BMJ Open

Impact of urinary sodium excretion on the prevalence and incidence of metabolic syndrome: a population-based study

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To cite: Yin L, Li S, He Y, *et al*. Impact of urinary sodium excretion on the prevalence and incidence of metabolic syndrome: a population-based study. *BMJ Open* 2023;**13**:e065402. doi:10.1136/bmjopen-2022-065402

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-065402).

Received 07 June 2022
Accepted 12 April 2023

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ABSTRACT

Objective To evaluate the association of metabolic syndrome (MetS) risk with 24-hour urinary sodium excretion (24hUNaE) estimated from spot urine samples.

Design Serial cross-sectional studies were conducted, and those with multiple repeated examinations were used to assess the MetS incidence risk.

Setting and Participants A health check-up programme was conducted between 2018 and 2021 and enrolled 59 292 participants to evaluate the relationship between MetS risk and 24hUNaE in the Third Xiangya Hospital, Changsha, China. Among these participants, 9550 had at least two physical examinations during this period, which were used to evaluate the association of a new occurrence of MetS with 24hUNaE.

Outcomes Guidelines for the prevention and treatment of dyslipidaemia in Chinese adults (revised in 2016) were used to define prevalent and incident MetS.

Results The prevalence of MetS was 19.3% at the first check-up; among individuals aged ≤55 years, the risk was higher in men than women, while among older individuals, a similar prevalence was observed in both sexes. A significant increase in MetS prevalence was observed per unit increase in 24hUNaE (adjusted OR (AOR) 1.11; 95% CI 1.09 to 1.13), especially for the prevalence of central obesity and elevated blood pressure. Additionally, 27.4% of the participants among the 7842 participants without MetS at the first check-up (male vs female: 37.3% vs 12.9%) were found to have a new occurrence of MetS at the second, third and/or fourth check-ups. A 25% increase in MetS incidence was observed per unit increase in 24hUNaE (95% CI 1.19 to 1.32), which was more prominent in the participants with a new occurrence of central obesity and elevated fasting blood glucose.

Conclusions Although the prevalence of MetS seemed stable, new occurrences of MetS remained high, which might result in MetS recurrence. The influence of sodium intake on MetS development is probably attributed to the increase in blood pressure and central obesity, but a new occurrence of MetS may develop through elevated blood glucose and central obesity.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Trends in metabolic syndrome (MetS) prevalence have not been evaluated since 2017.
⇒ This is the first study to assess the potential association of new occurrences of MetS with urinary sodium thus far in China.
⇒ Different trends of MetS prevalence with increasing age were observed in women and men.
⇒ The variation in MetS prevalence may be due to the change in sodium intake at various ages.
⇒ Our results may be limited in their generalisation to other populations due to the inclusion of only one centre.

INTRODUCTION

Metabolic syndrome (MetS) is estimated to affect approximately one-quarter of the world's population and is defined by the WHO as a pathological condition characterised by abdominal obesity, insulin resistance, hypertension and hyperlipidaemia.[1] Hence, MetS is not a single disease but is associated with cardiovascular diseases, diabetes, dyslipidaemia, cancer and disabilities, and has been defined by various organisations in slightly different ways.[2] With lifestyle changes and economic development, the prevalence of MetS is increasing in China, which has had serious effects on Chinese health. During 2000–2017, four national surveys across 31 provinces, autonomous regions and municipalities of mainland China found that the standardised prevalence of MetS had increased from 13.7% to 31.1%, although the definitions of MetS were slightly different, mainly due to the modification of the waist circumference (WC) cut-off.[3–6] To our knowledge, recent trends in MetS prevalence and its components have not been evaluated since 2017.

Although a moderate number of studies have suggested that people can control their blood pressure by reducing their sodium intake,[7–9] both low sodium intake and high sodium intake are related to increased

mortality and cardiovascular events compared with medium sodium intake.[10 11] In a Chinese population-based cohort study, the lowest risk was observed among those with sodium excretions of 3–5 g/day,[12] which exceeded all recommendations (WHO: <2 g/day and China: <2.4 g/day).[13 14] As MetS is regarded as the 'precursor' of cardiovascular diseases, it is particularly important to determine the comprehensive benefits of sodium intake in controlling blood pressure, blood glucose, blood lipids and obesity. A recent meta-analytical review including 17 cross-sectional studies explored the potential association between sodium intake and MetS, indicating that those with MetS had significantly higher levels of sodium than those with a healthy metabolic profile.[15] However, most individual studies evaluated this association using 24-hour urine samples, so the sample size is limited,[16–23] including one Chinese study.[23] Only three Korean studies used estimated sodium intake from spot urine samples.[24–26] As we know, spot urine samples are suggested as a practical and attractive alternative to 24-hour urine collection in large-scale population surveys, and are regarded as more accurate than dietary and food questionnaires due to better capturing of discretionary sodium use. Hence, we included urine tests in health check-up programmes beginning in 2018 to evaluate the associations of MetS prevalence and its components with estimated 24-hour urinary sodium excretion (24hUNaE), and further subgroup analyses were performed to compare the potential variations between women and men, as well as younger adults and elderly adults. Additionally, we also explored the relationships of new occurrences of MetS and its components with 24hUNaE among participants with at least two physical examinations during 2018–2021.

METHODS

Study subjects

During 2018–2021, 68 647 eligible random urine samples were collected among individuals who underwent a routine health check-up in the Health Management Center of the Third Xiangya Hospital, Changsha, China. A total of 20 427, 19 615, 16 307 and 12 298 participants came to the centre to check their health status in 2018, 2019, 2020 and 2021, respectively. When data from multiple check-ups were available, we selected the earliest check-up. After checking repeated measurements using unique Chinese residential ID card numbers, 61 039 participants underwent at least one physical examination during 2018–2021, among which 51 489 (84.35%) underwent only one check-up, 7975 (13.07%) underwent two, 1397 (2.3%) underwent three and 178 (0.3%) underwent four check-ups. Ultimately, data from 9550 participants who had undergone at least two check-ups were used to explore the potential influence of 24hUNaE on new occurrences of MetS.

Patient and public involvement

Because of the nature of this study being a fully data-based analyses based on the existing check-up databases, there was no specific involvement of patients or the public in the design, conduct, review and analysis of the study.

Inclusion criteria

Participants who met the following criteria were included in the final analyses: (1) were aged 18 years or older; (2) did not have missing values for main data, including age, sex, systolic blood pressure (SBP), diastolic blood pressure (DBP), WC, triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), fasting blood glucose (FBG), and urinary sodium, potassium and creatinine excretion values; (3) did not have exception values of blood pressure measurements: those with an SBP <70 mm Hg or SBP >260 mm Hg or a DBP <40 mm Hg or DBP >140 mm Hg were excluded; (4) did not have outliers of blood lipid levels: those with a TG level <0.2 mmol/L or TG level >30 mmol/L or an HDL-C level <0.1 mmol/L or HDL-C level >10.0 mmol/L were excluded; and (5) had plausible 24hUNaE values: those with a 24hUNaE ≥12 g/day were excluded.

