

# Global prevalence of hyperuricemia in adolescents from 2000 to 2019: A meta-analysis

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## Research article

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# Abstract

**Background:** Studies of the prevalence of hyperuricemia in adolescents have been limited to specific areas and the global prevalence is unknown. This study was to determine the prevalence of hyperuricemia in adolescents worldwide. **Methods:** A comprehensive search was conducted to identify all relevant studies in multiple databases. A meta-analysis was performed to determine the prevalence of hyperuricemia in adolescents worldwide. **Results:** The meta-analysis included 13 articles. The pooled prevalence of hyperuricemia in adolescents was 14.4% (95% CI 9.2–19.5%). Publication bias was observed but the results did not change after a trim and fill test, indicating that the impact of this bias was likely insignificant. **Conclusions:** Hyperuricemia prevalence in adolescents is high and continues to increase. The prevalence varies with geography, gender, and time. Effective measures should be taken to prevent any further increase in the incidence of adolescent hyperuricemia. **Keywords:** prevalence, hyperuricemia, adolescents

## Background

In hyperuricemia, the serum uric acid levels are elevated due to various *in vitro* and *in vivo* factors. Long-term hyperuricemia can cause gout and complications such as hypertension, cardiovascular disease, and chronic kidney disease (1). The onset age of hyperuricemia is continuing to fall and adolescent cases are not rare. Early onset patients have higher cholesterol, triglyceride, low-density lipoprotein cholesterol, aspartate aminotransferase, and alanine aminotransferase levels, and lower high-density lipoprotein cholesterol and estimated glomerular filtration rates than healthy people (2). Early onset juvenile patients are more likely to exhibit dyslipidemia and impaired liver and renal dysfunction. Hence, it is important to study adolescent hyperuricemia.

Most studies on the prevalence of hyperuricemia in adolescents have been limited to a specific region or country. There are regional and temporal differences in the prevalence of hyperuricemia in adolescents. For example, the prevalence of hyperuricemia in male adolescents in Taiwan was 3.5% in 1991–1994, 4.4% in 1995–1998, and 4.5% in 1999–2002 (3). In 9,405 pediatric patients in Japan, the prevalence of hyperuricemia was 3.7% (4). The prevalence of hyperuricemia in 5,531 young people ( $19 \pm 2$  years old) in Mexico was reported as 13.9% (5). In America, the overall prevalence of hyperuricemia in adolescents is approximately 10% (6). To increase our understanding of adolescent hyperuricemia and enhance awareness, a comprehensive epidemiological study of adolescent hyperuricemia is needed. We performed a meta-analysis to determine the global prevalence of hyperuricemia in adolescents.

## Methods

**Search strategy:** The PubMed, Embase, and Cochrane library databases were searched. All articles on the prevalence of hyperuricemia in adolescents published from Jan 1, 2000 to Dec 10, 2019 were searched comprehensively using the keywords “Adolescents”, “Adolescence”, “Teens”, “Teen”, “Teenagers”, “Teenager”, “Youth”, “Youths”, “Adolescents, Female”, “Adolescent, Female”, “Female Adolescent” or

“Female Adolescents”, “Adolescents, Male” or “Adolescent, Male”, “Male Adolescent” or “Male Adolescents”, “Infant” “Infants”, “Child, Preschool”, “Preschool Child”, “Children, Preschool”, “Preschool Children”, “Child”, “Children”, “Hyperuricemia”, “asymptomatic hyperuricemia”, “HUA”, “HU”, “uric acid”, “Prevalence”, “Incidence”, “Epidemiology”, “Prevalences”, and “Incidences”.

*Inclusion and Exclusion Criteria:* Papers were included if they met all of the following criteria: (1) all study participants were adolescents; (2) study data were general (i.e., population- rather than hospital-based); (3) original research; (4) clearly stated study date; and (5) the most detailed study among duplicate studies of the same population (where applicable).

Studies were excluded if they (1) were not original research, such as a review or case report, (2) included participants with concomitant diseases or a history of taking medications known to affect uric acid metabolism, (3) were animal studies or (4) cohort studies, or (5) had a small sample size.

