

Review Article

Detection rate of psychogenic cough in patients with chronic cough in Chinese hospital: a meta analysis

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Abstract: Objective: This study aimed to systematically evaluate the prevalence of psychogenic cough in patients with chronic cough in China by meta-analysis, which may provide evidence for the empirical diagnosis and treatment of chronic cough and for the updating of related guidelines. Methods: Based on the pre-defined inclusion and exclusion criteria, studies were searched in databases. Studies (English or Chinese) published before June 2015 were collected, and the prevalence of psychogenic cough in Chinese patients with chronic cough was analyzed. Results: The overall prevalence of psychological cough was 3.02% (95% CI: 2.53%-3.60%). There were heterogeneity and publication bias among these studies. Subgroup analysis: the prevalence of psychological cough in children was lower than in other patients (2.82%, OR=0.90, 95% CI: 2.21%-3.59%); the prevalence of psychological cough in children aged 7-14 years was higher than in children aged 3-6 years (6.22%, OR=2.14, 95% CI: 4.30%-8.90%); the prevalence of psychological cough in first class hospitals was lower than in other hospitals (2.73%, OR=0.66, 95% CI: 2.26%-3.30%); the prevalence of psychological cough in southern coastal areas was higher than in northern coastal areas, southern inland areas and northern inland areas and northern inland areas, respectively (3.94%, 95% CI: 3.11%-4.98%, OR=2.18, 1.56 and 1.53) (P<0.05 for all). Conclusion: In available studies, the prevalence of psychological cough in Chinese inpatients with chronic cough is 3.02% and higher in non-paediatrics departments, school-age children, non-first class hospitals and southern coastal areas. There are heterogeneity and publication bias in available studies.

Keywords: Cough, epidemiology, meta-analysis

Introduction

Psychogenic cough refers to the chronic cough due to serious psychological problems and has descriptive and exclusive diagnostic features. The typical symptom is daytime cough [1], but it never occurs during sleep or when the patient focuses on a thing. In addition, it is often accompanied by symptoms of anxiety [2]. Psychogenic cough is also known as “barking cough of puberty” [3], psychogenic cough tic [4], operant cough [5], neurogenic cough [6], psychogenic habit cough [7], “psychogenic cough”, “habit cough”, “neurogenic cough”, “cough related to psychological factors” and “Somatic Cough Syndrome” [8]. In the present study, psychogenic cough as recommended in

the Chinese Guideline for the Prevention and Treatment of Cough was used.

Psychogenic cough is an uncommon cause of chronic cough, and the diagnostic criteria for psychogenic cough are still controversial, which usually cause misdiagnosis and missed diagnosis [9]. In China, psychogenic cough was not reported [10, 11] or included in the unknown causes in studies focusing on the causes of chronic cough [12-15]. However, the exclusive diagnostic feature of psychogenic cough suggests that the diagnosis of psychogenic cough can not be neglected, and increasing attention has been paid to the diagnosis of psychogenic cough in recent years [16]. In available studies, the proportion of psychogenic cough as a cause

of chronic cough varies between studies, and studies on psychogenic cough are usually conducted in either children or other populations. To date, no study has been conducted to systematically analyze the prevalence of psychogenic cough in Chinese patients. In this study, the prevalence of psychogenic cough was investigated since the publication of guidelines of Paediatrics Department [1] and Respiratory Department [17], aiming to provide evidence for the empirical diagnosis and treatment of psychogenic cough and for the modification of guidelines.

Methods

Literature searching

Two authors independently searched the PUBMED, EMBASE, Chinese Biological Literature Service System (CBM), Chinese National Knowledge Infrastructure (CNKI), Chinese Science and Technology Journal Databases (VIP), Wangfang Databases and master and doctor thesis database. Studies in English and Chinese and reporting the psychogenic cough in Chinese inpatients with chronic cough were searched, and studies were published before June 17, 2015. The Chinese terms for searching included 1) psychological cough, psychogenic cough, habit cough, and neurogenic cough; 2) cough and chronic cough; 3) Neurosis; depression; depressive neurosis; anxiety; anxiety disorder; neurasthenia; hypochondriac; obsessive-compulsive disorder; phobia; hysteria; mental disorder; mental illness; psychiatric; somatic disorder; conversion disorder. 4) Pandemics; prevalence; incidence. The English terms included 1) Psychogenic cough; Habit cough; tic cough; vocal tic; operant cough; barking cough; nervous cough; Psychogenic habit cough; functional cough; honking cough; Involuntary cough. 2) Cough; chronic cough. 3) mental; depression; anxiety; Psycho*; stress; somatic. (4) Prevalence; inciden*; epidemic*; rate. Studies were confined to humans. In addition, the references of identified literatures were also manually searched for more studies.

