Prevalence of chronic cough in China: a systematic review and meta-analysis

Hanwen Liang1,2†, Weiyan Ye1†, Zhufeng Wang1†, Jingyi Liang1, Fang Yi1, Mei Jiang1* and Kefang Lai1*

Abstract

Background: Individual studies have indicated variable prevalence for chronic cough, but thus far, there has been no systematic report on the prevalence of this condition.

Methods: In this study, we performed a systematic review and meta-analysis by searching databases including PubMed, Cochrane Library, Web of Science, China National Knowledge Infrastructure, Chinese biomedical literature service system, Wanfang Database, and VIP database, for studies on chronic cough in China published before December 28, 2020. A random effects model was used to calculate pooled prevalence estimates with 95% confidence interval [95%CI], weighted by study size.

Results: Fifteen studies with 141,114 community-based adults were included in the study, showing a prevalence of 6.22% (95% CI 5.03–7.41%). And 21 studies with 164,280 community-based children were included, presenting a prevalence of 7.67% (95% CI 6.24–9.11%). In subgroup meta-analyses, the prevalence in adults was 4.38% (95% CI 2.74–6.02%) in southern China and 8.70% (95% CI 6.52–10.88%) in northern China. In the children population, the prevalence in northern China was also higher than in southern China (northern vs. southern: 7.45% with a 95% CI of 5.50–9.41%, vs. 7.86% with a 95% CI of 5.56–10.16%).

Conclusions: Our population-based study provides relatively reliable data on the prevalence of chronic cough in China and may help the development of global strategies for chronic cough management.

Keywords: China, Cough, Chronic diseases, Meta-analysis, Prevalence

Background

Cough is an essential defense mechanism, which prevents the aspiration of excessive respiratory secretions and foreign bodies [1]. However, cough is also one of the most common symptoms and subject of complaints among patients seeking help from respiratory specialists and community outpatient clinics [2]. Chronic cough is defined as a cough that lasts eight weeks or longer in adults, or four weeks or longer in children [3–7], seriously impairs life quality, and results in a heavy social and economic burden [8–10]. Worldwide, more than 10% percent of the adults suffer from chronic cough, and in China, patients with chronic cough account for more than a third of the total patients in respiratory clinics [11, 12].

Previously, chronic cough was considered a concomitant symptom in various diseases, including in asthma, rhinitis, and gastro-esophageal acid reflux disease, and was ignored [13]. However, recent evidence suggests that chronic cough is a clinical syndrome with a distinct and intrinsic pathophysiology, characterized by neuronal hypersensitivity, significant association with a drastic decrease of lung function, and an increase risk of hospitalization [14–16].

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Chronic cough has gained increasing attention in recent years and emerged as a serious public health problem. Since the first Cough Guideline launched in 1998, countries have successively issued guidelines to standardize the definition and the treatments of chronic cough [17]. Recent research has focused on risk factors, mechanisms and treatments for chronic cough in China. Yet, the epidemiology of chronic cough, also important for its management, is rapidly changing with the urbanization of China [1, 18–21]. Although a research letter published in 2015 [12] reviewed the global burden of chronic cough, the prevalence of chronic cough in China had not been systematically and independently reported. Considering the role of host–environment interactions, we hypothesized that chronic cough might have distinct characteristics in China. As there are more than 1.4 billion people in China, epidemiological information on chronic cough in this country cannot be ignored, and may contribute to the definition of global strategies for the management of this distressing disease. The whole world, as China, urgently requires updated information on chronic cough prevalence and burden among the general population.

We performed a systematic review of the studies performed on the Chinese population that reported chronic cough prevalence in different regions and over different periods of time. We hypothesized that these data would provide crucial updates regarding chronic cough disease burden in China and bring useful information to plan appropriate strategies for the allocation of healthcare resources. We pooled chronic cough prevalence estimates from different regions and provinces of China and analyzed the prevalence of chronic cough among Chinese adults and children. Understanding the epidemiologic patterns of chronic cough in the Chinese population will lead to a better management of this disease in China and provide data to estimate the burden of chronic cough worldwide.

Methods
This systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA) 2020 [22]. Besides, we prospectively submitted the systematic review protocol for registration on PROSPERO (CRD42021247623).

Search strategies and selection criteria
A systematic search using a combination of keywords including “chronic cough” or “prevalence” and “China,” was performed independently in seven different databases, including PubMed, Cochrane Library, Web of Science, China National Knowledge Infrastructure, Chinese biomedical literature service system, Wanfang Database, and VIP database. The search strategies were drafted independently by H.W. and Z.F. and evaluated according to the inclusion criteria. Disagreements were discussed until a consensus was reached. To minimize missingness, a manual search in the bibliography of reference articles, as well as in previously published relevant reviews was performed. A quality control of the literature search was conducted by M.J. All suitable articles published before the 28th of December 2020 were identified and subsequently catalogued using EndNote X9. All articles published in Chinese or English were included. The detailed search strategy is described in Supporting Information (Additional file 1).

