

# Metabolic Syndrome and 5-Year Incident Hyperuricemia Among Older Chinese Adults: A Community-Based Cohort Study

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**Background:** There was a lack of studies focusing on older adults about the longitudinal association between metabolic syndrome (MetS) and hyperuricemia (HUA). We aimed to assess the association of baseline MetS and incident HUA among older Chinese adults, with a special focus on the associations between different combinations of MetS components and HUA.

**Methods:** Data of 3247 Chinese adults aged 60 years or older included in a community-based longitudinal cohort study were analyzed. Anthropometric examinations and collection of blood sample were conducted both at baseline and follow-up. HUA was defined as 7 mg/dl or above for men and 6 mg/dl or greater for women. MetS was assessed based on the National Cholesterol Education Program-Adult Treatment Panel III, and older adults with the presence of at least three of MetS components were considered as having MetS.

**Results:** MetS and its components, including high blood pressure (BP), high body mass index, diabetes mellitus and high triglycerides, were significantly related to incident HUA. The association between high BP and incident HUA is strongest among the five MetS components. Among all combinations of MetS components, the group consisting of diabetes mellitus, high BP and high triglycerides had the highest odds for incident HUA (OR = 13.07, 95% CI = 4.95–34.54).

**Conclusion:** MetS and its components, except for low high-density lipoprotein cholesterol, could increase the risk of HUA among community-dwelling older adults, and high BP may be the most important determinant.

**Keywords:** hyperuricemia, metabolic syndrome, older adults, epidemiology

## Background

Hyperuricemia (HUA), an important risk factor for gout,<sup>1</sup> is a worldwide public health problem with high prevalence across different ethnic groups.<sup>2,3</sup> The prevalence of HUA increased with age and was higher among older adults.<sup>4,5</sup> HUA could increase the risk of cardiovascular events and all-cause mortality,<sup>6</sup> and therefore understanding the risk factors for HUA is important for the prevention of gout and cardiovascular events. Specific metabolic abnormalities such as blood glucose, pressure and lipids have been suggested to be involved in the development of HUA.<sup>7–9</sup> Metabolic syndrome (MetS) is a constellation of major metabolic disorders and understanding its association with HUA could more comprehensively and accurately evaluate how metabolic abnormalities plays a role in the pathological mechanism of HUA.

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The prevalence of HUA was higher in MetS when compared to those without MetS,<sup>10</sup> and serum uric acid (SUA) was also reported to be increased in individuals with MetS.<sup>11,12</sup> Moreover, studies assessing the longitudinal associations between MetS and SUA/HUA indicated that MetS could predict elevated SUA or incident HUA.<sup>13,14</sup> However, some key questions remain unanswered. First, there was a lack of studies focusing on older adults, who have a high prevalence and incidence of both conditions compared with younger generations. Second, MetS includes 5 major components and which combination of these components best predicts the incidence of HUA has not been elucidated.

To address this gap, we performed a community-based longitudinal cohort study to assess the association of baseline MetS and incident HUA among Chinese adults aged 60 years or older, with a special focus on the associations between different combinations of MetS components and the occurrence of HUA. The findings would be conducive to tackling modifiable risk factors for the prevention of HUA and gout.

## Methods

### Study Design and Procedure

This was a community-based cohort study, which was conducted among older adults, aged 60 years or older, who lived in Weitang town of Suzhou located in the eastern part of China. Details of the baseline study have been described elsewhere.<sup>15–17</sup> In the baseline examinations, 6030 families who had an older adult aged 60 years or older based on local official records received an invitation letter, which explained the nature of the study and invited the older adults to participate. Exclusion criteria applied to those who had been living there shorter than six months, had migrated from the residing address, or had deceased. Of the 5613 eligible older adults, 4611 attended the baseline clinical examinations from August 2014 to February 2015. The final sample at baseline consisted of 4579 older adults who had a complete data of anthropometric examinations, questionnaires and blood sample analyses. Five years later, these participants were invited to attend the anthropometric examination and collection of blood sample. Home visits or revisits were conducted to encourage older adults who did not participate in the follow-up examinations to attend with the aim of improving the follow-up rate of study. Older adults at baseline were excluded when they declined to participate, moved away and could not be contacted or deceased before the follow-up examination. Older adults with HUA at baseline or without data about SUA at the follow-

up examination were excluded. Official death registration forms were used to identify the death of individuals at baseline.

Both baseline and follow-up studies were conducted to abide by the tenets of the Helsinki Declaration and were approved by the Institutional Review Board of Soochow University.

### Clinical and Biochemical Measurements

Blood samples of participants were collected and frozen at  $-80^{\circ}\text{C}$  before transferring to laboratory technicians to find related data including SUA, fasting plasma glucose (FPG), high-density lipoprotein cholesterol (HDL-C) and blood triglycerides.

Blood pressure (BP) was measured using an automatic blood pressure monitor (Dinamap model Pro Series DP110X-RW, 100V2; GE Medical Systems Information Technologies, Inc., Milwaukee, Wisconsin, United States) when older adults had a rest of 5 minutes or longer. The recorded BP was the average value of the last two readings. Body height and weight of older adults without shoes and with light clothing were measured using a wall-mounted measurement tape and digital scale, separately. Body mass index (BMI,  $\text{kg}/\text{m}^2$ ) was calculated as the weight in kilograms divided by the square of the height in meters.

These clinical and biochemical indicators were examined with similar procedures for both baseline and follow-up study participants.