Screening of literatures

Inclusion criteria: 1) Observational studies and epidemiological studies on current situation; 2) chronic cough inpatients with psychogenic

cough were included; 3) The diagnosis of chronic cough patients in non-pediatrics departments (≥ 14 years) was based on the guideline developed by the Asthma Group of Respiratory Diseases Branch (duration of cough: >8 weeks) [2, 17]; the diagnosis of chronic cough patients in department of pediatrics (<14 years) was based on the guideline developed by the Respiratory Disease Group of Pediatrics branch (duration of cough: >4 weeks); (4) The detection rate of psychogenic cough was present in studies or data available in studies were able to be used to calculate the detection rate of psychogenic cough.

Exclusion criteria: 1) Patients did not meet the diagnostic criteria for chronic cough; 2) Data were abnormal or incomplete, or data extraction was impossible; 3) Different studies focused on the sample patient population or the same data were used repeatedly; studies with incomplete data were excluded; 4) non-human studies were excluded; 5) review, case report, comment, meeting minutes and studies with incomplete publication were excluded; 6) studies with incomplete or unclear information were excluded.

Literatures were input into EndnoteX5, and repeated literatures were excluded. Then, two authors screened the remaining literatures. Initial screening was conducted by reviewing the titles and abstracts, which was confirmed by reading the full text. Whether the study was included was based on the exclusion criteria. Any discrepancy was resolved by discussion with a third author.

Data extraction

All the data were extracted by two authors independently and then cross-checked, and any discrepancy was resolved by discussion with a third author.

Quality assessment

According to the Strengthening the Reporting of Observational studies in Epidemiology (STROB) [18, 19], the quality of title, abstract, introduction, methods, results and discussion were assessed. A total of 22 items were assessed, and each has a score of 1 with the total score of 22. Assessment was done by two authors independently and an average was obtained.