Comprehensive inclusion and exclusion criteria were predefined to facilitate the objective screening of the articles (Table 1). Suitable reports identified by manual search were also included for review. The references of system review and meta-analysis were also reviewed. Two reviewers (H.W. and Z.F.) independently reviewed all reports in accordance with the preset criteria. The outcome of this initial review was then cross checked by the two reviewers. Conflicting opinions and uncertainties were discussed and resolved by reaching a consensus with a third reviewer.

Data extraction and quality assessment
A full text review was performed for all selected article and the data were extracted and sorted by two reviewers (H.W. and Z.F.) using independent spreadsheets, into the following variables: first author, publication year, title, region, participants’ demographic characteristics, diagnostic criteria for chronic cough, number of cases, sample size, journal type, and prevalence of chronic cough. When data were missing, the corresponding authors of the concerned articles were contacted to obtain relevant information. For studies containing data from different provinces or age groups, the relevant data were extracted separately according to provinces and age categories (adults ≥ 18 years, or children). The two reviewers (H.W. and J.Y.) assessed independently the quality of the included studies using an 11-item checklist recommended by the Agency for Healthcare Research and Quality (AHRQ) (Additional file 2). An item was scored “0” if it was answered “NO” or “UNCLEAR,” and “1” if it was answered “YES.” According to this scoring, the article quality was defined as follows: low quality = 0–3; moderate quality = 4–7; high quality = 8–11 [23, 24]. If no consensus could be reached between the two reviewers, a third reviewer (W.Y.) was consulted. The grading of recommendations assessment, development, and evaluation (GRADE) algorithm was used to assign quality levels to the meta-analysis evidence. The overall confidence could be judged as “high,” “moderate,” “low,” or “very low” [25].
Statistical analysis
The pooled prevalence was calculated using the inverse-variance random-effects model or fixed-effect model, which was presented as percentage with 95% confidence intervals. Heterogeneity was assessed using the $I^2$ statistic. Subgroup analysis as well as heterogeneity regression analysis were performed to determine if the prevalence data was influenced by age, region, AHRQ, diagnosis criteria, year of publication, sample size, prevalence definition, chronic cough definition, and sampling method. Publication bias was assessed by funnel plots and Begg's test. Sensitivity analyses were conducted by plotting the pooled effect size and excluding one study at a time to estimate its individual effect on the results overall (The pooled results was robust, if we removing any particular study not change the pooled effect size or significance of the remaining studies). Stata 14.0 was used for the analysis. The significance level was defined as (two-tailed) $P < 0.05$.

Quality assessment
All selected articles were assessed for methodological quality. Among the studies reporting the prevalence of chronic cough in adults, two were of high quality [26, 27], and thirteen were of moderate quality [28–40]. Among the studies reporting the prevalence of chronic cough in children, 2 were of high quality [41, 42], and 19 were of moderate quality [36, 43–60]. No articles ranked as low-quality (Additional file 4). For studies in adults and children, the AHRQ score was 5.46±1.46 and 5.05±1.24, respectively. The GRADE evidence of all outcomes was judged as “moderate”, “low”, or “very low”. These results are shown in Table 2.

Geographical coverage
The 35 selected studies, 1 nationwide epidemiological investigation and studies from 12 provinces and autonomous regions of China. Several studies covered more than one region. The detail of the geographical coverage is shown in Table 2.

Characteristics of participants
In total, the 35 studies included 305,394 participants (141,114 adults and 164,280 children), of which 20,177 (6,940 adults and 13,237 children) were patients with chronic cough. The characteristics of the participants are presented in Tables 2, 3 and Additional file 5.

