Epidemiology of childhood asthma in mainland China (1988–2014): A meta-analysis

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ABSTRACT

Background: *After the promotion of the two-child policy in recent years, the population of children in mainland China was bound to have a rapid growth, which would bring great challenges to public health. A number of cross-sectional studies on the epidemic of childhood asthma in mainland China were recently conducted, and varied prevalences were reported. Thus, knowing the epidemiology of childhood asthma in mainland China is of great necessity.*

Objective: *Our study aimed to summarize the pooled prevalence of childhood asthma in mainland China and its time trend, gender difference, regional distribution, and age structure.*

Methods: *Studies that reported the prevalence of childhood asthma in mainland China were identified via a systematic data base search through July 1, 2016. Meta-analysis was used to estimate the prevalence of childhood asthma and its subgroups, including gender, age groups, years, and regions. The regional distribution of the prevalence was set by province with the help of a geographic mapping software. The autoregressive integrated moving average model was used to predict the current prevalence of asthma.*

Results: *A total of 117 studies published from 1988 to 2014 in mainland China with a total sample size of 2,678,696 were included. The overall current prevalence and lifetime prevalence of childhood asthma was 2.112% (95% confidence interval [CI], 1.977–2.247%) and 2.502% (95% CI, 2.166–2.838%), respectively. The difference of the prevalences between male and female patients was significant: odds ratio 1.54 (95% CI, 1.47–1.62) for the current prevalence and odds ratio 1.61 (95% CI, 1.47–1.77) for the lifetime prevalence.*

Conclusion: *The prevalence of childhood asthma in mainland China was low but has been increasing remarkably since 1998. Boys are more likely to have asthma throughout most of their childhood. Preschoolers (3–6 years old) showed a higher prevalence than the other age groups. The current prevalence of childhood asthma probably increased slightly from 2017 to 2019.*

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Asthma is a chronic airway inflammation characterized by variable symptoms, such as wheezing, breathlessness, chest tightness, cough, and reversible airflow limitation. The prevalence and burden of asthma have markedly increased recently in children.[1,2] The International Study of Asthma and Allergies in Childhood (ISAAC) phase III reported that 13.7% of the population of children worldwide experienced asthmatic symptoms. As the second most costly respiratory disease,[2] and one of the top 10 causes of disability-adjusted life years lost among the population ages 5–14 years, asthma accounted for 0.9% of the overall global estimate of disability-adjusted life years lost in 2010.[3]

After the formation of the People's Republic of China, the disease spectrum shifted from infectious diseases to chronic diseases in an unprecedentedly fast speed.[4] Consequently, the prevalence, mortality, and burden of asthma showed a remarkable increase. The Global Initiative for Asthma[3] focused on the global burden of asthma, and reported that China possessed the highest asthma case fatality rate (36.7 deaths per 100,000 patients with asthma) in the 5–34-year-old age group. After promoting the two-child policy, the population of children in mainland China grew rapidly, which brought great challenges to public health.

Assessing the situation of the epidemiology of common pediatric diseases, including asthma, is a critical task. Three national surveys on the prevalence of childhood asthma were conducted in 1990, 2000, and 2010[5–7]_ENREF_5 showed the current prevalences as 0.91% (1990), 1.54% (2000), and 2.32% (2010), and the lifetime prevalences as 1.97% (2000) and 3.02% (2010), which presented an increasing trend and indicated higher burdens in all directions. Studies based on different regions in mainland China showed great differences. The current prevalence in Xining, Qinghai, was 0.665%

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in 2013,[8] whereas it was 8.618% in Weihai, Shandong.[9] However, the detailed epidemic patterns of both the time trend and regional variation are unclear.

Yangzong *et al.*[10] summarized_ENREF_10 the epidemiology of childhood asthma in China in 2012 and noted a generally low prevalence. However, the regional variations and time trend in the prevalence were not summarized in the article. Knowing the geographic distribution of the prevalence is important and significant for the health resource allocation because of the great differences among the elevations, climates, pollution levels, economic development, and living habits of regions in mainland China. Similarly, the time trend provides valuable information on the epidemic of the disease, public health planning, and etiologic inference of asthma. The epidemiology status of childhood asthma in mainland China may have changed, and new studies[11–13] have been conducted. A meta-analysis is necessary for a better understanding of the epidemiology of childhood asthma in mainland China.

This study aimed to summarize the pooled prevalence and other epidemic characteristics of childhood asthma in mainland China, reveal the status quo, and contribute to future practices in health decision-making. The overall prevalence and its time trend, predicted prevalence, gender difference, regional distribution, and age structure are studied. The results may contribute to future practices in health decision-making.

METHOD

Search Strategy

PubMed (Bethesda, MD) and Embase (London, UK & Amsterdam, Netherlands), with Chinese National Knowledge Infrastructure (Beijing, China), Chinese Biologic Medical Literature (Beijing, China), Chinese Wanfang (Beijing, China), and Chongqing VIP (Chongqing, China) data bases were searched from inception to July 1, 2016. The key words searched included "asthma," "bronchial disease," "wheezing," "prevalence," "incidence," "epidemiology," "epidemiologic," "occurrence," "China," and "Chinese," with the language restricted to English or Chinese. The reference lists of the studies included were reviewed to identify other potentially eligible studies. Two authors (Z.L., X.G.) independently completed the literature search and study selection. X. Guo, Z.L., and W. Ling are co–first authors.

Selection Criteria

Inclusion Criteria. Inclusion criteria were the following: (1) Cross-sectional studies among children ages 0–14 years old reported with a prevalence of childhood asthma; (2) in mainland China (excluding Hong Kong, Macao, and Taiwan); and (3) diagnosed as using two-stage screening (a questionnaire for primary screening and formal diagnosis by physicians according to the conventional diagnostic criteria in China. See Online Supplemental Material).

Exclusion Criteria. Exclusion criteria were the following: (1) Repetition; when the same data were retrieved from both a national level study and a provincial study or from a provincial level study and a city level study, we gave preference to the provincial level study, which possesses more robust data and better reliability; (2) specific populations, such as hospital in-patients or volunteers; (3) studies that corresponded to one of these clauses, (a) diagnostic criteria unclear or (b) unconventional diagnostic tools; (4) small sample sizes (<1000); and (5) unclear survey date.

Data Extraction

Two researchers (Z.L., X.G.) independently extracted the following data: first author, survey date, territorial level, province, urban or rural, age range, screening tool, diagnostic tool, sampling method, participation rate, sample size (total, boys or girls, urban or rural), case (current or lifetime), and prevalence of childhood asthma (current or lifetime, boys or girls, urban or rural, typical asthma or cough-variant asthma, age group). A third researcher (J. Long) was involved in reaching a consensus when differences in opinions occurred.

