META-ANALYSIS

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Prevalence of short stature among children in China: A systematic review

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ABSTRACT

Importance: The prevalence and characteristics of short stature (SS) among children in China should be assessed to provide guidance for planning and implementation of nationwide public health policies. Thus far, there have been no accurate estimates of the prevalence of SS in China.

Objective: To analyze the prevalence of SS among children in China and to explore the influences of sex, area, age, study year, and study site on prevalence rates.

Methods: Relevant literature was identified by searching the following databases: PubMed, Embase, The Cochrane Library, Chinese Biomedical Literature, China Knowledge Resource Integrated, WeiPu, and WanFang databases. Meta-analysis was carried out using STATA 11.2.

Results: This meta-analysis included 39 studies with 348 326 Chinese participants; the studies covered 20 provinces, municipalities, and autonomous regions. The pooled prevalence of SS was 3.2% (95% confidence interval [*CI*], 2.6%–3.7%; I^2 = 99.8%). The prevalence of SS in boys and girls were 3.1% (95% *CI*, 2.5%–3.7%) and 3.2% (95% *CI*, 2.6%–3.9%), respectively. The sex difference was not statistically significant ($P > 0.05$). The prevalence of SS was higher in rural areas than in urban areas (4.7% [95% *CI*, 3.6%–5.8%] vs. 2.8% [95% *CI*, 2.2%–3.4%]; $P < 0.001$). The prevalence of SS was higher in West China (5.2%; 95% *CI*, 4.4%–6.0%) than in Northeast China (0.6%; 95% *CI*, 0.3%–0.8%), East China (2.3%; 95% *CI*, 1.9%–2.8%), or Central China (2.9%; 95% *CI*, 1.9%–3.9%).

Interpretation: The prevalence of SS among children was higher in western and rural areas of China. Close attention to children's growth and development is needed to prevent the occurrence of SS.

KEYWORDS
Prevalence, Short stature, Meta-analysis, China

INTRODUCTION

Short stature (SS) is individual height that is <2 standard deviations below (or below the third percentile of) the average height among children with the same ethnicity, age, and sex under similar living conditions.[1,2] Individual height is affected by genetic and environmental factors such as nutrition, disease, and physiology. Hormonal therapy, nutritional regulation, and reasonable exercise can promote height growth before epiphyseal closure. Many

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studies have shown that children with SS lack confidence and have different degrees of adjustment disorder, cognitive disorders, and self-consciousness disturbance. Moreover, treatment for SS is both extensive and expensive, constituting an economic burden for families and society.[3-5]

Numerous investigations of stature characteristics have been performed at different sites and areas of China. These investigations showed that in 2018, the total rate of SS among children ages 6–23 months in the middle region of China (i.e., Anhui, Henan, Hubei, Hunan, Jiangxi, and Shanxi Provinces) was 5.9%.[6] Wang et al[1] found that the average detection rate of SS in primary and middle school students was 3.16% in Anhui province in 2015. A recent investigation of 213 795 Han school children from 30 provinces/municipalities/autonomous regions showed that the prevalence of SS was 3.70% of children aged 7–18 years in China.[7] To the best of our knowledge, there has been no systematic review of the stature characteristics of children in China; no exact statistical data are available regarding the prevalence of SS in these children. Here, we performed a systematic review and meta-analysis of published literature regarding SS among children in China. Specifically, we explored the prevalence with respect to various characteristics including sex, area, age, study time, and study site in subgroup analyses.

METHODS

Search strategy

The literature search process is shown in Figure 1. Two investigators (Qianlong Zhao and Junyi Chen) independently searched the literature using the following databases: PubMed, Embase, Cochrane Library, Chinese Biomedical Literature, China Knowledge Resource Integrated, WeiPu, and WanFang databases; databases were searched from inception until February 2019. Search terms included “short stature”, “stunting”, “growth retardation”, “incidence”, “prevalence”, “epidemiology”, and “China”. The literature search included original articles, review articles, and meta-analyses. Literature search strategy was shown in Figure S1.