Psychogenic cough detection in chronic cough patients

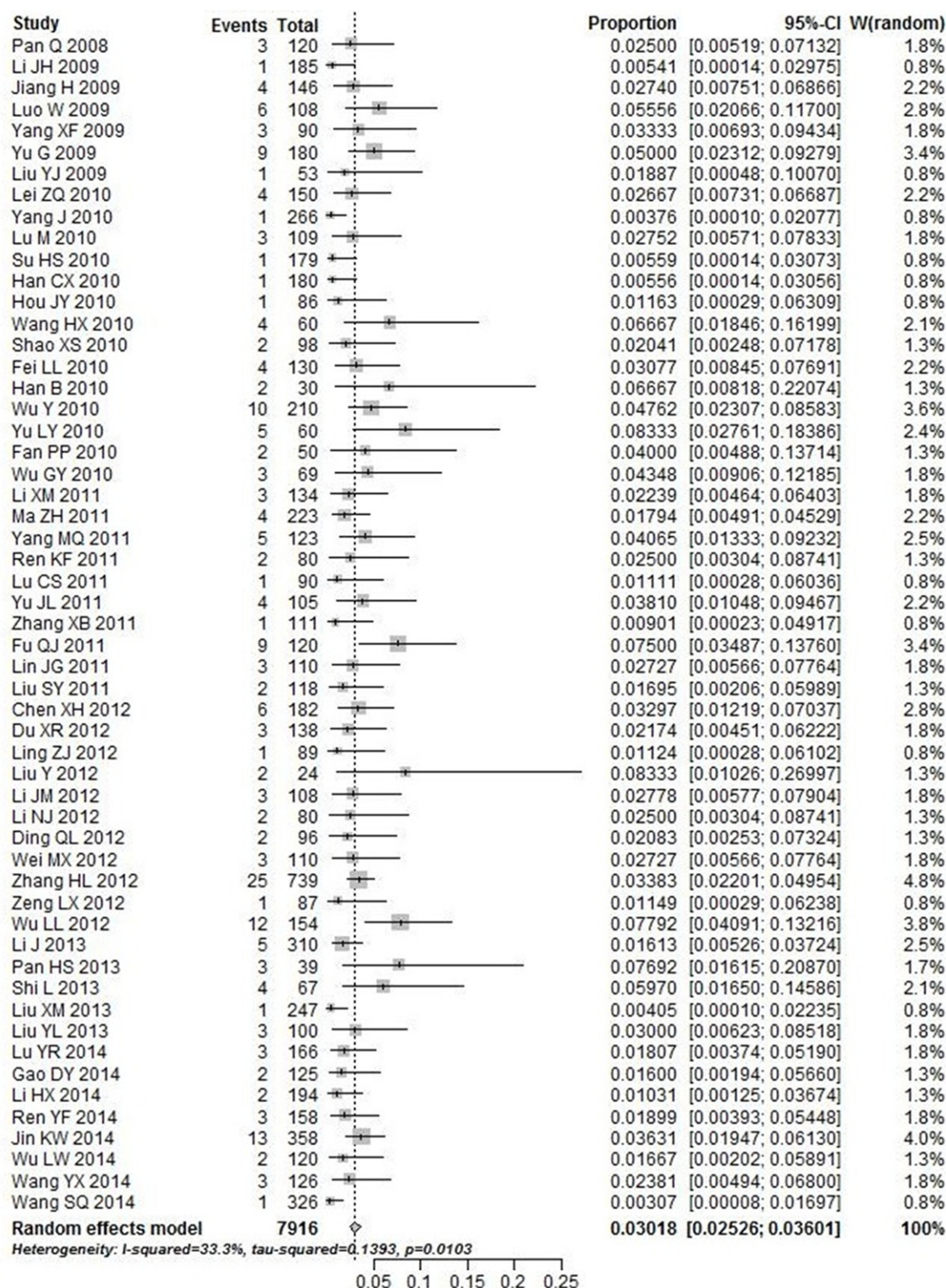


Figure 1. Forest plot of detection rate of psychogenic cough in Chinese inpatients with chronic cough.

Statistical analysis

The extracted data were subjected to meta analysis with R-3.1.2 software. Each detection

rate was subjected to double arcsine conversion, and the combined value was calculated according to the weight of sample size in each study. Finally, the reverse conversion was con-