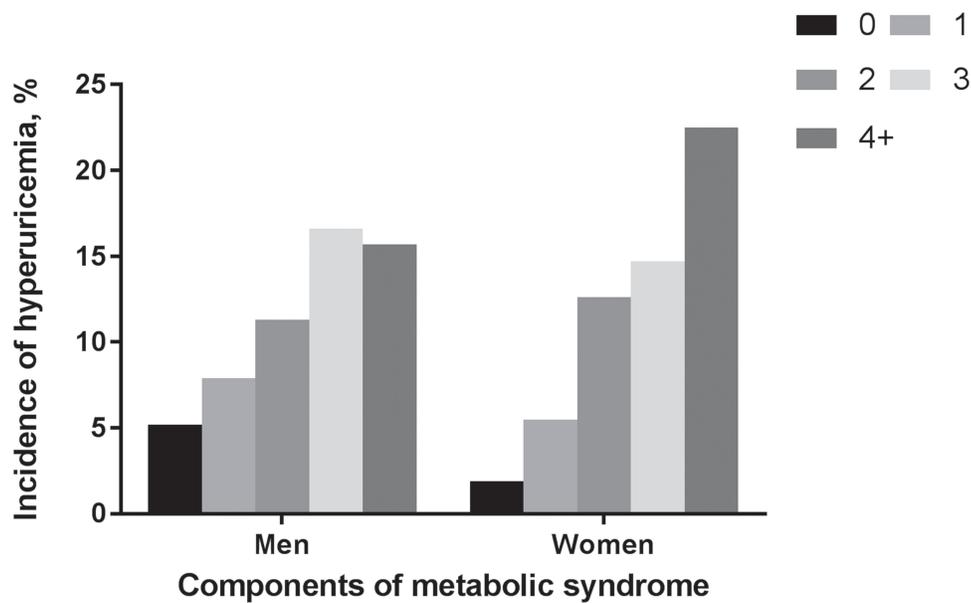
### Definitions of HUA and MetS

HUA was defined as 7 mg/dl or above for men and 6 mg/dl or greater for women.<sup>18</sup>

The MetS of participants was assessed based on the National Cholesterol Education Program-Adult Treatment Panel III.<sup>19</sup> MetS was diagnosed when participants met three or more of the following components: (1) BMI of  $25 \text{ kg}/\text{m}^2$  or above; (2) high BP (BP of 130/85 mmHg or greater or on antihypertensive drug treatment); (3) elevated blood triglycerides (1.7 mmol/L or higher); (4) diabetes mellitus defined as FPG of 7.0 mmol/L or above or with diabetes; (5) low HDL-C (lower than 1.0 mmol/L in men and 1.3 mmol/L in women).

### Assessment of Main Covariates

Information on participants' socio-demographic characteristics including age, gender, marriage status (living with spouse/living without spouse), educational level (primary and below education/secondary education or above) and monthly income ( $\leq 1000/1001\text{--}3000/>3000$  Chinese Yuan)



**Figure 1** Incidence of hyperuricemia by increasing metabolic syndrome components in men and women.

as well as lifestyle habits was collected using a pre-designed questionnaire. Data regarding lifestyle habits such as smoking, alcohol intake, tea consumption and physical activity were also collected during the questionnaire interview. Smoking was queried through the question: “Have you ever smoked?”<sup>20</sup> Older adults who have drunk alcohol in the past three months were classified as alcohol intake.<sup>21</sup> Status of tea consumption was inquired with the question: “Do you usually drink tea?” and subjects who answered “yes” were coded as habitual tea drinkers.<sup>22</sup> Physical activity was queried with the question: “How long do you exercise every day?” and older adults with physical activity were participants who spent time on exercise.<sup>23</sup>

## Statistics Analysis

Chi-square test and Student’s *t*-test were separately used to compare categories and continuous variables of participants according to HUA status at follow-up, and percentage as well as mean  $\pm$  standard deviation were calculated to express the comparison, as appropriate. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using two logistic regression models to estimate the effects of baseline MetS and its components on 5-year incident HUA. The first model adjusted for age and gender only, and the second one additionally adjusted for marriage status, educational level, monthly income, lifestyle habits including alcohol intake, smoking status, tea consumption, physical activity and baseline SUA. In addition, in logistic regressions of assessing linear trends, quartiles of MetS

components at baseline were treated as continuous variables by assigning each quartile with a median. Logistic regression model was also used to investigate the influences of different combinations of baseline MetS components on incident HUA and those without any MetS components were treated as the “reference group”. A stratified-analysis was performed to evaluate the associations of baseline MetS components with incident HUA in different statuses of diabetes mellitus component.

Data were analyzed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA) and statistical significance was considered if a *p*-value was less than 0.05.

## Results

The prevalence of HUA at baseline was 15.8%. Among 4579 older adults at baseline, 183 (4.0%) deceased before the follow-up examination and 526 (11.5%) refused to participant or were out of touch. Of the 3870 participants enrolled in the follow-up examination, 608 older adults with HUA at baseline and 15 participants without data about SUA at follow-up examination were excluded. Eventually, 3247 older adults were included in this longitudinal analysis.

This study sample consisted of 1517 men and 1730 women with a respective average SUA of 5.4 mg/dl and 4.4 mg/dl at baseline. In Total, 308 (9.5%) developed HUA among 3247 participants free of HUA at baseline. As shown in Figure 1, incidence of HUA increased with elevated number of MetS components in both men and women (both *p* values for trend <0.001). In participants

with MetS, the incidence of HUA is similar in men and women (17.0% versus 16.3%). Participants' characteristics by HUA status at follow-up are displayed in Table 1. Compared to participants without HUA at follow-up, older adults with HUA were more likely to have higher level of SBP, DBP, BMI, FPG, TG and a lower level of HDL-C.

