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# BMJ Open

## Temporal trends in Hyperuricemia among Adults in Wuhan City, China from 2010-2019: a cross-sectional study

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9 3 **Temporal trends in Hyperuricemia among Adults in Wuhan City, China from**  
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12 4 **2010-2019: a cross-sectional study**  
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17 6 Zhengce Wan,<sup>1</sup> Lulu Song,<sup>2</sup> Liu Hu,<sup>1</sup> Xiaomei Lei,<sup>1</sup> Yuancheng Huang,<sup>1</sup> Yongman Lv<sup>1</sup>  
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52 19 **Word count:** 250 for the abstract, 2639 for the text  
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## 21 Abstract

22 **Objectives:** Hyperuricemia is a risk factor for gout attacks, kidney damage and  
23 cardiovascular events. Evidence on the burden of hyperuricemia in Wuhan city, China  
24 was limited. The present study aimed to estimate the prevalence of and a decade trend  
25 in hyperuricemia in Wuhan city.

26 **Design:** Cross-sectional study.

27 **Setting:** Health management center of Tongji hospital.

28 **Participants:** A total of 732527 adult participants from the general population who  
29 took a physical examination in the health management center between 2010 and 2019.

30 **Main outcome measures:** Prevalence of and trends in hyperuricemia.

31 **Results:** The overall prevalence of hyperuricemia was 25.8% (36.6% in men and 10.8%  
32 in women) in 2019. Serum uric acid levels among men and women gradually increased  
33 from  $363.02 \pm 74.32$  mmol/L and  $255.87 \pm 57.58$  mmol/L in 2010 to  $395.62 \pm 83.69$   
34 mmol/L and  $277.48 \pm 64.32$  mmol/L in 2019, respectively, *P* values < 0.05. From 2010  
35 through 2019, hyperuricemia prevalence significantly increased in each age category  
36 and it increased most sharply among participants aged 20-39 years. The multivariate-  
37 adjusted prevalence among men was 25.2% (24.6% - 25.7%) in 2010, 30.3% (29.8% -  
38 30.8%) in 2015, and 34.5% (34.1% - 34.8%) in 2019, while among women it was 5.6%  
39 (5.3% - 6.0%) in 2010, 7.1% (6.8% - 7.4%) in 2015, and 10.1% (9.9% - 10.4%) in 2019.

40 **Conclusions:** hyperuricemia was highly prevalent among adults in Wuhan city. More  
41 attention should be paid to the increasing burden of hyperuricemia, especially for those  
42 at higher risks.

43 **Key Words:** Hyperuricemia, uric acid, epidemiology, temporal trend

44

45 **Strengths and limitations of this study**

- 46 ➤ This study included a large sample size of participants (more than 730000 adults)
- 47 from the general population, which made our findings more convincing.
- 48 ➤ This study firstly estimated the prevalence of and trends in hyperuricemia over the
- 49 recent decade (2010-2019) among adults in Wuhan city.
- 50 ➤ The multivariate logistic model was used to correct selection biases and
- 51 confounding biases as possible by adjusting for potential confounders.
- 52 ➤ Since participants in the present study were recruited from a health management
- 53 center, selection biases could not be avoided.

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## 55 Introduction

56 Serum uric acid (SUA) is the final product of purine nucleotides metabolism. The  
57 overproduction or inefficient renal or gut excretion of SUA can consequently lead to  
58 hyperuricemia. Hyperuricemia is generally recognized as the major contributor to the  
59 onset of gout.<sup>1</sup> Moreover, many studies have demonstrated a positive association of  
60 hyperuricemia or a high level of SUA with several chronic diseases such as chronic  
61 kidney disease, type 2 diabetes mellitus, hypertension, metabolic syndrome, and  
62 cardiovascular events.<sup>2-6</sup> These diseases accounted for a large part of global deaths and  
63 disability-adjusted life-year losses,<sup>7 8</sup> resulting in a particular urgency to prevent and  
64 control hyperuricemia.

65 Previous studies have documented an increasing trend of hyperuricemia prevalence  
66 in the past few decades across the world, especially in western countries.<sup>9-11</sup>  
67 Additionally, hyperuricemia is reported to be more prevalent in developed countries  
68 than in developing countries.<sup>12</sup> The prevalence among US adults was substantial (20.2%  
69 in men and 20.0% in women) during 2015-2016.<sup>13</sup> In China, the prevalence estimated  
70 from national surveys were 8.4% in 2009-2010,<sup>14</sup> 13.0% in 2007-2011,<sup>15</sup> and 6.4%  
71 among the middle-aged and elderly in 2011-2012.<sup>16</sup> Besides, a meta-analysis of 38  
72 studies from mainland China reported that the pooled prevalence of hyperuricemia  
73 among Chinese adults was 13.3% in 2000-2014.<sup>17</sup> Obviously, the data above were not  
74 able to clearly illustrate the trend of hyperuricemia prevalence among Chinese adults.

75 China is a large developing country with unbalanced economic development and  
76 marked regional differences. Hyperuricemia prevalence among Chinese adults varied

77 greatly by geographical regions, with a report of 18.6% in south China, 12.9% in east  
78 China, 13.9% in southwest China, 10.3% in northwest China, 10.1% in northeast China,  
79 and 13.2% in north China.<sup>17</sup> Noteworthy, evidence on hyperuricemia prevalence in  
80 central China was limited. Wuhan, the capital city of Hubei province in central China,  
81 was characterized by rapid economic growth and urbanization in the recent decade. Its  
82 gross domestic products (GDP) per capita increased from 50117 yuan in 2009 to  
83 123831 yuan in 2017.<sup>18 19</sup> Studies from developing countries showed that a rapidly  
84 growing economy in the short term and subsequently changed lifestyles would increase  
85 the risk of several metabolic disorders.<sup>20 21</sup>

86 To date, few studies have investigated the burden of hyperuricemia in Wuhan city.  
87 Therefore, we performed a large cross-sectional study to estimate the sex-specific  
88 prevalence of and trends in hyperuricemia among the general adults from 2010 through  
89 2019. This general population-based study used data collected from consecutive healthy  
90 adults in a health management center.

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## 92 **Methods**

### 93 **Study population**

94 We conducted a cross-sectional study, of which consecutive participants who had a  
95 health check-up in the Health Management Center of Tongji Hospital in Wuhan city,  
96 China between January 2010 and December 2019 were included. All the participants  
97 came from the general population. Most of them were urban citizens working in  
98 government organizations or large enterprises. Each participant completed the basic  
99 items of the physical examination including demographic information collection,  
100 biochemical tests, and anthropometric measurements. Supplemental Figure 1 shows the  
101 procedures for selecting participants in the study. A total of 732527 participants aged  $\geq$   
102 20 years were recruited. After excluding participants with missing data, we included  
103 676478 participants. As reduced renal function may affect uric acid excretion, we  
104 further excluded 5027 participants who had an estimated glomerular filtration rate  
105 (eGFR) of less than 60 mL/min/1.73m<sup>2</sup>. Finally, 671451 participants were included in  
106 the analyses.

107 We used the STROBE cross sectional reporting guidelines in the present study.<sup>22</sup>  
108 The study was conducted in accordance with the Declaration of Helsinki and it was  
109 approved by the ethics committee of Tongji Hospital, Tongji Medical College,  
110 Huazhong University of Science and Technology. Written informed consent was  
111 obtained from every participant.

### 112 113 **Assessment of main variables**

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4 114 Overnight fasting blood samples were collected to test the biochemical variables. SUA  
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6 115 concentrations were measured by the enzymatic colorimetry using an automated  
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9 116 analyzer (Roche Cobas 8000, Basel, Switzerland). Additionally, the method of SUA  
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12 117 measurement did not change during the whole study period. In the current study,  
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14 118 hyperuricemia was defined according to the level of SUA: male  $\geq 416$  mmol/L (7  
15  
16 119 mg/dL), female  $\geq 357$  mmol/L (6 mg/dL). Participants were asked to wear light clothes  
17  
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19 120 and bare foot before their height and weight were measured. The body mass index (BMI)  
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22 121 was calculated as weight in kilograms divided by height in meters squared. For Chinese  
23  
24 122 adults, obesity was defined as BMI  $\geq 28$  Kg/m<sup>2</sup> and overweight was defined as BMI  $\geq$   
25  
26 123 24 Kg/m<sup>2</sup>.<sup>23</sup> Hypertension was identified if any of the following criteria was satisfied:  
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28 124 systolic blood pressure  $\geq 140$  mmHg, or diastolic blood pressure  $\geq 90$  mmHg, or use of  
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30 125 antihypertensive medication, or self-reported physician diagnosis of hypertension.  
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33 126 Information on age and sex was provided by the participants.  
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### 128 **Patient and public involvement**

129 Patients or the public were not involved in the design, or conduct, or reporting, or  
130 dissemination plans of our research. Patients or the public were not invited to contribute  
131 to the writing or editing of this article for readability or accuracy.

### 133 **Statistical analysis**

134 Due to the marked difference in levels of SUA between males and females, the sex-  
135 specific prevalence of and trends in hyperuricemia were estimated. Categorical

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4 136 variables were expressed in percentages, whereas continuous variables were reported  
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6 137 as means  $\pm$  standard deviation (SD) for normally distributed data or median  
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9 138 (interquartile range) for skewed data. We used data collected in 2019 to estimate the  
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11 139 SUA level, the hyperuricemia prevalence and their 95% confidence intervals (CIs),  
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14 140 stratified by sex (male or female), age (20 - 29, 30 - 39, 40 - 49, 50 - 59, 60 - 69, or  $\geq$   
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16  
17 141 70 years), BMI ( $< 24$ , 24 - 27.9, or  $\geq 28$  kg/m<sup>2</sup>, the cut-off values of overweight and  
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19 142 obesity for Asian), and hypertension status (hypertensive or normotensive). In this part,  
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22 143 the prevalence of hyperuricemia was compared using the Cochran-Armitage test for  
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25 144 trend. The level of SUA was compared using one-way analysis of variance (ANOVA).

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27 145 Sex- and age- specific trends in hyperuricemia from 2010 through 2019 were then  
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30 146 analyzed. We performed tests for trends by including the observation year as a  
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33 147 continuous variable in a linear or logistic regression model. The sex-specific  
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35 148 multivariate-adjusted prevalence of hyperuricemia from 2010 through 2019 were  
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38 149 estimated using logistic regression models after adjustment for age, BMI, eGFR, and  
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41 150 hypertension. All statistical analyses were performed using Stata version 12.0 (Stata  
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43 151 Corp LP, College Station, TX, USA). Graphs were drawn using an available R package:  
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45 152 ggplot2. Two-sided *P* values  $< 0.05$  were considered statistically significant.  
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## 154 **Results**

### 155 **The crude prevalence of hyperuricemia in 2019**

156 Table 1 shows the crude prevalence of hyperuricemia and the level of SUA in  
157 participants aged  $\geq 20$  years during the year 2019. A total of 66998 men and 48385  
158 women in 2019 were included, with an average age of  $42.0 \pm 12.6$  years. The overall  
159 hyperuricemia prevalence was 25.8%. The crude prevalence of hyperuricemia and level  
160 of SUA in men were significantly higher than those in women (36.6% versus 10.8%,  
161  $395.62 \pm 83.69$  mmol/L versus  $277.48 \pm 64.31$  mmol/L; both  $P$  values  $< 0.05$ ).  
162 Hyperuricemia prevalence was around 9.0% in women aged  $< 50$  years and it rapidly  
163 increased with advancing age in women aged  $\geq 50$  years, with the highest prevalence  
164 of 26.1% for women aged  $\geq 70$  years. The burden of hyperuricemia among men was  
165 high across all age groups and it was particularly marked in young men (39.3% for 20-  
166 29 years and 40.5% for 30-39 years). Hyperuricemia prevalence and level of SUA  
167 dramatically increased with elevating BMI in both sexes ( $P$  values  $< 0.05$ ); the  
168 prevalence (95% CI) was 55.9% (55.0% - 56.9%) in obese men and 34.6% (32.8% -  
169 36.5%) in obese women. Hypertensive participants had a higher hyperuricemia  
170 prevalence and higher levels of SUA than normotensive participants ( $P$  values  $< 0.05$ ).