Psychogenic cough detection in chronic cough patients

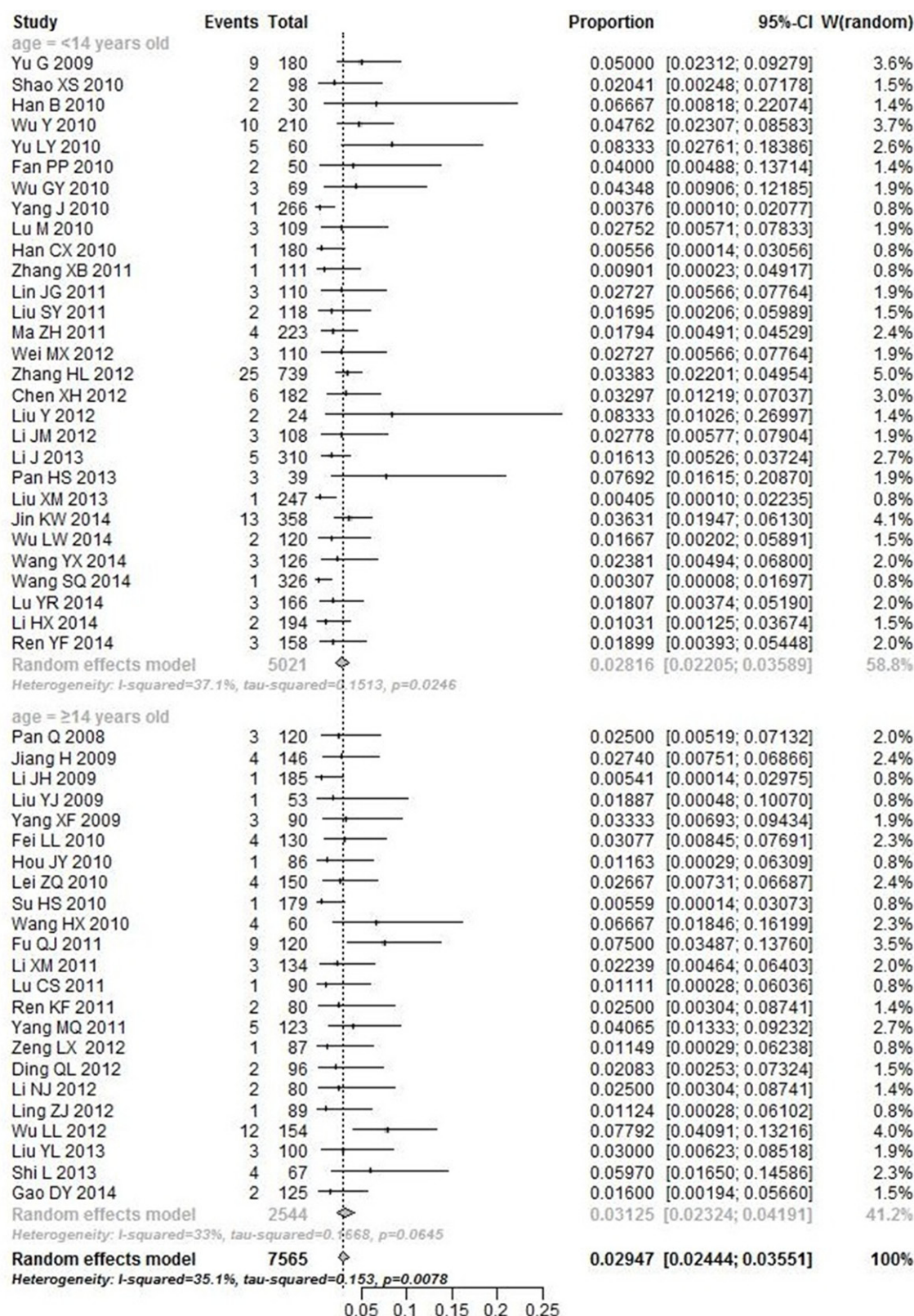


Figure 2. Forest plot of detection rate of psychogenic cough in paediatrics department and non-paediatrics departments.

Psychogenic cough detection in chronic cough patients

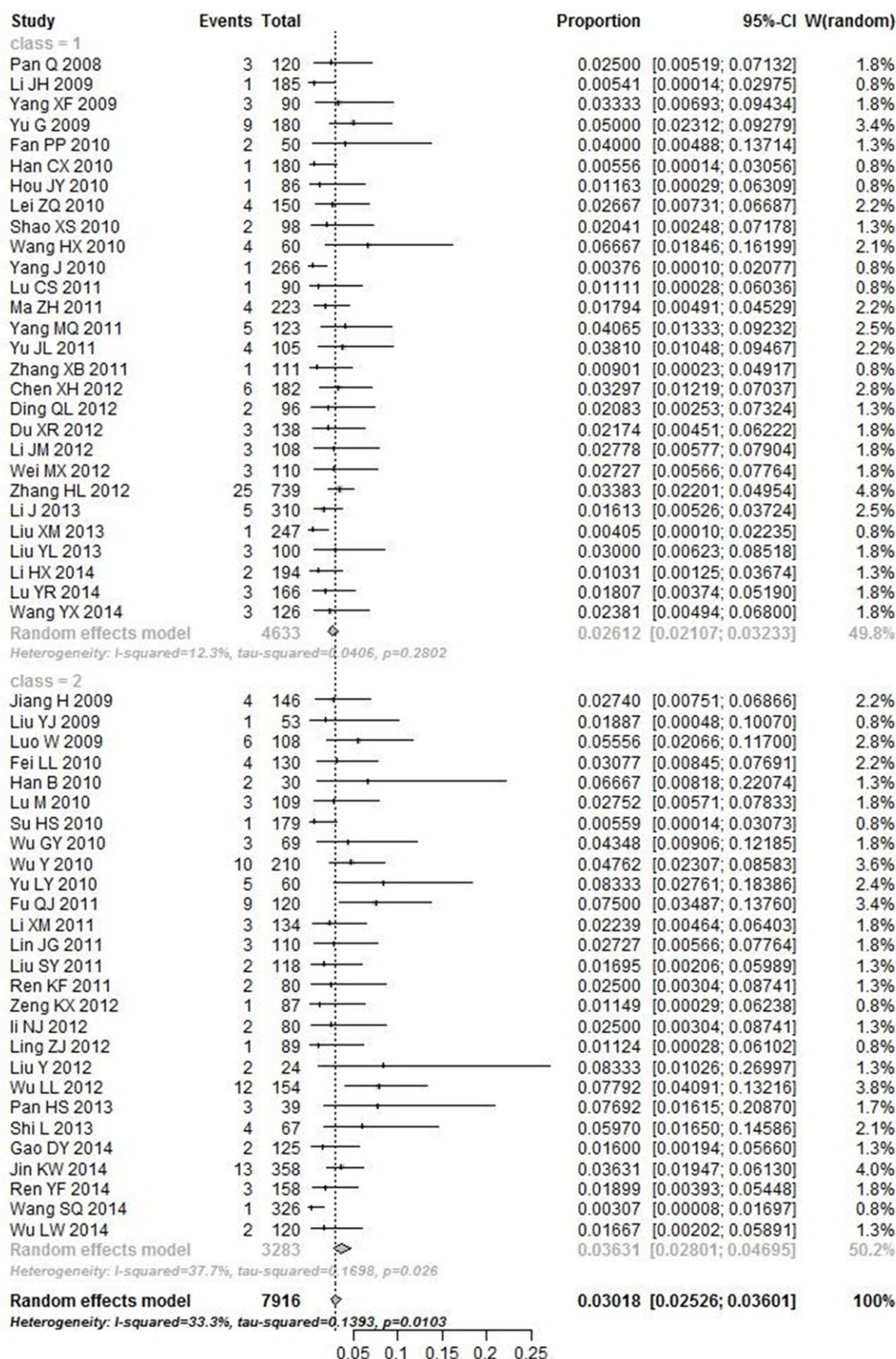


Figure 3. Forest plot of detection rate of psychogenic cough in first class hospitals and non-first class hospitals.

