

# Prevalence of hyperuricemia in adolescents from 2000 to 2019 in Asia: 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 prevalence in Asia is unknown.

**Objectives:** This study was to determine the prevalence of hyperuricemia in adolescents in Asia from 2000 to 2019.

**Data sources:** A comprehensive search was conducted to identify all relevant cross-sectional studies in Pubmed, Embase, and Cochrane library databases.

**Study eligibility criteria:** “hyperuricemia” and “adolescent” were the two critical inclusion criteria.

**Participants, and interventions:** Adolescents;

**Study appraisal and synthesis methods:** Two reviewers independently extracted data and assessed study quality using STROBE check list. Extracted information included the first author, study year, country, publication year, sample size, number of cases, and age of onset. Heterogeneity among studies was evaluated using the Q test and quantified using the  $I^2$  statistic. Subgroup analyses were performed to identify the source of the heterogeneity. The possibility of publication bias was assessed using Egger’s test.

**Results:** The meta-analysis included 11 articles. The pooled prevalence of hyperuricemia in adolescents in Asia was 15.4% (95% CI 9.5-21.2%) and the prevalence of adolescents in Taiwan was higher than that in mainland China. The prevalence in coastal areas was higher than that in inland areas. The prevalence of men was higher than that of women. After excluding the high prevalence study in Taiwan, the prevalence of adolescents has been increasing year by year. 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.

**Limitations:** The diagnostic criteria for hyperuricemia for adolescents varied among the studies; some studies used their own cut-off values for hyperuricemia in adolescents.

**Conclusions and implications of key findings:** 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.

**Systematic review registration number:** Not applicable.

## Background

Hyperuricemia has been kept on increasing in worldwide. Long-term hyperuricemia can cause gout and complications such as hypertension, cardiovascular disease, and chronic kidney disease (1). What ’s

more serious is that its complications are more harmful in adolescents which were defined as people aged 10–19 years by The World Health Organization (2) than those of adults. Both early onset and juvenile hyperuricemic patients have more severe dyslipidemia, impaired liver and renal dysfunction (3, 4). Up to now, there is no unanimously accepted cut off for hyperuricemia in adolescents. Data on the prevalence of hyperuricemia are lacking and hyperuricemia of children under the age of 20 which accounting for one-third of the population(5) has not attracted enough attention.

The health status of the adolescent population is related to the future of the country. Obtaining an accurate prevalence of hyperuricemia is important to help us formulate appropriate local public health policies. Due to varied geographic locations that include diverse populations and different socioeconomic conditions, a unified epidemiological investigation about the prevalence of hyperuricemia in adolescents remains difficult, so we performed a meta-analysis to determine the prevalence of hyperuricemia in adolescents in Asia from 2000 to 2019.

## 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”, “Child”, “Children”, “Hyperuricemia”, “asymptomatic hyperuricemia”, “HUA”, “HU”, “uric acid”, “Prevalence”, “Incidence”, “Epidemiology”, “Prevalences”, and “Incidences”.

The following search strategy was used for Pubmed:

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("Adolescent"[Mesh] OR "Adolescents" OR "Adolescence" OR "Teens" OR "Teen" OR "Teenagers" OR "Teenager" OR "Youth" OR "Youths" OR "Adolescents, Female" OR "Adolescent, Female" OR "Female Adolescent" OR "Female Adolescents" OR "Adolescents, Male" OR "Adolescent, Male" OR "Male Adolescent" OR "Male Adolescents") AND (((("Gout"[Mesh]) OR "Hyperuricemia"[Mesh]) OR "asymptomatic hyperuricemia" OR "HUA" OR "HU" OR "uric acid") AND (((("Prevalence"[Mesh]) OR "Incidence"[Mesh]) OR "Epidemiology"[Mesh] OR "Prevalences" OR "Incidences") AND (("2000/01/01"[Pdat] : "2019/12/10"[Pdat]) AND Humans[Mesh] AND English[lang])
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Searches were restricted to English publications and human studies. In addition, we searched the reference lists of all identified relevant studies. Our meta-analysis was conducted fundamentally according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines (PRISMA).