Quality Assessment

The quality of the studies included were assessed by using the "The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement" guidelines,[14] a scoring criterion that presents the risk of selection and performance bias. The scale contains five items that describe the sample population (0–2 points), sample size (0–2 points), participation rate (0–2 points), outcome assessment (0–2 points), and analytical methods to control the bias (0–2 points). For each item, low risk is 2 points, moderate risk is 1 point, and high risk is 0 point.

Statistical Analysis

The pooled prevalences were estimated *via* STATA 12.0 (Stata Corp., College Station, TX). A random-effects model was used when the heterogeneity was significant ($I^2 \geq 50\%$ or $p < 0.05$), otherwise a fixed-effects model was used. Funnel plot, Egger's and Begg's tests, sensitivity analysis, and meta-regression were conducted to estimate the publication bias and to explore the sources of heterogeneity. Review Manager 5.0 software (The Cochrane Collaboration; The Nordic Cochrane Centre, Copenhagen, Denmark) was used for comparing the differences of the prevalences by gender

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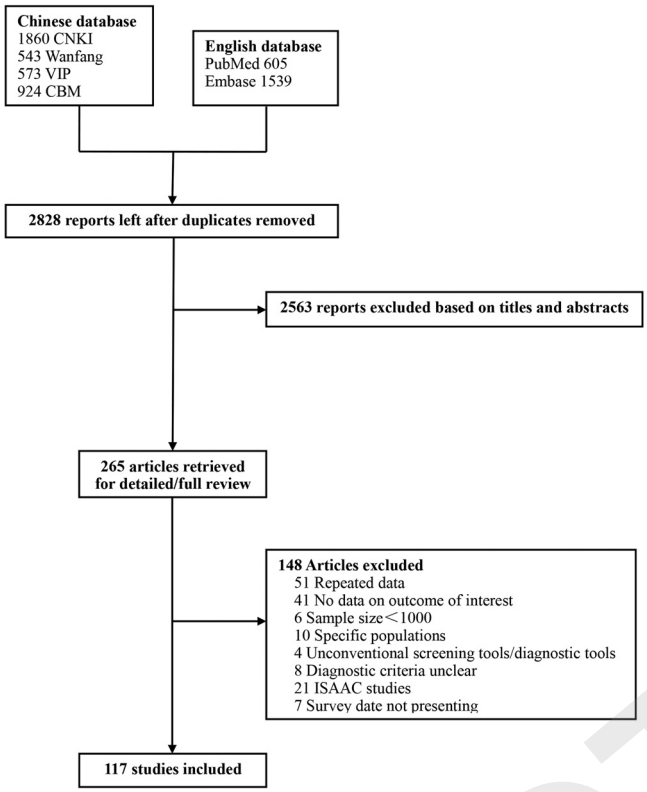

Figure 1. *Search strategies.*

and by area. When I^2 was ≥50%, we used the random-effects model to access the odds ratios (OR) with 95% confidence intervals (CI), otherwise, the fixed-effects model was used. The autoregressive integrated moving average (ARIMA) model was used to fit the pooled prevalence data from 1996 to 2011, and prevalence data from 2012 to 2014 were used to validate the models. Through EViews version 6.0 (Quantitative Micro Software Co., US), the ARIMA model was finally determined to be (4, 1, 3) which was the best model to predict the prevalence data 5 years into the future. When considering the difference in the regional distributions, the pooled prevalence of different regions was set by province in mainland China by using ArcGis 10.2 software (Stanford University, CA).

RESULTS

Study Selection

A detailed flowchart of the search and selection process is shown in Fig. 1. A total of 6044 reports were identified from the initial searches of the data bases, and 3216 reports were excluded as duplicates among the data bases; then, 2563 unrelated reports were excluded based on the titles and abstracts. After carefully viewing the full text of the remaining articles (n = 265), we excluded 148 articles; 117 studies remained.

Description of Included Studies

The 117 studies[5–9,11–13,15–123] (115 in Chinese and 2 in English) involved 22 provinces, 4 municipalities, and 5 autonomous regions, with a sample size of 2,678,696, and ranged from 1988 to 2014. In the quality assessment, 32 studies obtained 8 points, 31 studies obtained lower points, and 54 studies obtained higher points. More details are shown in Table 1.

Prevalence of Childhood Asthma

Overall Prevalence

The current and the lifetime prevalences of childhood asthma were 2.112% (95% CI, 1.977–2.247%) and 2.502% (95% CI, 2.166–2.838%) (Fig. 2; Table 1).

Prevalence by Gender

The current and the lifetime prevalences for boys were 2.589% (95% CI, 2.343–2.835%) and 3.920% (95% CI, 3.072–4.769%). For girls, the current and the lifetime prevalences were 1.651% (95% CI, 1.489–1.813%) and 2.495% (95% CI, 1.947–3.043%). A significant difference was found between the genders (current: OR 1.54 [95% CI, 1.47–1.62]; lifetime: OR 1.61 [95% CI, 1.47–1.77]) (Fig. 3).

Prevalence by Age Group

Based on the age distribution, the target populations were divided into infants (ages 0–2 years), preschoolers (ages 3–6 years), and school-age children (ages 7–14 years); the current prevalences of the three groups were 1.911% (95% CI, 1.578–2.149%), 3.577% (95% CI, 3.084–4.070%), and 1.887% (95% CI, 1.621–2.152%), respectively (Fig. 4); and the lifetime prevalences were 2.049% (95% CI, 1.526–2.572%), 4.285% (95% CI, 3.102–5.467%), and 3.027% (95% CI, 2.253–3.800%), respectively.

Prevalence by Year

Demonstrated in Fig. 5 is the time trend of the current prevalence of childhood asthma by year, from 1988 to 2014. The yearly pooled current prevalence values of childhood asthma in mainland China from 1996 to 2011 was used to fit the model (4, 1, 3), which illustrated no seasonal variation and a slightly increasing trend (Fig. 5). Log transformation and the nonseasonal (d = 1) difference were set to eliminate numerical instabilities. Also, we predicted the 5-year prevalence future of childhood asthma *via* a single ARIMA model (4, 1, 3). The predicted current prevalences in 2015, 2016, 2017, 2018, and 2019 were 3.234, 3.352, 3.296, 3.305, and 3.504% respectively, are shown in Attached Fig. 1.