Psychogenic cough detection in chronic cough patients

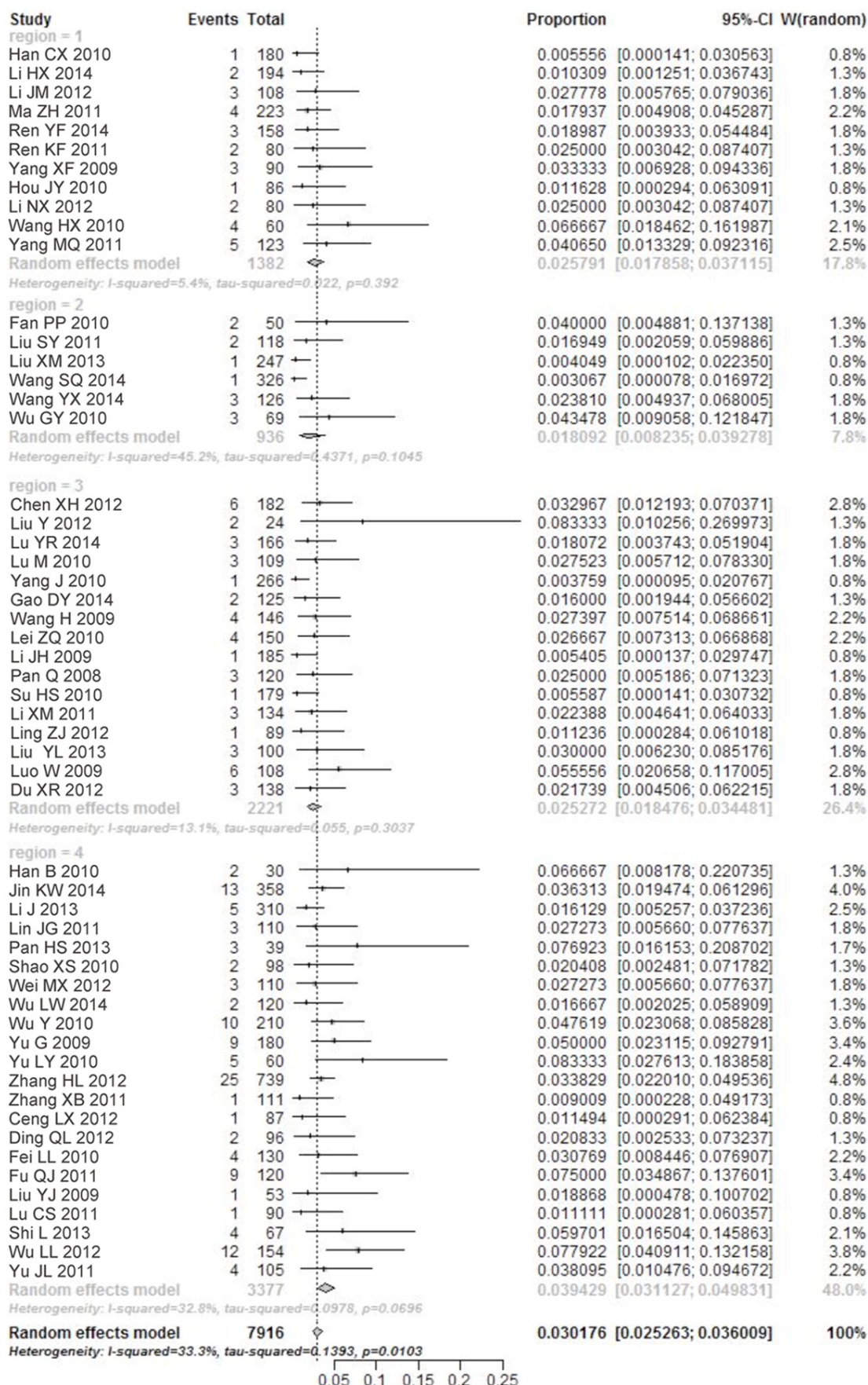


Figure 4. Forest plot of detection rate of psychogenic cough in Northern inland areas, northern coastal areas, southern inland areas and southern coastal areas.