*Eligibility 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) cross-sectional studies; (5) clearly stated study date; and (6) 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; (6) low Study quality.

Studies were imported into an EndNote X8 database and duplicates were removed. LHC and SGH screened the titles and abstracts of all studies against inclusion and exclusion criteria, respectively. The full text of potentially eligible studies were reviewed in duplicate by LHC and SGH against inclusion and exclusion criteria using a predesigned electronic assessment form. Discrepancies were resolved by discussion between the reviewers, with arbitration by a third reviewer (HBC) in case of disagreement.

*Definitions of Hyperuricemia:* The diagnostic criteria used for hyperuricemia for adolescents varied among the studies; we united the measurement unit of uric acid as mg/dL and listed the criteria in Table 1.

*Data extraction:* Two researchers (LHC, SGH) screened the literature independently and the screening results were cross-checked. 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 STROBE checklist to assess the quality of the research. Using this evaluation tool, we will evaluate six core components, including study design, participants, measurement, bias, descriptive data, and outcome data. Study quality was assessed independently by three reviewers (LHC, SGH, HBC). If two or three reviewers were in agreement, the study was included in the meta-analysis. If the score of the Study quality less than 4, we think it is low quality, and it will be eliminated in the final analysis. All data included in the study were tabulated.

*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 1,980 potentially relevant papers, among which 1,797 remained after removing duplicate articles. The 1,735 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. 11

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 15.4% (95% CI 9.5-21.2%)

*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 15.4% (95% CI 9.5-21.2%), which fell to 10.8% (95% CI 4.7–16.9%) after excluding Taiwan. In Taiwan, the prevalence of adolescent hyperuricemia was 27.4% (95% CI 22.5–32.2%) and that in mainland China was 20.3% (95% CI 10.3-30.3%). The prevalence rate inland was 13.8% (95% CI 6.1-21.5%), while that in coastal areas was 16.0% (95% CI 8.9-23.0%). The prevalence rate was 22.1% (95% CI 10.6-33.5%) in males and 11.2% (95% CI 7.5-15.0%) in females. The prevalence rate in adolescents was highest in 2013–2018 (18.0%), followed by 2000–2005 (16.6%), and 2006–2011 (12.1%). 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 (7.5%; 95% CI 0.0–15.1%). 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. Then we performed a trim and fill method to address the problem of publication bias. However, it became unchanged after we applied the trim and fill method.

## Discussion

We analyzed 11 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 15.4%, which is higher than that in adults in some regions. The prevalence of hyperuricemia among Chinese adults in 2009–2010 was 8.4% (17). In Saudi Arabia, the prevalence of hyperuricemia was 8.42% (18). The overall prevalence of hyperuricemia in Thai adults was 10.6%(19). The age-standardized prevalence of hyperuricemia in the general Korean population was 11.4%(20). In Italy, the prevalence was 11.9% during the period 2005–2009(21). In our study, the prevalence in adolescents in mainland China was 20.3% 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(22).

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 high, 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(23). 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 (24). 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 (25, 26). 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.*(27) 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 (28-30). The high incidence of hyperuricemia in men is thought to be associated with the protective effects of estrogen in women (31). Kubota *et al.*(32) 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(33). 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 (34). 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. FJL, XTC and SC participated in the revision of 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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## Tables

Table 1: Characteristics of studies on the prevalence of hyperuricemia.