Inclusion and exclusion criteria

Articles were included if they met the following criteria: 1) they described a cross-sectional survey conducted in China (only baseline data were extracted); 2) participants were <18 years of age; 3) the diagnosis of SS was established in accordance with the guidelines of the genetic metabolic endocrine group of pediatrics branch in Chinese Medical Association,[2] such that one of the following conditions was met: i) height < 2 standard deviations of average height for children of the same ethnicity, sex, and age; ii) height below the third percentile of average height (−1.88 standard deviations) for children of the same ethnicity, sex, and age; iii) bone age less than chronological age by > 2 years; iv) height growth rate below the 25th percentile based on bone age (annual growth rate of 4.5-year-old children to adolescent children ≥ 5 cm; annual growth rate of adolescent children ≥ 6 cm).

Data collection and extraction

After removal of duplicate references, two investigators (Fulun Li and Ke Liu) independently screened the titles and abstracts of all records to identify articles that met the inclusion criteria. Any disagreements were resolved by consensus or by consultation with a senior researcher (Jing Yang). We used a predefined form to extract relevant characteristics of included literature such as title, the first author, study year, sample size, and age and sex of participants.

Quality assessment

The methodological quality of the included literature was evaluated using the Joanna Briggs Institute Prevalence Critical Appraisal Tool (Table 1),[8] which incorporates 10 domains. A study was considered to be of low quality if 0–5 criteria were met, whereas it was considered to be of high quality if 5–10 criteria were met. Two reviewers (Fulun Li and Ke Liu) independently assessed methodological quality. Disagreements were resolved by consultation with a senior researcher (Jing Yang).

Statistical analysis

The pooled prevalence of SS in the included studies were determined and reported with 95% confidence intervals (*CI*). Statistical analyses in this study were conducted using STATA software (version 11.2; StataCorp, College Station, TX, USA). Subgroup analyses were conducted based on sex, age, area, study time, and study site. Heterogeneity between studies was assessed by the Q test and I^2 statistic (no heterogeneity: I^2 = 0%–25%; moderate heterogeneity: 25%–50%; large heterogeneity: 50%–75%; and extreme heterogeneity: 75%–100%).[9] Fixed effects model analysis was used when $P \geq 0.10$ or $I^2 < 50\%$; otherwise, random effects model analysis was used. Publication bias was assessed using Egger’s funnel plot. All P values were two-tailed and $P < 0.05$ was considered statistically significant.

RESULTS

Characteristics of the included studies

In total, 3630 eligible articles were identified in the initial literature search; of these, 39 met the inclusion criteria after screening of titles, abstracts, and full texts, as well as removal of duplicates (Figure 1).

The 39 studies included a total of 1 348 326 participants (Table 1).[1,10-47] One study was published in English, while the remaining 38 were published in Chinese. Sample sizes ranged from 2000 to 581 016 participants. Participant age ranged from 6 months to 18 years old. All studies

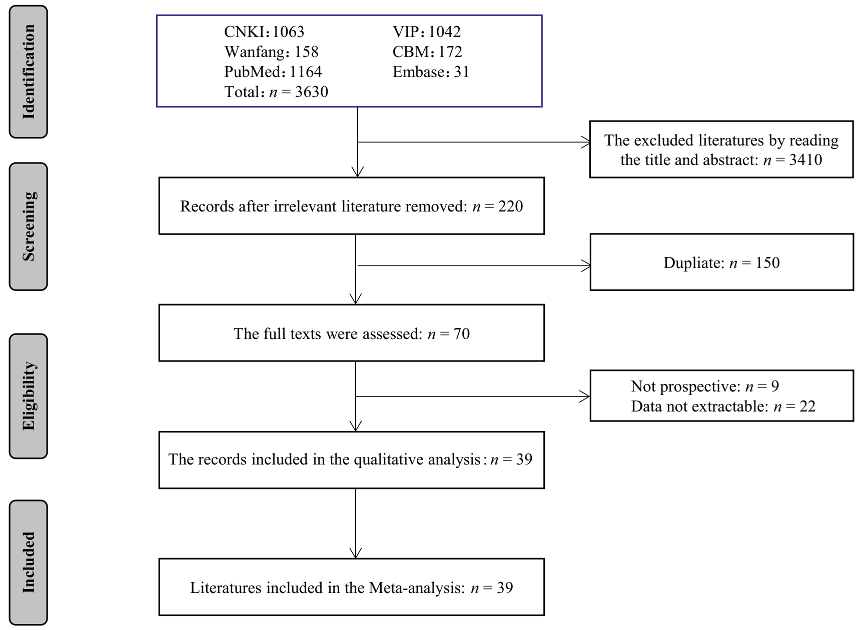

FIGURE 1 Flow diagram for the included studies in this meta-analysis.

were conducted from 1989 to 2018 in 20 provinces/municipalities/autonomous regions in China. Stratification based on China's four major economic regions revealed that five studies were conducted in Northeast China, 20 were conducted in East China, eight were conducted in Central China, and 15 were conducted in West China.