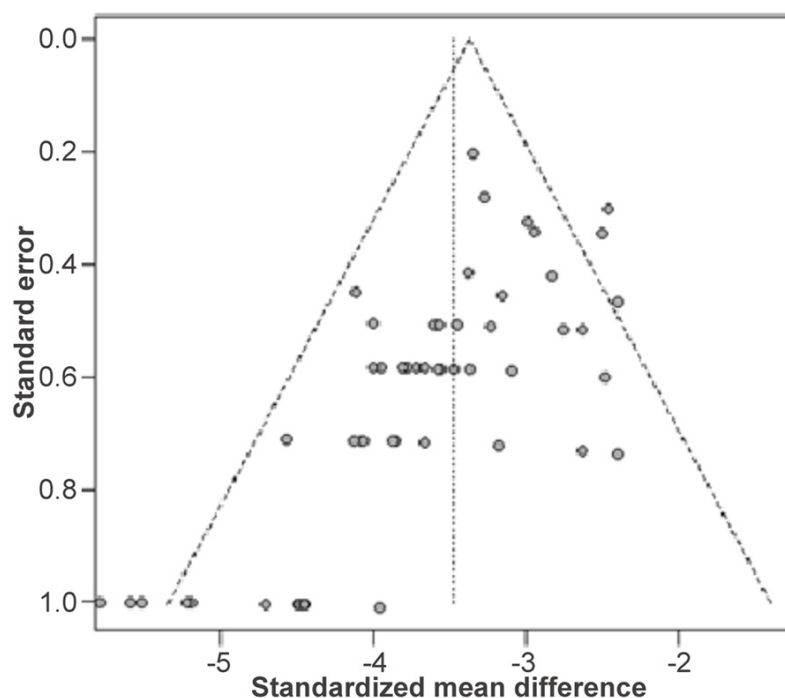


Figure 5. Funnel plot of detection rate of psychogenic cough in Chinese in patients with chronic cough.

ducted to obtain the combined detection rate and its 95% confidence interval. The heterogeneity was examined with Homogeneity test (Q test; $\alpha=0.1$). At the same time, the heterogeneity was quantified with I^2 . The P of ≥ 0.10 and I^2 of $\leq 50\%$ suggest the homogeneity and fixed effects model was used for meta analysis; on the contrary, there was heterogeneity, and random effects model was used. Publication bias was tested with Eggers' test. After removing the studies with the lowest quality, the combined value was re-calculated for the analysis of sensitivity with $\alpha=0.05$. According to the factors potentially affecting the heterogeneity among studies, subgroup analysis was conducted. To differentiate different age groups and different groups determined by guidelines, age groups included children group (preschool children: 3-6 years; school children: 7-14 years) and non-children group (>14 years); different area groups included Northern coastal group, northern inland group, southern coastal group and southern inland group. The China mainland is divided into northern China and southern China along the Qinling-Huaihe line. The north-

ern China includes Beijing, Tianjin, Hebei, Shanxi, Inner Mongolia Autonomous Region, Liaoning, Jilin, Heilongjiang, Shanghai, Gansu, Qinghai, Ningxia Hui Autonomous Region, Xinjiang Uygur Autonomous Region, Shandong and Henan). The southern China includes Jiangsu, Zhejiang, Shanghai, Hubei, Hunan, Sichuan, Anhui, Chongqing, Guizhou, Yunnan, Guangxi Zhuang Autonomous Region, Jiangxi, Fujian, Guangdong, Hainan and Tibet Autonomous Region. According to the Problems in the Division between Coastal Cities and Inland Cities (State Planning Commission and National Bureau of Statistics) in 1982, the coastal regions include Liaoning, Hebei, Beijing,

Tianjing, Shandong, Jiangsu, Shanghai, Zhejiang, Fujian, Guangdong, Guangxi, Hainan, Taiwan and Aomen. The hospitals are divided into first class hospitals and non-first class hospitals. For statistical analysis, t test, analysis of variance and Wilcoxon signed rank test were employed for the comparisons of detection rates among studies depending the characteristics of data.

Results

Baseline characteristics of included studies

A total of 1155 studies were identified, and finally, 55 studies were included for analysis. All of them were published in Chinese and from China mainland.

Quality evaluation

STROBE assessment showed the lowest score was 9 and the highest score was 20 with a mean score of 14 ± 3 . Moreover, results published in these studies were reliable ($ICC=0.88$). Of these studies, 10 had the score of ≤ 11 , sug-

gesting a low quality, and following factors affected the quality of these studies: missing values were not addressed in 96.35% of studies, rationale determining the sample size was not described in 98.18% of studies, follow up was not conducted to modify the diagnosis in 61.82% of studies, and the characteristics of patients and/or specific therapies were not introduced in 14.55% of studies.

Heterogeneity test

There was Heterogeneity among 55 studies included ($I^2=33.3\%$, $P=0.010$, $P<0.1$) and thus Random effects model was used for further analysis. In addition, subgroup analysis was performed on the basis of potential confounding factors.