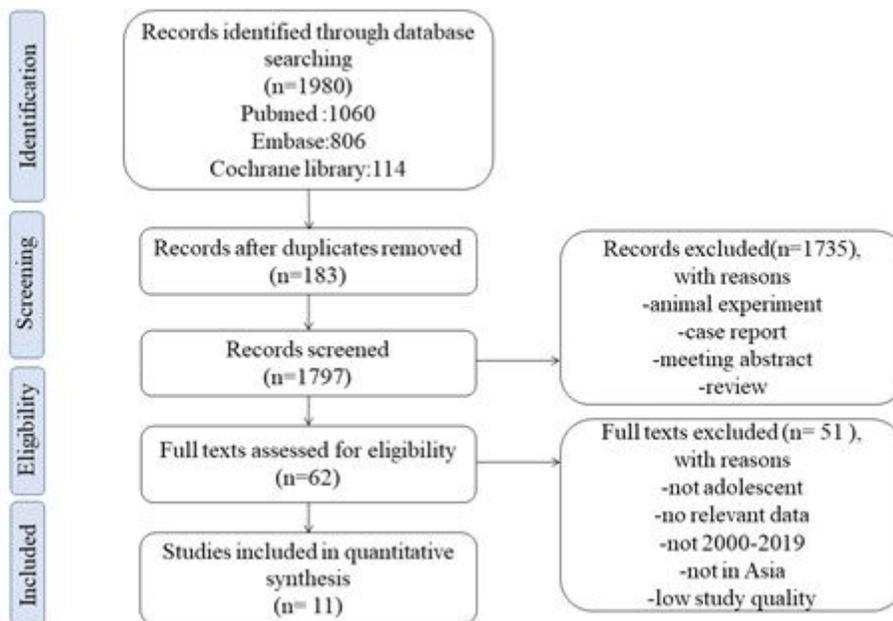
st Author	Publication year	Area	Diagnostic criterion(mg/dL) (boy/girl)	Inland/coastal	Study Age year	Sample size	Case (%)	Prevalence	Study quality
ttikomin(6)	2018	Thailand	$\geq 7/\geq 6$	Inland	2013 12- 18	689	135	19.6	5
ng(7)	2015	Northeast China	$> 7/> 5.7$	Inland	2010- 11- 2011 16	936	142	15.2	6
en(8)	2012	Taiwan	$\geq 7.7/\geq 5.7$	Coastal	2010 12- 19	2090	535	25.6	5
lemezoglu(9)	2012	Turkey	5-11years: $>6.6$ >11years: $>7.7/ >5.7$	Coastal	2007- 5-18 2008	3174	28	0.9	5
ngo (10)	2010	Japan	$\geq 7.0$	Inland	2006- 12.1- 2008 15	958	65	6.8	5
ə (11)	2007	Taiwan	$\geq 7.0$	Coastal	2001- 6-12 2002	2284	524	22.9	6
l (12)	2003	Taiwan	$\geq 7/>6$	Coastal	2001 4-13	414	146	35.3	6
ura (13)	2004	Japan	$>7.6$	Coastal	1999- 18- 2002 19	5338	240	4.5	5
ama (14)	2006	Japan	$\geq 7.0$	Coastal	2003 9.1- 15	1729	86	5.0	5
ə(15)	2019	Korea	10-11years: $>6.6$ 12-18years: $>7.7 />5.7$	Coastal	2016- 10- 2017 18	1256	115	9.2	6
(16)	2019	China	$\geq 7.0$	Coastal	2017- 13- 2018 19	9371	2379	25.3	7

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	15.4(9.5-21.2)	11	99.7	<0.001	4395/28239
Taiwan	27.4(22.5,32.2)	3	92.0	<0.001	1205/4788
China mainland	20.3(10.3,30.3)	2	98.5	<0.001	2521/10307
<b>Coast/inland</b>					
Inland	13.8(6.1,21.5)	3	97.2	<0.001	342/2583
Coast	16.0(8.9,23.0)	8	99.8	<0.001	4053/25656
<b>Sex</b>					
Male	22.1(10.6-33.5)	8	99.4	<0.001	2784/9070
Female	11.2(7.5-15.0)	8	99.1	<0.001	808/8567
<b>Study Year</b>					
2000-2005	16.6(8.3,24.9)	4	99.5	<0.001	996/9765
	4.6(4.1,5.1)*	2	0	0.422	326/7076
2006-2011	12.1(0.9-23.3)	4	99.6	<0.001	770/7158
	7.5(0,15.1)*	3	99.0	<0.001	235/5068
2013-2018	18.0(6.6,29.5)	3	99.3	<0.001	2629/11316
<b>Age</b>					
11-19	16.2(6.4,25.9)	6	99.7	<0.001	3496/19382
Total	15.4(9.5-21.2)	11	99.7	<0.001	4395/28239