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### 172 **Trends in the crude prevalence of hyperuricemia**

173 A total of 671451 participants were included in the study between 2010 and 2019. As  
174 is shown in Table 2, the crude prevalence of hyperuricemia significantly increased over  
175 the years in both men and women ( $P$  values  $< 0.05$ ). SUA levels among men and women

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4 176 gradually increased from  $363.02 \pm 74.32$  mmol/L and  $255.87 \pm 57.58$  mmol/L in 2010  
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6 177 to  $395.62 \pm 83.69$  mmol/L and  $277.48 \pm 64.32$  mmol/L in 2019, respectively (*P* values  
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8 178  $< 0.05$ ). A significantly increasing trend in hyperuricemia prevalence was observed  
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10 179 during the observation period in each age category of both sexes (Figure 1 and Figure  
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12 180 2). The prevalence increased most sharply among participants aged 20-39 years. It  
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14 181 increased from 22.5% (21.6% - 23.3%) in 2010 to 40.1% (39.6% - 40.6%) in 2019  
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16 182 among young men, whereas among young women it increased from 2.5% (2.1% - 2.9%)  
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18 183 in 2010 to 9.0% (8.6% - 9.4%) in 2019.  
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### 185 **Trends in multivariate-adjusted prevalence of hyperuricemia**

186 The multivariate-adjusted prevalence of hyperuricemia was calculated using logistic  
187 regression models. Figure 3 shows an increasing trend in multivariate-adjusted  
188 prevalence of hyperuricemia during the observation years in both sexes (*P* values  $<$   
189 0.05). The prevalence among men was 25.2% (24.6% - 25.7%) in 2010, 30.3% (29.8%  
190 - 30.8%) in 2015, and 34.5% (34.1% - 34.8%) in 2019, while among women it was  
191 5.6% (5.3% - 6.0%) in 2010, 7.1% (6.8% - 7.4%) in 2015, and 10.1% (9.9% - 10.4%)  
192 in 2019.  
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## 194 Discussion

195 The present study revealed that hyperuricemia was highly prevalent (36.6% in men and  
196 10.8% in women) among adults in Wuhan city, China during 2019. The burden of  
197 hyperuricemia among men was substantial in all age groups. Hyperuricemia prevalence  
198 varied distinctly by gender, age, BMI, and hypertension status, with young men, old  
199 women, obese adults, and the hypertensives having a significantly higher prevalence.

200 This study also investigated the trend of hyperuricemia over a decade period (from  
201 2010 to 2019) and revealed a significantly increasing trend in multivariate-adjusted  
202 prevalence of hyperuricemia in both sexes. Moreover, it was observed that the  
203 prevalence increased most sharply among young adults during the observation period,  
204 which meant that hyperuricemia occurred more and more frequently in young adults.

205 The estimated prevalence in our study (25.8% in 2019) was much higher than those  
206 reported in America (20.1% in 2015-2016),<sup>13</sup> Italy (11.9% in 2009),<sup>10</sup> Korea (11.4% in  
207 2016),<sup>24</sup> and a previous national survey in China (13.0% in 2007-2011).<sup>15</sup> A cross-  
208 sectional study from Bangkok, Thailand used data of the annual physical examination  
209 and reported a prevalence rate of 24.4% in urban residents,<sup>25</sup> which was close to our  
210 result. Epidemiological studies demonstrated that urban individuals had a higher  
211 prevalence of hyperuricemia than rural residents.<sup>14 16</sup> In the present study, almost all the  
212 participants included were urban citizens, which may help explain the high  
213 hyperuricemia prevalence. Overweight or obesity was a well-accepted risk factor for  
214 hyperuricemia,<sup>26</sup> which was validated in our study. We found that hyperuricemia  
215 prevalence increased significantly with elevating BMI in both sexes. Based on

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4 216 information in Table 1, it could be calculated that nearly 61.0% of men were overweight  
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6 217 or obese and 44.5% of them were identified as hyperuricemia. The heavy burden of  
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9 218 overweight or obesity may be another reason to explain the highly prevalent  
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12 219 hyperuricemia.

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14 220 The present study found that hyperuricemia prevalence was higher among women  
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17 221 aged  $\geq 50$  years and it further increased with advancing age. Several studies from Asian  
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20 222 and European countries revealed a roughly positive association of hyperuricemia  
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22 223 prevalence with age among women,<sup>10 11 15 24</sup> which accorded with our results. Given the  
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25 224 huge gender difference in hyperuricemia prevalence, we thought that sex hormones may  
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28 225 play a key role. One explanation was that female sex hormones had protective effects  
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31 226 against hyperuricemia. A cross-sectional study of 58870 South Korean women  
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33 227 demonstrated that hyperuricemia prevalence significantly increased with the  
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36 228 menopausal stage, after controlling for potential confounders.<sup>27</sup> Postmenopausal  
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39 229 women are characterized by materially declined levels of female sex hormones  
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42 230 (especially estradiol and progesterone). When they grow older, levels of estradiol and  
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45 231 progesterone would decline further. The BioCycle study demonstrated that SUA levels  
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48 232 were inversely associated with these two hormones.<sup>28</sup> Until now, how estradiol and  
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51 233 progesterone lower SUA levels was not fully understood. They probably effect via  
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54 234 promoting renal excretion of uric acid.<sup>29 30</sup>

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56 235 Data from the National Health and Nutrition Examination Survey demonstrated  
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59 236 that hyperuricemia prevalence among American adults significantly increased from  
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237 18.2% in 1988-1994 to 21.4% in 2007-2008 and concluded that the increasing trend of

238 hyperuricemia was likely due to rising prevalence of obesity and hypertension.<sup>9</sup>  
239 However, in the present study, we did not observe an increasing trend in obesity and  
240 hypertension over the years (Table 2). Thus, it might be some other factors responsible  
241 for the increasing prevalence of hyperuricemia among our study participants. We  
242 thought that gradually westernized dietary structure and rising consumption of fructose-  
243 sweetened soft drinks might be the main causes. Western diets contained much more  
244 purine than the traditional Chinese diets, leading to a higher risk of developing  
245 hyperuricemia. In addition, accumulating evidence showed that fructose-sweetened  
246 drinks, although containing no purines, could induce hyperuricemia.<sup>31-33</sup> Fructose  
247 intake per capita has dramatically increased during the past few decades,<sup>34-36</sup> in parallel  
248 with the increasing burden of hyperuricemia.

249 To the best of our knowledge, the present study firstly revealed age-specific trends  
250 in hyperuricemia over a decade among Chinese adults and found that hyperuricemia  
251 prevalence increased most sharply among young adults during the observation period.  
252 A large analysis of 128014 Irish adults revealed an increasing trend in hyperuricemia  
253 from 2006 through 2014 across all age groups, with the most increment among young  
254 participants aged 18-39 years;<sup>11</sup> a finding that was similar to our result. In addition to  
255 hyperuricemia, several hyperuricemia-related diseases such as diabetes and  
256 cardiovascular events also occurred more frequently among young adults over the past  
257 years,<sup>37 38</sup> posing a serious threat to public health. Based on the trend revealed in our  
258 study, hyperuricemia prevalence was much likely to continue rising in the coming years.  
259 Policy-makers should pay more attention to the burden of hyperuricemia, especially



260 among young adults.

261 The strengths of the present study were distinct. This study included a large sample  
262 size of participants (more than 730000 adults) from the general population, which made  
263 our findings more convincing. In addition, to the best of our knowledge, this was the  
264 first study to estimate the prevalence of and trends in hyperuricemia over the recent  
265 decade (2010-2019) among adults in Wuhan city, contributing to the management of  
266 hyperuricemia in this area.

267 The study also had several limitations. First, as the participants in the present study  
268 were recruited from a health management center, selection biases could not be avoided.  
269 The participants may be not a representative sample of the general population in  
270 community. Therefore, it should take caution to interpret the findings of this study.  
271 Second, hyperuricemia prevalence may be underestimated in our study. We diagnose  
272 hyperuricemia only according to SUA levels. However, participants with  
273 hyperuricemia might have normal SUA levels if they were undergoing SUA-lowering  
274 therapies. Third, our study did not collect data on diets and lifestyles that were related  
275 to hyperuricemia. Changes of these variables such as fructose intake over the years may  
276 help explain the trends in hyperuricemia.

277

## 278 **Conclusions**

279 In summary, a high burden of hyperuricemia was found among adults in Wuhan city.  
280 Moreover, hyperuricemia occurred more and more frequently in young adults. Our  
281 study also revealed an significantly increasing trend in multivariate-adjusted prevalence

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4 282 of hyperuricemia among adults from 2010 through 2019. Effective measures to prevent  
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6 283 and control hyperuricemia should be taken urgently, especially among young adults,  
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9 284 postmenopausal women, obese adults and the hypertensives, for they were at higher  
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12 285 risks.  
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For peer review only

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289

290 **Author contributions** All authors are in agreement with the content of the  
291 manuscript. ZW designed the study and drafted the article. LS, LH, and YL contributed  
292 to the conception, analysis, and critically revised the manuscript. XL and YH  
293 participated in the data collection and revised the manuscript.

294

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297

298 **Competing interests** None declared.

299

300 **Patient consent for publication** Not required.

301

302 **Data availability statement** Data are available upon reasonable request.