*Definitions of Hyperuricemia and Gout:* The diagnostic criteria used for hyperuricemia for adolescents varied among the studies; we have listed the criteria in Table 1.

*Data extraction:* Two researchers screened the literature independently and the screening results were cross-checked. For studies where suitability for inclusion was difficult to determine, group discussions were held to reach a consensus. According to the pre-designed data extraction table, the data were extracted independently, and the extraction results were cross-checked. The extracted data included the first author, study year, country, publication year, sample size, number of cases, and age of onset. We used the framework proposed by the Cochrane Partnership to assess the quality of the research. Study quality was assessed independently by three reviewers. If two or three reviewers were in agreement, the study was included in the meta-analysis. All data included in the study were tabulated and bias was determined during the quality-assessment phase.

*Data analysis:* The statistical analyses were performed using STATA software (ver. 15.0; StataCorp., College Station, TX, USA). First, a heterogeneity test was performed on the included studies. The heterogeneity statistic,  $I^2$ , was classified as follows: 25%, low heterogeneity; 50%, high heterogeneity; and 75%, high heterogeneity. If the heterogeneity among the included studies was low ( $I^2 \leq 50\%$ ,  $P > 0.05$ ), a fixed effect model was used; when there was high heterogeneity among the included studies ( $I^2 > 50\%$ ,  $P < 0.05$ ), a random effect model was adopted. Subgroup analyses were also performed according to gender, age, and region.

## Results

The search identified 2,983 potentially relevant papers, among which 2,844 remained after removing duplicate articles. The 2,782 articles that clearly did not meet the inclusion criteria were excluded after reading the title and abstract; the remaining 62 articles were further screened by reading the full text. Thirteen articles were eventually included in the meta-analysis. Figure 1 summarizes the literature screening process. The basic characteristics of the included articles are shown in Table 1.

*Pooled prevalence of hyperuricemia:* As shown in Figure 2, the pooled prevalence of adolescent hyperuricemia was 14.4% (95% CI 9.2–19.5%).

*Subgroup analysis:* We performed subgroup analyses of the prevalence of hyperuricemia in adolescents according to gender, age, region, study year, and residence (coastal or inland). The prevalence of hyperuricemia in adolescents in Asia was 15.8% (95% CI 9.7–21.8%), which fell to 11.3% (95% CI 4.7–17.8%) after excluding Taiwan; the prevalence in non-Asian areas was 6.8% (95% CI –4.8–18.5%). In Taiwan, the prevalence of adolescent hyperuricemia was 27.4% (95% CI 22.5–32.2%) and that in mainland China was 15.2% (95% CI 1.1–29.3%). The prevalence rate inland was 11.5% (95% CI 5.6–17.4%), while that in coastal areas was 15.6% (95% CI 9.1–22.1%). The prevalence rate was 22.1% (95% CI 13.1–31.2%) in males and 11.8% (8.2–15.5%) in females. The prevalence rate in adolescents was highest in 2013–2018 (16.7%), followed by 2000–2005 (16.6%), and 2006–2011 (10.6%). After excluding the high-prevalence Taiwanese studies, the pooled prevalence of hyperuricemia in 2000–2005 was 4.6% (95% CI 4.1–5.1%), which was lower than that in 2006–2011 (6.9%; 95% CI 1.7–12%). The prevalence of hyperuricemia in adolescents was high in Asia, and higher in Taiwan than in mainland China. The prevalence of hyperuricemia in adolescents was also higher in males and coastal areas (Table 2).

*Analysis of heterogeneity and publication bias:* Heterogeneity analysis showed very high heterogeneity in the studies of the prevalence of hyperuricemia in adolescents, and there was no decrease in heterogeneity in the subgroup analyses. Egger's test also indicated publication bias.