Prevalence
The overall pooled prevalence of chronic cough was 6.22% (95% CI 5.03–7.41%) in adults and 7.67% (95% CI 6.24–9.11%) in children. There was significant heterogeneity between the studies that reported the prevalence of

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Table 1 Inclusion and exclusion criteria for article selection used in the systematic review, according to the PICOS Framework

| Component | Inclusions | Exclusion |
|-----------|------------|-----------|
| Population | Community-based or unselected populations of China | 1. Reports that focused only on specific sub-groups (e.g., soldiers and patients with occupational diseases) 2. Participants are from studies based on respiratory clinic or focused on a defined disease like bronchitis, COVID-19, influenza virus, mycoplasma pneumoniae infection etc 3. Studies using duplicated samples |
| Intervention and comparator | Any | 1. Studies published neither in English nor Chinese 2. Full text not accessible 3. Studies reported the proportion of chronic cough based on population for medical care |
| Outcome | Studies reporting the prevalence of chronic cough, or data that can be converted into prevalence, such as calculate the prevalence according to the formulation of $\frac{[(\text{number of female chronic cough patients} + \text{number of male chronic cough patients})}{(\text{number of female participants} + \text{male participants})] \times 100\%}$. Studies with chronic cough or other conceptually equivalent terms, such as prolonged cough or persistent cough | |
| Study design | Observational study, such as cohort study and cross-sectional study | Case reports, case series, comments, conference papers, technical reports, popular science literature, and animal experiments |

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Results
Study selection
The literature search yielded a total of 2531 potentially relevant citations, of which 652 were duplicates, i.e., the investigations were performed in population or subset of population already included. After screening (title, abstract), a total of 254 articles were retained for full-text review. After comprehensive full-text review, 35 articles (21 in Chinese and 14 in English) were finally included, of which 15 involved adults and 21 involved children. Figure 1 and Additional file 3 details the process of studies selection and the reasons of exclusion.

Quality assessment
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Prevalence
The overall pooled prevalence of chronic cough was 6.22% (95% CI 5.03–7.41%) in adults and 7.67% (95% CI 6.24–9.11%) in children. There was significant heterogeneity between the studies that reported the prevalence of
chronic cough in adults ($I^2 = 99.1\%, P < 0.001$) and children ($I^2 = 99.3\%, P < 0.001$) (Figs. 2, 3, 4 and Additional file 6: Fig. S1). A subsequent meta regression analysis to explore the source of heterogeneity and the results showed that the year of publication, sample size, diagnostic definition, classification of prevalence, and region were not associated with heterogeneity between studies (adults: adjusted $R^2$: –8.31%, $P = 0.581$; children: adjusted $R^2$: –27.36%, $P = 0.988$).

**Subgroup analyses**
We ran separate meta-analyses on adult studies for subgroup effects by region, diagnostic criteria, AHQR, age, sample size, population sampling method, prevalence definition and year of publication, using the random effects model. The prevalence of chronic cough was 4.38% (95% CI 2.74–6.02%) in southern China, and 8.70% (95% CI 6.52–10.88%) in northern China (Additional file 6: Fig. S2). The pooled prevalence, according to the diagnostic criteria: “cough lasting for more than three weeks”, “cough lasting for more than eight weeks”, and “cough lasting for more than three months”, was 3.47% (95% CI 2.76–4.18%), 8.76% (95% CI 1.82–15.69%) and 6.14% (95% CI 4.32–7.96%), respectively (Additional file 6: Fig. S3). According to the update of the Chinese Guideline for Cough, the included studies were divided into four periods of time (1988–2004; 2005–2009; 2010–2014; and 2015–2020). Compared with the other three periods, the prevalence during 2005–2009 was dramatically low (2.66%, 95% CI 1.72–3.60%) (Additional file 6: Fig. S3).
Table 2  Principal characteristics of studies in adults included in the meta-analysis