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4 419 **Figure legends**  
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8 420 Figure 1. Age-specific trends in hyperuricemia prevalence (95% CI) among men, 2010-  
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10 421 2019. CI, confidence interval.  
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15 422 Figure 2. Age-specific trends in hyperuricemia prevalence (95% CI) among women,  
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17 423 2010-2019. CI, confidence interval.  
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23 424 Figure 3. Sex-specific trends in multivariate-adjusted hyperuricemia prevalence (95%  
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25 CI) among participants aged  $\geq 20$  years, 2010-2019. The prevalence was adjusted for  
26 425 age, BMI, eGFR, and Hypertension. CI, confidence interval; BMI, body mass index;  
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28 426 age, BMI, eGFR, and Hypertension. CI, confidence interval; BMI, body mass index;  
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30 427 eGFR, estimated glomerular filtration rate.  
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429 Table 1. Crude prevalence of hyperuricemia and levels of SUA according to sex, age,  
 430 BMI, and hypertension status in participants aged  $\geq 20$  years, 2019

Variables	N	Cases	Hyperuricemia, %		SUA (mmol/L)	
			Prevalence (95% CI)	<i>P</i>	Mean $\pm$ SD	<i>P</i>
<b>Sex</b>				< 0.001		< 0.001
Men	66998	24511	36.6 (36.2-36.9)		395.62 $\pm$ 83.69	
Women	48385	5202	10.8 (10.5-11.0)		277.48 $\pm$ 64.31	
<b>Men</b>						
Age (years)				< 0.001		< 0.001
20-29	11413	4489	39.3 (38.4-40.2)		402.86 $\pm$ 81.58	
30-39	21613	8757	40.5 (39.9-41.2)		404.68 $\pm$ 83.96	
40-49	15415	5672	36.8 (36.0-37.6)		396.08 $\pm$ 82.91	
50-59	12744	4119	32.3 (31.5-33.1)		385.08 $\pm$ 83.15	
60-69	4119	1031	25.0 (23.7-26.4)		369.67 $\pm$ 81.57	
$\geq 70$	1694	443	26.2 (24.1-28.3)		369.34 $\pm$ 83.23	
BMI (Kg/m <sup>2</sup> )				< 0.001		< 0.001
<24	26072	6309	24.2 (23.7-24.7)		370.61 $\pm$ 75.08	
24-27.9	29864	12013	40.2 (39.7-40.8)		403.11 $\pm$ 81.94	
$\geq 28$	11062	6189	55.9 (55.0-56.9)		434.34 $\pm$ 88.76	
Hypertension status				< 0.001		< 0.001
Hypertensive	18905	7991	42.3 (41.6-43.0)		407.10 $\pm$ 89.38	
Normotensive	48093	16520	34.4 (33.9-34.8)		391.11 $\pm$ 80.90	
<b>Women</b>						
Age (years)				< 0.001		< 0.001
20-29	10003	926	9.3 (8.7-9.8)		275.53 $\pm$ 61.07	
30-39	15051	1329	8.8 (8.4-9.3)		272.00 $\pm$ 61.34	
40-49	11180	917	8.2 (7.7-8.7)		268.82 $\pm$ 61.18	
50-59	7679	1065	13.9 (13.1-14.7)		288.14 $\pm$ 67.09	
60-69	3334	668	20.0 (18.7-21.4)		300.11 $\pm$ 72.13	
$\geq 70$	1138	297	26.1 (23.6-28.8)		313.99 $\pm$ 78.80	
BMI (Kg/m <sup>2</sup> )				< 0.001		< 0.001
<24	35238	2409	6.8 (6.6-7.1)		266.81 $\pm$ 57.91	
24-27.9	10529	1886	17.9 (17.2-18.7)		298.92 $\pm$ 68.15	
$\geq 28$	2618	907	34.6 (32.8-36.5)		334.91 $\pm$ 77.14	
Hypertension status				< 0.001		< 0.001
Hypertensive	7461	1625	21.8 (20.8-22.7)		304.94 $\pm$ 74.88	
Normotensive	40924	3577	8.7 (8.5-9.0)		272.48 $\pm$ 60.88	

431 SUA, serum uric acid; BMI, body mass index; CI, confidence interval; SD, standard deviation.

Table 2. Sex- specific characteristics of participants aged  $\geq 20$  years, 2010-2019

Variables	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	<i>P</i>
<b>Men</b>											
N	23535	24776	26574	27316	29416	32183	42222	51179	59921	66998	
Age (years)	43.80 $\pm$ 13.03	43.35 $\pm$ 12.67	42.83 $\pm$ 12.72	42.87 $\pm$ 12.43	43.39 $\pm$ 12.73	43.19 $\pm$ 12.40	41.71 $\pm$ 12.24	42.11 $\pm$ 12.53	42.34 $\pm$ 12.44	42.34 $\pm$ 12.49	< 0.001
eGFR (mL/min/1.73m <sup>2</sup> )	108.48 $\pm$ 20.81	107.53 $\pm$ 20.01	107.89 $\pm$ 19.23	101.62 $\pm$ 17.99	104.07 $\pm$ 18.92	101.95 $\pm$ 18.05	100.49 $\pm$ 17.36	99.33 $\pm$ 16.86	99.55 $\pm$ 16.84	98.97 $\pm$ 16.75	< 0.001
Obesity, n (%)	3346 (14.2)	3659 (14.8)	4156 (15.6)	4414 (16.2)	4523 (15.4)	4849 (15.1)	5855 (13.9)	7336 (14.2)	9561 (16.0)	11062 (16.5)	< 0.001
Hypertension, n (%)	7683 (32.6)	7982 (32.2)	8845 (33.3)	9138 (33.5)	9609 (32.7)	9699 (30.1)	11194 (26.5)	14355 (27.9)	15965 (26.6)	18905 (28.2)	< 0.001
SUA (mmol/L)	363.02 $\pm$ 74.32	367.28 $\pm$ 75.22	366.09 $\pm$ 75.39	373.68 $\pm$ 77.71	372.13 $\pm$ 78.58	381.22 $\pm$ 81.80	387.53 $\pm$ 82.52	391.09 $\pm$ 83.62	393.89 $\pm$ 84.11	395.62 $\pm$ 83.69	< 0.001
Hyperuricemia, % (95% CI)	21.8 (21.2-22.3)	24.1 (23.6-24.7)	23.1 (22.6-23.7)	26.6 (26.1-27.1)	25.7 (25.2-26.2)	29.9 (29.4-30.4)	32.8 (32.4-33.3)	34.8 (34.4-35.2)	35.9 (35.5-36.3)	36.6 (36.2-37.0)	< 0.001
<b>Women</b>											
N	15759	19212	17867	19544	21643	26816	32552	40347	44606	48385	
Age (years)	42.94 $\pm$ 13.44	42.43 $\pm$ 13.01	42.10 $\pm$ 12.95	41.64 $\pm$ 12.88	42.37 $\pm$ 13.20	41.42 $\pm$ 12.90	39.95 $\pm$ 12.65	40.79 $\pm$ 12.76	41.15 $\pm$ 12.66	41.52 $\pm$ 12.62	< 0.001
eGFR (mL/min/1.73m <sup>2</sup> )	130.36 $\pm$ 28.22	130.69 $\pm$ 27.51	130.71 $\pm$ 26.16	123.06 $\pm$ 25.14	126.08 $\pm$ 26.08	123.95 $\pm$ 24.54	122.58 $\pm$ 23.67	117.46 $\pm$ 22.86	120.28 $\pm$ 23.03	119.11 $\pm$ 22.67	< 0.001
Obesity, n (%)	938 (6.0)	1041 (5.4)	1035 (5.8)	1156 (5.9)	1252 (5.8)	1439 (5.4)	1652 (5.1)	1939 (4.8)	2279 (5.1)	2618 (5.4)	< 0.001
Hypertension, n (%)	2974 (18.9)	3440 (17.9)	3196 (17.9)	3523 (18.0)	3841 (17.7)	4385 (16.4)	4697 (14.4)	6234 (15.6)	6524 (14.6)	7461 (15.4)	< 0.001
SUA (mmol/L)	255.87 $\pm$ 57.58	256.43 $\pm$ 57.78	256.47 $\pm$ 57.40	260.28 $\pm$ 57.99	259.99 $\pm$ 58.22	264.21 $\pm$ 60.38	269.96 $\pm$ 61.87	273.26 $\pm$ 62.79	275.29 $\pm$ 63.43	277.48 $\pm$ 64.32	< 0.001
Hyperuricemia, % (95% CI)	5.2 (4.9-5.6)	5.5 (5.2-5.8)	5.3 (5.0-5.6)	5.9 (5.6-6.3)	6.1 (5.8-6.4)	7.1 (6.8-7.4)	8.6 (8.3-8.9)	9.8 (9.5-10.1)	10.1 (9.8-10.4)	10.8 (10.5-11.0)	< 0.001

Data were shown as Mean  $\pm$  SD or percentages. eGFR, estimated glomerular filtration rate; SUA, serum uric acid; CI, confidence interval.

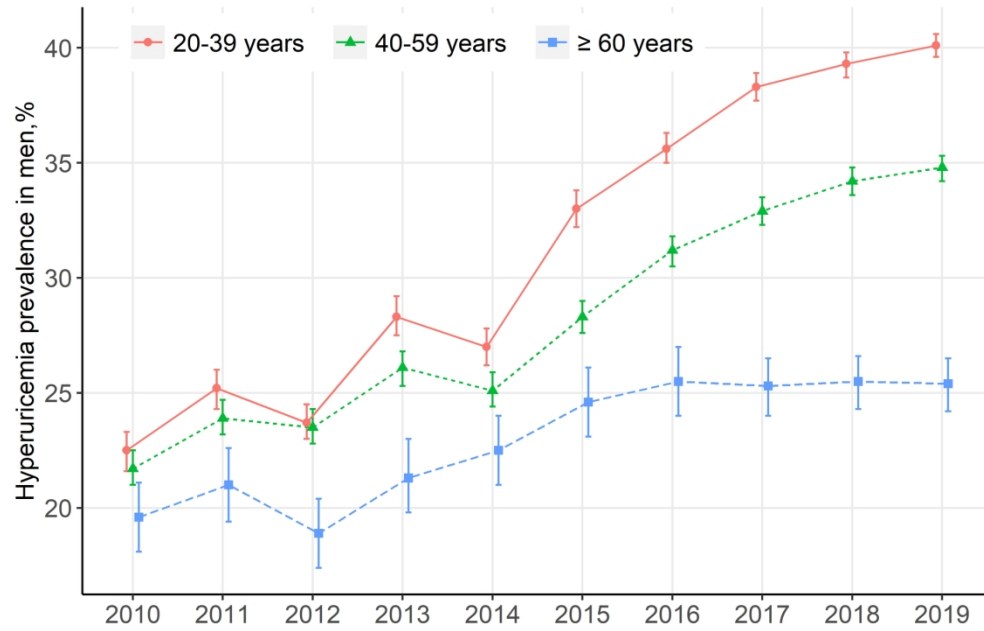


Figure 1. Age-specific trends in hyperuricemia prevalence (95% CI) among men, 2010-2019. CI, confidence interval.

170x114mm (300 x 300 DPI)

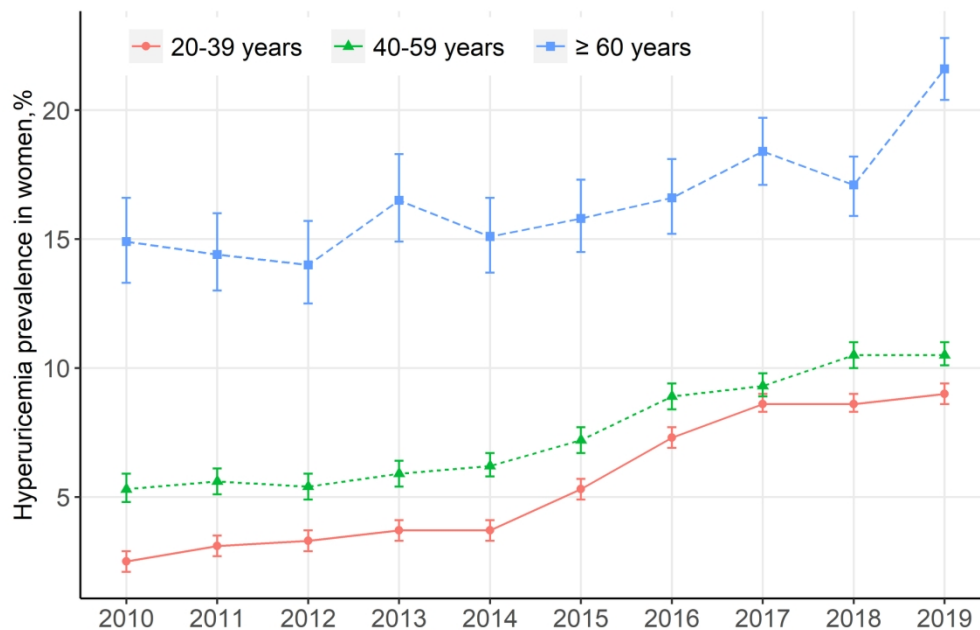


Figure 2. Age-specific trends in hyperuricemia prevalence (95% CI) among women, 2010-2019. CI, confidence interval.

