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A Systematic Review of the Prevalence of Acne in Mainland China

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Abstract

Introduction Acne, a very common skin disease, can result in psychological distress and sustained impairment in quality of life. Data on the prevalence of acne and their difference in gender, region and age is sketchy. The aim of this review is to estimate the prevalence of acne in mainland China comprehensively and to quantify its association with gender, region and age.

Methods We searched electronic databases with predetermined search terms to identify relevant studies published between January 1, 1996 and September 30, 2016. We pointed out repeated results using Note Express software and evaluated the studies for inclusion. Two independent reviewers extracted data. Then statistical analyses were performed using Comprehensive Meta-Analysis version 2.0. A random-effects model was adopted to calculate the overall pooled prevalence and to merge categories, including gender, region and age for subgroup analyses. Logistic meta-regression analysis was used to clarify the associations between acne and the predictors age, gender, and region using odds ratios and their associated 95% confidence intervals.

Results 25 relevant studies were included in this meta-analysis. The overall pooled prevalence rates of acne were 39.2% (95% CI=0.310-0.479). The prevalence rates in different age groups were 10.2% overall (95% CI=0.059-0.171), 50.2% for primary and secondary students (95% CI=0.451-0.554), and 44.5% for undergraduates (95% CI=0.358-0.534); by gender, the prevalence rates were 35.7% for females (95% CI=0.274-0.451) and 39.7% for males (95% CI=0.317-0.482); and by region, the prevalence rates were 34.2% for northern China (95% CI=0.242-0.458) and 46.3% for southern China (95% CI=0.374-0.555). The associations between acne and the predictors age, gender, and region were statistically significant.

Conclusions In mainland China, primary and secondary students exhibited higher prevalence rates than undergraduate students, males had higher prevalence rates of acne than females, and the prevalence rates of acne in southern China was higher than northern China.

Strengths and limitations

To our knowledge, this was the first meta-analysis of its scope which will give us a detailed understanding of the prevalence of acne in mainland China and its associations with age, gender, and region and provide a sound basis for the future provision of health services.

This systematic review, covering 12 different provinces, represents near-complete capture of the demographic for more than 80 thousand people over a 41-year period.

Some limitations should be considered: the diagnostic criteria for acne differed among included studies; the age of the survey population could not be subdivided.

Introduction

Acne, a very common skin disease among adolescents, was the fourth most common reason for patients aged 11–21 years to visit a doctor in the USA[1]. In addition, there is increasing epidemiological data suggesting that acne also affects a considerable number of adults[2,3] and women are more frequently affected by adult acne than men[4]. Several studies have shown that the estimated prevalence rate of acne varies from 8.1% to 85.1% in China[5-7], depending on the region, subjects' ages, and the nationality studied.

The clinical features of acne include papules, pustules, cysts, comedos, and nodules. Acne occurs primarily on the face, neck, and upper trunk and can lead to scar formation if treated improperly. Thus, acne can result in psychological distress and

have profound effects on patients' self-esteem, may leading to anxiety, depression, diminished self-confidence, and communication difficulties[8, 9].

To date, many large population-based studies have been conducted to estimate the prevalence rates of acne in regional populations. Because China comprises 34 province-level administrative regions, with 56 nations and a population of 1.3 billion people, a country-wide, population-based study of the prevalence rates of acne in China was needed.

In this review, we examined the prevalence of acne in mainland China systematically and to analyse the effects of gender, region and age on acne.

Methods

Search strategy

Studies were aggregated from six databases between January 1, 1996 and September 30, 2016, including PubMed, EMBASE, the Web of Science, the China National Knowledge Infrastructure, the VIP Database for Chinese Technical Periodicals, and the Wan Fang Database for Chinese Periodicals. In addition, a manual search was performed by checking the reference lists of the reports that were examined. The following search terms were used to retrieve relevant studies, (acne), (prevalence or incidence) AND (China or Chinese).

Inclusion criteria

Studies that met all of the following criteria were included in the meta-analysis,

(1) the study was a population-based survey;

(2) the study evaluated the prevalence/incidence of acne;

(3) the investigation involved random sampling or cluster sampling;

(4) the sample size was >300;

A flow chart illustrating the article search process is presented in Figure 1.

Data management

Any duplicate studies was removed by Note Express. Two reviewers(Qiang Chen and Danhui Li) independently evaluated the title and abstract of all studies identified through the search against the inclusion and exclusion criteria. The full text of all eligible studies will then be retrieved. Any disagreement will be resolved by a third reviewer. Excluded studies and the reasons for exclusion will be recorded.