The pooled current prevalences of childhood asthma in the past: 1990, 1991–2000, 2001–2010, and 2011 were 0.959% (95% CI, 0.790–1.129%), 1.914% (95% CI, 1.635–2.193%), 2.600% (95% CI, 2.241–2.959%), and 4.043%

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Table 1 **The prevalence of childhood asthma and subgroups**

Childhood Asthma	No. Studies	No. Cases	Population, no.	Prevalence (95% CI), %	OR (95% CI)
Current					
Overall	153	43,064	2,678,696	2.112 (1.977–2.247)	
Age					
0–2 y	48	2635	160,176	1.911 (1.678–2.149)	
3–6 y	37	5443	234,567	3.577 (3.084–4.070)	
7–14 y	41	6170	374,645	1.887 (1.621–2.152)	
Gender					1.54 (1.47–1.62)
Boys	65	12,274	651,058	2.589 (2.343–2.835)	
Girls	65	7649	605,167	1.651 (1.489–1.813)	
Region					1.10 (0.74–1.63)
Urban	17	5071	396,047	2.006 (1.652–2.359)	
Rural	17	6582	511,689	1.662 (1.354–1.969)	
Time trend					
–1990	31	12,929	1,316,311	0.959 (0.790–1.129)	
1991–2000	44	10,844	587,091	1.914 (1.635–2.193)	
2001–2010	69	17,513	722,715	2.600 (2.241–2.959)	
2011–	9	1778	52,579	4.043 (2.924–5.161)	
Asthma					
Typical	48	12,744	842,854	1.843 (1.600–2.087)	
Cough variant	39	1440	573,064	0.272 (0.233–0.311)	
Lifetime					
Overall	51	15,041	603,687	2.502 (2.166–2.838)	
Age					
0–2 y	14	524	27,193	2.049 (1.526–2.572)	
3–6 y	13	1961	47,361	4.285 (3.102–5.467)	
7–14 y	13	2562	88,485	3.027 (2.253–3.800)	
Gender					1.61 (1.47–1.77)
Boys	17	4125	104,611	3.920 (3.072–4.769)	
Girls	17	2401	97,464	2.495 (1.947–3.043)	
Time trend					
1991–2000	20	5122	283,139	1.915 (1.541–2.290)	
2001–2010	28	8696	286,301	2.807 (2.234–3.244)	
Asthma					
Typical	27	8828	347,005	2.739 (2.234–3.244)	
Cough variant	25	733	327,263	0.226 (0.176–0.276)	

CI = Confidence interval; OR = odds ratio.

(95% CI, 2.924–5.161%), respectively. The lifetime prevalences in 1991–2000 and 2001–2010 were 1.915% (95% CI, 1.541–2.290%) and 2.807% (95% CI, 2.249–3.364%), respectively (Table 1).

Prevalence by Area

The current prevalence in urban and rural populations were 2.006% (95% CI, 1.652–2.359%) and 1.662% (95% CI, 1.354–1.969%), respectively. Only a few studies provided the individual lifetime prevalence in urban and rural areas, so the pooled lifetime prevalence in urban and rural areas were not provided. The pooled prevalences varied in different provinces, municipalities, and autonomous regions in mainland China. The current prevalence ranged from 0.251% (Tibet) to 4.418% (Zhejiang). The colored maps that show the regional distribution of the pooled prevalence in different decades (Figs. 6 and 7) indicate that the prevalences in the east coastal areas were higher than those in inland China. The prevalences in the southern areas were higher than those in the northern areas. Densely populated regions, such as Shanghai, Shandong, and Jiangsu, had higher prevalences than those of Tibet, Qinghai, and Sinkiang, which had small populations.

Prevalence by Classification

The current and lifetime prevalences for typical asthma were 1.843% (95% CI, 1.600–2.087%) and

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Study ID	ES (95% CI)	% Weight
Anqing group 2002	2.44 (2.14, 2.74)	0.66
Cen et al 2005	4.85 (4.42, 5.28)	0.63
Chen 2015	1.91 (1.67, 2.15)	0.66
Chen et al 1990	1.64 (1.50, 1.79)	0.67
Chen et al 1993	1.65 (1.55, 1.76)	0.68
Chen et al 1995	0.88 (0.79, 0.97)	0.68
Chen et al 2002	0.48 (0.38, 0.57)	0.68
Chen et al 2007	2.87 (2.48, 3.26)	0.64
Cheng et al 2014	3.29 (2.95, 3.64)	0.65
Ding et al 2012	2.74 (2.40, 3.07)	0.65
Feng et al 1994	0.80 (0.77, 0.83)	0.68
Feng et al 2007	1.81 (1.23, 2.40)	0.60
Feng et al 2015	0.24 (0.03, 0.44)	0.67
Gansu Group 1992	0.58 (0.44, 0.71)	0.67
Gao et al 2005	1.88 (1.62, 2.13)	0.66
Gao et al 2011	0.79 (0.42, 1.16)	0.64
Gu et al 2012	2.36 (2.01, 2.71)	0.65
Guo et al 1992	0.73 (0.64, 0.82)	0.68
Hao et al 2002	2.50 (2.26, 2.74)	0.66
He et al 2001	1.65 (1.39, 1.90)	0.66
Hong et al 2000	3.94 (3.73, 4.15)	0.67
Hu et al 2014	2.68 (2.36, 3.00)	0.65
Huo et al 2000	2.96 (2.43, 3.49)	0.61
Jiang et al 1993	0.45 (0.38, 0.51)	0.68
Jin 2011	1.32 (1.10, 1.54)	0.67
Kong 2014	4.39 (3.86, 4.93)	0.61
Kong et al 2006	3.02 (2.70, 3.35)	0.65
Lei et al 2012	12.70 (11.88, 13.53)	0.54
Lei et al2005	0.44 (0.17, 0.72)	0.66
Li et al 2004	1.44 (1.28, 1.60)	0.67
Li et al 2006	1.87 (1.17, 2.57)	0.57
Li et al 2011	2.70 (2.38, 3.01)	0.65
Li et al 2012	1.40 (0.78, 2.03)	0.59
Li et al 2013(rural)	2.54 (2.13, 2.95)	0.64
Li et al 2013(urban)	3.95 (3.66, 4.23)	0.66
Li et al 2015	4.33 (3.94, 4.73)	0.64
Liaoning Group 2002	0.79 (0.67, 0.91)	0.67
Lin et al 1995	3.06 (2.84, 3.28)	0.67
Lin et al 2002	2.77 (2.45, 3.09)	0.65
Lin et al 2005	2.40 (1.74, 3.06)	0.58
Lin et al 2013	3.69 (3.32, 4.06)	0.65
Liu at al 2002	1.49 (1.28, 1.70)	0.67
Liu et al 2005	1.19 (1.01, 1.37)	0.67
Liu et al 2006	4.56 (3.94, 5.18)	0.59
Liu et al 2012	3.39 (3.05, 3.73)	0.65
Liu et al 2013	2.55 (2.29, 2.82)	0.66
Liu et al 2015	4.93 (3.88, 5.98)	0.48
Liu et al 2015(Rural)	2.03 (1.67, 2.39)	0.65
Liu et al 2015(Urban)	4.13 (3.77, 4.49)	0.65
Lu et al 2000	1.64 (1.41, 1.86)	0.67
Lu et al 2012	2.03 (1.76, 2.29)	0.66
Lv et al 2013	4.49 (4.10, 4.88)	0.64
Ma et al 2002	2.05 (1.77, 2.32)	0.66
Ma et al 2013	0.67 (0.46, 0.87)	0.67
Ma et al 2015	1.24 (1.04, 1.44)	0.67
Mo et al 2004	1.10 (0.90, 1.30)	0.67
NCGCA 2003(Chongqin)	3.34 (3.01, 3.67)	0.65
NCGCA 2003(Haikou)	1.44 (1.21, 1.67)	0.66
NCGCA 2003(Harbin)	0.92 (0.73, 1.11)	0.67
NCGCA 2003(Henan)	1.04 (0.90, 1.18)	0.67
NCGCA 2003(Lasa)	0.52 (0.35, 0.69)	0.67
NCGCA 2003(Nanchang)	1.03 (0.83, 1.23)	0.67
NCGCA 2003(Nanning)	1.77 (1.53, 2.01)	0.66
NCGCA 2003(Urumuqi)	0.61 (0.46, 0.76)	0.67
NCGCA 2003(Wuhan)	1.82 (1.55, 2.09)	0.66
NCGCA 2003(Yinchuan)	0.76 (0.59, 0.93)	0.67
NCGCA 2004(Changsha)	1.39 (1.15, 1.63)	0.66
NCGCA 2004(Fuzhou)	1.57 (1.41, 1.72)	0.67
NCGCA 2004(Guangzhou)	1.12 (0.92, 1.33)	0.67
NCGCA 2004(Harbin)	0.92 (0.70, 1.13)	0.67
NCGCA 2004(Henan)	0.65 (0.53, 0.77)	0.67
NCGCA 2004(Inner Mongolia)	0.37 (0.27, 0.48)	0.68
NCGCA 2004(Lasa)	0.09 (0.04, 0.14)	0.68
NCGCA 2004(Taiyuan)	0.51 (0.38, 0.65)	0.67
NCGCA 2004(Wuhan)	0.86 (0.72, 1.00)	0.67
NCGCA 2004(Xian)	0.66 (0.55, 0.77)	0.67
NCGCA 2013(Chongqin)	4.11 (3.75, 4.47)	0.65
NCGCA 2013(Guangzhou)	1.48 (1.26, 1.70)	0.67
NCGCA 2013(Haikou)	3.19 (2.85, 3.53)	0.65