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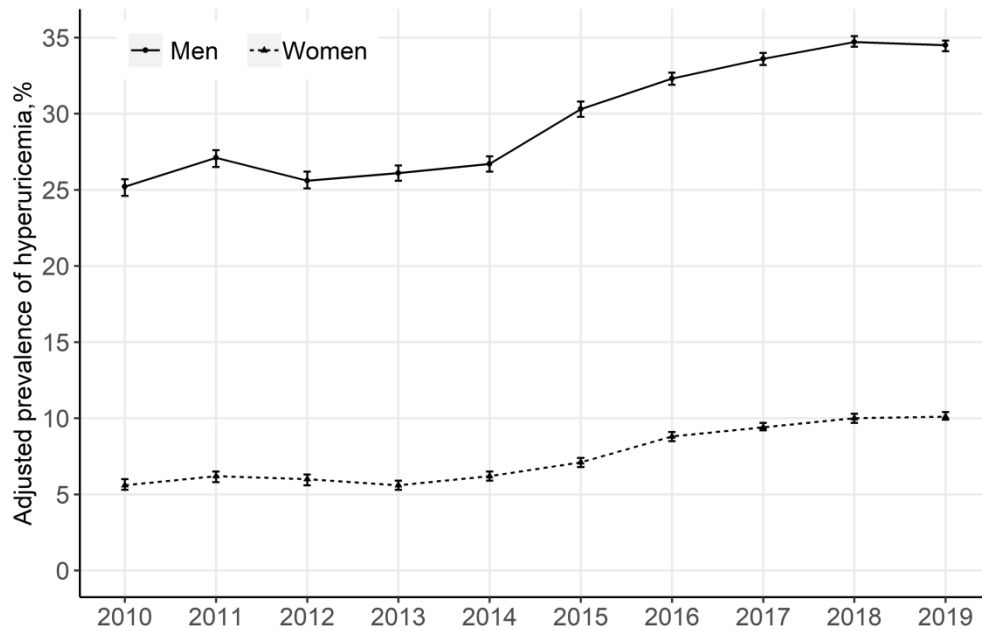
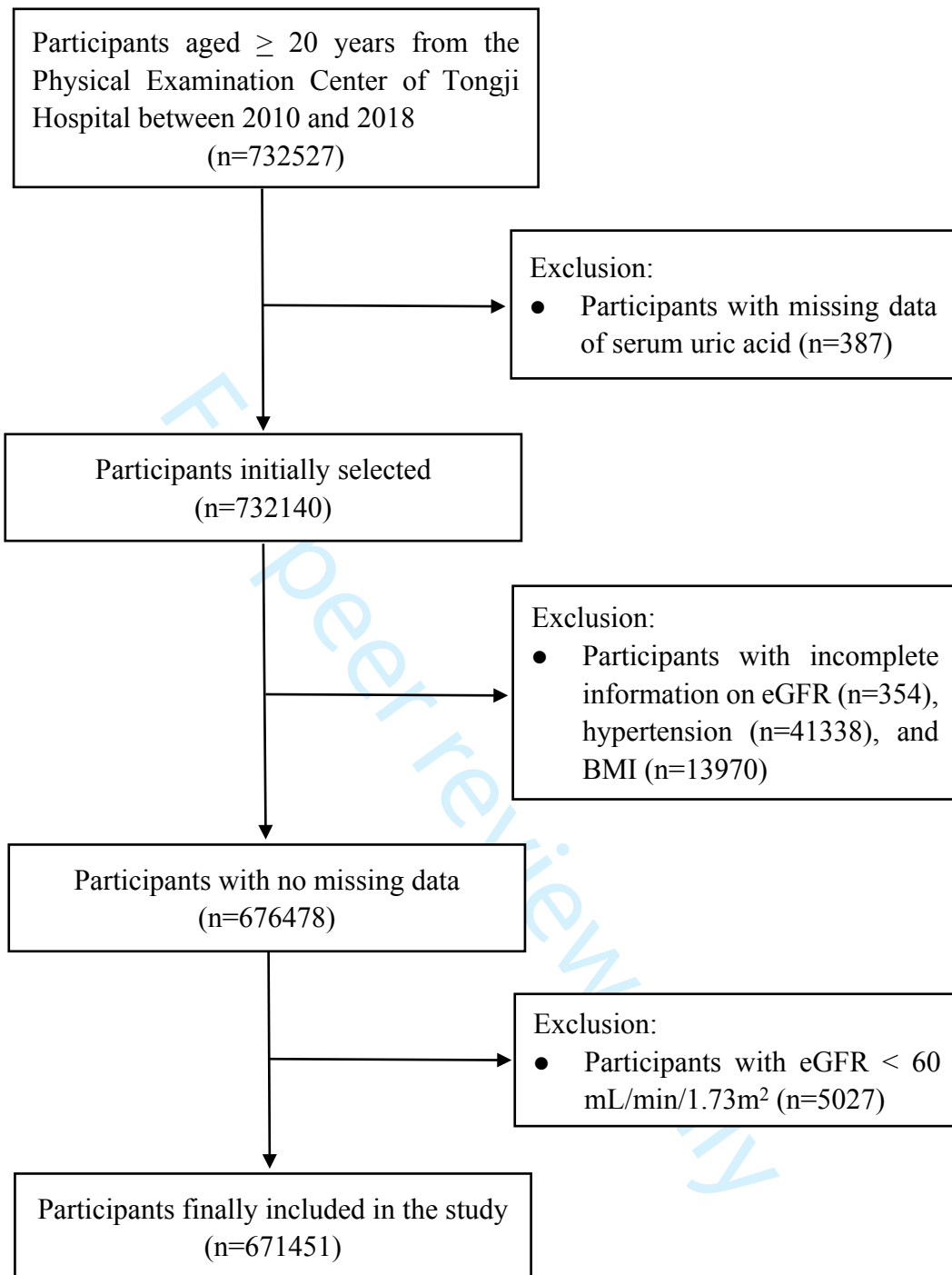


Figure 3. Sex-specific trends in multivariate-adjusted hyperuricemia prevalence (95% CI) among participants aged  $\geq 20$  years, 2010-2019. The prevalence was adjusted for age, BMI, eGFR, and Hypertension. CI, confidence interval; BMI, body mass index; eGFR, estimated glomerular filtration rate.

170x114mm (600 x 600 DPI)



Supplemental Figure 1. Flow chart for selection of the study participants.



# Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the STROBE cross sectional reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

	Reporting Item	Page Number
<b>Title and abstract</b>		
Title	<a href="#">#1a</a> Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	<a href="#">#1b</a> Provide in the abstract an informative and balanced summary of what was done and what was found	2
<b>Introduction</b>		
Background / rationale	<a href="#">#2</a> Explain the scientific background and rationale for the investigation being reported	4
Objectives	<a href="#">#3</a> State specific objectives, including any prespecified hypotheses	5
<b>Methods</b>		
Study design	<a href="#">#4</a> Present key elements of study design early in the paper	6

1	Setting	<a href="#">#5</a>	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
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6	Eligibility criteria	<a href="#">#6a</a>	Give the eligibility criteria, and the sources and methods of selection of participants.	6
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10		<a href="#">#7</a>	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
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15	Data sources / measurement	<a href="#">#8</a>	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	7
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24	Bias	<a href="#">#9</a>	Describe any efforts to address potential sources of bias	3, 8
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28	Study size	<a href="#">#10</a>	Explain how the study size was arrived at	6
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30	Quantitative variables	<a href="#">#11</a>	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	7-8
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35	Statistical methods	<a href="#">#12a</a>	Describe all statistical methods, including those used to control for confounding	7-8
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39	Statistical methods	<a href="#">#12b</a>	Describe any methods used to examine subgroups and interactions	7-8
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43	Statistical methods	<a href="#">#12c</a>	Explain how missing data were addressed	6
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47	Statistical methods	<a href="#">#12d</a>	If applicable, describe analytical methods taking account of sampling strategy	n/a
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51	Statistical methods	<a href="#">#12e</a>	Describe any sensitivity analyses	n/a
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54	<b>Results</b>			9
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57	Participants	<a href="#">#13a</a>	Report numbers of individuals at each stage of study— eg numbers potentially eligible, examined for eligibility,	9
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confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.

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5	Participants	<a href="#">#13b</a>	Give reasons for non-participation at each stage 6
6			
7	Participants	<a href="#">#13c</a>	Consider use of a flow diagram 6,supplemental Figure 1.
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11	Descriptive data	<a href="#">#14a</a>	Give characteristics of study participants (eg 9, Tabel 1-2 demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.
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20	Descriptive data	<a href="#">#14b</a>	Indicate number of participants with missing data for 6,supplemental each variable of interest Figure 1.
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23	Outcome data	<a href="#">#15</a>	Report numbers of outcome events or summary 9, Tabel 1-2 measures. Give information separately for exposed and unexposed groups if applicable.
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29	Main results	<a href="#">#16a</a>	Give unadjusted estimates and, if applicable, 9-10, Tabel 1-2, confounder-adjusted estimates and their precision (eg, Figure 1-3 95% confidence interval). Make clear which confounders were adjusted for and why they were included
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37	Main results	<a href="#">#16b</a>	Report category boundaries when continuous variables 9-10 were categorized
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41	Main results	<a href="#">#16c</a>	If relevant, consider translating estimates of relative risk n/a into absolute risk for a meaningful time period
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45	Other analyses	<a href="#">#17</a>	Report other analyses done—e.g., analyses of 10, Figure 1-2 subgroups and interactions, and sensitivity analyses
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49	<b>Discussion</b>		
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51	Key results	<a href="#">#18</a>	Summarise key results with reference to study 11 objectives
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55	Limitations	<a href="#">#19</a>	Discuss limitations of the study, taking into account 14 sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.
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1	Interpretation	<a href="#">#20</a>	Give a cautious overall interpretation considering	11-14
2			objectives, limitations, multiplicity of analyses, results	
3			from similar studies, and other relevant evidence.	
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6	Generalisability	<a href="#">#21</a>	Discuss the generalisability (external validity) of the	14
7			study results	
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10	<b>Other</b>			
11	<b>Information</b>			
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14	Funding	<a href="#">#22</a>	Give the source of funding and the role of the funders	16
15			for the present study and, if applicable, for the original	
16			study on which the present article is based	
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# BMJ Open

## Temporal trends in Hyperuricemia among Adults in Wuhan City, China from 2010-2019: a cross-sectional study

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3 **Temporal trends in Hyperuricemia among Adults in Wuhan City, China from**  
4 **2010-2019: a cross-sectional study**

5

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## 30 Abstract

31 **Objectives:** Hyperuricemia is a risk factor for gout attacks, kidney damage and  
32 cardiovascular events. Evidence on the trends in hyperuricemia burden in Wuhan city,  
33 China was limited. The present study aimed to estimate the prevalence of and a decade  
34 trend in hyperuricemia in Wuhan city.