## Discussion

We analyzed 13 studies of adolescent hyperuricemia conducted between 2000 and 2019, in the first meta-analysis of the prevalence of hyperuricemia in adolescents (to the best of our knowledge). The pooled prevalence of adolescent hyperuricemia was 14.4%, which is higher than that in adults in some regions. The prevalence of hyperuricemia among Chinese adults in 2009–2010 was 8.4% (20). In Saudi Arabia, the prevalence of hyperuricemia was 8.42% (21). The overall prevalence of hyperuricemia in Thai adults was 10.6% (22). The age-standardized prevalence of hyperuricemia in the general Korean population was 11.4% (23). In Italy, the prevalence was 11.9% during the period 2005–2009(24). In our study, the prevalence in adolescents in mainland China was 15.2% during the period 2000–2019, i.e., higher than that in adults; a meta-analysis of studies conducted in mainland China showed that the prevalence of hyperuricemia in adults was 13.3% during the period 2000–2014 (25).

The prevalence of hyperuricemia in adolescents is high and varies with geography, gender, and time. We found that the prevalence of hyperuricemia in adolescents in Asia was higher than that in other regions, with the highest prevalence being in Taiwan. This may be because little research has been conducted in other regions, or simply because the prevalence of hyperuricemia in adolescents in Taiwan is high. In one study, the prevalence of hyperuricemia among aboriginal people in Taiwan was higher than that of non-aboriginal people (26). Our meta-analysis included two studies of Taiwan aborigines; these studies reported hyperuricemia prevalence rates in aboriginal adolescents of 22.9% and 35.3%, respectively,

compared with 15.2% in adolescents in mainland China. In addition to environmental factors, the high prevalence of hyperuricemia among aboriginals in Taiwan may be associated with genetic factors (27). There are many aboriginal tribes in Taiwan, and since many laws prohibit non-aboriginal people from occupying aboriginal villages, there is a high rate of inbreeding within these tribes.

Considering the impact of the prevalence of hyperuricemia among aboriginal people in Taiwan on the overall prevalence, we excluded the data for Taiwan aboriginal adolescents from the subgroup analysis of time, and found that the prevalence of hyperuricemia increased with the year. The prevalence of hyperuricemia during the period 2006–2011 was 1.5 times that in 2000–2005, and that of hyperuricemia during the period 2013–2018 was three times that in 2000–2005. The increasing prevalence of hyperuricemia in adolescents with time is in accordance with the increasing prevalence of diabetes (28, 29). With economic development, people's living standards have improved, and their living and eating habits have changed. The prevalence of hyperuricemia in adolescents in coastal areas is higher than that in inland areas, which may also be related to lifestyle and eating habits. Miao *et al.* (30) showed that consumption of alcohol, meat, and seafood was associated with elevated blood uric acid levels in coastal residents of Shandong, China.

Studies have reported higher hyperuricemia prevalence in adult men than in adult women (31-33). The high incidence of hyperuricemia in men is thought to be associated with the protective effects of estrogen in women (34). Kubota *et al.* (4) showed that the serum uric acid level increased steadily from 1 to 15 years of age, and there was a significant difference in uric acid levels between boys and girls after the age of 13 years. However, because of limited amount of data in these studies, we did not perform subgroup analyses of specific age groups.

One limitation in our study was that the diagnostic criteria for hyperuricemia for adolescents varied among the studies; some studies used their own cut-off values for hyperuricemia in adolescents, which may also explain the high heterogeneity of prevalence. A study of schoolchildren in Brazil defined hyperuricemia as a serum uric acid  $\geq 5.5$  mg/dL (8). A study of school adolescents in northeast China used the 95<sup>th</sup> percentile of serum uric acid in their sample as the cutoff value for hyperuricemia (35). There is no accepted threshold for defining hyperuricemia in children and adolescents. In the future, it will be necessary to determine optimal cutoff values for hyperuricemia in children in China and elsewhere.

In summary, since previous studies have been limited to specific areas, our meta-analysis of adolescent hyperuricemia has important implications for public health policy. We found that the prevalence of hyperuricemia in adolescents is similar to that in adults, and is continuing to increase. The prevalence of hyperuricemia in Taiwanese aboriginals had a major impact on the overall prevalence. Large, well-designed multicenter surveys are needed to obtain information on the outcome and prognosis of hyperuricemia in adolescents. Effective measures should be taken to prevent the incidence of adolescent hyperuricemia from further increasing.