Figure 2. *A forest plot for the current prevalence of childhood asthma.*

2.739% (95% CI, 2.234–3.244%), and the current and lifetime prevalences for cough-variant asthma (CVA) were 0.272% (95% CI, 0.233–0.311%) and 0.226% (95% CI, 0.176–0.276%).

Meta-Regression

Notable heterogeneity was found in this meta-analysis (all $I^2 > 50\%$; $p < 0.001$) (Table 2). Years of investigation, sample size, province (Anhui, Shandong,

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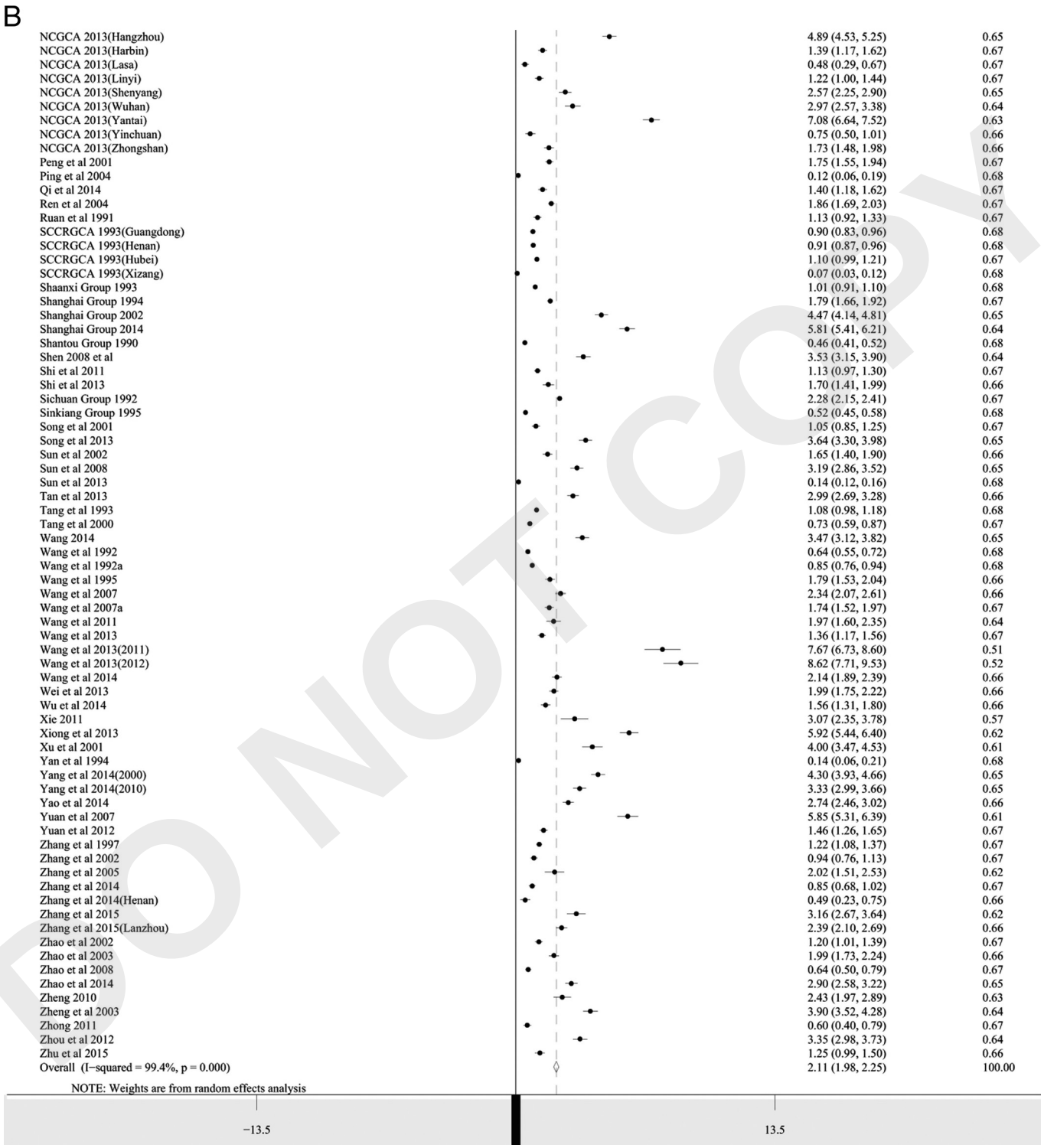

Figure 2. *Continued.*

Shanghai, Zhejiang), territorial level (county), age group of target population, and gender were the factors considered to be sources of heterogeneity for the current prevalence of childhood asthma. As to lifetime prevalence, potential sources of heterogeneity were years of investigation, province (Shanghai), territorial level (city), and gender.