Data collection

Trained physicians performed physical examinations, which included weight, height, WC, hip circumference, SBP and DBP measurements. Based on the Guidelines for Blood Pressure Measurement in China, blood pressure readings were taken on both arms using an OMRON automatic digital blood pressure monitor (OMRON HBP-9021, OMRON Healthcare, Scarborough, Ontario, Canada). Additionally, the collected information included age, sex, smoking status, drinking status and physical activities. Fasting blood samples were collected to test for FBG, total cholesterol, TG, low-density lipoprotein cholesterol and HDL-C levels using LEADMAN test kits (Beijing LEADMAN Biochemical Co, China).

A random urine sample was collected from each participant on the day of the physical examination. Simply speaking, a labelled urine container was provided for each subject to collect his/her midstream urine sample, which was transferred to the Department of Clinical Laboratory to test for sodium, potassium and creatinine within 2 hours. Sodium and potassium were examined by ion selective electrode method, and creatinine was examined by a dynamic enzymatic method (Beijing LEADMAN Biochemical Co, China). Blood and urine samples were measured using 7600 and 7170 Hitachi automatic biochemical analyser. More details of procedures for physical examination, blood and urine collection and measurements have been published elsewhere.[27–30]

Urinary sodium and potassium estimations

Sodium concentrations in fasting urine were measured and converted into an estimate of 24hUNaE using Tanaka equation, Kawasaki equation or INTERSALT equations.[31] These three methods have been evaluated and validated in a Chinese population, but all of the

methods underestimated the true 24hUNaE. Compared with the other two approaches, the Kawasaki equation had the lowest mean difference compared with the true 24hUNaE.[32] Therefore, we ultimately chose to use the Kawasaki method in the current study.[33]

Definitions of MetS and its components

Participants with three or more of the following factors were diagnosed as having MetS per the guidelines for the prevention and treatment of dyslipidaemia in Chinese adults (revised in 2016)[34]: (1) central obesity: a WC of ≥90 cm in men and ≥85 cm in women; (2) elevated TG: a fasting plasma TG level ≥1.7 mmol/L; (3) low HDL-C: a fasting plasma HDL-C level <1.0; (4) elevated blood pressure: an SBP ≥130 mm Hg or a DBP ≥85 mm Hg, the current use of blood pressure medication or having been diagnosed with hypertension by a physician; and (5) elevated FBG: an FBG level ≥6.1 mmol/L, the current use of antidiabetic medications or having been diagnosed with diabetes by a physician.

Statistical analyses

The Statistical Analysis System (SAS V.9.4 for Windows; SAS Institute) software was used for all statistical analyses in this study. Kolmogorov–Smirnov tests were used to assess the normal distribution of continuous variables. If a normal distribution ($p<0.05$), means and SD are presented, and two-sample t-tests are performed. On the contrary, continuous variables are shown as the median and IQR, and two-sample non-parametric Wilcoxon tests were used to compare the differences between participants with and without MetS. Categorical variables are presented as percentages (%) and numbers, and X^2 tests were performed. As independent variables, 24hUNaE at the first check-up was classified into four groups according to the sex-specific quartiles of the overall study population, and the lowest quartile was used as the reference. Binary logistic regression models were used to calculate ORs and their CIs of total MetS risk and five components, with quartiles of 24hUNaE and continuous 24hUNaE. Multivariate logistic regression models were used to assess the above-mentioned associations, adjusting for age, sex, current drinking, current smoking, physical activities and estimated 24-hour urinary potassium excretion (24hUKE). Restricted cubic splines (RCSs) were used to detect the possible non-linear dependency of the associations of MetS risk and its components with 24hUKE, using three knots at the 10th, 50th and 90th percentiles.[35] A scatter plot of 24hUNaE levels was created with a penalised B-spline in women and men. Subgroup analyses were conducted to evaluate the consistency between overall associations and each subgroup, including sex (female and male) and age (<60 years and ≥60 years).

RESULTS

A total of 61 071 participants were enrolled to provide random urine samples on the day of the physical examination in the Health Management Center between 2018 and 2021. A total of 213 participants aged <18 years were excluded. Of the remaining 60 858 participants aged ≥18 years, 1527 were excluded due to missing values of anthropometric measurements (n=1347), blood lipids (n=110), blood glucose (n=62) and blood pressure (n=8). Furthermore, 9 participants were excluded due to outliers of blood lipid and/or blood pressure values, and 30 were excluded due to 24hUNaE exception values. Ultimately, 59 292 participants were included in the final analyses (online supplemental appendix 1).

The prevalence of MetS and its components are illustrated in online supplemental appendix 2. Overall, 20 427, 19 615, 16 307 and 12 298 eligible participants were enrolled in our check-up programmes in 2018, 2019, 2020 and 2021, respectively, and men had a much higher risk of MetS than women. An increasing trend was observed in men (26.0% in 2018, 26.7% in 2019, 28.8% in 2020 and 32.1% in 2021; $p<0.01$), while the prevalence was stable in women (7.3%, 7.7%, 7.4% and 8.3%; $p=0.16$). Almost half of the female participants had at least one MetS component, but approximately 80% of the male participants had at least one component, which was stable from 2018 to 2021 (online supplemental appendix 3).

The characteristics of participants with MetS and without MetS are presented in table 1. Kolmogorov–Smirnov tests were used to assess the normal distribution of 18 continuous variables, none of which conformed to a normal distribution ($p>0.05$). After checking repeated measurements using unique Chinese residential ID card numbers, 59 292 participants had a mean age of 44.84±11.91 years at the first check-up. Participants with MetS were much older than those without MetS, and had worse profiles of obesity, blood pressure, blood lipids, blood glucose and salt intake (all $p<0.01$). MetS was more prevalent in men than women (28.08% vs 7.83%), and those aged ≥60 years had a higher risk of MetS than those who were younger (27.09% vs 18.32%). With the increase in the number of MetS components, the levels of 24hUNaE gradually increased in both sexes across all years (all $p<0.01$), and detailed data are shown in online supplemental appendix 4.