35 **Design:** Cross-sectional study.

36 **Setting:** Health management center of Tongji hospital.

37 **Participants:** A total of 732527 adult participants from the general population who  
38 took a physical examination in the health management center between 2010 and 2019.

39 **Main outcome measures:** Prevalence of and trends in hyperuricemia.

40 **Results:** The overall prevalence of hyperuricemia was 25.8% (36.6% in men and 10.8%  
41 in women) in 2019. The hyperuricemia prevalence and serum uric acid (SUA) levels  
42 were significantly higher in young men, old women, and participants with obesity,  
43 hypertension, diabetes, or dyslipidemia ( $P < 0.05$ ). SUA levels among men and women  
44 gradually increased from 358.0 (313.0-407.0) mmol/L and 250.0 (217.0-288.0) mmol/L  
45 in 2010 to 388.0 (338.0-445.2) mmol/L and 270.0 (233.0-314.0) mmol/L in 2019,  
46 respectively,  $P < 0.05$ . From 2010 through 2019, hyperuricemia prevalence  
47 significantly increased in each age category and it increased most sharply among  
48 participants aged 20-39 years. The multivariate-adjusted prevalence among men was  
49 26.1% (25.4% - 26.7%) in 2010, 30.9% (30.4% - 31.4%) in 2015, and 34.4% (34.1% -  
50 34.8%) in 2019, while among women it was 5.8% (5.4% - 6.2%) in 2010, 7.2% (6.9% -  
51 - 7.5%) in 2015, and 10.1% (9.9% - 10.3%) in 2019.

52 **Conclusions:** Hyperuricemia was highly prevalent among adults in Wuhan city. More  
53 attention should be paid to the increasing burden of hyperuricemia, especially for those  
54 at higher risks.

55 **Key Words:** Hyperuricemia, uric acid, epidemiology, temporal trend

56  
57 **Strengths and limitations of this study**

- 58 ➤ This study included a large sample size of participants (more than 730000 adults)  
59 from the general population, which made our findings more convincing.
- 60 ➤ This study firstly estimated the prevalence of and trends in hyperuricemia over the  
61 recent decade (2010-2019) among adults in Wuhan city.
- 62 ➤ The multivariate logistic model was used to correct selection biases and  
63 confounding biases as possible by adjusting for potential confounders.
- 64 ➤ Since participants in the present study were recruited from a health management  
65 center, selection biases could not be avoided.

## 67 **Introduction**

68 Serum uric acid (SUA) is the final product of purine nucleotides metabolism. The  
69 overproduction of SUA, as well as its inefficient renal or gut excretion, can  
70 consequently lead to hyperuricemia. Hyperuricemia is generally recognized as the  
71 major contributor to the onset of gout.<sup>1</sup> Moreover, many studies have demonstrated a  
72 positive association of hyperuricemia or a high level of SUA with increased all-cause  
73 mortality and several chronic diseases such as chronic kidney disease, cardiovascular  
74 events, reduced pulmonary function, obesity, glucose metabolism, dyslipidemia,  
75 hypertension, and metabolic syndrome.<sup>2-9</sup> These diseases accounted for a large part of  
76 global deaths and disability-adjusted life-year losses,<sup>10 11</sup> resulting in a particular  
77 urgency to prevent and control hyperuricemia.

78 Previous studies have documented an increasing trend of hyperuricemia prevalence  
79 in the past few decades across the world, especially in western countries.<sup>12-14</sup>  
80 Additionally, hyperuricemia is reported to be more prevalent in developed countries  
81 than in developing countries.<sup>15</sup> The prevalence among US adults was substantial (20.2%  
82 in men and 20.0% in women) during 2015-2016.<sup>16</sup> In China, the prevalence estimated  
83 from national surveys were 8.4% in 2009-2010,<sup>17</sup> 13.0% in 2007-2011,<sup>18</sup> and 6.4%  
84 among the middle-aged and elderly in 2011-2012.<sup>19</sup> Besides, a meta-analysis of 38  
85 studies from mainland China reported that the pooled prevalence of hyperuricemia  
86 among Chinese adults was 13.3% in 2000-2014.<sup>20</sup> Obviously, the data above were not  
87 able to clearly illustrate the trend of hyperuricemia prevalence among Chinese adults.

88 China is a large developing country with unbalanced economic development and

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4 89 marked regional differences. Hyperuricemia prevalence among Chinese adults varied  
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6 90 greatly by geographical regions, with a report of 18.6% in south China, 12.9% in east  
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9 91 China, 13.9% in southwest China, 10.3% in northwest China, 10.1% in northeast China,  
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11 92 and 13.2% in north China.<sup>20</sup> Noteworthy, evidence on hyperuricemia burden in central  
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14 93 China was limited. Wuhan, the capital city of Hubei province in central China, was  
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17 94 characterized by rapid economic growth and urbanization in the recent decade. Its gross  
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20 95 domestic products (GDP) per capita increased from 50117 yuan in 2009 to 123831 yuan  
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22 96 in 2017.<sup>21 22</sup> Studies from developing countries showed that a rapidly growing economy  
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25 97 in the short term and subsequently changed lifestyles would increase the risk of several  
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27 98 metabolic disorders.<sup>23 24</sup>

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30 99 To date, few studies have investigated a decade trend in hyperuricemia burden in  
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33 100 Wuhan city. Therefore, we performed a large cross-sectional study to estimate the sex-  
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35 101 specific prevalence of and trends in hyperuricemia among the general adults from 2010  
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38 102 through 2019. This general population-based study used data collected from  
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40 103 consecutive adults who underwent a health check-up in a health management center.

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## 105 **Methods**

### 106 **Study population**

107 We conducted a cross-sectional study, of which consecutive participants who had a  
108 health check-up in the Health Management Center of Tongji Hospital in Wuhan city,  
109 China between January 1, 2010 and December 31, 2019 were included. All the  
110 participants came from the general population. Most of them were urban citizens  
111 working in government organizations or large enterprises. Each participant completed  
112 the basic items of the physical examination including demographic information  
113 collection, biochemical tests, and anthropometric measurements. Supplemental Figure  
114 1 showed the procedures for selecting participants in the study. A total of 732527  
115 participants aged  $\geq 20$  years were recruited. This age range was selected in accordance  
116 with several previous studies.<sup>12 25</sup> After excluding participants with missing data, we  
117 included 676478 participants. As reduced renal function may affect uric acid excretion,  
118 we further excluded 5027 participants who had an estimated glomerular filtration rate  
119 (eGFR) of less than 60 mL/min/1.73m<sup>2</sup>. Finally, 671451 participants were included in  
120 the analyses. Due to the lack of information on ID card number, there existed some  
121 participants who underwent health check-ups for years during the study period.

122 We used the STROBE cross sectional reporting guidelines in the present study.<sup>26</sup>  
123 The study was conducted in accordance with the Declaration of Helsinki and it was  
124 approved by the ethics committee of Tongji Hospital, Tongji Medical College,  
125 Huazhong University of Science and Technology with a waiver of informed consent.  
126 The Institutional Review Board Approval Number was TJ-IRB20200513.

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## 127 **Assessment of main variables**

128 Overnight fasting blood samples were collected to measure the biochemical variables.

129 SUA concentrations were measured by the enzymatic colorimetry using an automated

130 analyzer (Roche Cobas 8000, Basel, Switzerland) according to standard laboratory

131 process of quality control. Additionally, the method of SUA measurement did not

132 change during the whole study period and the laboratory quality assessment was

133 reviewed. The intra-assay and inter-assay coefficients of variation were 4.25% and <5.7%

134 at level 1 (210 $\mu$ mol/L), <4.25% and <5.7% at level 2 (572 $\mu$ mol/L). In the current study,

135 hyperuricemia was defined according to SUA levels: men  $\geq$  416 mmol/L (7 mg/dL),

136 women  $\geq$  357 mmol/L (6 mg/dL).<sup>27 28</sup> Participants were asked to wear light clothes and

137 bare foot before their height and weight were measured. The body mass index (BMI)

138 was calculated as weight in kilograms divided by height in meters squared. For Chinese

139 adults, obesity was defined as BMI  $\geq$  28 Kg/m<sup>2</sup> and overweight was defined as BMI  $\geq$

140 24 Kg/m<sup>2</sup>.<sup>29</sup> Blood pressure was measured by trained nurses using electronic

141 sphygmomanometers (HBP-9020; OMRON, Dalian, China) in a seated position after

142 participants had rested for at least 5 minutes. Hypertension was identified if any of the

143 following criteria was satisfied: systolic blood pressure  $\geq$  140 mmHg, or diastolic blood

144 pressure  $\geq$  90 mmHg, or use of antihypertensive medication, or self-reported physician

145 diagnosis of hypertension. Diabetes was defined as fasting blood glucose  $\geq$  7.0 mmol/L,

146 or use of antidiabetic medication, or self-reported physician diagnosis of diabetes.

147 Dyslipidemia was diagnosed according to the 2016 Chinese Guideline for the

148 Management of Dyslipidemia in Adults<sup>30</sup> if any of the following criteria was satisfied:

149 total cholesterol  $\geq$  6.22 mmol/L, triglyceride  $\geq$  2.26 mmol/L, LDL-C  $\geq$  4.14mmol/L,  
150 HDL-C  $<$  1.04 mmol/L. Information on age and sex was provided by the participants.

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## 152 **Patient and public involvement**

153 Patients or the public were not involved in the design, or conduct, or reporting, or  
154 dissemination plans of our research. Patients or the public were not invited to contribute  
155 to the writing or editing of this article for readability or accuracy.

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## 157 **Statistical analysis**

158 Due to the marked difference in SUA levels between men and women, the sex-specific  
159 prevalence of and trends in hyperuricemia were estimated. Categorical variables were  
160 expressed in percentages, whereas continuous variables were reported as means  $\pm$   
161 standard deviation (SD) for normally distributed data or median (interquartile range)  
162 for skewed data. The normality of data is evaluated by Kolmogorov-Smirnov test. We  
163 used data collected in 2019 to estimate SUA levels, the hyperuricemia prevalence and  
164 their 95% confidence intervals (CIs), stratified by sex (male or female), age (20 - 29,  
165 30 - 39, 40 - 49, 50 - 59, 60 - 69, or  $\geq$  70 years), BMI ( $<$  24, 24 - 27.9, or  $\geq$  28 kg/m<sup>2</sup>,  
166 the cut-off values of overweight and obesity for Asian), hypertension (yes or no),  
167 diabetes (yes or no), and dyslipidemia (yes or no). In this part, the prevalence of  
168 hyperuricemia was compared using the Cochran-Armitage test for trend. SUA levels  
169 were compared using Kruskal-Wallis test.

170 Sex- and age- specific trends in hyperuricemia from 2010 through 2019 were then

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4 171 analyzed. We performed tests for trends by including the observation year as a  
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6 172 continuous variable in a linear or logistic regression model. The sex-specific  
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9 173 multivariate-adjusted prevalence of hyperuricemia from 2010 through 2019 were  
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12 174 estimated using logistic regression models after adjustment for age, BMI, eGFR,  
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14 175 hypertension, diabetes, and dyslipidemia. Age, BMI, and eGFR were included in the  
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17 176 logistic model as continuous variables, whereas hypertension, diabetes, and  
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20 177 dyslipidemia were included as dichotomous variables. The Stata commands used to  
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22 178 estimate the adjusted hyperuricemia prevalence were “logit” and “margins” in this  
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25 179 study. All statistical analyses were performed using Stata version 12.0 (Stata Corp LP,  
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28 180 College Station, TX, USA). Graphs were drawn using R software (version 3.6.1) with  
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30 181 an available package: ggplot2. Two-sided  $P < 0.05$  was considered statistically  
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33 182 significant.