Sensitivity Analysis

Sensitivity analysis was applied to examine the stability of our results. The overall current prevalence of childhood asthma was influenced after removing the National Cooperative Group on Childhood Asthma (NCGCA) [6] (Lasa), Ping *et al.*,[94] Yan *et al.*,[111] Sun,[41] or

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Study or Subgroup	male Events	male Total	female Events	female Total	Weight	Odds Ratio M-H, Random, 95% CI
Anqing group 2002	168	5196	83	5083	1.6%	2.01 [1.54, 2.63]
Chen 2015	166	7121	69	5110	1.5%	1.74 [1.31, 2.31]
Chen et al 1990	300	15265	187	14392	2.1%	1.52 [1.27, 1.83]
Chen et al 1995	212	22566	175	21411	2.0%	1.15 [0.94, 1.41]
Chen et al 2002	44	10437	44	8060	1.0%	0.77 [0.51, 1.17]
Chen et al 2007	112	3767	92	3341	1.6%	1.08 [0.82, 1.43]
Ding et al 2012	159	4815	92	4358	1.7%	1.58 [1.22, 2.05]
Feng et al 1994	1485	164049	1049	152258	2.8%	1.32 [1.22, 1.43]
Feng et al 2007	26	1103	10	883	0.4%	2.11 [1.01, 4.39]
Feng et al 2015	3	1061	2	1052	0.1%	1.49 [0.25, 8.93]
Gansu Group 1992	36	6117	32	5852	0.8%	1.08 [0.67, 1.74]
Gao et al 2011	11	1126	6	1028	0.2%	1.68 [0.62, 4.56]
Guo et al 1992	152	17986	95	16007	1.7%	1.43 [1.10, 1.85]
Hong et al 2000	764	16691	547	16283	2.6%	1.38 [1.23, 1.54]
Huo et al 2000	77	2043	41	1943	1.1%	1.82 [1.24, 2.67]
Jin 2011	94	5298	44	5161	1.2%	2.10 [1.47, 3.01]
Kong 2014	158	2920	88	2680	1.6%	1.68 [1.29, 2.20]
Kong et al 2006	204	5546	120	5175	1.9%	1.61 [1.28, 2.02]
Lei et al2005	5	1265	5	985	0.2%	0.78 [0.22, 2.69]
Li et al 2004	196	10936	107	10166	1.8%	1.72 [1.35, 2.17]
Li et al 2013	88	2844	54	2746	1.2%	1.59 [1.13, 2.24]
Li et al 2013(urban)	433	8935	268	8824	2.3%	1.63 [1.39, 1.90]
Lin et al 1995	372	12097	324	10654	2.4%	1.01 [0.87, 1.18]
Lin et al 2005	34	1059	15	983	0.5%	2.14 [1.16, 3.95]
Lin et al 2013	236	5126	136	4956	1.9%	1.71 [1.38, 2.12]
Liu at al 2002	115	6387	72	6144	1.5%	1.55 [1.15, 2.08]
Liu et al 2015	52	854	28	769	0.8%	1.72 [1.07, 2.75]
Lu et al 2000	132	6404	73	6179	1.5%	1.76 [1.32, 2.35]
Lv et al 2013	308	5723	172	4969	2.1%	1.59 [1.31, 1.92]
Ma et al 2002	147	5252	61	4911	1.4%	2.29 [1.69, 3.09]
Ma et al 2015	104	6047	44	5892	1.2%	2.33 [1.63, 3.31]
Peng et al 2001	188	9273	109	7724	1.8%	1.45 [1.14, 1.83]
Qi et al 2014	104	5489	46	5228	1.2%	2.18 [1.53, 3.08]
Ren et al 2004	265	11642	180	11642	2.1%	1.48 [1.23, 1.80]
Shaanxi Group 1993	263	22238	164	20167	2.1%	1.46 [1.20, 1.78]
Shanghai Group 1994	468	19837	218	18451	2.3%	2.02 [1.72, 2.38]
Shanghai Group 2002	439	7356	215	7106	2.3%	2.03 [1.72, 2.40]
Shantou Group 1990	153	26940	90	25350	1.7%	1.60 [1.23, 2.08]
Shi et al 2011	109	8199	77	8202	1.5%	1.42 [1.06, 1.91]
Sinkiang Group 1995	150	22870	80	21543	1.6%	1.77 [1.35, 2.32]
Sun et al 2002	97	5004	69	5042	1.4%	1.42 [1.04, 1.94]
Sun et al 2008	210	5782	138	5138	1.9%	1.37 [1.10, 1.70]
Sun et al 2013	86	5055	55	4809	1.3%	1.50 [1.06, 2.10]
Tan et al 2013	238	6631	142	6088	2.0%	1.56 [1.26, 1.92]
Tang et al 2000	60	4708	55	6739	1.1%	1.57 [1.09, 2.27]
Wang 2014	229	5379	134	5077	1.9%	1.64 [1.32, 2.04]
Wang et al 1992	217	21131	124	18869	1.9%	1.57 [1.26, 1.96]
Wang et al 1992a	117	15917	80	15065	1.5%	1.39 [1.04, 1.84]
Wang et al 1995	115	5545	75	5090	1.5%	1.42 [1.06, 1.90]
Wang et al 2007	179	6719	102	5311	1.7%	1.40 [1.09, 1.79]
Wang et al 2007a	136	6471	84	6142	1.6%	1.55 [1.18, 2.04]
Wang et al 2013	106	6984	79	6599	1.5%	1.27 [0.95, 1.71]
Xie 2011	43	1122	25	1108	0.8%	1.73 [1.05, 2.85]
Xiong et al 2013	326	5152	226	4273	2.2%	1.21 [1.02, 1.44]
Xu et al 2001	129	2640	80	2589	1.5%	1.61 [1.21, 2.14]
Yao et al 2014	231	6678	133	6101	1.9%	1.61 [1.30, 2.00]
Yuan et al 2007	273	3675	149	3451	2.0%	1.78 [1.45, 2.18]
Yuan et al 2012	116	7162	90	6974	1.6%	1.26 [0.95, 1.66]
Zhang et al 2002	72	5751	31	5164	1.0%	2.10 [1.38, 3.20]
Zhang et al 2005	32	1793	27	1130	0.7%	0.74 [0.44, 1.25]
Zhang et al 2015	103	2623	54	2353	1.3%	1.74 [1.25, 2.43]
Zhao et al 2003	129	5828	96	5499	1.6%	1.27 [0.98, 1.66]
Zheng et al 2003	247	5189	147	4916	2.0%	1.62 [1.32, 2.00]
Zhou et al 2012	194	4507	108	4495	1.8%	1.83 [1.44, 2.32]
Zhu et al 2015	58	3732	32	3477	0.9%	1.70 [1.10, 2.62]
Total (95% CI)		**651058**		**605167**	**100.0%**	**1.54 [1.47, 1.62]**
Total events	12275		7649			