The 24hUNaE levels were fitted using a penalised B-spline by age, and total MetS prevalence is described across various age groups for women and men, which is illustrated in figure 1. The data show that both MetS prevalence and sodium intake increase with age. In women, the urinary sodium excretion level progressively increased with age, peaking at the age of 55 years, and then stabilising. Likewise, the prevalence of MetS continuously increased with age, and a rapid increase was observed at the age of approximately 55 years. On the other hand, men's urinary sodium excretion levels peaked at approximately 30 years of age before decreasing, although the overall level of urinary sodium excretion was still significantly higher in men than in women. The prevalence of MetS in men (from 11.2% to 33.5%) also increased significantly with age before the age of 55 years. Women

Table 1 General characteristics of participants with physical examinations during 2018–2021

	Participants with repeated measurements			Participants with only one measurement		
Median (IQR) or % (n)	**MetS**	**No MetS**	**P value***	**MetS**	**No MetS**	**P value***
Sample size	13 283	55 364		11 428	47 864	
Male sex	83.36 (11 073)	51.53 (28 529)	<0.01	82.32 (9408)	50.35 (24 098)	<0.01
Age (years)	49 (41–56)	44 (35–53)	<0.01	49 (41–56)	44 (34–53)	<0.01
Height (cm)	167.3 (161.9–172.0)	162.6 (157.0–168.8)	<0.01	167.0 (161.5–171.7)	162.5 (156.8–168.5)	<0.01
Weight (kg)	76.0 (69.3–83.0)	61.5 (54.2–69.7)	<0.01	76.0 (69.1–83.0)	61.1 (54.0–69.3)	<0.01
BMI (kg/m^2)	27.20 (25.56–29.07)	23.32 (21.37–25.28)	<0.01	27.25 (25.57–29.12)	23.28 (21.31–25.25)	<0.01
WC (cm)	93 (90–98)	80 (73–86)	<0.01	93 (90–98)	80 (73–86)	<0.01
HC (cm)	99 (95–102)	93 (89.0–96.5)	<0.01	99 (95–102)	93 (89–96)	<0.01
WHR	0.95 (0.91–0.98)	0.86 (0.81–0.91)	<0.01	0.95 (0.91–0.98)	0.86 (0.81–0.90)	<0.01
SBP (mm Hg)	134 (126–142)	118 (109–128)	<0.01	134 (126–142)	118 (109–128)	<0.01
DBP (mm Hg)	84 (77–90)	72 (66–80)	<0.01	84 (77–90)	72 (66–80)	<0.01
FBG (mmol/L)	6.04 (5.38–6.85)	5.25 (4.95–5.60)	<0.01	6.03 (5.38–6.87)	5.25 (4.94–5.59)	<0.01
TC (mmol/L)	5.22 (4.59–5.95)	4.92 (4.34–5.55)	<0.01	5.22 (4.59–5.94)	4.91 (4.33–5.54)	<0.01
TG (mmol/L)	2.59 (1.94–3.87)	1.21 (0.86–1.72)	<0.01	2.59 (1.94–3.88)	1.20 (0.85–1.71)	<0.01
HDL-C (mmol/L)	1.07 (0.95–1.24)	1.33 (1.16–1.53)	<0.01	1.07 (0.95–1.24)	1.34 (1.17–1.54)	<0.01
LDL-C (mmol/L)	2.72 (2.07–3.35)	2.86 (2.38–3.39)	<0.01	2.72 (2.07–3.34)	2.86 (2.37–3.39)	<0.01
24hUCrE (g/day)	1.68 (1.44–1.89)	1.20 (1.00–1.66)	<0.01	1.68 (1.42–1.89)	1.17 (0.99–1.65)	<0.01
24hUNaE (g/day)	4.27 (3.48–5.10)	3.95 (3.21–4.75)	<0.01	4.30 (3.50–5.13)	3.97 (3.22–4.77)	<0.01
24hUKE (g/day)	2.10 (1.83–2.39)	1.99 (1.73–2.29)	<0.01	2.10 (1.84–2.40)	1.99 (1.73–2.29)	<0.01
Salt intake (g/day)	10.86 (8.85–12.98)	10.06 (8.15–12.07)	<0.01	10.93 (8.89–13.04)	10.11 (8.20–12.12)	<0.01
Current smoking	39.87 (5296)	23.17 (12 829)	<0.01	40.18 (4592)	23.42 (11 212)	<0.01
Current drinking	42.52 (5648)	26.17 (14 491)	<0.01	42.18 (4820)	25.83 (12 362)	<0.01
Physical activities	54.87 (7288)	56.95 (31 532)	<0.01	53.53 (6117)	55.84 (26 726)	<0.01

*P values were obtained by two-sample non-parametric Wilcoxon tests for continuous variables and X^2 tests for categorical variables.
BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HC, hip circumference; HDL-C, high-density lipoprotein cholesterol; 24hUCrE, 24-hour urinary creatinine excretion; 24hUKE, 24-hour urinary potassium excretion; 24hUNaE, 24-hour urinary sodium excretion; LDL-C, low-density lipoprotein cholesterol; MetS, metabolic syndrome; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WHR, waist-to-hip ratio.

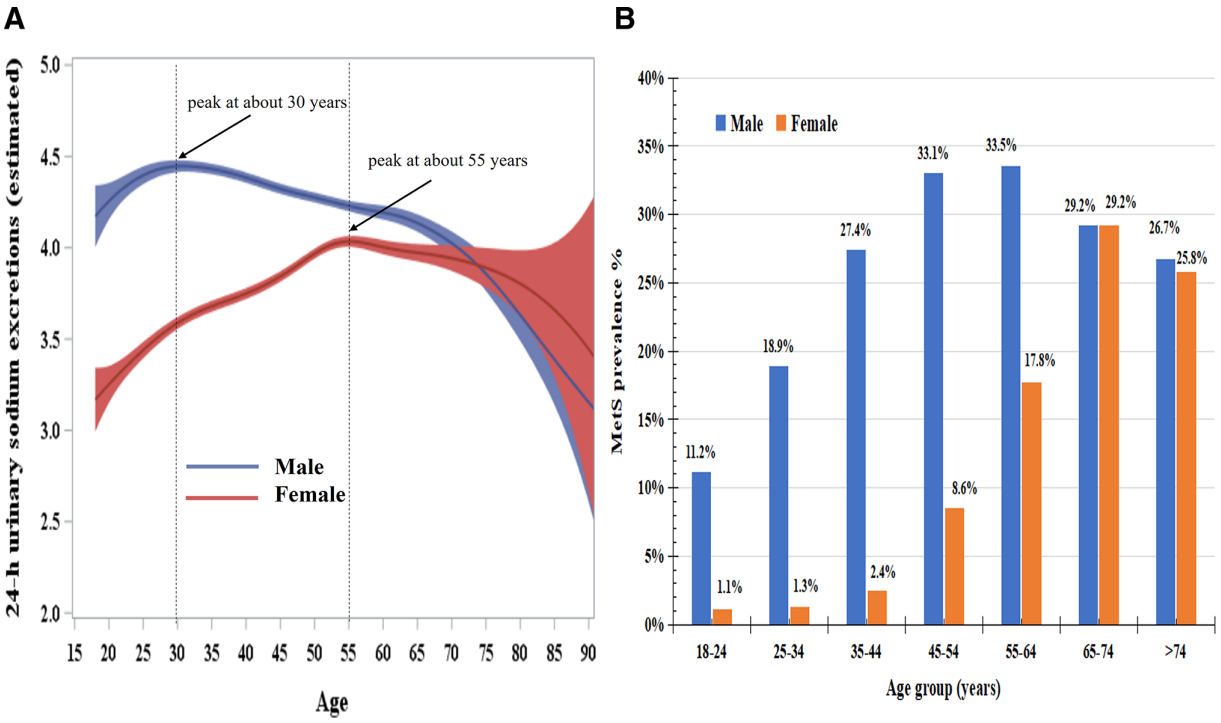

Figure 1 The trends of 24-hour urinary sodium excretion levels and MetS prevalence with increasing age. (A) Associations of 24-hour urinary sodium excretion levels with ageing with a penalised B-spline in men and women; (B) MetS prevalence across various age groups in men and women. MetS, metabolic syndrome.