Prevalence of SS

The pooled prevalence of SS among the 39 studies with available data was 3.2% (95% *CI*, 2.6%–3.7%; $I^2 = 99.8\%$) (Figure 2). The prevalence of SS in boys and girls were 3.1% (95% *CI*, 2.5%–3.7%) and 3.2% (95% *CI*, 2.6%–3.9%), respectively; the difference was not statistically significant (P = 0.775). Heterogeneity analysis showed great heterogeneity in the pooled prevalence of SS ($I^2 >$ 95%; $P < 0.05$); therefore, the random effects model was used to conduct subgroup analyses.

The prevalence of SS was significantly higher in rural areas than in urban areas (4.7% [95% *CI*, 3.6%–5.8%] vs. 2.8% [95% *CI*, 2.2%–3.4%]). The prevalence of SS was higher in children aged 6–12 years (3.3%; 95% *CI*, 2.7%–3.8%) than in children aged > 12 years (3.1%; 95% *CI*, 2.4%–3.8%) or < 6 years (2.4%; 95% *CI*, 1.6%–3.3%). The prevalence of SS was higher in studies conducted after 2010 (3.3%; 95% *CI*, 2.7%–4.0%) than in studies conducted before 2010 (2.5%; 95% *CI*, 1.8%–3.2%). The prevalence of SS was higher in West China (5.2%; 95% *CI*, 4.4%–6.0%) than in Northeast China (0.6%; 95% *CI*, 0.3%–0.8%), East China (2.3%; 95% *CI*, 1.9%–2.8%), or Central China (2.9%; 95% *CI*, 1.9%–3.9%) (Table 2).

Sensitivity analysis and publication bias

Egger's test revealed marginal publication bias for SS (t = 2.04, P = 0.047). The results of sensitivity analysis (trim and fill method) of the prevalence of SS indicated that the results were not significantly affected by exclusion of any single study, suggesting that the results were robust (Figures S2 and S3).

DISCUSSION

SS has been identified as a major global health priority and is the focus of several high-profile initiatives. Notably, SS is an important component of six global nutrition targets for 2025 that were adopted by the World Health Organization in 2012,[48] and may serve as an indicator for the post-2015 development agenda. The prevalence of SS is important for the surveillance of physical growth of children over time. Thus, information regarding the prevalence and characteristics of SS among children will provide guidance for planning and implementation of nationwide public health policies.[49,50]

Meta-analysis, as a statistical analysis method of evidence-based medicine, aims to increase the sample size by comprehensively analyzing the research results of multiple small samples on the same subject, thus improving the research efficiency of the original results and making the conclusions more representative.[51] This comprehensive meta-analysis of the prevalence of SS in China included 39 studies with 1 348 326 participants, covering 20 provinces/municipalities/autonomous regions. This results showed that the pooled prevalence of SS was 3.2% in China; notably, the prevalence of SS in children < 6 years of age was 2.4%. The United Nations Children's Fund reported the prevalence of SS in children < 5 years of age in multiple populations[52]: 37.9% in India (2015–2016), 33.4% in the Philippines (2015), 24.6% in Vietnam (2015),