Table 2 displays linear trends between baseline MetS components and risk of HUA. Older adults in the 4th quartiles of systolic BP, BMI, FPG and triglycerides had a greater risk of developing HUA compared to those in first quartiles ( $P < 0.05$ ). Even after adjusting for socio-demographic characteristics, lifestyle habits and baseline SUA, elevated quartiles of MetS components except diastolic BP and HDL-C quartiles were associated with an increasing risk of HUA (all  $p$  values for trend  $< 0.05$ ). MetS (OR = 1.73,  $P < 0.001$ ) and its components including high BP (OR = 2.16,  $P = 0.002$ ), high BMI (OR = 1.87,  $P < 0.001$ ), diabetes mellitus (OR = 1.76,  $P = 0.002$ ) and high triglycerides (OR = 1.44,  $P = 0.01$ ) were significantly related to incident HUA. The association between high BP and incident HUA is strongest among the five MetS components (Table 3). Moreover, increasing the number of MetS components at baseline was positively related to incident HUA though the presence of only one MetS component was not a significant predictor.

Table 4 presents the associations of specific combinations of MetS components at baseline with incident HUA. In this analysis, individuals free of MetS components were treated as the "reference group" and we found that the presence of a single MetS component had no influence on incident HUA. In combinations of two MetS components, groups of diabetes mellitus and high BP (2.1), high BP and high BMI (2.5), high BP and high triglycerides (2.6) as well as high BP and low HDL-C (2.7) were significantly related to incident HUA (all  $p$  values  $< 0.05$ ). Groups including both high BP and any other two MetS components were associated with higher risk of incident HUA (3.1, 3.2, 3.3, 3.7, 3.8, and 3.9). A combination of four MetS components without high triglycerides was not significantly linked to incidence of HUA while other four combinations showed significant associations. Participants with all five MetS components were associated with approximately five-fold odds of incident HUA (OR = 5.01, 95% CI = 1.31–19.26). Among all combinations of MetS components, the group consisting of diabetes mellitus, high BP and high triglycerides had the highest odds for incident HUA (OR = 13.07, 95% CI = 4.95–34.54). All combinations of MetS associated with incident HUA contained the component of high BP.

In stratified analysis by the presence of diabetes mellitus, high BP (OR = 3.17, 95% CI = 1.30–3.61), high BMI

**Table 1** Baseline Characteristics of Study Participants According to Development of Hyperuricemia

| Characteristic                     | No HUA (n = 2939) | HUA (n = 308) | P value |
|------------------------------------|-------------------|---------------|---------|
| Age, mean (SD), years              | 66.9 (5.5)        | 67.5 (5.8)    | 0.09    |
| Gender (women), n (%)              | 1565 (53.2)       | 165 (53.6)    | 0.91    |
| Primary and below education, n (%) | 2554 (86.9)       | 272 (88.3)    | 0.48    |
| Living with spouse, n (%)          | 2470 (84.0)       | 256 (83.1)    | 0.67    |
| Monthly income, n (%)              |                   |               | 0.39    |
| ≤1000 CNY                          | 1628 (55.4)       | 181 (58.8)    |         |
| 1001–3000 CNY                      | 1100 (37.4)       | 103 (33.4)    |         |
| >3000 CNY                          | 211 (7.2)         | 24 (7.8)      |         |
| Current smoking, n (%)             | 763 (26.0)        | 80 (26.0)     | 0.77    |
| Alcohol consumption, n (%)         | 629 (21.4)        | 76 (24.7)     | 0.19    |
| Tea consumption, n (%)             | 964 (32.8)        | 108 (35.1)    | 0.42    |
| Physical activity, n (%)           | 1231 (41.9)       | 127 (41.4)    | 0.86    |
| SBP, mean (SD), mmHg               | 143.2 (19.3)      | 148.2 (19.4)  | <0.001  |
| DBP, mean (SD), mmHg               | 85.2 (11.2)       | 87.2 (11.5)   | 0.003   |
| BMI, mean (SD), kg/m <sup>2</sup>  | 23.2 (5.0)        | 24.3 (2.7)    | <0.001  |
| FPG, mean (SD), mmol/L             | 5.6 (1.1)         | 5.8 (1.3)     | 0.001   |
| HDL-C, mean (SD), mmol/L           | 1.5 (0.4)         | 1.4 (0.4)     | <0.001  |
| TG, mean (SD), mmol/L              | 1.3 (0.7)         | 1.6 (0.9)     | <0.001  |

**Abbreviations:** HUA, hyperuricemia; SD, standard deviation; CNY, Chinese Yuan; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides.