had a total MetS prevalence of approximately 30% after the age of 65 years or older, while the prevalence in men stabilised at approximately 30%.

Among the 59 292 participants, unadjusted and adjusted logistic regression models were fitted for the total MetS prevalence and five components with 24hUNaE in online supplemental appendix 4 and table 2, and RCSs were also modelled using three knots, adjusting for age, sex, current smoking, current drinking, physical activities and 24hUKE values (shown in figure 2). A positive linear relationship was observed for the total MetS prevalence (adjusted OR (AOR) 1.11; 95% CI 1.09 to 1.13; p_{linear}<0.01), central obesity (AOR 1.19; 95% CI 1.17 to 1.21; p_{linear}<0.01), elevated TG (AOR 1.04; 95% CI 1.02 to 1.05; p_{linear}<0.01) and elevated blood pressure (AOR 1.25; 95% CI 1.23 to 1.27; p_{linear}<0.01) per unit increase in 24hUNaE, while a negative linear association was observed for low HDL-C (AOR 0.96; 95% CI 0.93 to 0.98; p_{linear}<0.01). A non-linear U-shaped association was observed for elevated FBG levels ($p_{non\text{-}linear}$<0.01), and the associations were significant in the second quartile (AOR 0.90; 95% CI 0.84 to 0.96) and the third quartile (AOR 0.89; 95% CI 0.83 to 0.96) compared with the first quartile.

Online supplemental appendix 5 and table 2 also show the subgroup analyses by sex and age. Strong linear associations of sodium intake were maintained with the total MetS prevalence, central obesity, and elevated blood pressure in both women and men. However, different results showed elevated TG, low HDL-C and elevated FBG in different sexes: (1) elevated TG: significance was not reached in men (p=0.61), although this association was significant in women (p<0.01); (2) low HDL-C: a negative linear relationship was observed only in men (p<0.01) but was not observed in women (p=0.92); and (3) elevated FBG: a 5% risk reduction was found per unit increase in 24hUNaE in men (AOR 0.95; 95% CI 0.93 to 0.98; p<0.01). Further subgroup analyses were performed by age group, and similar results were obtained only in those aged <60 years. A 6% risk reduction of elevated FBG (p=0.01) was observed among older adults (≥60 years) per unit increase in 24hUNaE, but significance was not found for elevated TG (p=0.39).

Online supplemental appendix 6 compares the difference across various examination times during 2018–2021, and the highest MetS prevalence was found among participants who underwent only one (19.41%), two (18.3%), three (16.7%) and four (10.1%) check-ups. After excluding participants with total MetS and its components at the first check-up, the incidence of total MetS, central obesity, elevated TG, low HDL-C, elevated blood pressure and elevated FBG levels was 27.4%, 12.6%, 17.6%, 7.0%, 16.0% and 7.1%, respectively, all of which were higher in men than women (total MetS: 37.3% vs 12.9%; central obesity: 17.9% vs 5.8%; elevated TG: 23.1% vs 11.3%; low HDL-C: 10.2% vs 2.1%; elevated blood pressure: 20.3% vs 10.1%; elevated FBG: 8.8% vs 4.2%). Table 3 presents the associations of the new occurrence of total MetS and the five components with 24hUNaE. Figure 3 illustrates the RCS models used to explore the potential non-linear relationships adjusting for age, sex, current smoking, current drinking, physical activities and 24hUKE at the first check-up, in which a