| References          | City       | Diagnostic criteria                                      | Age (y) | Events | Total   | Prevalence (%) | Bias score | GRADE\(^a\) | Source of information | Journal classification |
|---------------------|------------|----------------------------------------------------------|---------|--------|---------|----------------|------------|-------------|----------------------|------------------------|
| Koo et al. [36]     | Hongkong   | Cough more than 3 months                                 | 37.8    | 18     | 314     | 5.7            | 4          | Low         | Cluster random sampling | SCI \(^b\)              |
| Lai et al. [30]     | Hongkong   | Not mentioned                                            | ≥ 70    | 203    | 2032    | 10             | 4          | Low         | Stratified random sampling | SCI                    |
| Zhang et al. [35]   | Lanzhou    | Cough more than 3 months                                 | 18–49   | 83     | 1494    | 5.56           | 4          | Very low    | Cluster random sampling | Other                  |
| Zhang et al. [35]   | Wuhan      | Cough more than 3 months                                 | 18–49   | 47     | 1524    | 3.08           | 4          | Very low    | Cluster random sampling | Other                  |
| Zhang et al. [35]   | Guangzhou  | Cough more than 3 months                                 | 18–49   | 8      | 1090    | 0.73           | 4          | Very low    | Cluster random sampling | Other                  |
| Venners et al. [33] | Anhui      | Cough in the morning for three or more months during the winter | ≥ 18    | 73     | 2525    | 28.9           | 4          | Moderate    | Random samples          | SCI                    |
| Chen et al. [28]    | Guangzhou  | Cough more than 3 weeks                                  | 21 ±1   | 36     | 1087    | 3.3            | 6          | Low         | Cluster random sampling | The core journal of China |
| Wilson et al. [37]  | Liaoning   | Cough more than 3 months                                 | 477 ±15.2 | 729 | 31,704 | 2.3            | 5          | Low         | Cluster random sampling | SCI                    |
| Pan et al. [33]     | Guangzhou  | Cough more than 8 weeks                                  | 20 ±4   | 58     | 2588    | 2.24           | 4          | Very low    | Census                | Other                  |
| Wang et al. [27]    | Beijing    | Not mentioned                                            | ≥ 18    | 118    | 7614    | 1.55           | 8          | Very low    | Cluster random sampling | The core journal of China |
| Wang [29]           | Gansu      | Cough more than 3 months, for as much as 2 year          | ≥ 40    | 175    | 728     | 24.04          | 5          | Very low    | Not mentioned           | The core journal of China |
| Li [32]             | Shenzhen   | Cough more than 3 weeks                                  | ≥ 18    | 53     | 1468    | 3.6            | 5          | Low         | Cluster random sampling | Other                  |
| Yue [26]            | X’ian      | Not mentioned                                            | ≥ 60    | 73     | 758     | 9.6            | 8          | Low         | Cluster random sampling | Other                  |
| Hu et al. [38]      | Beijing    | Cough more than 8 weeks                                  | ≥ 35    | 156    | 1003    | 15.6           | 7          | Moderate    | Stratified random sampling | SCI                    |
| Huang et al. [40]   | Foshan      | Cough more than 8 weeks, which is the main or only symptom | ≥ 18    | 153    | 1769    | 8.65           | 5          | Low         | Multi-stage random sampling | The core journal of China |
| Zhang et al. [39]   | Beijing    | Cough more than 3 months                                 | ≥ 20    | 1894   | 26,166  | 7.2            | 6          | Moderate    | Cluster random sampling | SCI                    |
| Li [31]             | China      | Cough more than 3 months                                 | ≥ 40    | 2971   | 56,066  | 5.3            | 7          | Moderate    | Stratified multi-stage cluster sampling | The core journal of China |

\(^a\) GRADE, The Grading of Recommendations Assessment, Development, and Evaluation [25]

\(^b\) SCI, Science Citation Index
Table 3  Principal characteristics of studies in children included in the meta-analysis