**Table 2** Odds Ratios and 95% Confidence Intervals for the Risk of Hyperuricemia According to Quartiles of Metabolic Syndrome Components

| Characteristics                  | Age, Sex-Adjusted Model |                   | Multivariable-Adjusted Model* |                   |
|----------------------------------|-------------------------|-------------------|-------------------------------|-------------------|
|                                  | OR (95% CI)             | P value for Trend | OR (95% CI)                   | P value for Trend |
| SBP quartiles, mmHg              |                         | <0.001            |                               | 0.01              |
| 1 (≤130)                         | 1.00                    |                   | 1.00                          |                   |
| 2 (131–143)                      | 1.24 (0.86, 1.79)       |                   | 1.08 (0.73, 1.59)             |                   |
| 3 (144–156)                      | 1.59 (1.12, 2.27)       |                   | 1.35 (0.92, 1.96)             |                   |
| 4 (>156)                         | 1.85 (1.31, 2.62)       |                   | 1.51 (1.04, 2.19)             |                   |
| DBP quartiles, mmHg              |                         | 0.003             |                               | 0.18              |
| 1 (≤78)                          | 1.00                    |                   | 1.00                          |                   |
| 2 (79–85)                        | 1.21 (0.86, 1.72)       |                   | 0.99 (0.68, 1.44)             |                   |
| 3 (86–93)                        | 1.35 (0.96, 1.90)       |                   | 1.10 (0.76, 1.59)             |                   |
| 4 (>93)                          | 1.63 (1.17, 2.28)       |                   | 1.24 (0.87, 1.78)             |                   |
| BMI quartiles, kg/m <sup>2</sup> |                         | <0.001            |                               | <0.001            |
| 1 (≤21.91)                       | 1.00                    |                   | 1.00                          |                   |
| 2 (21.92–23.42)                  | 1.61 (1.09, 2.37)       |                   | 1.36 (0.90, 2.04)             |                   |
| 3 (23.43–24.09)                  | 1.83 (1.22, 2.73)       |                   | 1.45 (0.94, 2.23)             |                   |
| 4 (>24.09)                       | 3.20 (2.23, 4.61)       |                   | 2.15 (1.45, 3.17)             |                   |
| FPG, mmol/L                      |                         | 0.001             |                               | 0.01              |
| 1 (≤4.98)                        | 1.00                    |                   | 1.00                          |                   |
| 2 (4.99–5.35)                    | 1.20 (0.84, 1.71)       |                   | 1.25 (0.86, 1.83)             |                   |
| 3 (5.36–5.83)                    | 1.29 (0.90, 1.83)       |                   | 1.28 (0.88, 1.87)             |                   |
| 4 (>5.83)                        | 1.73 (1.24, 2.42)       |                   | 1.61 (1.12, 2.31)             |                   |
| HDL-C, mmol/L                    |                         | <0.001            |                               | 0.05              |
| 1 (≤1.20)                        | 1.00                    |                   | 1.00                          |                   |
| 2 (1.21–1.43)                    | 0.66 (0.48, 0.90)       |                   | 0.73 (0.52, 1.02)             |                   |
| 3 (1.44–1.71)                    | 0.61 (0.44, 0.83)       |                   | 0.81 (0.58, 1.15)             |                   |
| 4 (>1.71)                        | 0.45 (0.31, 0.63)       |                   | 0.66 (0.45, 0.96)             |                   |
| TG, mmol/L                       |                         | <0.001            |                               | <0.001            |
| 1 (≤0.83)                        | 1.00                    |                   | 1.00                          |                   |
| 2 (0.84–1.12)                    | 1.15 (0.76, 1.71)       |                   | 0.96 (0.63, 1.47)             |                   |
| 3 (1.13–1.55)                    | 2.01 (1.39, 2.90)       |                   | 1.45 (0.98, 2.14)             |                   |
| 4 (>1.55)                        | 2.93 (2.06, 4.17)       |                   | 1.79 (1.22, 2.61)             |                   |

**Note:** \*Adjusted for age, sex, educational level, monthly income, marriage status, smoking status, alcohol intake, tea consumption, physical activity and baseline serum uric acid.

**Abbreviations:** SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; OR, odds ratio; CI, confidence interval.

(OR = 2.06, 95% CI = 1.52–2.80) and low HDL-C (OR = 1.39, 95% CI = 1.00–1.92) increased risk of HUA only in participants without diabetes mellitus. (Table 5)

## Discussion

This community-based cohort study among older Chinese adults aged 60 years or older indicated that MetS and its components of diabetes mellitus, high BP, high BMI and high triglycerides at baseline were associated with incident HUA. In addition, high BP may be the most important MetS component contributing to incidence of HUA. Older

adults with simultaneous high BP, diabetes mellitus and high triglycerides may be most likely to develop HUA among all possible combinations of MetS components.

The result, that baseline MetS was a risk factor for incident HUA, was not unexpected and was consistent with some studies carried out in other countries.<sup>13,14,24</sup> A cohort study in middle-aged men in South Korea demonstrated that the incidence of HUA increased across MetS at baseline with the hazard ratio being 1.41.<sup>13</sup> In studies conducted in North American countries, MetS was reported to be associated with incident HUA both in men