Table 2 Adjusted associations of MetS prevalence and its components with 24hUNaE

MetS and its components	Adjusted ORs (95% CIs) for 24hUNaE						
	Q1	Q2	Q3	Q4	P_{trend}	Per unit increase	P value
Overall*	14823	14823	14823	14823		59292	
Central obesity	1.00	1.07 (1.01, 1.13)	1.23 (1.16, 1.30)	1.63 (1.54, 1.72)	<0.01	1.19 (1.17, 1.21)	<0.01
Elevated TG	1.00	1.01 (0.96, 1.06)	1.09 (1.03, 1.14)	1.11 (1.05, 1.17)	<0.01	1.04 (1.02, 1.05)	<0.01
Low HDL-C	1.00	0.96 (0.89, 1.03)	0.95 (0.89, 1.03)	0.90 (0.83, 0.97)	0.04	0.96 (0.93, 0.98)	<0.01
Elevated BP	1.00	1.22 (1.15, 1.28)	1.40 (1.33, 1.48)	1.85 (1.75, 1.96)	<0.01	1.25 (1.23, 1.27)	<0.01
Elevated FBG	1.00	0.90 (0.84, 0.96)	0.89 (0.83, 0.96)	0.93 (0.87, 1.00)	<0.01	0.98 (0.96, 1.00)	0.11
Total MetS	1.00	1.02 (0.96, 1.09)	1.10 (1.03, 1.17)	1.32 (1.23, 1.40)	<0.01	1.11 (1.09, 1.13)	<0.01
Females†	6447	6446	6446	6447		25786	
Central obesity	1.00	1.07 (0.96, 1.20)	1.32 (1.18, 1.48)	1.87 (1.67, 2.09)	<0.01	1.27 (1.23, 1.32)	<0.01
Elevated TG	1.00	1.11 (1.01, 1.22)	1.15 (1.04, 1.26)	1.19 (1.08, 1.32)	<0.01	1.06 (1.03, 1.09)	<0.01
Low HDL-C	1.00	1.05 (0.87, 1.28)	1.01 (0.83, 1.24)	1.08 (0.88, 1.34)	0.86	1.00 (0.93, 1.07)	0.92
Elevated BP	1.00	1.13 (1.03, 1.24)	1.33 (1.21, 1.46)	1.85 (1.68, 2.03)	<0.01	1.28 (1.24, 1.32)	<0.01
Elevated FBG	1.00	0.93 (0.82, 1.05)	0.90 (0.79, 1.02)	1.03 (0.91, 1.17)	0.08	1.04 (0.99, 1.08)	0.11
Total MetS	1.00	1.07 (0.92, 1.24)	1.12 (0.97, 1.30)	1.52 (1.32, 1.77)	<0.01	1.19 (1.14, 1.25)	<0.01
Males†	8376	8377	8377	8376		33506	
Central obesity	1.00	1.06 (0.99, 1.13)	1.17 (1.09, 1.25)	1.45 (1.36, 1.55)	<0.01	1.14 (1.11, 1.16)	<0.01
Elevated TG	1.00	0.95 (0.89, 1.01)	1.02 (0.96, 1.08)	0.97 (0.91, 1.04)	0.12	1.00 (0.98, 1.02)	0.61
Low HDL-C	1.00	0.95 (0.87, 1.02)	0.94 (0.87, 1.02)	0.86 (0.79, 0.93)	<0.01	0.95 (0.93, 0.97)	<0.01
Elevated BP	1.00	1.24 (1.17, 1.33)	1.39 (1.30, 1.48)	1.72 (1.61, 1.84)	<0.01	1.20 (1.18, 1.23)	<0.01
Elevated FBG	1.00	0.88 (0.82, 0.96)	0.88 (0.81, 0.95)	0.87 (0.80, 0.95)	<0.01	0.95 (0.93, 0.98)	<0.01
Total MetS	1.00	1.01 (0.94, 1.08)	1.07 (1.00, 1.15)	1.20 (1.12, 1.29)	<0.01	1.07 (1.04, 1.09)	<0.01
Age <60 years†	13110	13208	13221	13285		52824	
Central obesity	1.00	1.07 (1.00, 1.14)	1.22 (1.15, 1.30)	1.63 (1.53, 1.73)	<0.01	1.19 (1.17, 1.21)	<0.01
Elevated TG	1.00	0.97 (0.92, 1.03)	1.06 (1.00, 1.12)	1.07 (1.01, 1.14)	<0.01	1.03 (1.01, 1.05)	<0.01
Low HDL-C	1.00	0.95 (0.88, 1.02)	0.95 (0.88, 1.03)	0.90 (0.83, 0.98)	0.09	0.96 (0.94, 0.99)	<0.01
Elevated BP	1.00	1.20 (1.13, 1.27)	1.39 (1.31, 1.47)	1.83 (1.73, 1.95)	<0.01	1.25 (1.22, 1.27)	<0.01
Elevated FBG	1.00	0.89 (0.82, 0.96)	0.91 (0.84, 0.98)	0.94 (0.87, 1.02)	0.01	0.99 (0.96, 1.01)	0.29
Total MetS	1.00	1.00 (0.93, 1.07)	1.10 (1.03, 1.18)	1.31 (1.22, 1.40)	<0.01	1.11 (1.08, 1.13)	<0.01
Age ≥60 years†	1713	1615	1602	1538		6468	
Central obesity	1.00	0.98 (0.85, 1.14)	1.17 (1.01, 1.36)	1.48 (1.27, 1.73)	<0.01	1.15 (1.10, 1.21)	<0.01
Elevated TG	1.00	1.10 (0.95, 1.27)	1.06 (0.91, 1.23)	1.11 (0.95, 1.30)	0.52	1.02 (0.97, 1.07)	0.39
Low HDL-C	1.00	1.08 (0.86, 1.36)	0.93 (0.73, 1.19)	0.78 (0.59, 1.03)	0.11	0.89 (0.82, 0.96)	<0.01
Elevated BP	1.00	1.35 (1.17, 1.57)	1.43 (1.24, 1.66)	1.87 (1.59, 2.19)	<0.01	1.23 (1.17, 1.29)	<0.01
Elevated FBG	1.00	0.87 (0.75, 1.01)	0.75 (0.64, 0.87)	0.81 (0.69, 0.96)	0.01	0.94 (0.89, 0.99)	0.01
Total MetS	1.00	1.07 (0.91, 1.25)	1.00 (0.85, 1.17)	1.22 (1.03, 1.44)	0.05	1.06 (1.01, 1.12)	0.02

*Adjusted for age, sex, current drinking, current smoking, physical activities and 24hUKE.
†Adjusted for age, current drinking, current smoking, physical activities and 24hUKE.
BP, blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; 24hUKE, 24-hour urinary potassium excretion; 24hUNaE, 24-hour urinary sodium excretion; MetS, metabolic syndrome; Q, quartile; TG, triglyceride.

linear association was found for the new occurrence of total MetS, central obesity, elevated TG and elevated FBG (p_{linear}<0.05). However, neither a linear nor non-linear relationship was detected for low HDL-C and elevated blood pressure. Healthy populations with higher 24hUNaE values at the first check-up were more likely to develop MetS per unit increase in 24hUNaE (AOR 1.25; 95% CI 1.19 to 1.32; p_{linear}<0.01), and similar results were also shown for the incidence of central obesity (AOR 1.24; 95% CI 1.16 to 1.34; p_{linear}<0.01), elevated TG (AOR 1.12; 95% CI 1.05 to 1.19; p_{linear}=0.02) and elevated FBG (AOR 1.22; 95% CI 1.13 to 1.33; p_{linear}<0.01). However,