TABLE 1 Characteristics of the included studies

Study year	First author	Reference number	Events	Sample size	Age range (year)	Region	Sampling methods	Diagnostic criteria	Quality appraisal
2014	Wang Q	1	380	12 009	7–18	Central of China	Stratified random cluster sampling	<2SD or <P3rd	9
2014	Yang X	10	26 662	581 016	0–5	West of China	Cluster sampling	<2SD	9
2014	Chen XJ	11	172	6082	7–12	Central of China	Stratified cluster sampling	<2SD or <P3rd	9
2015	Wang LF	12	735	63 049	3–14	East of China	Cluster sampling	<2SD	10
2012	Cao LF	13	301	4930	6–11	East of China	Random cluster sampling	<2SD or <P3rd	9
2000	Chen AY	14	75	7455	6–12	East of China	Cluster sampling	<2SD or <P3rd	8
2003	Cheng RQ	15	2658	70 431	6–18	East of China	Cluster sampling	<2SD	10
2012	Dou YR	16	3325	54 743	6–18	West of China	Stratified cluster sampling	<2SD	10
2010	Fu DL	17	107	5374	6–13	East of China	Cluster sampling	<2SD	9
2000	Liu HJ	18	99	15 479	7–13	East of China	Random cluster sampling	<2SD	9
2013	Li SL	19	770	8043	7–13	West of China	Cluster sampling	<2SD or <P3rd	7
2014	Liu SS	20	287	9095	6–16	East of China	Random cluster sampling	<2SD or <P3rd	10
2014	Liu Y	21	94	3593	7–18	Central of China	Stratified random cluster sampling	<P3rd	9
2000	Lou XM	22	104	3240	12–16	Central of China	Cluster sampling	<2SD	8
2014	Ma FF	23	18	2267	3–6	East of China	Random sampling	<2SD	8
2016	Qin Y	24	1640	30 000	3–14	Central of China	Cluster sampling	—	9
2003	Qiu XG	25	230	23 512	6–12	East of China	Cluster sampling	<2SD or <P3rd	9
2015	Rui QQ	26	58	2069	6–12	East of China	Cluster sampling	<2SD	9
2018	Sang MY	27	272	14 179	7–18	Central of China	Cluster sampling	<P3rd	10
2016	Tao XG	28	210	9338	0–14	East of China	Cluster sampling	<2SD	10
2018	Wang M	29	73	8090	6–12	Northeast of China	Stratified random cluster sampling	<P3rd	9
2012	Wang ZH	30	52	3722	3–5	Mixed	Multi-stage stratified cluster sampling	<P3rd	9
2018	Wen YH	31	586	9214	6–14	West of China	Random cluster sampling	<2SD or <P3rd	9
2017	Wu LH	32	98	2000	0–7	West of China	Random cluster sampling	<2SD	8
2011	Xiang J	33	1553	70 918	6–18	West of China	Cluster sampling	<2SD	10
2015	Xu JJ	34	194	10 436	6–12	Central of China	Cluster sampling	<2SD	10
2016	Yao X	35	118	8336	6–18	West of China	Cluster sampling	<2SD	10
2011	Ye ZZ	36	4746	109 600	3–6	West of China	Cluster sampling	<2SD	9
1989	Zhang JH	37	126	8783	6–13	Northeast of China	Cluster sampling	<2SD	9
2017	Zhou LH	38	54	3106	6–12	West of China	Random sampling	—	8
2012	Du FF	39	299	3394	6–14	West of China	Cluster sampling	<2SD	8
2012	Gao G	40	279	38 005	7–12	East of China	Cluster sampling	<2SD	10
2013	Liu J	41	172	2017	5–19	West of China	Cluster sampling	—	10
2011			29	13 300		Northeast of China			
2012	Liu WD	42	29	14 022	3–5	Northeast of China	Cluster sampling	<2SD	7
2013			30	14 676		Northeast of China			
2012	Peng HL	43	98	2735	3–5	West of China	Random sampling	<2SD	8
2008			331	3430		East of China			
2009	Qu BX	44	287	3054	3–7	East of China	Cluster sampling	<2SD	8
2010			180	3304		East of China			
2014	Xu HY	45	90	4436	3–7	Central of China	Cluster sampling	<2SD	8
2010			180	5048		West of China			
2011	Yang Y	46	458	5798	3–5	West of China	Cluster sampling	<2SD	10
2012			315	5724		West of China			
2006			47	12 966		East of China			
2007			43	12 922		East of China			
2008	Yu WP	47	30	13 766	3–6	East of China	Cluster sampling	<2SD	10
2009			25	14 349		East of China			
2010			24	15 271		East of China			

Diagnostic criteria: <2SD, height <2 standard deviation (SD) of average height in same ethnicity, sex, and age; <P3rd, height below the third percentile (−1.88 SD) of average height in same ethnicity, sex, and age; —, not mentioned. Quality appraisal was evaluated using the Joanna Briggs Institute Prevalence Critical Appraisal Tool.