**Table 3** Risk of Developing Hyperuricemia According to Metabolic Syndrome and Its Components

| Characteristics             | Age, Sex-Adjusted Model |         | Multivariable-Adjusted Model* |         |
|-----------------------------|-------------------------|---------|-------------------------------|---------|
|                             | OR (95% CI)             | P value | OR (95% CI)                   | P value |
| MetS                        |                         |         |                               |         |
| Absent                      | 1.00                    |         | 1.00                          |         |
| Present                     | 2.43 (1.87, 3.16)       | <0.001  | 1.73 (1.30, 2.30)             | <0.001  |
| High BP component           |                         |         |                               |         |
| Absent                      | 1.00                    |         | 1.00                          |         |
| Present                     | 2.76 (1.73, 4.39)       | <0.001  | 2.16 (1.33, 3.50)             | 0.002   |
| High BMI component          |                         |         |                               |         |
| Absent                      | 1.00                    |         | 1.00                          |         |
| Present                     | 2.44 (1.88, 3.17)       | <0.001  | 1.87 (1.41, 2.47)             | <0.001  |
| Diabetes mellitus component |                         |         |                               |         |
| Absent                      | 1.00                    |         | 1.00                          |         |
| Present                     | 1.65 (1.19, 2.28)       | 0.003   | 1.76 (1.23, 2.52)             | 0.002   |
| Low HDL-C component         |                         |         |                               |         |
| Absent                      | 1.00                    |         | 1.00                          |         |
| Present                     | 1.73 (1.31, 2.27)       | <0.001  | 1.23 (0.92, 1.66)             | 0.17    |
| High TG component           |                         |         |                               |         |
| Absent                      | 1.00                    |         | 1.00                          |         |
| Present                     | 1.98 (1.53, 2.57)       | <0.001  | 1.44 (1.08, 1.90)             | 0.01    |
| Number of MetS components   |                         |         |                               |         |
| 0                           | 1.00                    |         | 1.00                          |         |
| 1                           | 1.77 (1.00, 3.14)       | 0.05    | 1.41 (0.78, 2.55)             | 0.26    |
| 2                           | 3.48 (1.96, 6.19)       | <0.001  | 2.38 (1.31, 4.34)             | 0.005   |
| 3                           | 4.73 (2.60, 8.60)       | <0.001  | 2.70 (1.44, 5.07)             | 0.002   |
| 4+                          | 6.80 (3.51, 13.17)      | <0.001  | 3.57 (1.77, 7.18)             | <0.001  |

**Note:** \*Adjusted for age, sex, educational level, monthly income, marriage status, smoking status, alcohol intake, tea consumption, physical activity and baseline serum uric acid.

**Abbreviations:** MetS, metabolic syndrome; BP, blood pressure; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; OR, odds ratio; CI, confidence interval.

and women.<sup>14,24</sup> Moreover, a study with participants from three urban areas and one rural county of Beijing showed a 2.0-fold risk of HUA among community elderly with MetS,<sup>25</sup> which was similar to our results.

It was in line with some studies that MetS components of high BP, high BMI, diabetes mellitus and high triglycerides at baseline were related to an increased risk of HUA.<sup>24,26</sup> In this study, 96.6% of older adults were found to have abnormal BP, defined as 130/85 mmHg or greater, among individuals suffering from MetS. The high BP component may act as an important risk factor related to the incidence of HUA in this population. A longitudinal study has reported that those with hypertension were at a 1.65-fold risk of HUA.<sup>26</sup> Hypertension may result in the vascular disease related to decreased renal blood flow and finally stimulate urate reabsorption.<sup>27</sup> The other processes

of hypertension causing HUA may be through blocking urate excretion and generating increased xanthine oxidase associated with production of uric acid.<sup>8,28,29</sup> In our study, high BMI also had a higher impact on incident HUA. According to a study conducted among large cohorts, the increment of risk of HUA was 7.5% per 4 kg/m<sup>2</sup> increased in BMI.<sup>30</sup> Insulin resistance may be a link between obesity and HUA. Obesity may, through chronic adipose tissue inflammation, cause the insulin resistance,<sup>31</sup> which may lead to the enhanced activity of hexose monophosphate shunt and eventually contribute to increased purine biosynthesis and turnover.<sup>32</sup> Moreover, higher serum leptin concentration in individuals with obesity could induce oxidative stress in endothelial cells.<sup>33,34</sup> The oxidative stress has been reported to be associated with increased SUA concentration.<sup>34</sup>

**Table 4** Associations Between Individual and Specific Combinations of Metabolic Syndrome Components and Risk of Hyperuricemia