## Declarations

**Ethics approval and consent to participate:** Not applicable

**Consent for publication:** Not applicable

**Availability of data and materials:** Not applicable

**Competing interests:** The authors declare that they have no competing interests

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**Authors' contributions:** HBC designed the research, LHC and SGH analyzed the data and wrote the manuscript. All authors were involved in the acquisition and/or interpretation of the data. H.B.C. was the guarantor of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final manuscript.

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## Table 1

Table1: Characteristics of studies on the prevalence of hyperuricemia.

## Table 2

First Author	Publication Area year	Diagnostic criterion	Inland/coastal	StudyAge year	Sample size	Case size	Prevalence (%)
Suttikomin (7)	2018	Thailand. $\geq 6$ mg/dL in girls $\geq 7$ mg/dL in boys	inland	2013 12-18	689	135	19.6
Reis (8)	2017	Brazil $\geq 5.5$ mg/dL	coast	2014-7-17 2015	2335	299	12.8
Wang (9)	2015	northeast > 420 $\mu$ mol/L for boys $\square$ SUA China > 340 $\mu$ mol/L for girls	inland	2010-11-16 2011	936	142	15.2
Li (10)	2014	northeast SUA $\geq 95$ th percentile China	inland	2010-11~16 2011	16910	45	4.9
Chen (11)	2012	Taiwan $\geq 460$ mmol/L in males $\geq 340$ mmol/L in females	coast	2010 12-19	2090	535	25.6
Soylemezoglu (12)	2012	turkey >6.6 mg/dL for 5-11 years of age, >7.7 mg/dL for boys above 11 years of age and >5.7 mg/dL for girls above 11 years of age	coast	2007-5-18 2008	3174	28	0.9
Hongo (13)	2010	Japan $\geq 7.0$ mg/d	inland	2006-12.1- 2008 15	958	65	6.8
Lee (14)	2007	Taiwan $\geq 7.0$ mg/dl	coast	2001-6-12 2002	2284	524	22.9
Liu (15)	2003	Taiwan $\square 416.5 \mu$ mol/l in boys and $\square 357 \mu$ mol/l in girls.	coast	2001 4-13	414	146	35.3
Ogura (16)	2004	Japan >7.6mg/dl	coast	1999-18-19 2002	5338	240	4.5
Oyama (17)	2006	Japan $\geq 7.0$ mg/dl	coast	2003 9.1-15	1729	86	5.0
Lee (18)	2019	Korea >6.6 mg/dL at 10-11 years of age, >7.7 mg/dL for males at 12-18 years of age and >5.7	coast	2016-10-18 2017	1256	115	9.2