Heterogeneity: Tau² = 0.02; Chi² = 158.13, df = 64 (P < 0.00001); I² = 60%
Test for overall effect: Z = 17.00 (P < 0.00001)

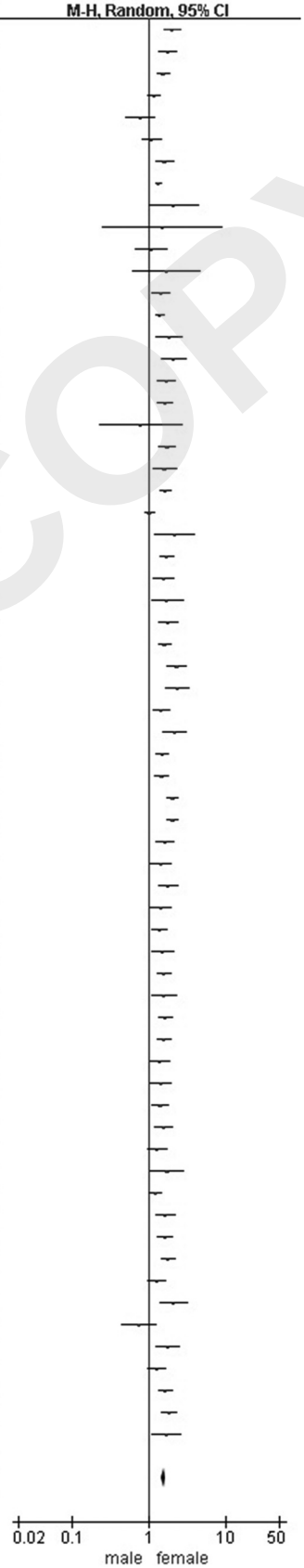

Figure 3. A forest plot for the current prevalence of childhood asthma by gender.

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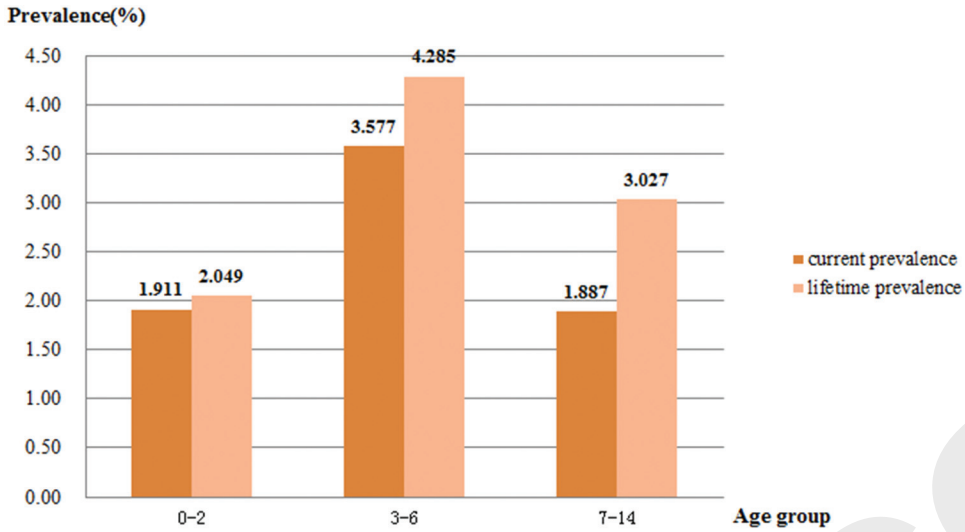

Figure 4. The prevalence of childhood asthma by age group.

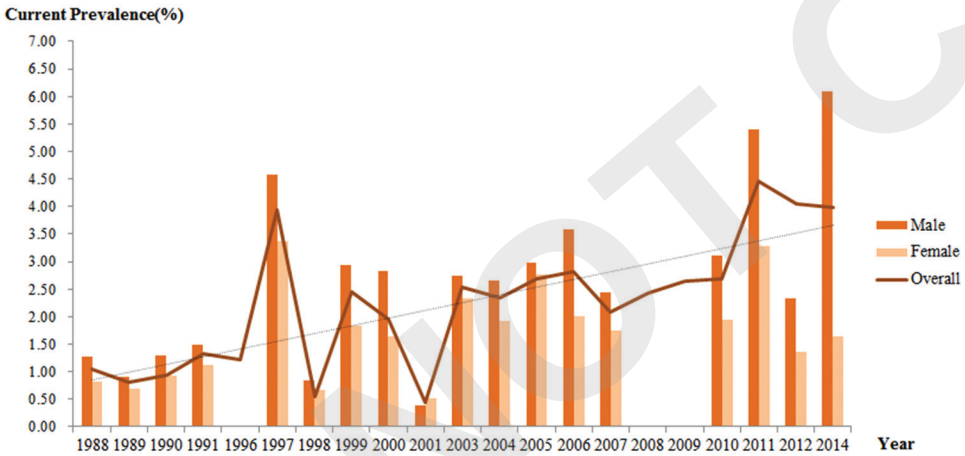

Figure 5. The current prevalence of childhood asthma by year.

Dong and Zhao[61] (Tibet). The lifetime prevalences were affected by NCGCA[6] (Lasa), NCGCA 2004[6] (Urumuqi), Ping *et al.*,[94] NCGCA[7] (Lasa), NCGCA[7] (Linyi), and Chen *et al.*[60]

Publication Bias

A funnel plot indicated a publication bias (Online Supplemental fig. 2). Results of the Begg's test indicated a publication bias (current: $z = 8.56$, $p < 0.001$; and lifetime: $z = 7.72$, $p < 0.001$). Results of the Egger's test also indicated a significant value, current and lifetime: $t = 16.64$, $p < 0.001$; and $t = 11.40$, $p < 0.001$, respectively.

DISCUSSION

In 2012, Yangzong *et al.*[10] reviewed studies on the epidemiology of childhood asthma in China, and 12 studies[10] followed the ISAAC protocol,[1] whereas 62 studies[10] followed the two-stage Chinese diagnostic process. They reported generally low prevalences in both groups. The ISAAC survey[124] was widely conducted worldwide and provided important information on the epidemiology of childhood asthma, but few ISAAC studies[125–128] were held in mainland China after 2012. Studies[12,63,77] in subregions of mainland China, especially a nationwide survey[7] conducted in 2010, were conducted based on the Chinese diagnostic process. Questions on changes in the prevalence of childhood asthma in mainland China after 4 years were asked. Is there any variation among the populations, times, and regions? A meta-analysis that involved 117 studies that followed the two-stage Chinese diagnostic process with a total sample size of 2,678,696 in 1988–2014 was conducted for this reason.