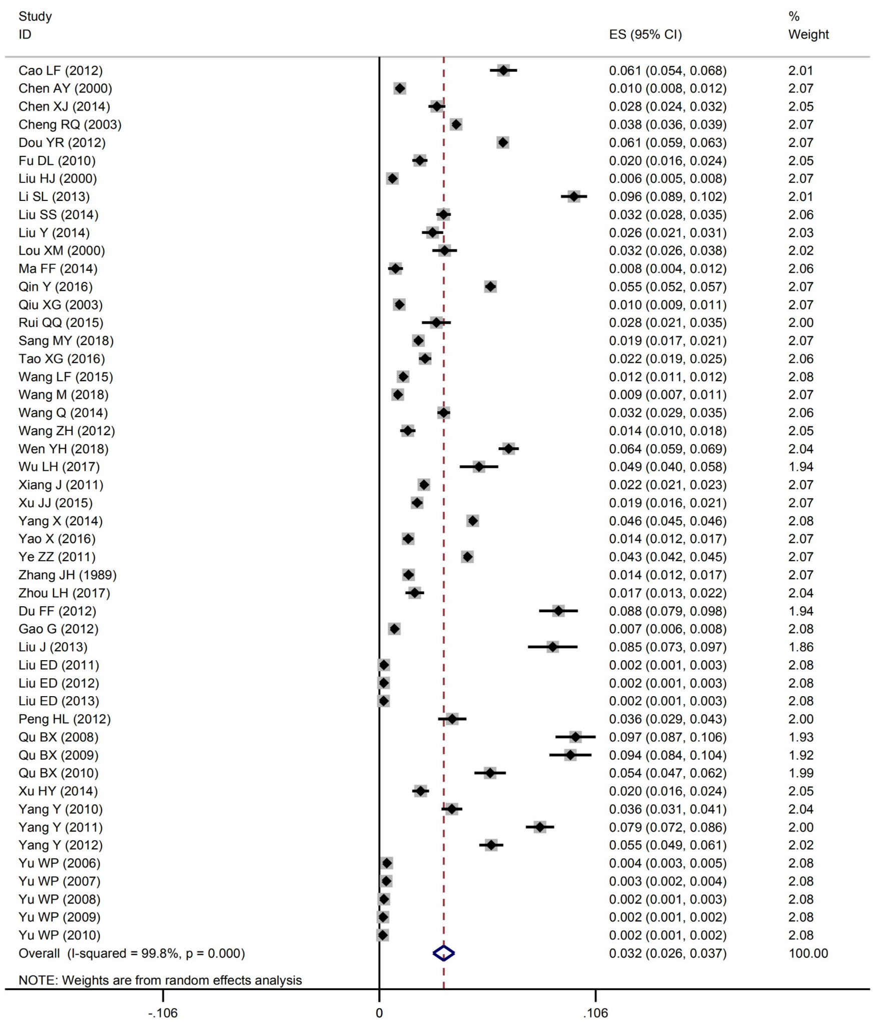

FIGURE 2 Forest plot of prevalence estimates of short stature with 95% confidence intervals among children in China.

10.5% in Thailand (2015–2016), 7.1% in Japan (2010), 7.0% in Brazil (2006–2007), and 2.5% in the Republic of Korea (2008–2011). The results of this meta-analysis showed that the prevalence of SS in children < 6 years of age in China was lower than the prevalence in these developing countries.

The prevalence of SS (3.3%) was higher in primary school students (aged 6–12 years) than in students aged > 12 years (3.1%) or < 6 years (2.4%). This difference is potentially because children aged 0–6 years can fully obtain nutrition under the care of their parents (children of this age have not yet begun to attend school). Moreover, since 2009, the Chinese government has provided a free Supplementary Nutrition Program for children from 6 months to 2 years of age[53-54]; this program provides a variety of vitamins and minerals for the growth and development of children. Notably, the prevalence of SS was high in primary school students (aged 6–12 years). Children of this age have begun to attend school; notably, some rural children live in boarding houses during school attendance (separate from their parents' care) and may be unable to achieve satisfactory nutrition, thereby resulting in restricted growth and development. After the age of 13 years, students' self-care ability may be increased, such that they adequately monitor nutrition. In recent years, the rate of SS detection has increased, as indicated in Table 2: the prevalence of SS was slightly higher in studies conducted after 2010 than in studies conducted before 2010. This may be because with the improvement of living standards, SS in children has become an important concern to the families and society. The increase in the number of children who went to hospital for the diagnosis of SS can increase the detection rate of SS to some extent. At the same time, with the improvement of the medical level, the recognition and diagnosis of SS by specialists can further increase the prevalence of SS.