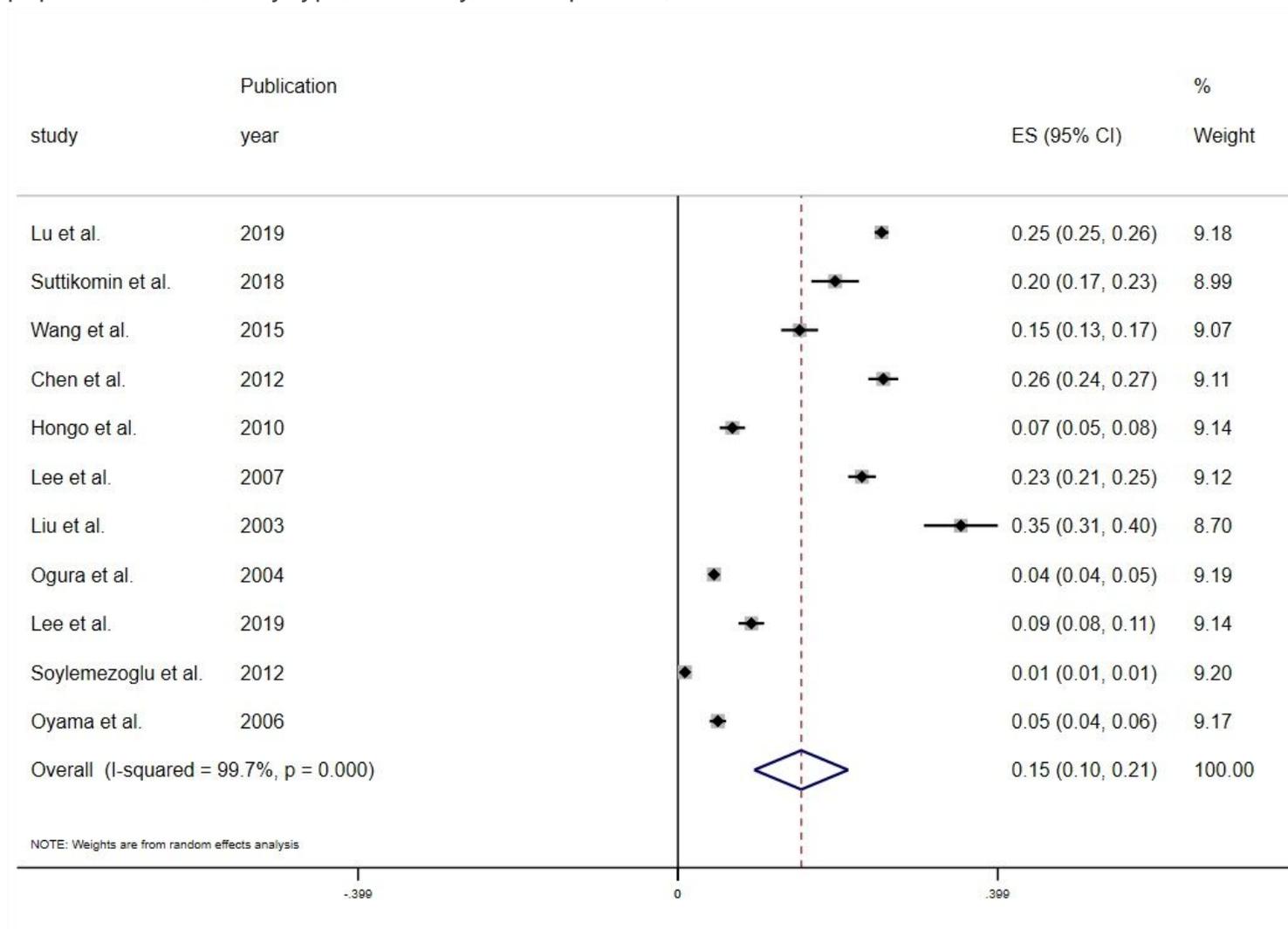
\* after excluding studies in Taiwan

## Figures



**Figure 1**

Flow diagram for the literature-search process. A total of 1,980 articles were identified. After screening for population base, study type, relevancy, and duplicates, 11 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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- [PRISMA2009checklist.pdf](#)