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## 184 **Results**

### 185 **The crude prevalence of hyperuricemia in 2019**

186 Table 1 showed crude prevalence of hyperuricemia and SUA levels in participants aged  
187  $\geq 20$  years during the year 2019. A total of 66998 men and 48385 women in 2019 were  
188 included, with an average age of  $42.0 \pm 12.6$  years. The overall hyperuricemia  
189 prevalence was 25.8%. The crude prevalence of hyperuricemia and SUA levels in men  
190 were significantly higher than those in women (36.6% versus 10.8%,  $388.0$  ( $338.0$ -  
191  $445.2$ ) mmol/L versus  $270.0$  ( $233.0$ - $314.0$ ) mmol/L; both  $P < 0.05$ ). Hyperuricemia  
192 prevalence was around 9.0% in women aged  $< 50$  years and it rapidly increased with  
193 advancing age in women aged  $\geq 50$  years, with the highest prevalence of 26.1% for  
194 women aged  $\geq 70$  years. The burden of hyperuricemia among men was high across all  
195 age groups and it was particularly marked in young men (39.3% for 20-29 years and  
196 40.5% for 30-39 years). Hyperuricemia prevalence and 1 SUA levels dramatically  
197 increased with elevating BMI in both sexes ( $P < 0.05$ ); the prevalence (95% CI) was  
198 55.9% (55.0% - 56.9%) in obese men and 34.6% (32.8% - 36.5%) in obese women. In  
199 the whole population, participants with hypertension, diabetes, or dyslipidemia had  
200 significantly higher hyperuricemia prevalence and SUA levels than the normal groups  
201 ( $P < 0.05$ ).

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### 203 **Trends in the crude prevalence of hyperuricemia**

204 A total of 671451 participants were included in the study between 2010 and 2019. As  
205 shown in Table 2, the crude prevalence of hyperuricemia significantly increased over

the years in both men and women ( $P < 0.05$ ). SUA levels among men and women gradually increased from 358.0 (313.0-407.0) mmol/L and 250.0 (217.0-288.0) mmol/L in 2010 to 388.0 (338.0-445.2) mmol/L and 270.0 (233.0-314.0) mmol/L in 2019, respectively ( $P < 0.05$ ). A significantly increasing trend in hyperuricemia prevalence was observed during the observation period in each age category of both sexes (Figure 1). The prevalence increased most sharply among participants aged 20-39 years. It increased from 22.5% (21.6% - 23.3%) in 2010 to 40.1% (39.6% - 40.6%) in 2019 among young men, whereas among young women it increased from 2.5% (2.1% - 2.9%) in 2010 to 9.0% (8.6% - 9.4%) in 2019.

### **Trends in multivariate-adjusted prevalence of hyperuricemia**

The multivariate-adjusted prevalence of hyperuricemia was calculated using logistic regression models. Figure 2 showed an increasing trend in multivariate-adjusted prevalence of hyperuricemia during the observation years in both sexes ( $P < 0.05$ ). The prevalence among men was 26.1% (25.4% - 26.7%) in 2010, 30.9% (30.4% - 31.4%) in 2015, and 34.4% (34.1% - 34.8%) in 2019, while among women it was 5.8% (5.4% - 6.2%) in 2010, 7.2% (6.9% - 7.5%) in 2015, and 10.1% (9.9% - 10.3%) in 2019.

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## 224 Discussion

225 The present study revealed that hyperuricemia was highly prevalent (36.6% in men and  
226 10.8% in women) among adults in Wuhan city, China during 2019. The burden of  
227 hyperuricemia among men was substantial in all age groups. Hyperuricemia prevalence  
228 varied distinctly by sex, age, BMI, hypertension, diabetes, and dyslipidemia, with  
229 young men, old women, and participants with metabolic disorders having a  
230 significantly higher prevalence.

231 This study also investigated the trend of hyperuricemia over a decade period (from  
232 2010 to 2019) and revealed a significantly increasing trend in multivariate-adjusted  
233 prevalence of hyperuricemia in both sexes. Moreover, it was observed that the  
234 prevalence increased most sharply among young adults during the observation period,  
235 which meant that hyperuricemia occurred more and more frequently in young adults.

236 The estimated prevalence in our study (25.8% in 2019) was much higher than those  
237 reported in America (20.1% in 2015-2016),<sup>16</sup> Italy (11.9% in 2009),<sup>13</sup> Korea (11.4% in  
238 2016),<sup>31</sup> and a previous national survey in China (13.0% in 2007-2011).<sup>18</sup> A cross-  
239 sectional study from Bangkok, Thailand used data of the annual physical examination  
240 and reported a prevalence rate of 24.4% in urban residents,<sup>32</sup> which was close to our  
241 result. Epidemiological studies demonstrated that urban individuals had a higher  
242 prevalence of hyperuricemia than rural residents.<sup>17 19</sup> In the present study, almost all the  
243 participants included were urban citizens, which may help explain the high  
244 hyperuricemia prevalence.

245 Overweight or obesity was a well-accepted risk factor for hyperuricemia,<sup>33</sup> which

was validated in our study. We found that hyperuricemia prevalence increased significantly with elevating BMI in both sexes. Based on information in Table 1, it could be calculated that nearly 61.0% of men were overweight or obese and 44.5% of them were identified as hyperuricemia. The prevalence of overweight or obesity among men was reported to be 38.6% in a representative sample of Wuhan community residents aged 15-69 years.<sup>34</sup> Compared to this representative sample, the working population in the present study had markedly higher ratios of men, labor force, and overweight or obesity. The heavy burden of overweight or obesity may be another reason to explain the highly prevalent hyperuricemia. It was also observed that hyperuricemia was closely correlated with hypertension, diabetes, and dyslipidemia, which accorded with the previous studies.<sup>6-9</sup> These metabolic disorders were common comorbidities in participants with hyperuricemia, leading to higher risk of renal and cardiovascular diseases.

The present study found that hyperuricemia prevalence was higher among women aged  $\geq 50$  years and it further increased with advancing age. Several studies from Asian and European countries revealed a roughly positive association of hyperuricemia prevalence with age among women,<sup>13 14 18 31</sup> which accorded with our results. Given the huge sex difference in hyperuricemia prevalence, we thought that sex hormones may play a key role. One explanation was that female sex hormones had protective effects against hyperuricemia. A cross-sectional study of 58870 South Korean women demonstrated that hyperuricemia prevalence significantly increased with the menopausal stage, after controlling for potential confounders.<sup>35</sup> Postmenopausal

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4 268 women are characterized by materially declined levels of female sex hormones  
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6 269 (especially estradiol and progesterone). When they grow older, levels of estradiol and  
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9 270 progesterone would decline further. The BioCycle study demonstrated that SUA levels  
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11 271 were inversely associated with these two hormones.<sup>36</sup> Until now, how estradiol and  
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13 272 progesterone lower SUA levels was not fully understood. They probably effect via  
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15 273 promoting renal excretion of uric acid.<sup>37 38</sup> Another two explanations would be the  
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17 274 higher prevalence of obesity and alcohol drinking in men than women,<sup>34 39</sup> as obesity  
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19 275 and alcohol drinking are well-established risk factors for hyperuricemia.  
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25 276 Data from the National Health and Nutrition Examination Survey demonstrated  
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27 277 that hyperuricemia prevalence among American adults significantly increased from  
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29 278 18.2% in 1988-1994 to 21.4% in 2007-2008 and concluded that the increasing trend of  
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31 279 hyperuricemia was likely due to rising prevalence of obesity and hypertension.<sup>12</sup>  
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33 280 However, in the present study, we did not observe an increasing trend in obesity and  
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35 281 hypertension over the years (Table 2). Thus, it might be some other factors responsible  
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37 282 for the increasing prevalence of hyperuricemia among our study participants. We  
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39 283 thought that gradually westernized dietary structure and rising consumption of fructose-  
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41 284 sweetened soft drinks might be the main causes. Western diets contained much more  
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43 285 purine than the traditional Chinese diets, leading to a higher risk of developing  
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45 286 hyperuricemia. In addition, accumulating evidence showed that fructose-sweetened  
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47 287 drinks, although containing no purines, could induce hyperuricemia.<sup>40-42</sup> Fructose  
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49 288 intake per capita has dramatically increased during the past few decades,<sup>43-45</sup> in parallel  
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51 289 with the increasing burden of hyperuricemia. Alcohol consumption and several lifestyle  
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290 habits like inactivity and sedentary behaviors have been established as risk factors for  
291 hyperuricemia. There are no studies directly investigating the associations between  
292 these risk factors and the increasing trends in hyperuricemia prevalence. However,  
293 findings from the China Kadoorie Biobank reported a modest increase in alcohol  
294 consumption, drinking frequency and heavy episodic drinking prevalence among men  
295 in the past decade, particularly among the young men,<sup>39</sup> which may help explain our  
296 results.

297 To the best of our knowledge, the present study firstly revealed age-specific trends  
298 in hyperuricemia over a decade among Chinese adults and found that hyperuricemia  
299 prevalence increased most sharply among young adults during the observation period.  
300 A large analysis of 128014 Irish adults revealed an increasing trend in hyperuricemia  
301 from 2006 through 2014 across all age groups, with the most increment among young  
302 participants aged 18-39 years,<sup>14</sup> a finding that was similar to our result. In addition to  
303 hyperuricemia, several hyperuricemia-related diseases such as diabetes and  
304 cardiovascular events also occurred more frequently among young adults over the past  
305 years,<sup>46 47</sup> posing a serious threat to public health. Based on the trend revealed in our  
306 study, hyperuricemia prevalence was much likely to continue rising in the coming years.  
307 Policy-makers should pay more attention to the burden of hyperuricemia, especially  
308 among young adults.

309 The strengths of the present study were distinct. This study included a large sample  
310 size of participants (more than 730000 adults) from the general population, which made  
311 our findings more convincing. In addition, to the best of our knowledge, this was the

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4 312 first study to investigate the trend in hyperuricemia prevalence over the recent decade  
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6 313 (2010-2019) among adults in Wuhan city, contributing to the management of  
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9 314 hyperuricemia in this area.

11 315 The study also had several limitations. First, as the participants in the present study  
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14 316 were recruited from a health management center, selection biases could not be avoided.  
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17 317 The participants may be not a representative sample of the general population in  
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20 318 community. Therefore, it should take caution to interpret the findings of this study. In  
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23 319 fact, as almost all the participants were urban citizens working in government  
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25 320 organizations or enterprises across every district of Wuhan city, the study participants  
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27 321 were more likely a sample of working populations than community residents.  
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30 322 Additionally, we estimated the hyperuricemia prevalence after controlling several  
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32 323 confounders (shown in Figure 2), which would help reduce the bias through statistical  
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35 324 analyses. Second, hyperuricemia prevalence may be underestimated in our study. We  
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38 325 diagnose hyperuricemia only according to SUA levels. However, participants with  
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40 326 hyperuricemia might have normal SUA levels if they were undergoing SUA-lowering  
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43 327 therapies. Third, our study did not collect data on diets and lifestyles that were related  
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46 328 to hyperuricemia. Changes of these variables such as fructose intake over the years may  
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48 329 help explain the trends in hyperuricemia. Forth, in the study population, there existed  
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51 330 participants who underwent health check-ups more than once during the study period.  
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53 331 Their multiple medical records were included in the analyses, which may finally  
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56 332 influence the accuracy of our results. Fifth, the definition of hyperuricemia highlights  
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59 333 the measurement of SUA on two different days under the normal purine diet. However,  
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334 SUA was measured only once in the present study, which would affect the screening  
335 rate of hyperuricemia.