Our results showed no significant difference in the prevalence of SS between boys and girls. Similar findings regarding sex differences in SS were demonstrated in studies conducted in Arab countries. A study in Saudi Arabia showed no significant difference in the prevalence of SS between boys and girls (5–17 years of age),[55] as

TABLE 2 Prevalence of short stature among children in each subgroup

Variables	Number of studies	Events	Sample size	Heterogeneity of the studies		Prevalence (%)	95% Confidence interval	Comparison of the groups (*P*)
				I^2 (%)	*P*			
Sex								0.775
boys	25	7583	248 846	99.10	<0.001	3.1	2.5–3.7	
girls	25	7104	232 014	99.40	<0.001	3.2	2.6–3.9	
Area								<0.001
Urban	16	5121	188 763	98.90	<0.001	2.8	2.2–3.4	
Rural	16	8373	201 703	99.50	<0.001	4.7	3.6–5.8	
Age (years)								<0.001
<6	20	33 222	841 883	99.90	<0.001	2.4	1.6–3.3	
6–12	25	7746	311 889	99.40	<0.001	3.3	2.7–3.8	
>12	14	3036	104 940	97.60	<0.001	3.1	2.4–3.8	
Study year								<0.001
<2010	11	3980	181 932	99.70	<0.001	2.5	1.8–3.2	
≥2010	38	44 736	1 166 394	99.90	<0.001	3.3	2.7–4.0	
Study site								<0.001
Northeast of China	5	287	58 871	99.80	<0.001	0.6	0.3–0.8	
East of China	20	6024	330 066	99.50	<0.001	2.3	1.9–2.8	
Central of China	8	2946	83 975	98.70	<0.001	2.9	1.9–3.9	
West of China	15	39 434	871 692	99.50	<0.001	5.2	4.4–6.0	

did a study in Ankara, Turkey regarding the prevalence of SS in 7–15-year-old school-aged children.[56] However, we found that the prevalence of SS was high in rural (4.7%) and West China (5.2%). Potential explanations for this result are as follows: first, the economic progress of rural areas and West China is very uneven, which directly affects the nutritional status of children living in those areas. For example, the growth and development of school-aged children (aged 6–12 years) in western rural areas remains suboptimal. Secondly, the educational levels of caregivers are also low in these areas. Children rely on their caregivers to prevent malnutrition; the educational levels of caregivers affect whether they use evidence-based methods to determine how to feed and care for their children.[57] The educational level of caregivers could also affect family income, thus indirectly affect the nutritional status of their children.[58,59]

The methodology quality of included studies was evaluated using the Joanna Briggs Institute Prevalence Critical Appraisal Tool. Of the 39 studies included in this meta-analysis, 18 had inadequate sample size and 11 had unclear sampling methods; however, these aspects did not have substantial impact on the results of this meta-analysis. Therefore, these studies were considered to be of high quality. In addition, the included studies did not have incomplete data reports or missing data, and all baselines were comparable.

There were some limitations in this meta-analysis. First, heterogeneity was present among the included studies. Heterogeneity is difficult to avoid in epidemiological studies.[60] Second, the diagnosis of SS was made on the basis of the physical growth and development of children in China, excluding the National Center for Health Statistics/World Health Organization reference data. This method may have caused some bias in the resulting data. Third, publication bias was present in our meta-analysis because of unclear randomization and concealment methodology in some studies; the prevalence of SS in the included studies demonstrated heterogeneity because of differences in age, area, sample size, study time, and study site. Fourth, the studies included in this meta-analysis covered only 20 provinces/municipalities/autonomous regions in China; thus, they did not cover all possible areas. Finally, relevant factors (e.g., socioeconomic, nutritional, and environmental variables) were not recorded in most studies; therefore, it was difficult to evaluate their impacts on the prevalence of SS.

In conclusion, this meta-analysis showed that the prevalence of SS among children in China was 3.2%. However, the prevalence of SS among children in western and rural areas of China was relatively high, which suggests that governmental care and support should be increased to prevent development of SS among children in these areas.

CONFLICT OF INTEREST

The author declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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