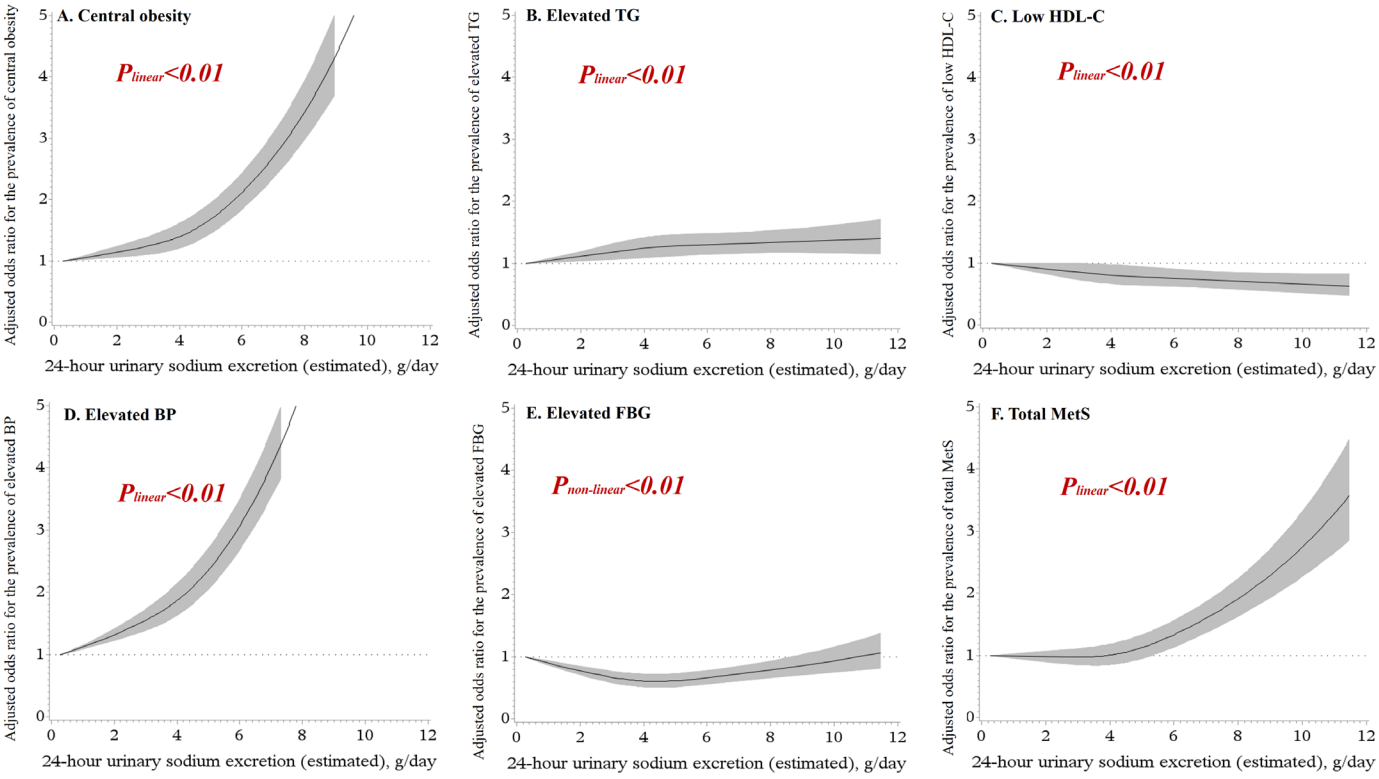

Figure 2 Adjusted associations of 24hUNaE with total MetS prevalence and its components using RCS. (A) central obesity; (B) elevated TG; (C) low HDL-C; (D) elevated BP; (E) elevated FBG; (F) total MetS. 24hUNaE, 24-hour urinary sodium excretion; BP, blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome; RCS, restricted cubic spline; TG, triglyceride.

no significance was obtained for low HDL-C (p_{linear}=0.81) and elevated blood pressure (p_{linear}=0.06).

Further subgroup analyses were conducted in women and men, and only positive associations of 24hUNaE with central obesity incidence were obtained in women (AOR 1.20; 95% CI 1.02 to 1.42; p=0.03), with total MetS incidence in women (AOR 1.24; 95% CI 1.11 to 1.39; p<0.01), with central obesity incidence in men (AOR 1.16; 95% CI 1.07 to 1.26; p<0.01), with elevated FBG incidence in men (AOR 1.19; 95% CI 1.08 to 1.30; p<0.01) and with new total MetS in men (AOR 1.15; 95% CI 1.08 to 1.21; p<0.01). Another subgroup analysis among those aged <60 years presented positive associations of 24hUNaE with the incidence of total MetS (AOR 1.19; 95% CI 1.12 to 1.25; p<0.01), central obesity (AOR 1.18; 95% CI 1.09 to 1.27; p<0.01), elevated TG (AOR 1.07; 95% CI 1.00 to 1.15; p=0.04) and elevated FBG (AOR 1.19; 95% CI 1.12 to 1.25; p<0.01). However, no significance was detected for total MetS and its components in those aged ≥60 years.

DISCUSSION

In this study, 19.3% of the participants were diagnosed as having MetS at the first check-up, and the prevalence of MetS in women was stable at approximately 8%; however, an increasing trend was observed in men (from 26% to 32%) between 2018 and 2021. Based on the spot urine sodium excretion estimates, the mean estimated 24hUNaE value was higher in those with MetS (4.34±1.23 g/day) than in those without MetS (4.04±1.15 g/day), both of which are more than double the recommended level (WHO: <2 g/day and China: <2.4 g/day).[13 14] It is noteworthy that similar trends were shown in the mean levels of sodium excretion and MetS prevalence in men and women with increasing age. The association between sodium intake and MetS risk might be attributed to the increase in blood pressure and central obesity. However, new occurrences of MetS may develop through elevating blood glucose levels and central obesity, and elevated blood pressure levels or hypertension did not occur as we expected.

Based on data from four China Nutrition and Health Surveillance surveys (2000–2017), the prevalence of MetS among residents aged 20 years or older in China is increasing, especially among women.[3–6] In our study, however, MetS was more prevalent in men (28.1%) than women (7.8%) in Changsha, Hunan Province, located in central South China. Sex differences in the prevalence of MetS have been observed in previous studies, but the results were inconsistent; some studies reported a higher prevalence of MetS in men,[5 36–39] while others found a higher prevalence of MetS in women.[3 4 6 16 17 25 40 41] A possible explanation may be due to the age distribution of the respective study population and the proportion of middle-aged and older adults. Because postmenopausal status may be associated with an increased risk of central obesity, hyperglycaemia, hypertension and insulin