336

### 337 **Conclusions**

338 In summary, a high burden of hyperuricemia was found among adults in Wuhan city.  
339 Moreover, hyperuricemia occurred more and more frequently in young adults. Our  
340 study also revealed a significant increasing trend in multivariate-adjusted prevalence of  
341 hyperuricemia among adults from 2010 through 2019. Promoting dietary change,  
342 weight loss and physical activity in community or workplace would be effective  
343 measures to prevent and control hyperuricemia. These measures should be taken  
344 urgently, especially among young adults, postmenopausal women, and participants  
345 with metabolic disorders, for they were at higher risks.

346



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349

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351 manuscript. ZW designed the study and drafted the article. LS, LH, and YL contributed  
352 to the conception, analysis, and critically revised the manuscript. XL and YH  
353 participated in the data collection and revised the manuscript.

354

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357

358 **Competing interests** None declared.

359

360 **Patient consent for publication** Not required.

361

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363 Tongji Medical College, Huazhong University of Science and Technology.

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365 **Data availability statement** Data are available upon reasonable request.

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4 507 **Figure legends**

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8 508 Figure 1. Sex and age-specific trends in hyperuricemia prevalence (95% CI), 2010-2019.

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10 509 CI, confidence interval.

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15 510 Figure 2. Sex-specific trends in multivariate-adjusted hyperuricemia prevalence (95%

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17 511 CI) among participants aged  $\geq 20$  years, 2010-2019. The prevalence was adjusted for

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19 512 age, BMI, eGFR, hypertension, diabetes, and dyslipidemia. CI, confidence interval;

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21 513 BMI, body mass index; eGFR, estimated glomerular filtration rate.

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28 514 Supplemental Figure 1. Flow chart for selection of the study participants.

Table 1. Crude prevalence of hyperuricemia and levels of SUA in participants aged  $\geq 20$  years, 2019

Variables	The whole population			Men			Women		
	Cases/ participants	Hyperuricemia, Prevalence (95% CI)	SUA (mmol/L), Median (IQR)	Cases/ participants	Hyperuricemia, Prevalence (95% CI)	SUA (mmol/L), Median (IQR)	Cases/ participants	Hyperuricemia, Prevalence (95% CI)	SUA (mmol/L), Median (IQR)
In total	29713/115383	25.8 (25.5-26.0)	338.3 (274.0-407.3)	24511/66998	36.6 (36.2-36.9)	388.0 (338.0-445.2)	5220/48385	10.8 (10.5-11.0)	270.0 (233.0-314.0)
Age (years)									
20-29	5415/21416	25.3 (24.7-25.9)	335.0 (269.0-405.1)	4489/11413	39.3 (38.4-40.2)	394.8 (347.0-451.0)	922/10003	9.3 (8.7-9.8)	269.0 (234.0-310.0)
30-39	10086/36664	27.5 (27.1-28.0)	343.0 (273.1-415.1)	8757/21613	40.5 (39.9-41.2)	396.1 (346.0-455.0)	1339/15051	8.8 (8.4-9.3)	265.0 (229.6-306.8)
40-49	6589/26595	24.8 (24.3-25.3)	335.0 (268.0-406.0)	5672/15415	36.8 (36.0-37.6)	389.0 (338.0-445.5)	917/11180	8.2 (7.7-8.7)	262.3 (226.8-303.0)
50-59	5184/20423	25.4 (24.8-26.0)	341.0 (283.0-406.0)	4119/12744	32.3 (31.5-33.1)	378.0 (328.0-435.0)	1065/7679	13.9 (13.1-14.7)	280.1 (242.0-327.0)
60-69	1699/7453	22.8 (21.8-23.8)	330.5 (278.4-389.5)	1031/4119	25.0 (23.7-26.4)	363.3 (315.3-416.0)	636/3334	20.0 (18.7-21.4)	292.1 (249.0-342.3)
$\geq 70$	740/2832	26.1 (24.5-27.8)	340.8 (288.8-398.0)	443/1694	26.2 (24.1-28.3)	360.0 (312.0-419.9)	277/1138	26.1 (23.6-28.8)	306.5 (258.0-359.0)
BMI (Kg/m <sup>2</sup> )									
<24	8718/61310	14.2 (13.9-14.5)	300.0 (249.0-363.0)	6309/26072	24.2 (23.7-24.7)	365.0 (320.0-414.0)	2449/35238	6.8 (6.6-7.1)	260.9 (227.0-300.7)
24-27.9	13899/40393	34.4 (33.9-34.9)	371.8 (312.5-432.8)	12013/29864	40.2 (39.7-40.8)	396.3 (346.9-452.0)	1886/10529	17.9 (17.2-18.7)	292.0 (252.0-338.1)
$\geq 28$	7096/13680	51.9 (51.0-52.7)	411.0 (349.6-475.4)	6189/11062	55.9 (55.0-56.9)	428.0 (374.0-489.0)	997/2618	34.6 (32.8-36.5)	327.7 (282.0-377.0)
Hypertension									
Yes	9616/26366	36.5 (35.9-37.1)	372.0 (310.0-439.0)	7991/18905	42.3 (41.6-43.0)	399.0 (345.0-461.0)	1625/7461	21.8 (20.8-22.7)	266.0 (230.6-307.6)
No	20097/89017	22.6 (22.3-22.9)	328.0 (265.0-396.9)	16520/48093	34.4 (33.9-34.8)	384.0 (335.1-439.0)	3577/40924	8.7 (8.5-9.0)	296.6 (252.0-348.8)
Diabetes									
Yes	1496/5339	28.0 (26.8-29.2)	348.0 (294.0-413.7)	1136/4047	28.1 (26.7-29.5)	361.4 (309.0-424.0)	320/1292	27.9 (25.4-30.4)	307.0 (255.0-363.0)
No	28217/110044	25.6 (25.4-25.9)	338.0 (273.0-407.0)	23375/62951	37.1 (36.8-37.5)	389.6 (340.0-446.6)	4842/47093	10.3 (10.0-10.6)	269.0 (232.8-312.5)
Dyslipidemia									
Yes	16294/37925	43.0 (42.5-43.5)	393.0 (334.0-456.0)	14503/30847	47.0 (46.5-47.6)	410.0 (357.3-469.0)	1721/7078	25.3 (24.3-26.3)	306.0 (263.0-357.0)
No	13419/77458	17.3 (17.1-17.6)	311.2 (256.0-376.0)	10008/36151	27.7 (27.2-28.1)	371.1 (325.0-422)	3411/41307	8.3 (8.0-8.5)	264.3 (229.8-306.0)

All *P* for tests < 0.001; SUA, serum uric acid; BMI, body mass index; CI, confidence interval; IQR, interquartile range.

Table 2. Sex- specific characteristics of participants aged  $\geq 20$  years, 2010-2019

Variables	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	P for trend
<b>Men</b>											
N	23535	24776	26574	27316	29416	32183	42222	51179	59921	66998	
Age (years)	43.80 $\pm$ 13.03	43.35 $\pm$ 12.67	42.83 $\pm$ 12.72	42.87 $\pm$ 12.43	43.39 $\pm$ 12.73	43.19 $\pm$ 12.40	41.71 $\pm$ 12.24	42.11 $\pm$ 12.53	42.34 $\pm$ 12.44	42.34 $\pm$ 12.49	< 0.001
eGFR (mL/min/1.73m <sup>2</sup> )	108.48 $\pm$ 20.81	107.53 $\pm$ 20.01	107.89 $\pm$ 19.23	101.62 $\pm$ 17.99	104.07 $\pm$ 18.92	101.95 $\pm$ 18.05	100.49 $\pm$ 17.36	99.33 $\pm$ 16.86	99.55 $\pm$ 16.84	98.97 $\pm$ 16.75	< 0.001
Obesity, n (%)	3346 (14.2)	3659 (14.8)	4156 (15.6)	4414 (16.2)	4523 (15.4)	4849 (15.1)	5855 (13.9)	7336 (14.2)	9561 (16.0)	11062 (16.5)	< 0.001
Hypertension, n (%)	7683 (32.6)	7982 (32.2)	8845 (33.3)	9138 (33.5)	9609 (32.7)	9699 (30.1)	11194 (26.5)	14355 (27.9)	15965 (26.6)	18905 (28.2)	< 0.001
Diabetes, n(%)	1426 (6.1)	1611 (6.5)	1567 (5.9)	1653 (6.1)	1876 (6.1)	2145 (6.7)	2602 (6.2)	3231 (6.4)	3718 (6.3)	4047 (6.0)	0.958
Dyslipidemia, n(%)	7265 (39.6)	9299 (40.2)	11116 (41.9)	13391 (49.0)	13713 (46.6)	12952 (40.3)	18497 (44.9)	22349 (43.5)	27350 (46.7)	30847 (46.0)	< 0.001
SUA (mmol/L)	358.0 (313.0-407.0)	362.0 (316.0-413.0)	360.0 (315.0-411.0)	367.9 (320.7-419.9)	365.2 (318.8-417.8)	373.9 (325.7-428.5)	380.0 (331.0-435.5)	388.0 (335.0-443.0)	386.0 (336.0-443.0)	388.0 (338.0-445.2)	< 0.001
Hyperuricemia, % (95% CI)	21.8 (21.2-22.3)	24.1 (23.6-24.7)	23.1 (22.6-23.7)	26.6 (26.1-27.1)	25.7 (25.2-26.2)	29.9 (29.4-30.4)	32.8 (32.4-33.3)	34.3 (34.4-35.2)	35.9 (35.5-36.3)	36.6 (36.2-37.0)	< 0.001
<b>Women</b>											
N	15759	19212	17867	19544	21643	26816	32552	40347	44606	48385	
Age (years)	42.94 $\pm$ 13.44	42.43 $\pm$ 13.01	42.10 $\pm$ 12.95	41.64 $\pm$ 12.88	42.37 $\pm$ 13.20	41.42 $\pm$ 12.90	39.95 $\pm$ 12.65	40.09 $\pm$ 12.76	41.15 $\pm$ 12.66	41.52 $\pm$ 12.62	< 0.001
eGFR (mL/min/1.73m <sup>2</sup> )	130.36 $\pm$ 28.22	130.69 $\pm$ 27.51	130.71 $\pm$ 26.16	123.06 $\pm$ 25.14	126.08 $\pm$ 26.08	123.95 $\pm$ 24.54	122.58 $\pm$ 23.67	114.46 $\pm$ 22.86	120.28 $\pm$ 23.03	119.11 $\pm$ 22.67	< 0.001
Obesity, n (%)	938 (6.0)	1041 (5.4)	1035 (5.8)	1156 (5.9)	1252 (5.8)	1439 (5.4)	1652 (5.1)	1939 (4.8)	2279 (5.1)	2618 (5.4)	< 0.001
Hypertension, n (%)	2974 (18.9)	3440 (17.9)	3196 (17.9)	3523 (18.0)	3841 (17.7)	4385 (16.4)	4697 (14.4)	6234 (15.6)	6524 (14.6)	7461 (15.4)	< 0.001
Diabetes, n(%)	501 (3.2)	556 (2.9)	487 (2.7)	500 (2.6)	643 (3.0)	773 (2.9)	830 (2.6)	1030 (2.7)	1157 (2.6)	1292 (2.7)	0.001
Dyslipidemia, n(%)	1719 (14.5)	2290 (13.7)	2573 (14.4)	3260 (16.7)	3361 (15.5)	3692 (13.8)	4523 (14.7)	5637 (14.1)	6319 (14.7)	7078 (14.6)	0.339
SUA (mmol/L)	250.0 (217.0-288.0)	251.0 (216.0-289.0)	250.0 (217.5-289.0)	253.7 (221.2-292.7)	253.7 (220.3-292.2)	257.7 (222.8-297.9)	263.0 (228.0-304.1)	266.2 (232.0-311.0)	268.0 (232.0-311.0)	270.0 (233.0-314.0)	< 0.001
Hyperuricemia, % (95% CI)	5.2 (4.9-5.6)	5.5 (5.2-5.8)	5.3 (5.0-5.6)	5.9 (5.6-6.3)	6.1 (5.8-6.4)	7.1 (6.8-7.4)	8.6 (8.3-8.9)	9.9 (9.5-10.1)	10.1 (9.8-10.4)	10.8 (10.5-11.0)	< 0.001

Data were shown as Mean  $\pm$  SD, Median (IQR) or percentages. eGFR, estimated glomerular filtration rate; SUA, serum uric acid; CI, confidence interval.

