosclerosis* 2007; 191: 305–312.
32. Chandola T, Brunner E, Marmot M. Chronic stress at work and the metabolic syndrome: prospective study. *BMJ* 2006; 332: 521–525.
33. Ingelsson E, Massaro JM, Sutherland P, *et al.* Contemporary trends in dyslipidemia in the Framingham Heart Study. *Arch Intern Med* 2009; 169: 279–286.
34. Kheirandish M, Asgari S, Lotfaliany M, *et al.* Secular trends in serum lipid levels of a Middle Eastern adult population; 10 years follow up in Tehran lipid and glucose study. *Lipids Health Dis* 2014; 13: 20.
35. Liu M, Wang J, Jiang B, *et al.* Increasing Prevalence of Metabolic Syndrome in a Chinese Elderly Population: 2001–2010. *PLoS One* 2013; 8: e66233.
36. Lorenzo C, Williams K, Gonzalez-Villalpando C, *et al.* The prevalence of the metabolic syndrome did not increase in Mexico City between 1990–1992 and 1997–1999 despite more central obesity. *Diabetes Care* 2005; 28: 2480–2485.
37. Stevens J, Katz EG, Huxley RR. Associations between gender, age and waist circumference. *Eur J Clin Nutr* 2010; 64: 6–15.
38. Carroll MD, Lacher DA, Sorlie PD, *et al.* Trends in serum lipids and lipoproteins of adults, 1960–2002. *JAMA* 2005; 294: 1773–1781.
39. Park YM, Sui X, Liu J, *et al.* The effect of cardiorespiratory fitness on age-related lipids and lipoproteins. *J Am Coll Cardiol* 2015; 65: 2091–2100.
40. Cheung BM, Li M, Ong KL, *et al.* High density lipoprotein-cholesterol levels increase with age in American women but not in Hong Kong Chinese women. *Clin Endocrinol* 2009; 70: 561–568.
41. Weijenberg MP, Feskens EJ, Kromhout D. Age-related changes in total and high-density-lipoprotein cholesterol in elderly Dutch men. *Am J Public Health* 1996; 86: 798–803.
42. Song PK, Li H, Man Q-Q, *et al.* Trends in Determinants of Hypercholesterolemia among Chinese Adults between 2002 and 2012: Results from the National Nutrition Survey. *Nutrients* 2017; 9: 279.
43. Du S, Neiman A, Batis C, *et al.* Understanding the patterns and trends of sodium intake, potassium intake, and sodium to potassium ratio and their effect on hypertension in China. *Am J Clin Nutr* 2014; 99: 334–343.
44. Syauqy A, Hsu C-Y, Rau H-H, *et al.* Association of Dietary Patterns with Components of Metabolic Syndrome and Inflammation among Middle-Aged and Older Adults with Metabolic Syndrome in Taiwan. *Nutrients* 2018; 10: 143.
45. Wang L, Zhang B, Wang H, *et al.* Intakes of energy and macronutrient among the elderly in nine provinces (autonomous region), China during 1991–2015. *Wei Sheng Yan Jiu* 2019; 48: 700–705.
46. Khaw KT, Sharp SJ, Finikarides L, *et al.* Randomised trial of coconut oil, olive oil or butter on blood lipids and other cardiovascular risk factors in healthy men and women. *BMJ Open* 2018; 8: e020167.

47. Rhee EJ, Kim HC, Kim JH, *et al.* 2018 Guidelines for the management of dyslipidemia. *Korean J Intern Med* 2019; 34: 723–771.
48. Li JH, Wang LM, Mi SQ, *et al.* [Awareness rate, treatment rate and control rate of dyslipidemia in Chinese adults, 2010]. *Zhonghua Yu Fang Yi Xue Za Zhi* 2012; 46: 687–691.
49. Liu X, Yu S, Mao Z, *et al.* Dyslipidemia prevalence, awareness, treatment, control, and risk factors in Chinese rural population: the Henan rural cohort study. *Lipids Health Dis* 2018; 17: 119.
50. Xing L, Liu S, Jing L, *et al.* Trends in prevalence, awareness, treatment, and control of hypertension in rural Northeast China: 2008 to 2018. *Biomed Res Int* 2020; 2020: 1456720.
51. Boyle JP, Thompson TJ, Gregg EW, *et al.* Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence. *Popul Health Metr* 2010; 8: 29.
52. Rahib L, Smith BD, Aizenberg R, *et al.* Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. *Cancer Res* 2014; 74: 2913–2921.
53. Chan JCN, Lim L-LL, Wareham NJ, *et al.* The Lancet Commission on diabetes: using data to transform diabetes care and patient lives. *Lancet* 2021; 396: 2019–2082.
54. Monteiro CA, Moura EC, Conde WL, *et al.* Socioeconomic status and obesity in adult populations of developing countries: a review. *Bull World Health Organ* 2004; 82: 940–946.
55. Wu H, Bragg F, Yang L, *et al.* Sex differences in the association between socioeconomic status and diabetes prevalence and incidence in China: cross-sectional and prospective studies of 0.5 million adults. *Diabetologia* 2019; 62: 1420–1429.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Methods S1 | Estimating direct medical costs for cardiovascular diseases (CVD) in Chinese adults in Shanghai.

Table S1 | Reported risk ratios and estimated population attributable fraction of metabolic syndrome, metabolic syndrome components and metabolic type of overweight for cardiovascular diseases.

Table S2 | Reported crude prevalence of metabolic syndrome based on the NCEP ATP III criteria in 2002–2003, 2009 and 2017 in other populations.

Figure S1 | Flow chart of subject selection in the 2002–2003 (A), the 2009 (B) and the 2017 surveys (C).

Figure S2 | Clusters of metabolic syndrome components in all subjects (A) and in subjects with MS (B) in the three population-based surveys.