mg/dL for females at 12-18

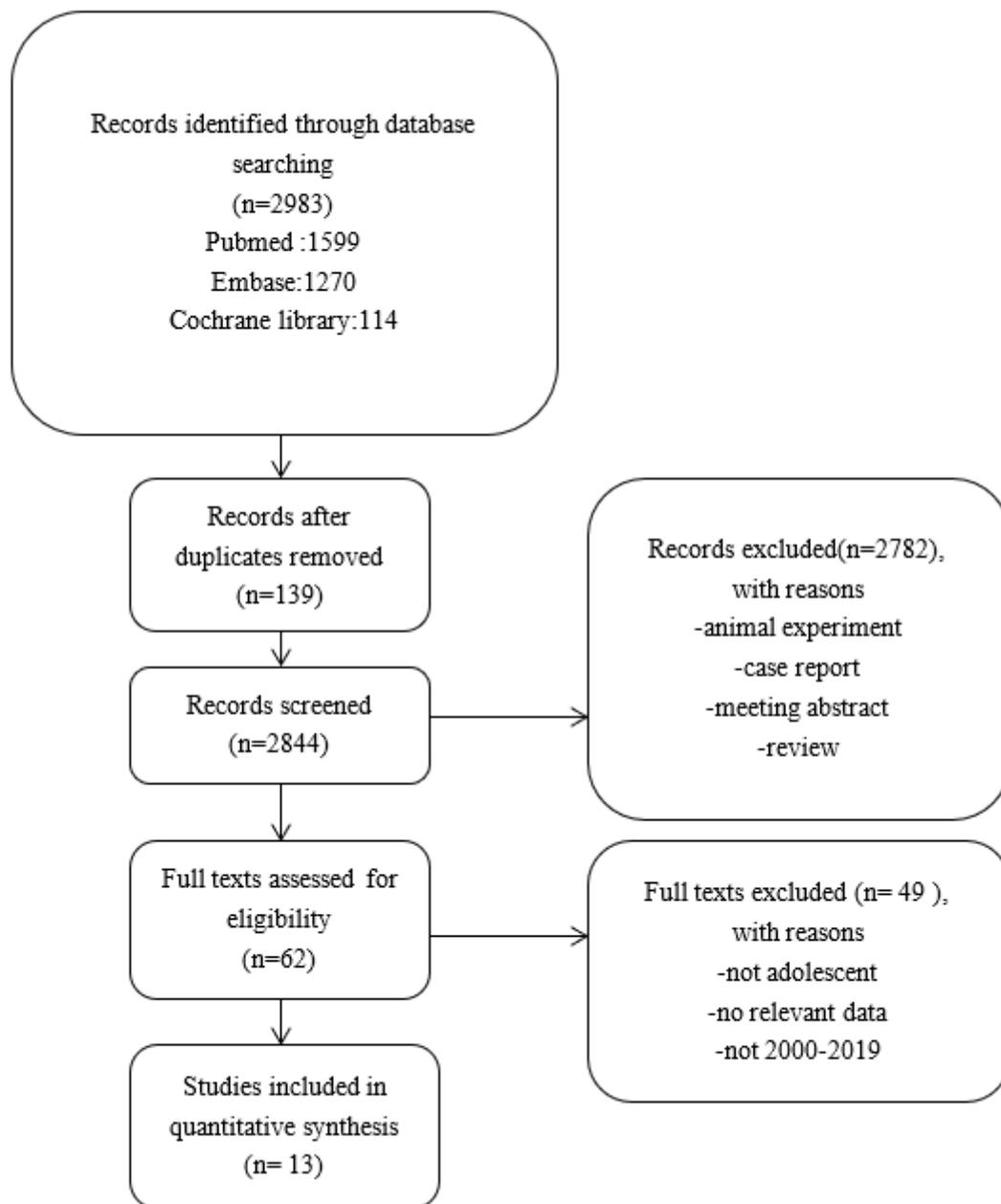
years of age

Lu (19)	2019	China	sUA $\geq$ 7.0 mg/dL	coast	2017-13-19	9371	237925.3
2018							

Table 2: Stratified prevalence of hyperuricemia in adolescents.