|  | Diabetes Mellitus | Metabolic Syndrome Components |          |         |           | Hyperuricemia                 |         |
|--|-------------------|-------------------------------|----------|---------|-----------|-------------------------------|---------|
|  |                   | High BP                       | High BMI | High TG | Low HDL-C | Age, Sex-Adjusted OR (95% CI) | P value |
| Absence of any components of MetS<br>I     |                   |                               |          |         |           | 1.00                          |         |
| Individual component of MetS               |                   |                               |          |         |           |                               |         |
| 1  | √                 |                               |          |         |           | 1.69 (0.21, 13.68)            | 0.62    |
| 2  |                   | √                             |          |         |           | 1.77 (1.00, 3.14)             | 0.05    |
| 3  |                   |                               | √        |         |           | 3.58 (0.95, 13.42)            | 0.06    |
| 4  |                   |                               |          | √       |           | 1.44 (0.18, 11.54)            | 0.73    |
| 5  |                   |                               |          |         | √         | –                             |         |
| Combination of two components of MetS      |                   |                               |          |         |           |                               |         |
| 1  | √                 | √                             |          |         |           | 3.20 (1.50, 6.83)             | 0.003   |
| 2  | √                 |                               | √        |         |           | –                             |         |
| 3  | √                 |                               |          | √       |           | –                             |         |
| 4  | √                 |                               |          |         | √         | 8.11 (0.79, 83.73)            | 0.08    |
| 5  |                   | √                             | √        |         |           | 4.55 (2.41, 8.61)             | <0.001  |
| 6  |                   | √                             |          | √       |           | 2.77 (1.34, 5.71)             | 0.01    |
| 7  |                   | √                             |          |         | √         | 3.50 (1.75, 7.00)             | <0.001  |
| 8  |                   |                               | √        | √       |           | –                             |         |
| 9  |                   |                               | √        |         | √         | –                             |         |
| 10   |                   |                               |          | √       | √         | –                             |         |
| Combination of three components of MetS    |                   |                               |          |         |           |                               |         |
| 1  | √                 | √                             | √        |         |           | 3.07 (1.05, 8.96)             | 0.04    |
| 2  | √                 | √                             |          | √       |           | 13.07 (4.95, 34.54)           | <0.001  |
| 3  | √                 | √                             |          |         | √         | 3.29 (1.02, 10.66)            | 0.05    |
| 4  | √                 |                               | √        | √       |           | –                             |         |
| 5  | √                 |                               | √        |         | √         | –                             |         |
| 6  | √                 |                               |          | √       | √         | –                             |         |
| 7  |                   | √                             | √        | √       |           | 6.77 (3.06, 15.02)            | <0.001  |
| 8  |                   | √                             | √        |         | √         | 5.40 (2.37, 12.28)            | <0.001  |
| 9  |                   | √                             |          | √       | √         | 3.58 (1.76, 7.29)             | <0.001  |
| 10   |                   |                               | √        | √       | √         | –                             |         |
| Combination of four components of MetS     |                   |                               |          |         |           |                               |         |
| 1  | √                 | √                             | √        | √       |           | 11.54 (3.52, 37.79)           | <0.001  |
| 2  | √                 | √                             | √        |         | √         | 1.63 (0.20, 13.20)            | 0.65    |
| 3  | √                 | √                             |          | √       | √         | 4.29 (1.54, 11.94)            | 0.01    |
| 4  | √                 |                               | √        | √       | √         | –                             |         |
| 5  |                   | √                             | √        | √       | √         | 9.48 (4.42, 20.34)            | <0.001  |
| Combination of all five components of MetS |                   |                               |          |         |           |                               |         |
| I  | √                 | √                             | √        | √       | √         | 5.01 (1.31, 19.26)            | 0.02    |

**Note:** √Presence of the component of metabolic syndrome.

**Abbreviations:** BP, blood pressure; BMI, body mass index; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome.

**Table 5** Associations Between Components of Metabolic Syndrome and Risk of Hyperuricemia by Status of Diabetes Mellitus Component

| Components of MetS | With Diabetes Mellitus Component    |         | Without Diabetes Mellitus Component |         |
|--------------------|-------------------------------------|---------|-------------------------------------|---------|
|                    | Multivariable-Adjusted* OR (95% CI) | P value | Multivariable-Adjusted* OR (95% CI) | P value |
| High BP            | 1.02 (0.20, 5.26)                   | 0.98    | 2.17 (1.30, 3.61)                   | 0.003   |
| High BMI           | 1.03 (0.48, 2.20)                   | 0.95    | 2.06 (1.52, 2.80)                   | <0.001  |
| High TG            | 1.97 (0.99, 3.90)                   | 0.05    | 1.30 (0.94, 1.78)                   | 0.11    |
| Low HDL-C          | 0.51 (0.24, 1.11)                   | 0.09    | 1.39 (1.00, 1.92)                   | 0.05    |

**Note:** \*Adjusted for age, sex, educational level, monthly income, marriage status, smoking status, alcohol intake, tea consumption, physical activity and baseline serum uric acid.

**Abbreviations:** MetS, metabolic syndrome; BP, blood pressure; BMI, body mass index; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol.

In this study, socio-demographic characteristics, lifestyle habits were adjusted for predicting HUA. Among these covariates, alcohol intake was the primary variable influencing the associations of MetS and its components with incident HUA. It has been reported that alcohol intake is a modifiable risk factor for HUA.<sup>35,36</sup> Ethanol could inhibit the excretion of SUA by kidneys and accelerate the degradation of purine which eventually leads to the elevated SUA levels.<sup>37</sup> We also identified that some combinations of MetS components that made older adults at high risk of incident HUA. Various combinations of different components of MetS were associated with a 2.77–13.07-fold risk of HUA. However, there are several combinations of MetS having similar risk, and some groups including three or four components of MetS showed higher risk of incident HUA compared to the group with all five MetS components. The high prevalence of high BP in this study may partially explain the results. When participants of this study were divided into 32 groups according to specific combinations of MetS components, the number of subjects in each group was small, and therefore more researches are needed to be conducted to explore these relationships.

The findings of our study added to the evidence of the impact of MetS and its components at baseline on incident HUA. It has been reported that programmed HUA intervention could optimize their cardiovascular lesions.<sup>38</sup> A combination of high BP, diabetes mellitus and high triglycerides was associated with the highest risk of incident HUA among all possible combinations of MetS components. This result may help to identify community-dwelling older adults at high risk of developing HUA and thus take measures to prevent HUA through modifying these common diseases among older adults. In addition, realizing the importance of MetS on incident HUA may be beneficial to make interventions and the clinical management of MetS as well as HUA, which may eventually reduce the risk of HUA-related cardiovascular events.

The strengths of this study included community-based sample, longitudinal design, reasonable follow-up rate and sufficient numbers of individuals with incident HUA. However, there were also several limitations, which should be noted. First, although we have adjusted a wide range of confounders, residual confounding may still exist. For example, dietary habits might have an impact on SUA levels. Consumption of purine-rich foods like seafood may increase SUA levels but information on this issue was not collected in this study.<sup>39</sup> Second, the under ascertainment and misclassification of outcome measures are possible because the incident cases might have been underestimated. Information on anti-hyperuricemia medication intake had been collected but few were reported. Recall bias or social desirability bias may lead to the underestimation of the incidence of HUA and distort the association of MetS and its components at baseline with incident HUA.