| References       | City          | Diagnostic criteria                                                                 | Age (y) | Events | Total  | Prevalence (%) | Bias score | GRADEa | Source of information         | Journal classification |
|------------------|---------------|--------------------------------------------------------------------------------------|---------|--------|--------|----------------|------------|--------|------------------------------|------------------------|
| Koo et al. [36]  | Hongkong      | Cough more than 3 months                                                             | 10.1    | 22     | 314    | 7.00           | 4          | Low    | Cluster random sampling       | SCIb                   |
| Xi et al. [54]   | Liaoning      | Cough more than 3 months                                                             |         |        |        |                 |            |        | Cluster random sampling Other |                       |
| Zhang et al. [56]| Guangzhou     | Coughed for at least 1 month per year either with or apart from colds               | 54–16.2 | 166    | 2216   | 7.49           | 4          | Low    | Cluster random sampling SCI   |                       |
| Zhang et al. [56]| Wuhan         | Coughed for at least 1 month per year either with or apart from colds               | 54–16.2 | 211    | 2307   | 9.17           | 4          | Low    | Cluster random sampling SCI   |                       |
| Zhang et al. [56]| Lanzhou       | Coughed for at least 1 month per year either with or apart from colds               | 54–16.2 | 157    | 1438   | 10.94          | 4          | Low    | Cluster random sampling SCI   |                       |
| Zhang et al. [56]| Chongqing     | Coughed for at least 1 month per year either with or apart from colds               | 54–16.2 | 101    | 1431   | 7.06           | 4          | Low    | Cluster random sampling SCI   |                       |
| Xi et al. [55]   | Benxi         | Cough more than 3 months                                                             |         |        |        |                 |            |        | Cluster random sampling The core journal of China |                       |
| Cai and Luo [43]| Liaoning      | Cough more than 4 weeks                                                              | 0–14    | 329    | 9947   | 3.31           | 4          | Very low | Cluster random sampling The core journal of China |                       |
| Dong et al. [46]| Liaoning      | Cough more than 4 days per week for as much as 3 months of the year either with or apart from colds | School-age children, toddler | 1480 | 14,556 | 10.17          | 6          | Low    | Cluster random sampling Other |                       |
| Salo et al. [42] | Wuhan         | Cough almost every day in the absence of colds during the past 12 months             | 152 ±0.6| 176    | 4146   | 4.30           | 8          | Moderate | Cluster random sampling SCI   |                       |
| Liu et al. [51]  | Benxi         | Not mentioned                                                                        |         |        |        |                 |            |        | Cluster random sampling The core journal of China |                       |
| Dong et al. [59] | Liaoning      | Cough more than 4 days per week for as much as 3 months of the year                  | 1–13    | 1347   | 14,729 | 9.15           | 5          | Low    | Stratified random sampling SCI |                       |
| Wu [47]          | Shanghai      | Cough more than 3 weeks                                                               | 4–17    | 519    | 6551   | 7.92           | 4          | Low    | Cluster random sampling Other |                       |
| Niu et al. [52]  | Shanghai      | Cough on most days (64 days per week) for as long as 3 months of the year, either together with or separately from cold | 4–17    | 565    | 6551   | 8.60           | 5          | Low    | Stratified random sampling The core journal of China |                       |
| References       | City     | Diagnostic criteria                                                                 | Age (y) | Events | Total   | Prevalence (%) | Bias score | GRADEa | Source of information           | Journal classification |
|------------------|----------|--------------------------------------------------------------------------------------|---------|--------|----------|----------------|------------|--------|---------------------------------|------------------------|
| Pan et al. [53]  | Liaoning | Cough on most days (54 days per week) for as long as 3 months of the year, either together with or separately from cold | 3–12    | 1123   | 11,860   | 9.47           | 4          | Moderate | Cluster random sampling | SCI                    |
| Zhang et al. [50] | Zhongshan| Cough more than 4 weeks                                                              | 2–12    | 260    | 3947     | 6.587          | 5          | Low     | Cluster random sampling | The core journal of China |
| Gao [48]         | Wenzhou  | Cough more than 4 weeks                                                              | 0–14    | 1544   | 5843     | 26.42          | 5          | Very low | Cluster random sampling | Other                  |
| Huang et al. [41]| Zhongshan| Cough more than 4 weeks                                                              | 3–14    | 889    | 15,763   | 5.64           | 8          | Moderate | Cluster random sampling | The core journal of China |
| Li et al. [58]   | Lanzhou  | Cough more than 4 days per week for as much as 3 months of the year                  | 8–13    | 15     | 929      | 1.60           | 6          | Very low | Cluster random sampling | The core journal of China |
| Gao et al. [45]  | Hongkong | Not mentioned                                                                        | 8–10    | 104    | 2203     | 4.72           | 6          | Low     | Cluster random sampling | SCI                    |
| Wang et al. [60] | Liaoning | Cough more than 4 days per week for as much as 3 months of the year                  | 2–14    | 2846   | 30,056   | 9.47           | 5          | Low     | Stratified random sampling | SCI                    |
| Zhu et al. [57]  | Beijing  | Not mentioned                                                                        | 5–11    | 197    | 4241     | 4.65           | 5          | Low     | Cluster random sampling | The core journal of China |
| Fan et al. [44]  | Chongqing| Not mentioned                                                                        | 8–10    | 28     | 695      | 4.03           | 6          | Very low | Cluster random sampling | The core journal of China |
| Li et al. [49]   | Hebei    | Cough more than 4 weeks                                                              | 2–12    | 117    | 1602     | 7.30           | 4          | Low     | Random sampling            | Other                  |

*a* GRADE, The Grading of Recommendations Assessment, Development, and Evaluation [29]  
*b* SCI, Science Citation Index
The prevalence of older adults (9.89%; 95%CI: 8.78–11.00%) was higher than non-elderly adults (3.25%; 95%CI: 1.85–4.64%) significantly (Additional file 6: Fig. S5). The prevalence of random sampling is 5.63% (95%CI: 4.40–6.85%). The prevalence of the census-based study and the study without mentioning sampling are 2.24% (95%CI: 1.67–2.81%) and 24.04% (95%CI: 20.94–27.14%), respectively. Compared with the prevalence of all eligible studies, those of random sampling is slightly lower (Additional file 6: Fig. S6). The analyses considering other subgroups are shown in Additional file 6: Figs. S7–S10.