Sensitivity analysis

Studies with score of ≤ 11 were deleted, and the combined rate was 2.91%. After stepwise deletion of studies with a low quality, the I^2 increased slightly without significance. This implies that the quality of included studies has little influence on the results, and combined results are stable.

Combination of effect value and subgroup analysis

Overall detection rate: After weighted combination of all the studies, the overall detection rate of psychogenic cough was 3.02% (95% CI: 2.53%-3.60%) (**Figure 1**).

Detection rate in subgroups: (1) Grouping according to diagnostic criteria and age: On the basis of guideline developed by the Asthma Group of Respiratory Diseases Branch, the combined detection rate was 3.13% (95% CI: 2.32%-4.19%) in non-pediatrics departments; on the basis of guideline developed by the Respiratory Diseases Group of Pediatrics Branch, the combined detection rate was 2.82% (95% CI: 2.21%-3.59%). The detection rate in pediatrics department was significantly lower than in non-pediatrics departments (OR=0.90, $\tau^2=0.0153$, $P<0.001$) (**Figure 2**). In addition, the detection rate in children aged 7-14 years was significantly higher than in children aged 3-6 years (6.22%, OR=2.14, 95% CI: 4.30%-8.90%, $\tau^2=0.2433$, $P<0.001$). (2) In first class hospitals, the detection rate was sig-

nificantly lower than in non-first class hospitals (2.73%, OR=0.66, 95% CI: 2.26%-3.30%, $\tau^2=0.139$, $P=0.0210<0.05$) (**Figure 3**). (3) In northern inland areas, northern costal areas, southern inland area and southern costal areas, the combined detection rate was 2.58% (95% CI: 1.79%-3.71%), 1.81% (95% CI: 0.82%-3.93%), 2.53% (95% CI: 1.85%-3.45%) and 3.94% (95% CI: 3.11%-4.98%), respectively, showing significant difference among these groups ($\tau^2=0.139$, $P=0.030176<0.05$) (**Figure 4**).

Evaluation of publication bias

Egger funnel plot was delineated with 55 studies (**Figure 5**). Although the funnel plot was relatively symmetrical, Egger's test showed $P<0.001$, suggesting a publication bias.

Discussion

Main findings

In this study, we for the first time conducted interdisciplinary meta analysis of detection rate of psychogenic cough in Chinese inpatients with chronic cough, and subgroup analysis was performed according to the diagnostic criteria, age, areas and hospital level.

A total of 55 studies published in Chinese were included in this meta analysis. Results showed the overall detection rate of psychogenic cough was 3.02% (95% CI: 2.53%-3.60%) in Chinese inpatients with chronic cough. Factors affecting the detection rate included age, hospital level and areas. The detection rate in non-pediatrics departments, school children, non-first class hospitals and southern costal areas was significantly higher than in pediatrics department, pre-school children, first class hospital and other areas, respectively.

There was heterogeneity among studies and stratified analysis reduced the heterogeneity among studies. In the present study, the overall detection rate was slightly lower than in previous studies (5% [20] and 5.7% [21]). This discrepancy may be related to the differences in the inclusion criteria, patients' selection, areas, races, seasons, diets and sample sizes. Of these factors, the most important factors are the definition and diagnostic criteria of psychogenic cough which vary between countries.

In this study, subgroup analysis was conducted according to the different guidelines. Although the duration of cough changing from 4 weeks to 8 weeks tended to reduce the detection rate in non-pediatrics department, the detection rate in non-pediatrics department was still markedly higher than in pediatrics department. This may be explained as follows: (1) In adolescents and adults, the social pressure is higher and they pay more attention to their health; (2) the content and statistical method were different. The recent 2 editions of guideline for non-pediatrics patients are highly consistent, and studies on non-pediatrics patients were recruited within 9 years; (3) Tic disorders are more likely diagnosed as psychogenic cough in non-pediatrics department, especially in adolescents. Tic disorders and psychogenic cough share the psychological symptoms, but symptoms of tic disorders occurs unconsciously and may stopped spontaneously within short time. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM; 5th edition), tic disorders are classified as Tourette syndrome, chronic motor or vocal tic disorder, and transient tic disorder. The simple vocal tic disorder and Tourette syndrome with neglected manifestations of motor tic disorder should be paid attention to, and both of them might be misdiagnosed as psychogenic cough [22, 23]. Patients with tic disorders are no older than 18 years and most patients with tic disorders are aged 10-12 years [24]. In recent years, non-pediatrics guideline broadly addresses this disease [2]. Physicians in non-pediatrics departments are not familiar with the tic disorders with a low incidence, which may reduce the detection rate in non-pediatrics departments [25]. Thus, it is should be emphasized in the modification of specific guideline. Subgroup analysis according to age showed the detection rate in children aged 7-14 years was higher than in pre-school children aged 3-6 years, which may be associated with environmental change and academic pressure. These findings were consistent with previously reported [26].