Data extraction

Customised data information was extracted independently by two investigators. The following information was collected for each study: (1) the name of the first author; (2) the location of the investigation area; (3) the year in which the investigation occurred; (4) the age range of the subjects; (5) the sample size (male, female, and overall); (6) the prevalence rates obtained for males, females, and overall; (7) the method used to sample subjects; (8) the criteria used to diagnose acne; and (9) the response rate.

Risk of bias (quality) assessment

Four key criteria[10, 11] were used by two independent investigators (Qiang Chen and Danhui Li) to estimate study quality: (1) the sampling scheme (random or consecutive); (2) whether the study included an adequate description of the characteristics of the study population; (3) whether a clear definition of the prevalence rate was provided; and (4) whether the response rate exceeded 75%. The scoring rule used was the following, for each quality item, “clear or adequate” was scored as 1 point, whereas “no” was scored as 0 points. The study was considered to be of adequate quality if the quality score was greater than or equal to 3. The two reviewers carefully assessed the included studies independently and agree on the final grading. An additional reviewer was consulted should there be any uncertainty or disagreement.

Ethics and dissemination

Since primary data will not be collected, formal ethical approval will not be required. The results will be disseminated through peer-reviewed publications, conference presentations and the media.

Statistical analysis

The statistical analyses were performed using Comprehensive Meta-Analysis version 2.0 (Biostat, Englewood Cliffs, NJ, USA; http,//www.meta-analysis.com). We calculated the pooled prevalence estimates as proportions and 95% CIs for the subgroup categories weighted by the sample sizes of the individual studies and then pooled these data to derive an overall proportion and its associated 95% CI. The heterogeneity of the pooled prevalence was estimated using the χ^2-based Q statistic. Meanwhile, I^2 metrics were calculated to quantify heterogeneity. A random-effects model was used if heterogeneity was observed ($p<0.05$); otherwise, a fixed-effects model was applied. All studies were classified into one of two groups (north versus south) according to the geographical regions in which the studies were conducted. Similarly, the studies were classified into three groups based upon the age of the participants in the samples, overall, undergraduate, and primary and secondary students ("p and s"). Subjects were also classified as male and female. The associations of age, gender, and region with the prevalence of acne were evaluated using a logistic meta-regression model. The associations between age, gender, region and risk of acne were expressed as ORs and 95% CIs. A value of $p<0.05$ was considered statistically significant.

Analysis of the publication bias

To examine the authenticity of data, Egger test and Funnel plots were made by Comprehensive Meta-Analysis version 2.0. There is no publication bia if the studies

arrange around the center line symmetrically and a value of p>0.05, otherwise there exists publication bia.

Results

Characteristics of the studies

Using the initial search strategy, 166 studies were identified, and 141 studies were subsequently excluded (Figure 1). A total of 25 studies[5-7, 12-33] involving 83,008 Chinese individuals were included in this meta-analysis. Detailed characteristics of each included study were presented in Table 1. The overall quality of all included studies was found to be adequate (Table 2).

The overall prevalence rates of acne in mainland China

A total of 25 studies involving 83,008 Chinese people were included in this meta-analysis. However, there was significant heterogeneity in this meta-analysis (I^2=99.797%, Q=11823.369, P<0.001). Thus, a random-effects model was selected for the analysis. The overall pooled prevalence of acne was 39.2% (95% CI=0.310-0.479; Figure 2).

The prevalence rates of acne in mainland China by gender

A total of 24 studies involving 40,712 males and 41,907 females were included in this subgroup meta-analysis. However, there was significant heterogeneity among both the males (I^2=99.582%, Q=5508.959, P<0.001) and females (I^2=99.614%, Q=5957.125, P<0.001) in this meta-analysis. Thus, a random-effects model was selected for the analysis. Males (39.7%, 95% CI=0.317-0.482) exhibited a higher prevalence of acne than did females (35.7%, 95% CI=0.274-0.451, Z=3.903, p<0.001) in the subgroup analysis (Figure 3).

The prevalence rates of acne in mainland China by region

A total of 24 studies involving 65,663 Chinese were included in this subgroup

meta-analysis. 10 of these studies were conducted in northern China (19,377 Chinese), and 14 studies were conducted in southern China (46,286 Chinese). However, significant heterogeneity was found both in the north (I^2=99.573%, Q=2109.204, P<0.001) and in the south (I^2=99.689%, Q=4176.791, P<0.001) in this meta-analysis. Thus, a random-effects model was selected for the analysis. The south (46.3%, 95% CI=0.374-0.555) had a higher prevalence of acne than did the north (34.2%, 95% CI=0.242-0.458, Z=2.498, p=0.012) in the subgroup analysis (Figure 4).