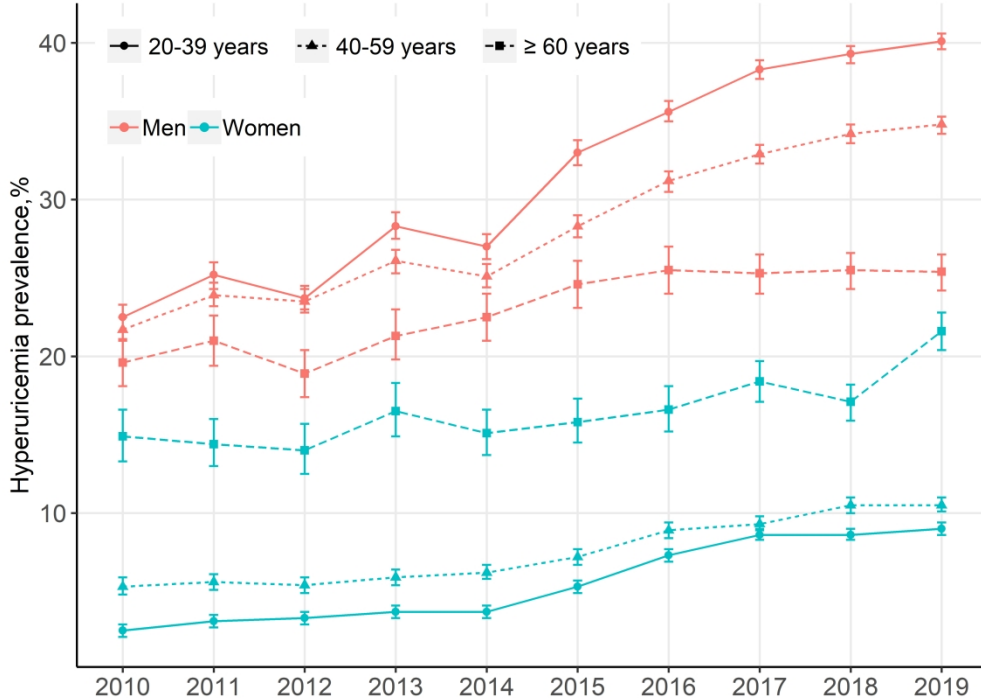


Figure 1. Sex and age-specific trends in hyperuricemia prevalence (95% CI), 2010-2019. CI, confidence interval.

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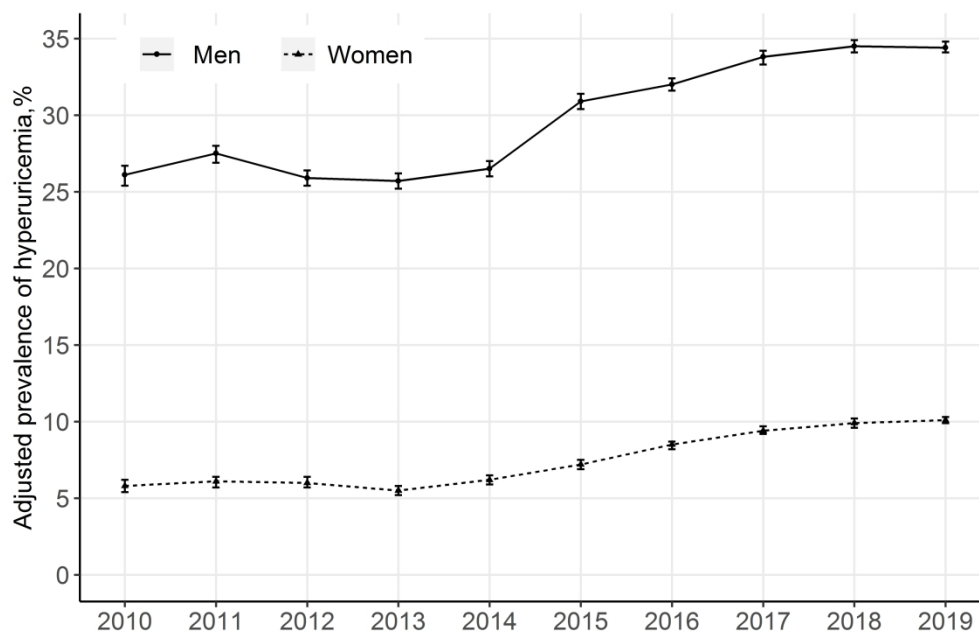
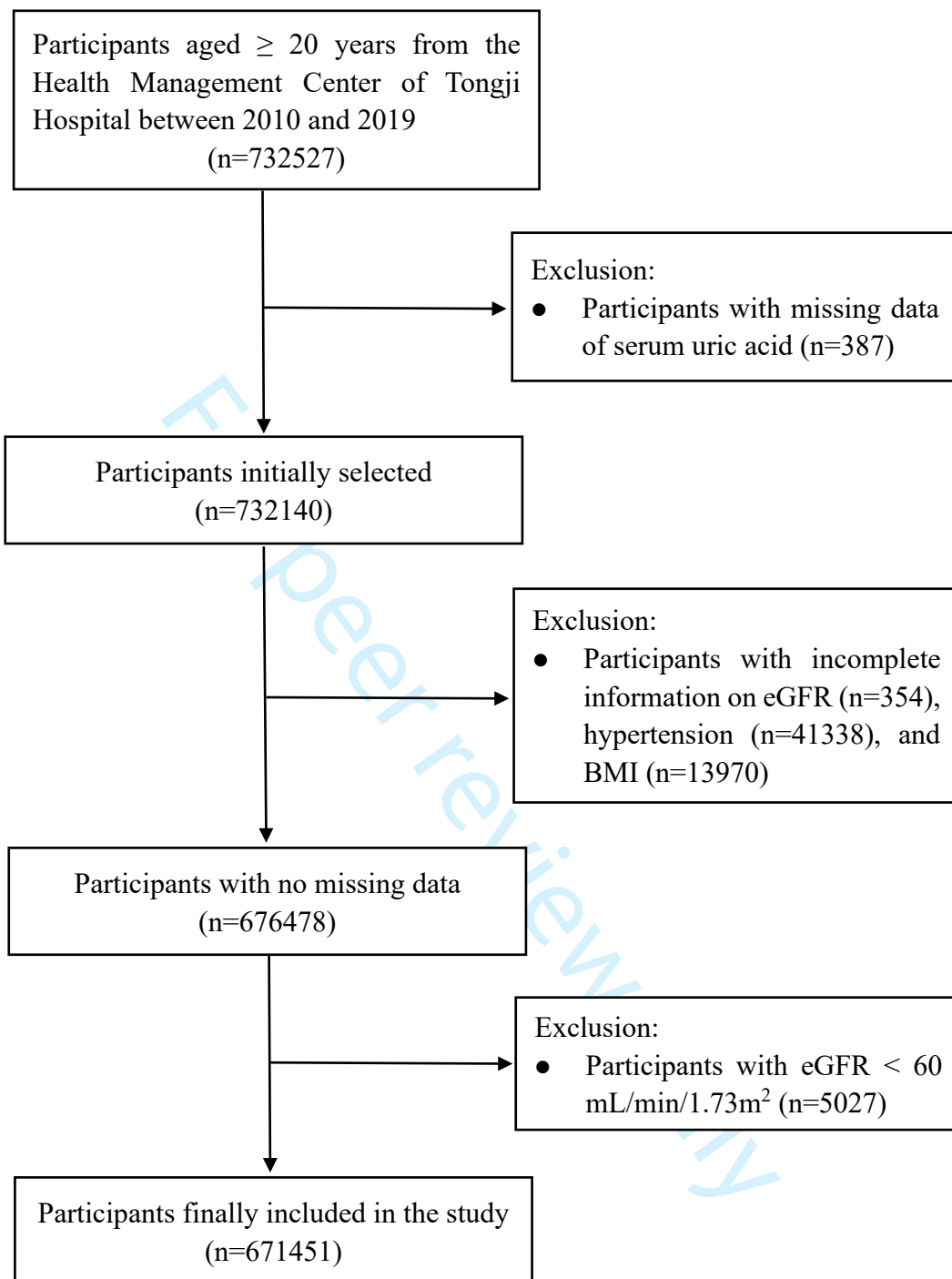


Figure 2. Sex-specific trends in multivariate-adjusted hyperuricemia prevalence (95% CI) among participants aged  $\geq 20$  years, 2010-2019. The prevalence was adjusted for age, BMI, eGFR, hypertension, diabetes, and dyslipidemia. CI, confidence interval; BMI, body mass index; eGFR, estimated glomerular filtration rate.

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Supplemental Figure 1. Flow chart for selection of the study participants.

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

Section/Topic	Item #	Recommendation	Reported on page #
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 or 3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 3-4
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	Page 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 7
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	Page 7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 8
Bias	9	Describe any efforts to address potential sources of bias	Page 7,10
Study size	10	Explain how the study size was arrived at	Page 7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 9-10
		(b) Describe any methods used to examine subgroups and interactions	Page 9-10
		(c) Explain how missing data were addressed	Page 7
		(d) If applicable, describe analytical methods taking account of sampling strategy	Not applicable
		(e) Describe any sensitivity analyses	Not applicable
<b>Results</b>			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page7, Supplemental Figure 1
		(b) Give reasons for non-participation at each stage	Page7, Supplemental Figure 1
		(c) Consider use of a flow diagram	Page7, Supplemental Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 11-12
		(b) Indicate number of participants with missing data for each variable of interest	Page7, Supplemental Figure 1
Outcome data	15*	Report numbers of outcome events or summary measures	Page 11-12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 11-12
		(b) Report category boundaries when continuous variables were categorized	Page 11-12
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 11-12
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 11-12
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	Page 13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 17-18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 13-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 17
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 19

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



1  
2 **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE  
3 checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at  
4 <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).  
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