Our results of childhood asthma in mainland China were consistent with the studies by Yangzong *et al.*[10] (<3%) and Song *et al.*[126] The results showed that the prevalences for current (2.112%) and lifetime (2.502%) were below the global average level.[124] These results were definitely lower than that of some countries, such as the United States (current prevalence, 8.69%; lifetime prevalence, 12.06%),[129] Australia (current prevalence, 11.3%; lifetime prevalence, 31%),[130] Great Britain (current prevalence, 15.4%; lifetime prevalence, 27.3%),[131] and Korea (current prevalence, 7.4%).[132] We

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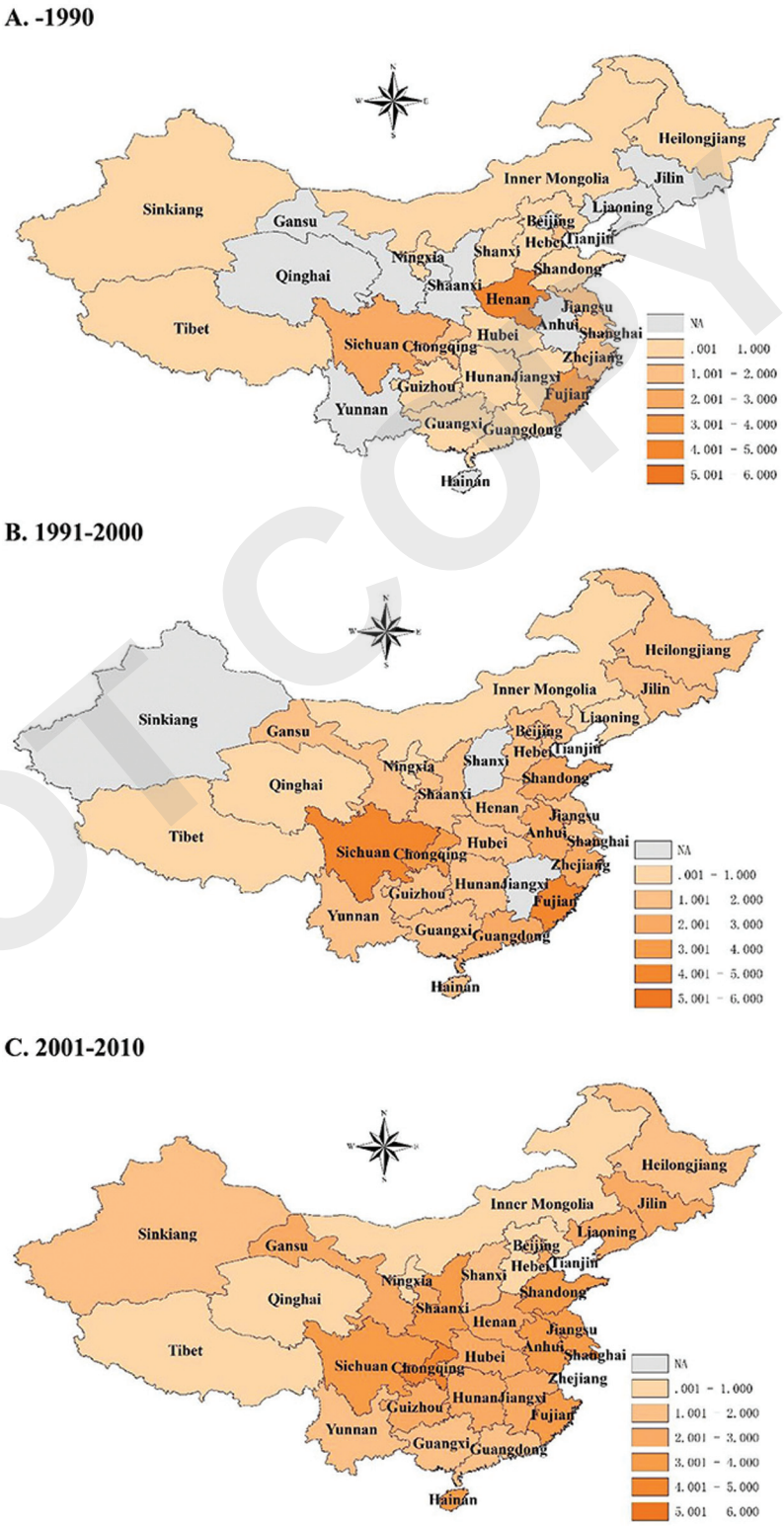

Figure 6. Regional distribution of current prevalence of childhood asthma in mainland China.

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also estimated the prevalence of two types of asthma as follows: typical asthma (current, 1.843%; lifetime: 2.739%) and CVA (current, 0.272%; lifetime: 0.226%). Particularly, an erroneous diagnosis and a missed diagnosis happen frequently in cough-variant asthma. The NCGCA[7] reported that only 58.6% of children who are ill were correctly diagnosed. Clinicians should attract enough attention to CVA, a particular form of asthma with chronic cough, which was often misdiagnosed as bronchitis.

The boys (current, 2.589%; lifetime, 3.920%) were at a significantly higher risk of childhood asthma than

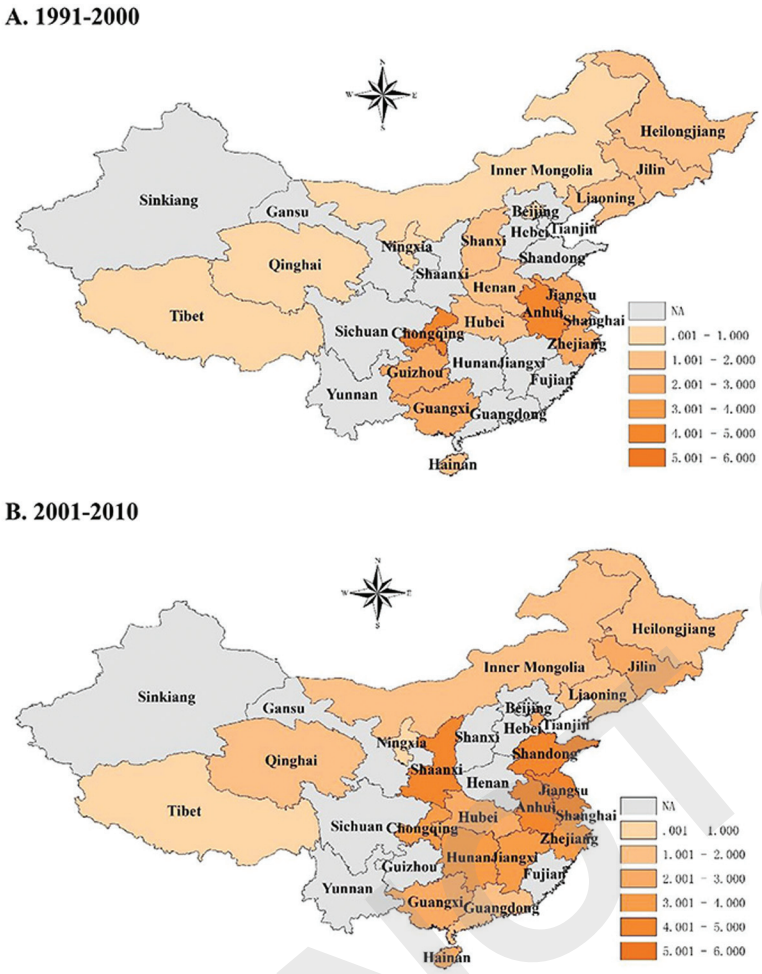

Figure 7. *Regional distribution of lifetime prevalence of childhood asthma in mainland China.*