The prevalence rates of acne in mainland China by age

A total of 25 studies, consisting of 4 studies that examined the overall population, 10 p-and-s studies, and 11 undergraduate studies, were included in this subgroup meta-analysis. However, significant heterogeneity was found overall (I^2=99.534%, Q=643.149, P<0.001), for the p and s subgroup (I^2=98.860%, Q=789.719, P<0.001), and for the undergraduates (I^2=99.130%, Q=1149.658, P<0.001) in this meta-analysis. Thus, a random-effects model was selected for the analysis. The prevalence of acne over all ages was 10.2% (95% CI=0.059-0.171). The primary and secondary students (50.2%, 95% CI=0.451-0.554) had a higher prevalence of acne than did the undergraduates (44.5%, 95% CI=0.358-0.534, Z=2.411, p=0.016) in the subgroup analysis (Figure 5).

Logistic meta-regression analysis of the associations between age, gender, and region and the prevalence of acne

The associations between acne and the predictors age, gender, and region were statistically significant (Table 3) as measured by the corresponding ORs and their associated 95% CIs. The OR of acne prevalence was 1.217 (95%CI=0.109-14.681, p=0.024) between male and female. Chinese male were 1.217 times more likely than female to have acne. The OR between north China and south China were 1.184

(95%CI=0.002-3.833, p=0.028) for acne. South Chinese people were 1.184 times more likely than north Chinese people to have acne. The OR between primary and secondary school students and undergraduate were 3.127 (95%CI=0.001-3.838, p=0.012) for acne. Primary and secondary school students were 3.127 times more likely than undergraduate to have acne.

Analysis of the publication bias

There were no obvious asymmetries in the Funnel plots and the value of p>0.05 for the following groups: the overall pooled studies(t=0.031, p=0.976, 95%CI=-0.215~0.222) (Supplementary file: Figure6), male subgroup(t=0.346, p=0.733, 95% CI=-0.185~0.132) (Supplementary file: Figure7),female subgroup(t=0.143, p=0.887, 95%CI=-0.164~0.188) (Supplementary file: Figure8), subgroup of overall-age -layer (t=0.501, p=0.666, 95%CI -0.831~0.658) (Supplementary file: Figure9), subgroup of primary and secondary school students (t=0.580, p=0.578, 95%CI=-0.246~0.147) (Supplementary file: Figure10), subgroup of undergraduates(t=1.061, p=0.316, 95%CI=-0.121~0.335) (Supplementary file: Figure11) and Southern subgroup(t=0.441, p=0.667, 95%CI=-0.194~0.293)(Supplementary file: Figure12). Except the studies of Northern China subgroup existed publication bia(t=3.369, p=0.01, 95%CI=-0.520~-0.974).(Supplementary file: Figure 13).

Discussion

This meta-analysis, based on 83,008 subjects, derived from 25 studies, covering 12 provinces and municipalities in China, enable us to assess reliable prevalence of acne at the national level. Our results showed that the overall pooled prevalence of acne was 39.2%. Males (39.7%) exhibited a higher prevalence of acne than females (35.7% Z=3.903, p<0.001) in the subgroup analysis of gender. Meanwhile, the south (46.3%)

had a higher prevalence of acne than north (34.2%,Z=2.498, p=0.012) in the regional subgroup analysis. Moreover, the primary and secondary students (50.2%) had a higher prevalence of acne than undergraduates (44.5%Z=2.411, p=0.016) in the subgroup analysis of age. There was heterogeneity among the 25 included studies in this meta-analysis (I2=99.797%, Q=11823.369, P<0.001) and following reasons may explain the phenomenon. (1) Differences existed in the design of studies, such as non-unified age range, collection of data and research objects, prevalence of acne had deviation. (2) Evidence for seasonality was observed, with lower lipid production and reduced barrier function during the winter[34]. And there was a correlation between the incidence of acne and skin surface lipid[26,35]. The included articles may research in different seasons[18, 21, 27, 32], which resulted in different incidence of acne.