Further, a separate meta-analysis, using the random effects model, was performed on the studies with children according to same geographical subgrouping as for the studies with adults. In southern China, 7.45% (95% CI 5.50–9.41%) of the children presented with chronic cough, against 7.86% (95% CI 5.56–10.16%) in northern China (Additional file 6: Fig. S11). The pooled prevalence, according to the diagnostic criteria “cough lasting for more than four weeks”, “cough lasting for more than three months”, and “coughing more than four days per week during three months”, was respectively of 9.78% (95% CI 4.98–14.58%), 3.96% (95% CI 3.27–4.65%), and 8.10% (95% CI 6.35–9.85%) (Additional file 6: Fig. S12). When considering the different periods of publication, the pooled prevalence during the first period (1988–2004) was 6.65% (95% CI 4.90–8.40%), and sharply increased to 9.53% (95% CI 7.93–11.13%) during the second period (2005–2009). From the second to the fourth period, the prevalence of chronic cough in children showed a decreasing trend (Additional file 6: Fig. S13). The analyses considering other subgroups are shown in Supplementary Materials (Additional file 6: Figs. S14–S17).

### Bias and sensitivity analyses

Bias tests were performed on both the adult- and children-related studies. The funnel plots and by the Begg's test (z = 1.29, P = 0.198) indicated that there was no publication bias in the included studies on adults (Additional file 6: Fig. S18). We performed the sensitivity analyses by removing individual studies, which did not change the direction or significance of the pooled results, revealed that the pooled prevalence for the adult population was robust (Additional file 6: Figs. S19-S21). Similarly, no publication bias existed in the included studies involving children (Additional file 6: Fig. S22) (Begg's test: z = 1.22,
The sensitivity analyses revealed that the pooled prevalence for the children population was also robust (Additional file 6: Fig. S23).

**Discussion**

Our meta-analysis showed that the prevalence of chronic cough in China is 7.11% (6.22% in adults and 7.67% in children), suggesting that more than 90 million individuals in China are suffering from this condition [61] (Additional file 6: Fig. S24). Chronic cough continues being a major public health issue in China and worldwide, and should not be ignored. Although a meta-analysis reported a global prevalence of chronic cough of 9.6% (95% CI 7.6–11.7%), this previous study did not analyze the prevalence in China separately [12]. Considering the role of host-environment interactions in coughing, we thought that the prevalence of chronic cough in China might be different from the global prevalence. Therefore, data on global prevalence might be of limited value for the management of chronic cough in China.

Cough is one of the important reflexes of the respiratory system, and its mechanism is complex and has not been fully elucidated to date. Activation of TRPA1 and TRPV1 channels on airway sensory nerve terminals and airway inflammation involving various cytokines such as prostaglandins, IFN—γ, and ATP can induce cough [62–64]. Dysregulation of central regulation is also involved in the development of cough [65–67]. Drugs targeting on relevant channels are being developed. The antagonists of TRPA1, TRPV1 and the voltage-gated sodium channel (NaV1.7) showed poor effect [68–70], while P2X3 antagonists, neuropeptide receptor antagonists (NK-1 receptor antagonists) are promising, but further clinical trials are still needed [71, 72].

We found that the prevalence of chronic cough in China was lower than the global prevalence. [12] However, the research of global prevalence conducted by Song et al. [12] included studies covering on a shorter and earlier period from 1980 to 2013, while we included studies covering a period between 1988 and 2020. The number of participants enrolled through studies performed after
2013 represented a considerable proportion of the total participants. Our study also showed that the prevalence of chronic cough in children decreased during the past five years, compared with that between 2005 and 2014. The first guideline for cough in China was published in 2005 [73] and updated successively in 2009 [74] and 2015 [75]. We speculate that these updates, combined with a better understanding of the mechanisms of chronic cough, might have contributed to better management of chronic cough and lower prevalence in China. In addition, approximately half (48.89%) of the studies included in the meta-analysis performed by Song et al. [12] were focused on European populations, which presented a high prevalence (12.7%; 95% CI 10.4–15.2%) and might have biased the global prevalence. A nationwide investigation in China focused on adults over 40 years reported a prevalence of 5.3% for chronic cough, which is closer to the prevalence found for adults in our studies [31].

In adults, there were regional differences in the chronic cough prevalence within China, which was higher in northern than in southern China. To some degree, the prevalence of chronic cough was associated with the level of urbanization and severity of environmental pollution [75]. It has been reported that the concentration of air pollutants was higher in northern China than in southern China [76, 77]. Number of research reported that the air pollution is an important risk factor for chronic cough [19, 21, 32, 40, 49, 50]. The evidence mentioned above imply that environmental factors may account for the regional variation in the prevalence of chronic cough. Several studies showed that the prevalence of chronic cough in urban areas was higher than in countryside, suggesting that urbanization might also contribute to the regional variability [40, 50]. However, we were unable to examine this relationship because relevant information in the included studies was sparse.