## Conclusions

In conclusion, MetS and its components such as high BP, high BMI, diabetes mellitus and high triglycerides could increase the risk of HUA among community-dwelling older adults and high BP may be the most important determinant. A combination of high BP, diabetes mellitus and high triglycerides best predicts incident HUA. Additional studies are needed to confirm the findings in other ethnic groups and to further investigate the underlying mechanisms for the association. Randomized controlled trials are also warranted to investigate whether lowering BP in hypertensive patients or losing weight in obese populations could reduce the risk of HUA among the elderly.

## Compliance with Ethical Standards

The study adhered to the Declaration of Helsinki and ethics approval was obtained from the Institutional Review Board of the Soochow University. Written inform

consent was obtained from each participant at the recruitment stage of the study.

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## Disclosure

The authors report no conflicts of interest in this work.

## References

- Dalbeth N, Merriman TR, Stamp LK. Gout. *Lancet*. 2016;388(10055):2039–2052. doi:10.1016/S0140-6736(16)00346-9
- Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the national health and nutrition examination survey 2007–2008. *Arthritis Rheum*. 2011;63(10):3136–3141. doi:10.1002/art.30520
- Liu H, Zhang XM, Wang YL, Liu BC. Prevalence of hyperuricemia among Chinese adults: a national cross-sectional survey using multi-stage, stratified sampling. *J Nephrol*. 2014;27(6):653–658. doi:10.1007/s40620-014-0082-z
- Kumar AUA, Browne LD, Li X, et al. Temporal trends in hyperuricaemia in the Irish health system from 2006–2014: a cohort study. *PLoS One*. 2018;13(5):e0198197. doi:10.1371/journal.pone.0198197
- Wu J, Qiu L, Cheng XQ, et al. Hyperuricemia and clustering of cardiovascular risk factors in the Chinese adult population. *Sci Rep*. 2017;7(1):5456. doi:10.1038/s41598-017-05751-w
- Chen PH, Chen YW, Liu WJ, Hsu SW, Chen CH, Lee CL. Approximate mortality risks between hyperuricemia and diabetes in the United States. *J Clin Med*. 2019;8(12). doi:10.3390/jcm8122127
- Andrade JA, Kang HC, Greffin S, Garcia Rosa ML, Lugon JR. Serum uric acid and disorders of glucose metabolism: the role of glycosuria. *Braz J Med Biol Res*. 2014;47(10):917–923. doi:10.1590/1414-431X20143878
- Tsouli SG, Liberopoulos EN, Mikhailidis DP, Athyros VG, Elisaf MS. Elevated serum uric acid levels in metabolic syndrome: an active component or an innocent bystander? *Metabolism*. 2006;55(10):1293–1301. doi:10.1016/j.metabol.2006.05.013
- Tinahones JF, Perez-Lindon G, C-Soriguer FJ Pareja, A, Sanchez-Guijo P, Collantes E. Dietary alterations in plasma very low density lipoprotein levels modify renal excretion of urates in hyperuricemic-hypertriglyceridemic patients. *J Clin Endocrinol Metab*. 1997;82(4):1188–1191.
- Kang WM, Zhang JS, Wang MS, Gu YC, Yu JC. Prevalence of metabolic syndrome and its associations with other metabolic disorders and cardiovascular changes in health examination population in Beijing. *Chin Med Sci J*. 2009;24(4):227–230.
- Numata T, Miyatake N, Wada J, Makino H. Comparison of serum uric acid levels between Japanese with and without metabolic syndrome. *Diabetes Res Clin Pract*. 2008;80(1):e1–5. doi:10.1016/j.diabetes.2007.10.031
- Stiburkova B, Pavlikova M, Sokolova J, Kozich V. Metabolic syndrome, alcohol consumption and genetic factors are associated with serum uric acid concentration. *PLoS One*. 2014;9(5):e97646. doi:10.1371/journal.pone.0097646
- Ryu S, Chang Y, Zhang Y, et al. A cohort study of hyperuricemia in middle-aged South Korean men. *Am J Epidemiol*. 2012;175(2):133–143. doi:10.1093/aje/kwr291
- Muntner P, Srinivasan S, Menke A, Patel DA, Chen W, Berenson G. Impact of childhood metabolic syndrome components on the risk of elevated uric acid in adulthood: the Bogalusa Heart Study. *Am J Med Sci*. 2008;335(5):332–337. doi:10.1097/MAJ.0b013e31815574a4
- Yang XJ, Tian S, Ma QH, Sun HP, Xu Y, Pan CW. Leukocyte-related parameters in older adults with metabolic syndrome. *Endocrine*. 2020;68(2):312–319. doi:10.1007/s12020-020-02243-2
- Liu JH, Qian YX, Ma QH, Sun HP, Xu Y, Pan CW. Depressive symptoms and metabolic syndrome components among older Chinese adults. *Diabetol Metab Syndr*. 2020;12(1):18. doi:10.1186/s13098-020-00526-2
- Qian YX, Liu JH, Ma QH, Sun HP, Xu Y, Pan CW. Associations of sleep durations and sleep-related parameters with metabolic syndrome among older Chinese adults. *Endocrine*. 2019;66(2):240–248. doi:10.1007/s12020-019-02064-y
- Roubenoff R. Gout and hyperuricemia. *Rheum Dis Clin North Am*. 1990;16(3):539–550.
- Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). *JAMA*. 2001;285(19):2486–2497. doi:10.1001/jama.285.19.2486
- Qian J, Cai M, Gao J, Tang S, Xu L, Critchley JA. Trends in smoking and quitting in China from 1993 to 2003: national health service survey data. *Bull World Health Organ*. 2010;88(10):769–776. doi:10.2471/BLT.09.064709
- Yu M, Xu CX, Zhu HH, et al. Associations of cigarette smoking and alcohol consumption with metabolic syndrome in a male Chinese population: a cross-sectional study. *J Epidemiol*. 2014;24(5):361–369. doi:10.2188/jea.JE20130112
- Feng L, Yan Z, Sun B, et al. Tea consumption and depressive symptoms in older people in rural China. *J Am Geriatr Soc*. 2013;61(11):1943–1947. doi:10.1111/jgs.12496
- Ma DY, Wong CHY, Leung GTY, Fung AWT, Chan WC, Lam LCW. Physical exercise helped to maintain and restore functioning in chinese older adults with mild cognitive impairment: a 5-year prospective study of the Hong Kong Memory and Ageing Prospective Study (HK-MAPS). *J Am Med Dir Assoc*. 2017;18(4):306–311. doi:10.1016/j.jamda.2016.10.003
- Rivera-Paredes B, Macias-Kauffer L, Fernandez-Lopez JC, et al. Influence of genetic and non-genetic risk factors for serum uric acid levels and hyperuricemia in Mexicans. *Nutrients*. 2019;11(6):6. doi:10.3390/nu11061336
- Lu X, Li X, Zhao Y, Zheng Z, Guan S, Chan P. Contemporary epidemiology of gout and hyperuricemia in community elderly in Beijing. *Int J Rheum Dis*. 2014;17(4):400–407. doi:10.1111/1756-185X.12156
- McAdams-DeMarco MA, Law A, Maynard JW, Coresh J, Baer AN. Risk factors for incident hyperuricemia during mid-adulthood in African American and white men and women enrolled in the ARIC cohort study. *BMC Musculoskelet Disord*. 2013;14(1):347. doi:10.1186/1471-2474-14-347
- Messerli FH, Frohlich ED, Dreslinski GR, Suarez DH, Aristimuno GG. Serum uric acid in essential hypertension: an indicator of renal vascular involvement. *Ann Intern Med*. 1980;93(6):817–821. doi:10.7326/0003-4819-93-6-817
- Puig JG, Ruilope LM. Uric acid as a cardiovascular risk factor in arterial hypertension. *J Hypertens*. 1999;17(7):869–872. doi:10.1097/00004872-199917070-00001
- Friedl HP, Till GO, Trentz O, Ward PA. Role of oxygen radicals in tourniquet-related ischemia-reperfusion injury of human patients. *Klin Wochenschr*. 1991;69(21–23):1109–1112. doi:10.1007/BF01645168
- Palmer TM, Nordestgaard BG, Benn M, et al. Association of plasma uric acid with ischaemic heart disease and blood pressure: mendelian randomisation analysis of two large cohorts. *BMJ (Clinical Research Ed)*. 2013;347:f4262.