Table 3 Associations of MetS incidence and its components with 24hUNaE

MetS and its components	Sample size			Unadjusted model		Adjusted model*	
	Total	MetS (+)	MetS (–)	OR (95% CI)	P value†	OR (95% CI)	P value†
Overall							
Central obesity	6716	849	5867	1.34 (1.25, 1.43)	<0.01	1.24 (1.16, 1.34)	<0.01
Elevated TG	5972	1052	4920	1.18 (1.11, 1.25)	<0.01	1.12 (1.05, 1.19)	<0.01
Low HDL-C	8395	590	7805	1.15 (1.07, 1.23)	<0.01	1.07 (0.99, 1.16)	0.10
Elevated BP	6290	1009	5281	1.16 (1.09, 1.23)	<0.01	1.11 (1.04, 1.19)	<0.01
Elevated FBG	8232	584	7648	1.21 (1.12, 1.30)	<0.01	1.22 (1.13, 1.33)	<0.01
Total MetS	7842	2149	5693	1.33 (1.27, 1.39)	<0.01	1.25 (1.19, 1.32)	<0.01
Females							
Central obesity	2909	168	2741	1.37 (1.18, 1.60)	<0.01	1.20 (1.02, 1.42)	0.03
Elevated TG	2773	314	2459	1.16 (1.04, 1.30)	0.01	1.09 (0.97, 1.24)	0.16
Low HDL-C	3271	68	3203	1.16 (0.92, 1.47)	0.21	1.13 (0.88, 1.46)	0.33
Elevated BP	2637	267	2370	1.12 (0.99, 1.27)	0.08	1.07 (0.94, 1.23)	0.31
Elevated FBG	3085	129	2956	1.22 (1.03, 1.44)	0.02	1.14 (0.95, 1.36)	0.18
Total MetS	3179	411	2768	1.35 (1.22, 1.49)	<0.01	1.24 (1.11, 1.39)	<0.01
Males							
Central obesity	3807	681	3126	1.16 (1.07, 1.25)	<0.01	1.16 (1.07, 1.26)	<0.01
Elevated TG	3199	738	2461	1.05 (0.98, 1.13)	0.17	1.04 (0.96, 1.13)	0.30
Low HDL-C	5124	522	4602	0.98 (0.91, 1.06)	0.64	0.97 (0.89, 1.06)	0.51
Elevated BP	3653	742	2911	1.04 (0.97, 1.12)	0.25	1.04 (0.96, 1.13)	0.32
Elevated FBG	5147	455	4692	1.10 (1.01, 1.20)	0.03	1.19 (1.08, 1.30)	<0.01
Total MetS	4663	1738	2925	1.13 (1.07, 1.19)	<0.01	1.15 (1.08, 1.21)	<0.01
Age <60 years							
Central obesity	6225	771	5454	1.35 (1.26, 1.45)	<0.01	1.18 (1.09, 1.27)	<0.01
Elevated TG	5418	942	4476	1.20 (1.13, 1.28)	<0.01	1.07 (1.00, 1.15)	0.04
Low HDL-C	7667	553	7114	1.15 (1.06, 1.24)	<0.01	0.99 (0.91, 1.07)	0.72
Elevated BP	6017	928	5089	1.17 (1.10, 1.25)	<0.01	1.07 (1.00, 1.15)	0.06
Elevated FBG	7699	498	7201	1.24 (1.15, 1.34)	<0.01	1.19 (1.09, 1.30)	<0.01
Total MetS	7252	1898	5354	1.36 (1.30, 1.43)	<0.01	1.19 (1.12, 1.25)	<0.01
Age ≥60 years							
Central obesity	491	78	413	1.20 (0.95, 1.52)	0.13	1.24 (0.96, 1.60)	0.11
Elevated TG	554	110	444	1.01 (0.84, 1.21)	0.93	1.07 (0.87, 1.30)	0.54
Low HDL-C	728	37	619	1.13 (0.85, 1.51)	0.40	1.07 (0.78, 1.47)	0.68
Elevated BP	273	81	192	1.03 (0.81, 1.29)	0.84	0.94 (0.72, 1.22)	0.63
Elevated FBG	533	86	447	1.08 (0.88, 1.34)	0.46	1.13 (0.90, 1.41)	0.31
Total MetS	590	251	339	1.13 (0.97, 1.32)	0.11	1.11 (0.94, 1.31)	0.23

*Adjusted for age, sex, current drinking, current smoking, physical activities and 24-hour urinary potassium excretion (estimated).
†P values were obtained by logistic regression models.
BP, blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; 24hUNaE, 24-hour urinary sodium excretion; MetS, metabolic syndrome; TG, triglyceride.

resistance, the prevalence of MetS was significantly higher in postmenopausal women than in premenopausal women.[42 43] The reported age at natural menopause in Chinese women ranged from 32 to 58 years, with a median of 49 years,[44] and most women experienced menopause at 55 years or younger, which has been used as a surrogate age for postmenopause in previous studies when no menopausal age was reported.[45 46] It is interesting that both sodium excretion and MetS prevalence were also significantly associated with age and sex in our study. To avoid the premenopausal effect, the prevalence of MetS in women was compared between individuals

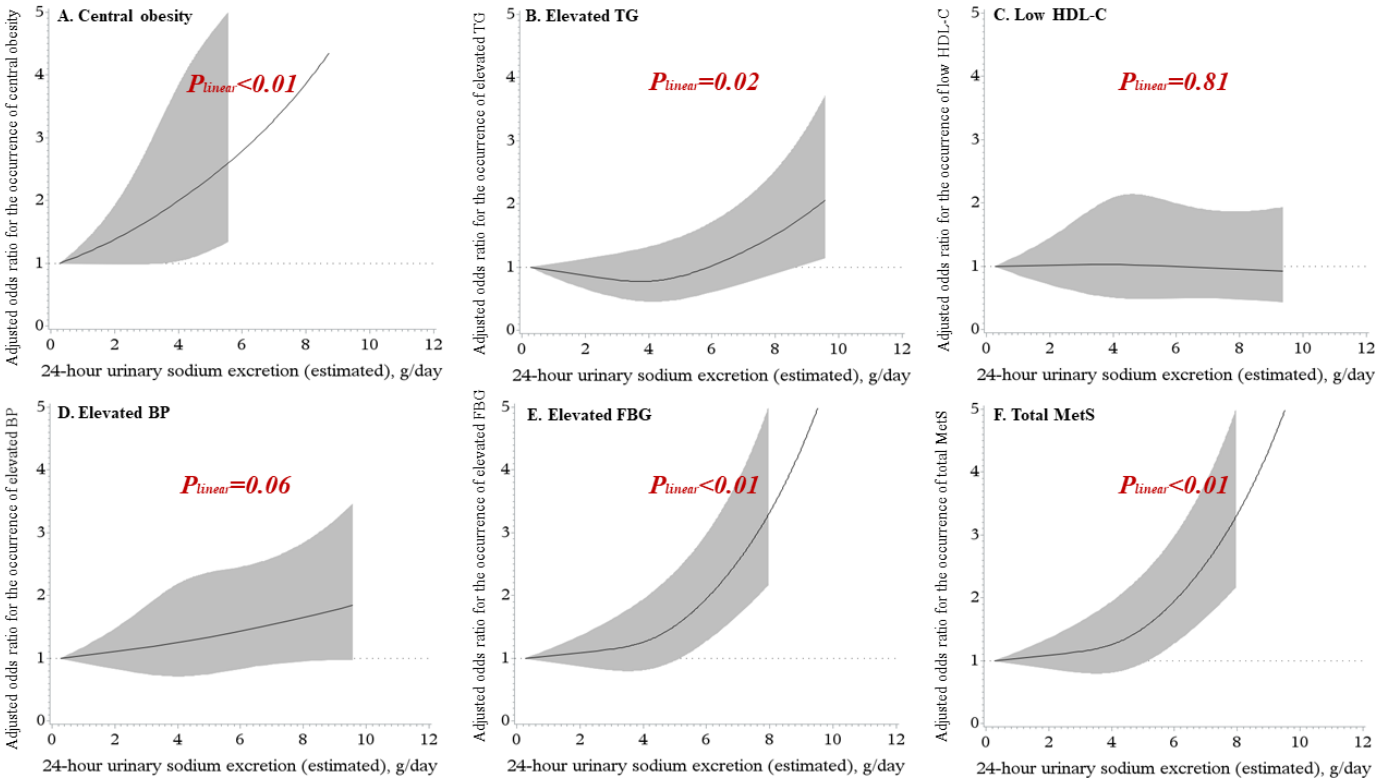

Figure 3 Adjusted associations of 24hUNaE with total MetS occurrence and its components using RCS. (A) Central obesity; (B) elevated TG; (C) low HDL-C; (D) elevated BP; (E) Elevated FBG; (F) total MetS. 24hUNaE, 24-hour urinary sodium excretion; BP, blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome; RCS, restricted cubic spline; TG, triglyceride.