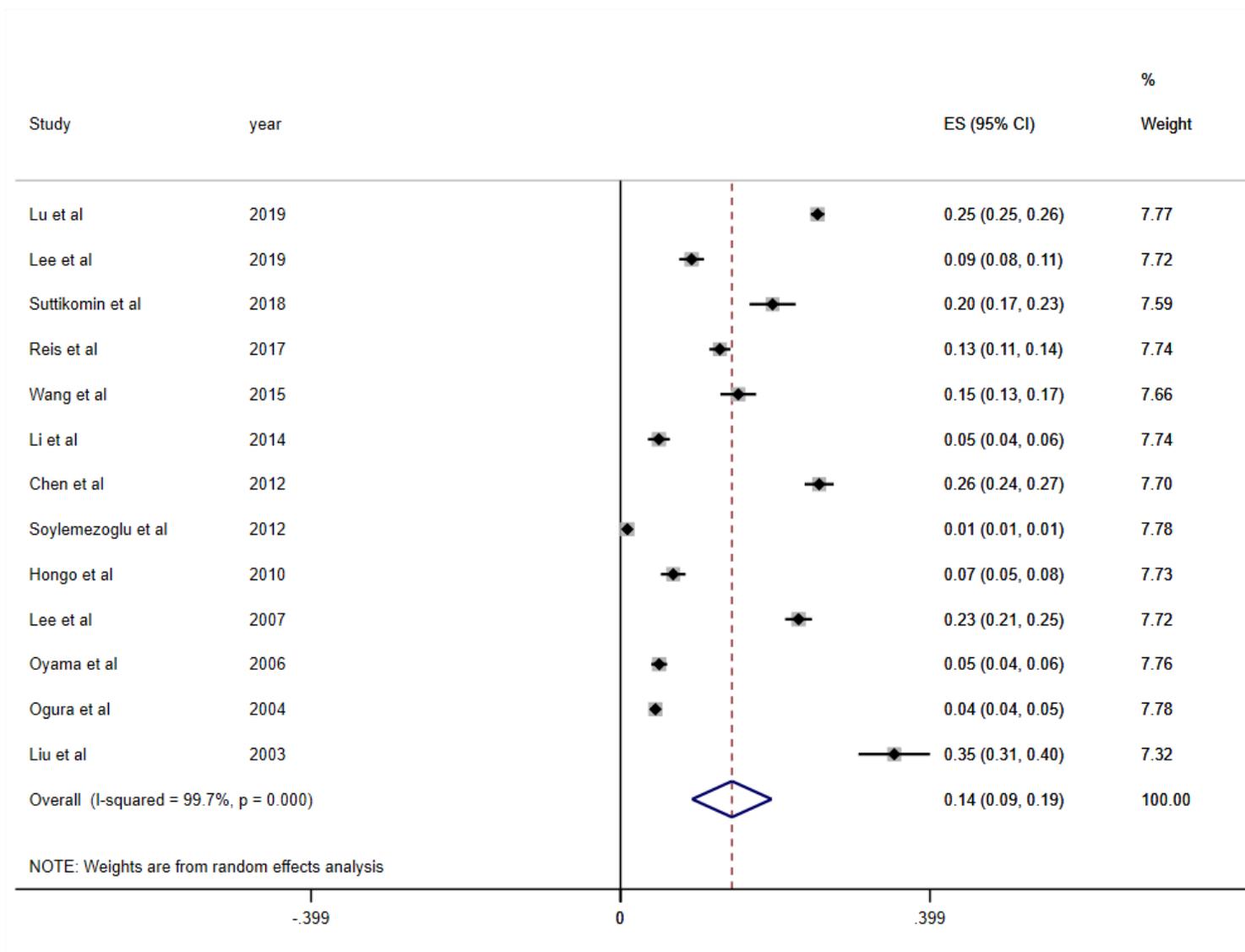
Subgroups	Prevalence(95%CI)	Number of studies	Heterogeneity		Case/Total
			I <sup>2</sup> %	P value	
<b>Location</b>					
Asia	15.8(9.7,21.8)	11	99.6	<0.001	4412/25975
Not Asia	6.8(-4.8,18.5)	2	99.6	<0.001	327/5509
Taiwan	27.4(22.5,32.2)	3	92.0	<0.001	1205/4788
China mainland	15.2(1.1,29.3)	3	99.7	<0.001	2566/11217
<b>Coast/inland</b>					
Inland	11.5(5.6,17.4)	4	97.4	<0.001	387/3493
Coast	15.6(9.1,22.1)	9	99.8	<0.001	4352/27991
<b>Sex</b>					
Male	22.1(13.1,31.2)	10	99.3	<0.001	3298/11330
Female	11.8(8.2,15.5)	10	99.1	<0.001	1117/10926
<b>Study Year</b>					
2000-2005	16.6(8.3,24.9)	4	99.5	<0.001	996/9765
2006-2011	10.6(2.5,18.8)	5	99.5	<0.001	815/8068
2013-2018	16.7(8.1,25.4)	4	99.3	<0.001	2928/13651
<b>Age</b>					
11-19	14.6(6.1,23.0)	7	99.7	<0.001	3541/20292
Total	14.4(9.2,19.5)	13	99.7	<0.001	4739/31484

## Figures



**Figure 1**

Flow diagram for the literature-search process. A total of 2,983 articles were identified. After screening for population base, study type, relevancy, and duplicates, 13 articles met our inclusion criteria.



**Figure 2**

Forest plot of the pooled prevalence of hyperuricemia in adolescents. Summary the prevalence of hyperuricemia in adolescents. The area of the squares reflects the study-specific weight. Weights are from random effects analysis. The diamond and the vertical dotted line represent the pooled prevalence and 95%CI.

## Supplementary Files

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