The variability of the definitions of chronic cough between studies might have introduced some heterogeneity and affected the calculation of prevalence. However, subgroup analyses taking the definitions of chronic cough into account dramatically showed that the most stringent temporal definition, for both adults and children (adults:
more than 3 months; children: more than 4 days per week for as much as 3 months of the year) did not lead the lowest prevalence. Heterogeneity of prevalence still existed in all subgroups, without significant decrease, implying that other factors may contribute to this heterogeneity. The first Chinese Guideline for Cough was published in 2005 [73], using as temporal definition “more than or equal to 8 weeks for adults”. However, this still varied between studies published after edition, implying that the guideline was not strictly followed by Chinese researchers and clinicians. The same problem was also found in studies related to the child populations. In our opinion, poor compliance to this guideline could not only lead to misdiagnosis, but also create difficulties for the management of chronic cough in China. In the future, more effort should be made to reach a consensus definition and promote the guideline across China.

Differences between chronic cough in adults and children have been widely reported. The etiology of pediatric chronic cough included asthma, postinfectious cough, bronchiectasis, airway malacia, and protracted bacterial bronchitis. In contrast, common causes of chronic cough in adults are gastroesophageal reflux, asthma, and upper airway syndrome (e.g., post-nasal drip) [78]. In our studies, we found that the pooled prevalence of chronic cough in adults was lower than that of children (adults vs. children: 6.22% [95% CI 5.03–7.41%] vs. 7.67% [95% CI 6.24–9.11%]). We supposed that the mechanisms described thereafter might contribute to the higher prevalence in children. Cough serves to prevent the lung from inhaling noxious agents and clean the airway of unwanted secretions [79]. In adults, mucus glands constitute about 12% of the bronchial wall, whereas in children, this area is approximately of 17% [80], resulting in greater mucus secretion during childhood. In addition, cough is also a neuromuscular phenomenon involving various respiratory and extra respiratory muscles, and activation by multiple peripheral (e.g., vagal nerves) and central neural circuits of cough reflex [81]. Exposure of the airways to noxious agents may cause more damage in children than in adults. Moreover, chronic cough in infants and children may lead to a greater vulnerability to infections due to irreversible gene upregulation in the vagal afferent nerves by airway inflammation triggered by allergens or viral infections [64, 82].

The present study has several strengths. Firstly, many studies focused on patients with chronic cough in specialized care centers or in general practitioner’s office and reported the proportion of chronic cough based on population for medical care. However, the proportion only based on population for medical care would overestimate the prevalence of general population. To our knowledge, our study is the first comprehensive review on the prevalence of chronic cough in China. In addition, we included only population-based data, which limited selection bias. Besides, the latest versions of the PRISMA and PROSPERO protocol were strictly observed, which makes our results more reliable.

Yet, we acknowledge several limitations in our study. First, the definitions of chronic cough were heterogeneous [83], and thus, the estimation of the prevalence might be biased. Second, our studies only covered 12 provinces or autonomous regions, which might have skewed the prevalence estimation for the whole China. Third, significant heterogeneity exists in our study. Despite our effort, the source of heterogeneity could not be identified because of the limited information in the primary studies. The effect of sex on the prevalence of chronic cough was controversial. Difference of prevalence between male and female could not be explored because of limited information in the included studies. Likewise, ethnic background was not emphasized in the included studies, for the relevant information was limited. However, further research focusing on the population of ethnic would be valuable. Finally, recall bias cannot be avoided in our study.

Although limitations exist, the present meta-analysis provides relatively robust results of the prevalence of chronic cough. The differences between northern and southern China suggest that the prevalence of chronic cough might be influenced by environmental factors. The methodological inconsistencies in the studies of chronic cough in China suggest that there is an urgent need for promoting the corresponding guidelines across China and standardizing the definition of chronic cough. What’s more, although the included studies were published before the COVID-19 pandemic, there is insufficient evidence to consider that the prevalence of chronic cough has significantly changed during the COVID-19 pandemic in China [84]. Hence, our data are still applicable now. Besides, because of the widespread fear of cough in the community, it’s significant to call for more social and academic attention to the impact and burden of cough in patients with chronic cough in this pandemic conditions.

Conclusions

This systematic review and meta-analysis provided relatively reliable data on the prevalence of chronic cough in China (6.22% in adults and 7.67% in children), which may help developing global strategies for chronic cough management.

**Abbreviations**

AHRQ: Agency for Healthcare Research and Quality; CI: Confidence intervals; ES: Effect size; GRADE: The Grading of Recommendations Assessment, Development, and Evaluation; PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses; SCI: Science Citation Index.
Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-022-01847-w.