aged <55 years and ≥55 years in our study, in which a much higher prevalence of MetS was observed in women aged ≥55 years (20.4%) than women aged <55 years (4.5%), but only a slight increase was observed in men (26.9% vs 32.3%). Further analyses based on more detailed age stratification also showed that the peak level of 24hUNaE was obtained in women at approximately 55 years of age, and the prevalence of MetS in women also reached the same level as that in men aged 65 years or older. On the other hand, the 24hUNaE levels overlapped in men and women with increasing age. A study in China reported that the risk of MetS in postmenopausal women increased with the number of years since menopause, reaching a peak level during the 5–9 years postmenopause and then decreasing.[47 48] However, available evidence is still limited, and more studies are required for further verification.

As approximately more than 95% of dietary sodium is excreted in the urine, 24-hour urinary excretion values were used to evaluate daily sodium intake as a gold-standard technique. The meta-analysis of seven studies involving 51 886 participants suggested that subjects in the highest categories of urinary sodium excretion levels had a 37% greater chance of developing MetS than those in the lowest category,[15] although this meta-analytical review also included individual studies using dietary sodium intake assessment methods from food records and 24-hour recalls and food frequency questionnaires, all of which tend to underestimate the mean sodium intake.[49–52] However, 24-hour collections are expensive and relatively burdensome for individuals, so most individual studies only used small sample sizes to evaluate the associations between urine sodium and MetS risk.[16–23 38] Only three Korean studies used estimated sodium intake from spot urine samples, one of which found that high salt intake was significantly associated with all five components of MetS and total MetS prevalence.[24] Two other Korean studies reported that sodium intake was associated with central obesity and elevated BP levels but not with dyslipidaemia or fasting glucose levels.[25 26] Results from both above-mentioned studies were reported in other previous studies regarding sodium intake based on 12-hour and 24-hour urine collections.[16 17 20 21 23 38] In our study, RCS models were used to explore the potential non-linear relationships between sodium intake and MetS risk, showing positive linear associations of sodium excretion with central obesity, elevated TG levels, elevated blood pressure levels and total MetS prevalence. In addition, negative linear relationships for low HDL-C and negative U-shaped associations for elevated FBG levels were observed. Hence, the positive association between MetS and sodium excretion originated mainly from the effects of elevated blood pressure levels and abdominal obesity, but it cannot be ignored that a high-salt diet may be associated with insulin resistance and fat metabolism in the development of MetS, especially for younger adults.

The population prevalence of one disease may depend mainly on the occurrence of new cases. To our knowledge, only a cross-sectional study design has been used to estimate the prevalence of MetS and assess the associations between sodium intake and MetS risk. Our study is the first to explore the potential influence of sodium intake on the incidence of MetS based on a 4-year check-up programme, although it was not a classic prospective cohort study. Generally, the incidence of MetS and the five components is still high, and men and older adults can get sick easily. Positive linear relationships were observed between sodium excretion and total MetS incidence, as well as each MetS component, but the relationships with low HDL-C and elevated blood pressure levels did not reach statistical significance. A high-sodium diet might play an important role in MetS development by inducing abdominal obesity and insulin resistance rather than by elevating blood pressure. The results of sensitivity analyses based on sex and age are not consistent with the overall population, which might be due to the small sample sizes in each subgroup. More relevant cohort studies are needed to draw a conclusion on the potential role of sodium intake on the occurrence of MetS.

Our study has potential limitations. First, the study population comprised only Chinese individuals, and only residents living in Changsha or nearby were included in our analyses. Most of the study participants were urban residents, and the salt intake in urban areas is usually lower than that in rural areas. Hence, our results may lack generalisability to other populations. Second, our urinary sodium excretion values were not determined by 24-hour urine collection but were estimated by spot urine measurements, which do not allow precise quantification for sodium intake throughout the day, especially for day-to-day varied diets in the Chinese population. Hence, our estimates might not represent actual sodium intake levels. Third, drug treatments for hypercholesterolaemia were not collected for participants with controlled elevated TG or low HDL-C levels during check-ups, and guidelines for the prevention and treatment of dyslipidaemia in Chinese adults (revised in 2016) were used to define a diagnosis of MetS in our study, in which no drug treatment of serum lipids was included in the definition of elevated TG and low HDL-C. Hence, the risk of hypercholesterolaemia may have been ignored due to good drug control, which may even have masked the true associations with sodium intake. However, the proportion of Chinese men and women whose hypercholesterolaemia status was aware, treated and controlled was only 8.8% and 7.5%, 3.5% and 3.4%, and 1.9% and 1.5%, respectively.[53] Fourth, we cleaned the data from check-ups in 4 natural years and analysed the association of new occurrences of MetS with sodium intake after deleting data from participants with MetS at the first check-up, but this is not a classic cohort study design. We could not evaluate the MetS status among those not presenting to our centre for later check-ups. Finally, major confounders were considered in our analyses, such as age, sex, smoking status, alcohol drinking and physical activities, but residual confounding factors were ruled out, including the estimated glomerular filtration rate, menopause status and daily energy intake, which may have led to the misinterpretation of the real relationship between sodium intake and MetS risk.

CONCLUSIONS

Although the prevalence of MetS seems to be stable, the incidence of MetS is high, which may lead to an increase in MetS prevalence. Men seemingly have a higher MetS risk than women, but the rapid increase in MetS risk in perimenopausal and postmenopausal women is alarming, and sodium restriction may be one of the treatment strategies. Our data further confirm that high estimated sodium excretion levels may be related to total MetS prevalence, which is more prominent for central obesity and elevated blood pressure levels. In addition, our team pioneered the assessment of the impact of sodium intake on the occurrence of MetS and found a linear association. However, individuals with a high-sodium diet are likely to have an increased incidence of central obesity and elevated FBG levels, but do not have for elevated blood pressure levels.

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Funding This work was supported by funding from the National Natural Science Foundation of China (81973324), Hunan Young Talent grant (2020RC3063), Natural Science Foundation of Hunan Province (2020JJ5858), and the Wisdom Accumulation and Talent Cultivation Project of the Third Xiangya Hospital of Central South University (YX202002).

Disclaimer The funders had no role in the study design, data collection and analysis, decision to publish or preparation of the manuscript.

Competing interests None declared.

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

Patient consent for publication Obtained.

Ethics approval This study involves human participants and ethics approval for research involving human participants was given by the Ethics Committee of the Third Xiangya Hospital, China (ID 2020-S498). All participants signed informed consent forms.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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