31. Zatterale F, Longo M, Naderi J, et al. Chronic adipose tissue inflammation linking obesity to insulin resistance and type 2 diabetes. *Front Physiol.* 2019;10:1607.
32. Modan M, Halkin H, Karasik A, Lusky A. Elevated serum uric acid—a facet of hyperinsulinaemia. *Diabetologia.* 1987;30(9):713–718. doi:10.1007/BF00296994
33. Bedir A, Topbas M, Tanyeri F, Alvur M, Arik N. Leptin might be a regulator of serum uric acid concentrations in humans. *Jpn Heart J.* 2003;44(4):527–536. doi:10.1536/jhj.44.527
34. Rahmouni K, Haynes WG. Endothelial effects of leptin: implications in health and diseases. *Curr Diab Rep.* 2005;5(4):260–266. doi:10.1007/s11892-005-0020-5
35. Choi HK, McCormick N, Lu N, Rai SK, Yokose C, Zhang Y. Population impact attributable to modifiable risk factors for hyperuricemia. *Arthritis Rheum.* 2020;72(1):157–165. doi:10.1002/art.41067
36. Rai SK, Fung TT, Lu N, Keller SF, Curhan GC, Choi HK. The dietary approaches to stop hypertension (DASH) diet, Western diet, and risk of gout in men: prospective cohort study. *BMJ (Clinical Research Ed).* 2017;357:j1794. doi:10.1136/bmj.j1794
37. Faller J, Fox IH. Ethanol-induced hyperuricemia: evidence for increased urate production by activation of adenine nucleotide turnover. *N Engl J Med.* 1982;307(26):1598–1602. doi:10.1056/NEJM198212233072602
38. Zhu WH, Fang LZ, Chen LY, Chen ZW, Dai HL, Chen JH. [Follow-up study of programmed intervention of hyperuricemia in the prevention and treatment of cardiovascular morbid change]. *Chin Med J.* 2010;90(10):662–666. Chinese.
39. Choi HK, Liu S, Curhan G. Intake of purine-rich foods, protein, and dairy products and relationship to serum levels of uric acid: the third national health and nutrition examination survey. *Arthritis Rheum.* 2005;52(1):283–289. doi:10.1002/art.20761

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