were the girls (current, 1.651%; lifetime, 2.495%) and constituted the majority of patients throughout most of their childhood, consistent with the previous studies.[46,104,123] However, the current prevalence in girls surpasses that among boys during puberty. The condition persists among adults. Almqvist *et al.*[133] found that hormonal changes and gender-specific differences in environmental exposures may influence the susceptibility to asthma. Similarly, Postma[134] found that both hormonal changes and genetic susceptibility contribute to the difference in prevalences between the genders in puberty.

Preschoolers (3–6 years old) possessed the highest prevalence (current, 3.577%; lifetime, 4.285%). A similar condition was reported in two nationwide surveys in mainland China.[6,7] Most of the preschoolers went to kindergarten, where many-to-one care for infants turned to one-to-many management. Staying in kindergarten may increase the risk of an upper respiratory infection, which was thought to be the main factor of childhood asthma[131,135] for children who have a weak immune system and low self-management abilities. Children acquire strengthened self-management abilities and stronger immunity as they grew older and showed lower prevalence. Thus, the management of preschools and kindergarten should merit sufficient attention.

Although the prevalence of childhood asthma in mainland China was still low up to now, a rising trend from 1988 to the present was shown in the time-line chart presented (Fig. 5). Within the global scope, Asher *et al.*[124] found that most countries showed an increased prevalence from ISAAC phases I to III,[124] whereas some countries showed decreased prevalences. They also found that the decreases in the prevalences were more common in countries with existing high prevalence, such as Australia, South Korea, and Singapore. The principle of divergent trends requires further research. With concern to the increasing prevalence in mainland China, the epidemiologic transition along with the rapid development of China may have played a potential role. The intensifying environmental degradation (especially air pollution[136]), developing living quality (higher consultations), and behavioral changes (Western life style,[10] decreased physical activity, high rates of smoking,[126] mental stress,[137] and other high-

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Table 2 **Meta-regression for prevalence of childhood asthma**

	Current Prevalence				Lifetime Prevalence			
	Covariates*	t	Coef. (95% CI)*	*p* Value	Covariates*	t	Coef. (95% CI)*	*p* Value
Years of investigation	—	5.75	0.931499 (0.0611166–0.1251832)	<0.0001	—	2.31	0.0959737 (0.012492–0.1794555)	0.025
Sample size	—	−2.33	−0.0000108 (−0.0000199 to 0.000002)	0.021	—			
Province	Sinkiang (Ref.)	—	—	—	Tianjin (Ref.)			
	Anhui	1.99	2.410014 (0.0090653–4.810963)	0.049	Shanghai	3.04	4.787903 (1.540373–8.035433)	0.006
	Shandong	2.31	2.686841 (0.3792168–4.994466)	0.023				
	Shanghai	2.28	2.932582 (0.390558–5.474606)	0.024				
	Zhejiang	2.85	3.509946 (1.072532–5.947361)	0.005				
Territorial level	Province (Ref.)	—	—	—	County (Ref.)			
	County	2.41	1.033171 (0.1851448–1.881198)	0.017	City	−2.58	−1.336017 (−2.377404 to −0.2946298)	0.013
Age group	—	−2.44	−1.061441 (−1.9224 to −0.2004813)	0.016				
Gender	—	−3.79	−0.9193107 (−1.399736 to −0.4388855)	0.000	—	−2.48	−1.412895 (−2.571222 to −0.2545678)	0.018

Coef. = Regression coefficient; Ref. = reference category.
**The estimated prevalence was calculated separately.*

risk behaviors) accelerate the prevalence of childhood asthma.

The predicted prevalence in 2015 showed a slight decrease and remained stable in the next 4 years. Many policy, social, and medical factors (*e.g.,* the promoting of the two-child policy in the recent years), all of which will affect the trend of the prevalence of childhood asthma. Ongoing monitoring is required to follow the epidemic of asthma. More attention should be given to promote reasonable disposition of health resources.

The current prevalences in urban and rural areas were 2.006 and 1.662%, respectively, without significant difference. However, some studies indicated that the prevalence in urban areas was higher.[16,138,139] Ege *et al.*[140] indicate that rural children exposed to a wider range of microbes than urban children so that they were less likely to develop asthma. However, most existing research[19,32,38] focused on metropolises, and only a small number of studies[16,19,43,111] focused on rural populations. Therefore, the comparison results may be insufficient to show the real state. Hence, the difference in the prevalences between urban and rural areas should still be taken into consideration.

A subgroup analysis by province was conducted, and the current prevalence ranged from 0.251% (Tibet) to 4.418% (Zhejiang). Highly developed regions demonstrated a higher prevalence than less-developed regions. The variation of the developments in different parts of China led to different epidemiologic circumstances. Air pollution, passive smoking, and a family history of respiratory disease are associated with children's asthma.[141,142] Moreover, methods of cooking and heating may contribute to different prevalences of children's asthma in different regions of China. The availability of unified heating in cold days could be an important factor. The resulting difference between the behaviors and environment may have played an important role on the difference in prevalence.

High heterogeneity in a meta-analysis based on epidemiologic surveys is common.[143,144] We conducted subgroup analyses and explored heterogeneity through meta-regression. Years of investigation, sample size, province (Zhejiang, Anhui, Shandong, and Shanghai), territorial level, age ranges of the study, and gender were considered to be the sources of heterogeneity. In response to this issue, we used the random-effect model and conducted subgroup analyses to examine the influence of these factors.

Several potential limitations cannot be ignored. First, the restriction of diagnosis tools and language contributed to the unavoidable publication bias that limited the accuracy of our results, although we attempted to discover all eligible studies in the literature. Second, despite the exclusion of studies with an unclear survey date or a small sample size (<1000) or the rigorous selection criteria for higher study qualities, some stud-

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ies still scored low (<8). After carefully viewing the studies that affected the results, we discovered that these studies reported distinctly lower prevalences than others, which resulted in a lower estimated prevalence.

CONCLUSION

The prevalence of childhood asthma in mainland China was low but increased remarkably since 1998. Boys are more likely to have asthma throughout most of their childhood. Preschoolers (3–6 years old) showed a higher prevalence than the other age groups. The predicted current prevalences of childhood asthma fluctuated from 2015 to 2019, and increased slightly since 2017.

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