Subgroup analysis according to the hospital level indicated that the detection rate of psychogenic cough in first class hospitals was markedly lower than in non-first class hospitals, which may be explained as follows: (1) complete adjunctive examinations reduce the misdiagnosis of psychogenic cough (bronchoscopy

is helpful for the diagnosis of bronchial lesions with secondary anxiety; 24 hour esophageal pH-monitoring is helpful for the diagnosis of gastroesophageal reflux cough). Thus, it reduces the possibility of secondary psychological symptoms misdiagnosed as psychogenic cough; (2) there is psychosomatic department in first class hospital, and some patients are diagnosed as having somatization disorder. Chronic cough is often accompanied by anxiety, depression and obsessive-compulsive disorder [22]. In available guideline for chronic cough, the objective diagnostic criteria for psychogenic cough are not clearly addressed. In non-first class hospitals without psychosomatic department, the misdiagnosis rate of psychogenic cough will increase; (3) the statistical method used for the analysis of psychogenic cough is different among hospitals of different levels. In 71.4% of studies from first class hospitals (n=20), there were patients with chronic cough of unknown causes; in non-first class hospitals, only 40.7% of studies (n=11) had patients with chronic cough of unknown causes. The chronic cough of unknown causes may cause misdiagnosis and bias our results; (4) the sample size is different between studies.

Subgroup analysis according to the areas showed the detection rate in southern costal areas was significantly higher than in inland areas and northern areas, which may be related to the rapid economic development and the higher pressure of work and living in southern costal areas.

In this study, the difference in the definition of chronic cough between different guidelines should be paid attention to. The guideline of Asthma Group of Respiratory Diseases Branch [2, 17] recommends the duration of cough should be longer than 8 weeks, but the guideline of Respiratory Diseases Group of Pediatrics Branch [1] recommends the duration of cough should be longer than 4 weeks. In addition, there is no clear cut-off age in both guidelines. In different countries, the cut-off age for children is different. In USA, UK and Belgium, the maximum age of children is 15 years, 12 years and 18 years, respectively [27-29]. In the present study, the maximum age of children was defined as 14 years according to the definition of Population Fund of United Nation. Thus, the guideline is freely used due to the unclear cut-

off age for children [25, 30, 31] (these studies were excluded in this meta analysis). In addition, following aspects should be improved: the description of patients' number in the diagnosis, follow up to confirm or modify the diagnosis and determination and therapy of specific disease among psychosomatic diseases.

Limitations

There were following limitations in this study: (1) Inpatients with chronic cough were investigated in this study. In China, no study has been conducted to investigate the epidemiology of psychogenic cough in general population, and thus it is difficult to analyze the incidence and prevalence of psychogenic cough; (2) The differences in the guidelines and cut-off age for children may affect our results. Especially in adolescents visiting the adult section, the cut-off age for children (4 weeks from guideline for pediatrics department to 8 weeks from guideline for non-pediatrics department) may reduce the detection rate of psychogenic cough in adolescents; (3) The diagnosis of psychogenic cough is confined to the field of cough and has no involvement of psychosomatic diseases; (4) In respect of causes of chronic cough, studies which investigated psychogenic cough or non-psychogenic cough, but had incomplete data were not included in meta analysis, which may increase the detection rate. (5) In the subgroup analysis, there is lacking of information for the analysis in different age groups and thus it is difficult to uncover the difference among adolescents, adults, menopausal patients and old patients. In addition, there is evidence showing that the prevalence of psychogenic cough is comparable between males and females [32], but a study in China showed the difference in the prevalence of psychogenic cough between males and females [33]. Thus, the difference between males and females is required to be further confirmed.

Significance

In the diagnosis of psychogenic cough, other causes of chronic cough (such as upper airway cough syndrome) should be excluded. Although psychogenic cough is an uncommon cause of chronic cough, the diagnosis of psychogenic cough should also be paid attention to. On one hand, it is necessary to elucidate the definition of psychogenic cough and to explore the objec-

tive scale and laboratory indicators for the diagnosis of psychogenic cough; on the other hand, the diagnostic criteria should reach a consensus in patients of different age groups, or the cut-off age for children should reach a consensus before the diagnosis of psychogenic cough. In addition, physicians may cooperate with those in Psychosomatic Division to conduct epidemiological survey on psychogenic cough and to explore the cause of psychogenic cough in psychogenic diseases.

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Disclosure of conflict of interest

None.

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