Meanwhile, age-related subgroup prevalence rates were calculated in this study. The prevalence of primary and secondary students was 50.2%, which consistent with the results(51.3%) of B Wei[36]. And primary and secondary students (50.2%) had a higher prevalence of acne than undergraduates (44.5%, Z=2.411, p=0.016), which was in agreement with the findings of Shen Y[5]. Moreover, by Logistic meta-regression analysis, we found the same results that primary and secondary school students were 3.127 times more likely than undergraduate to have acne. Gustavo Nunes[37] and Yentzer BA[38] also reported that primary and secondary students (89.3%) had a higher prevalence of acne than did the undergraduates (61.9%) in the US population. CW Choi[39] reported that in the patients with late onset acne, the number of comedones, the total number of acne lesions and the proportions of comedones were significantly less than in the patients with early onset acne. The age of onset had a negative correlation with the number of comedones and the proportion of comedones in the T-zone and the entire face, namely, acne. And the clinical differences in acne based on age appeared

to be mainly resulting from age of onset and not from the progression of the acne [40, 41].

In the present study, males (39.7%) had a 1.217 times higher prevalence rate of acne than did females (35.7%, Z=3.903, p<0.001). This result was in agreement with the findings of Schafer T[42] thatacne was more present in men (29.9%) than women (23.7%) in the city of Hamburg (Germany). This indicated that male had a higher risk of the occurrence and development of acne than females. (1)This difference might be related to lifestyle. It is well known to us all that males accounted for a larger proportion than female in drinking and smoking [43-45]. In several studies on acne, smoking appeared to be a strong disease-promoting factor [46-48]. (2)Besides this, males paid less attention to skin than females did in china. Nevertheless, inappropriate personal hygiene (use of abrasive soaps, harsh detergents, and excessive scrubbing) resulted in the pathological process of acne[49-50]. (3) Androgen levels. As we all know that increased androgen levels were a risk factors of acne[51]. Androgen levels were rise higher in male than female in adolescence. Adult women in different age categories have a lower prevalence of acne than adolescence. But recent researches have shown that acne is affecting an increasing number of adults, particularly females. Adult female acne should be considered as a specific acne subtype distinct from adolescent acne and to review topical and oral treatment options which may be particularly suitable for treating acne in adult females[4]. Therefore, several researches about adult female acne were expected in the future.

The prevalence rates of acne was also different in different regions. The prevalence of acne among individuals in southern China (46.3%) was higher than northern China (34.2%, Z=2.498, p=0.012). In consistent with Subramaniyan R[52], he considered that the prevalence of acne was different in the east of the Indian mainland from its

southern part. This difference may be due to several factors.(1) Climate. Enhanced sebum excretion, colonization of the pilosebaceous duct with Propionibacterium acnes and resultant inflammation were thought to play a critical role in the pathogenesis of acne[53]. The function of the sebaceous gland as an endocrine skin organ, which is mainly composed of sebocytes, took an important role in the occurrence and development of acne[54]. Excessive sebum production and its abnormal lipid ingredients from the sebaceous gland contributed to the formation of the primary acne lesions[55]. Sebocytes also produce inflammatory cytokines and they had a vital effect on formation and aggravation of acne lesions[56]. In China, southern China had longer hours of sunshine than northern China. Solar radiation contained ultraviolet radiation, which was an external environment factors causeing many skin disease. And ultraviiolet radiation can show some effects on the glands through direct or indirect pathways[57]. Sebaceous gland hyperplasia and increased sebum secretion after irradiation of ultraviolet (UV)-B has been widely accepted. The expression of inflammatory cytokines, especially IL-1b, IL-6, IL-8 and TNF-a was significantly increased in cultured sebocytes after treatment with UV-B[58]. Meanwhile, correlational research showed that time-distinct gene induction of TNF-a, IL-1b and matrilysin in cultured HaCaT cells may be involved in UV-induced cellular responses[59] . Although, mRNA level does not always correspond to protein level in vivo, mRNA level of inflammatory cytokines such as IL-1, IL-6 and TNF-a was also identified to be increased through studies using whole mouse skin and human skin exposed to UV-B[60, 61]. What's more, it has been known that epithelial keratinocytes contain a functional PPAR-c system and this system is a target for UV-B radiation[62]. The synthesis of free fatty acids by PPAR-c stimulates the production of pro-inflammatory cytokines, such as IL-1b and TNF-a, in sebaceous glands[58]. (2)Humidity. The humidity in south of

China was high than north of china was well known. Subramaniyan R et al[52] reported that the prevalence of dermatoses, including acne, much higher in humid regions than arid regions. (3) Diet. Chili was a favorite food for the residents of southern compared to the northern residents and southern residents ate more chili than northern. However, spicy food was risk factors for the acne[25]. In a word, environmental factors (climate and humidity) and diet may lead to the difference of prevalence between northern and southern China.