Additional file 1. Search strategies.
Additional file 2. Cross-sectional/prevalence study quality.
Additional file 3. Exclusion with reasons.
Additional file 4. Quality assessment of the included articles according to scale of Agency for Healthcare Research and Quality.
Additional file 5. Methodology of studies included in the meta-analysis.
Additional file 6. Fig. S1. Distribution of children with chronic cough across Mainland China. NOTE: Red star in the map represents Beijing City. The map was developed in XL Toolbox NG by ourselves, without the conflict of copyright. Fig. S2. Pooled chronic cough prevalence of adults stratified by region. Abbreviations: CI, confidence intervals. NOTE: The three author labels of ZHANG JF 1999 are from the same literature, and the two author labels of Venners 2001 are from the same literature. Fig. S3. Pooled chronic cough prevalence of adults stratified by diagnostic criteria. Abbreviations: CI, confidence intervals. NOTE: The three author labels of ZHANG JF 1999 are from the same literature, and the two author labels of Venners 2001 are from the same literature. Fig. S4. Pooled chronic cough prevalence of adults stratified by year of publication. Abbreviations: CI, confidence intervals. NOTE: The three author labels of ZHANG JF 1999 are from the same literature, and the two author labels of Venners 2001 are from the same literature. Fig. S5. Pooled chronic cough prevalence of adults stratified by age. Abbreviations: CI, confidence intervals. NOTE: The three author labels of ZHANG JF 1999 are from the same literature, and the two author labels of Venners 2001 are from the same literature. Fig. S6. Pooled chronic cough prevalence of adults stratified by sampling methods. Abbreviations: CI, confidence intervals. NOTE: The three author labels of ZHANG JF 1999 are from the same literature, and the two author labels of Venners 2001 are from the same literature. Fig. S7. Pooled chronic cough prevalence of adults stratified by sample size. Abbreviations: CI, confidence intervals; ES, Effect Size. NOTE: The three author labels of ZHANG JF 1999 are from the same literature, and the two author labels of Venners 2001 are from the same literature. Fig. S8. Pooled chronic cough prevalence of adults stratified by prevalence definitions. Abbreviations: CI, confidence intervals. NOTE: The three author labels of ZHANG JF 1999 are from the same literature, and the two author labels of Venners 2001 are from the same literature. Fig. S9. Pooled chronic cough prevalence of adults stratified by sample size. Abbreviations: CI, confidence intervals. NOTE: The three author labels of ZHANG JF 1999 are from the same literature, and the two author labels of Venners 2001 are from the same literature. Fig. S10. Pooled chronic cough prevalence of adults stratified by quality of articles assessed by AHRQ. Abbreviations: CI, confidence intervals; ES, Effect Size. NOTE: The three author labels of ZHANG JF 1999 are from the same literature, and the two author labels of Venners 2001 are from the same literature. Fig. S11. Pooled chronic cough prevalence of children stratified by region. Abbreviations: CI, confidence intervals. NOTE: The four author labels of ZHANG JF 2002 are from the same literature. Fig. S12. Pooled chronic cough prevalence of children stratified by diagnostic criteria. Abbreviations: CI, confidence intervals. NOTE: The four author labels of ZHANG JF 2002 are from the same literature. Fig. S13. Pooled chronic cough prevalence of children stratified by year of publication. Abbreviations: CI, confidence intervals. NOTE: The four author labels of ZHANG JF 2002 are from the same literature. Fig. S14. Pooled chronic cough prevalence of children stratified by sample size. Abbreviations: CI, confidence intervals. NOTE: The four author labels of ZHANG JF 2002 are from the same literature. Fig. S15. Pooled chronic cough prevalence of children stratified by prevalence definitions. Abbreviations: CI, confidence intervals. NOTE: The four author labels of ZHANG JF 2002 are from the same literature. Fig. S16. Pooled chronic cough prevalence of children stratified by quality of articles assessed by AHRQ. Abbreviations: CI, confidence intervals. NOTE: The four author labels of ZHANG JF 2002 are from the same literature. Fig. S17. Pooled chronic cough prevalence of children stratified by prevalence definitions. Abbreviations: CI, confidence intervals.

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Authors’ contributions
Study concept and design: MJ, KFL, HWL; Acquisition of data: WYY, ZFW, JYL; Analysis and interpretation of data: HWL, MJ; Writing – original draft: HWL, WYY; Writing – review & editing: HWL, WYY, ZFW, JYL, MJ, FY; Study supervision: MJ, KFL, FY; All authors had full access to the data and take responsibility for the integrity of the data and accuracy of the analysis. MJ is guarantor. All authors read and approved the final manuscript.

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Competing interests
All authors declare that they have no competing interests.

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