Conclusion

This systematic review will provide current evidence on the epidemiology of acne and its association between acne and gender, region and age,. The evidence generated from this paper may prove beneficial in terms of preventing skin lesion and improving the quality of life.

Footnotes

Contributors Shengjie Li and Danhui Li conceived the study, participated in drafting the final manuscript. Qiang Chen and Yi Liu analyzed the data and completed the final draft of the manuscript. TingTing Liu and Wenhui Tang prepared all the figures. All authors reviewed the manuscript.

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Competing interests None declared.

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Data sharing statement The data used to conduct this study are secondarily held data available to the public in peer reviewed journals. As such we do not own the data and have access to the data publicly. We therefore needed no special permissions to use the data and wish to inform BMJ Open that all data used in this document are

publicly held.

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Figure Legends

Figure1. Flow-chart illustrating the article search process

Figure2. Forest plot of the overall prevalence rates of acne. CI=confidence interval.

Figure3. Forest plot of the prevalence rates of acne according to gender. CI=confidence interval.

Figure4. Forest plot of the prevalence rates of acne according to region. CI=confidence interval.

Figure5. Forest plot of the prevalence rates of acne according to age. CI=confidence interval. All=overall age. P and s=primary and secondary students.

Tables

Table1. Characteristics of the populations examined in studies reporting the prevalence of acne in mainland China

Name	Region	Year	Age range	Sample size	Prevalence (%)		
					Male % (n)	Female % (n)	Total (%)
Zhang feng	Dong guan	2013	undergraduate	669	40.37 (379)	34.48 (290)	37.82
Liu lijuan	Shi jiazhuang	2013	undergraduate	742	42.11 (418)	36.11 (324)	39.49
Liu qing	Zi bo	2013	12-49	1455	9.4 (504)	11.5 (951)	8.32
Li shengjie	Tai an	2010	17-24	1416	39.85 (532)	46.61 (884)	44.07
Zhang zhiyong	Han dan	2010	undergraduate	1582	59.71 (834)	50.00 (748)	55.12
Cai xinduan	Guang dong	2010	9-18	2015	49.90 (986)	59.86 (1029)	54.99
Zhangjian	Yi chun	2011	18-26	448	45.16 (217)	32.03 (231)	38.39
Wang renli	Si chuan	2008-2009	all	10,503	19.3 (4319)	16.9 (6184)	18.1
Pei guangde	He nan	2008	all	1547	8.80 (742)	7.86 (805)	8.39
Chen ying	Guang zhou	2008	undergraduate	2252	34.7 (1253)	38.4 (999)	36.4
Zhang hong	Jiang men	2006-2008	17-18	12,450	55.9 (7134)	46.02 (5136)	51.83
Deng bin	Hai nan	2005	16-23	3500	34.8 (1990)	32.4 (1510)	33.8
Cui jianping	Xing tai	2007	10-18	2891	43.14 (1370)	35.44 (1521)	39.1
Min li	Fu jian	2007	15-23	1484	69.5 (836)	63.6 (648)	66.9
Feng jieying	Guang zhou	2004-2005	11-19	1561	51.95 (743)	60.76 (818)	56.57
Gao aili	Guang zhou	2004	12-20	2552	34.2 (1151)	31.6 (1305)	32.8
Wu tieqiang	Zhu hai	2004	10-18	3200	54.9 (1790)	51.6 (1410)	53.5
Sun zhenxiu	Nan jing	2005	16-23	2100	37.91 (1000)	22 (1100)	30.33
Liu zhaorui	Bei jing	2003	16-17	4933	67.1 (2364)	57.3 (2569)	62.0
Zhang aihua	Tai an, He ze	1996	14-23	1510	38.24 (829)	23.06 (581)	20.99
Fu rui	Ji ning	2012	11-17	2560	45.40 (1343)	47.80 (1177)	46.51
Li bing	Shan xi	2012	12-17	741	55.8 (335)	49.2 (406)	52.2
Yiwei Shen	China	2012	all	17,345	10.4 (7858)	6.1 (9487)	8.1
Law MP	Hong Kong	2010	undergraduate	389	N/A	N/A	85.1
Wu TQ	Guang dong	2007	10-18	3163	51.3 (1785)	58.6 (1378)	53.5

(n)= the number of participants, N/A= not available.

Table 2.Methodological quality of the studies reporting the prevalence of acne in mainland China

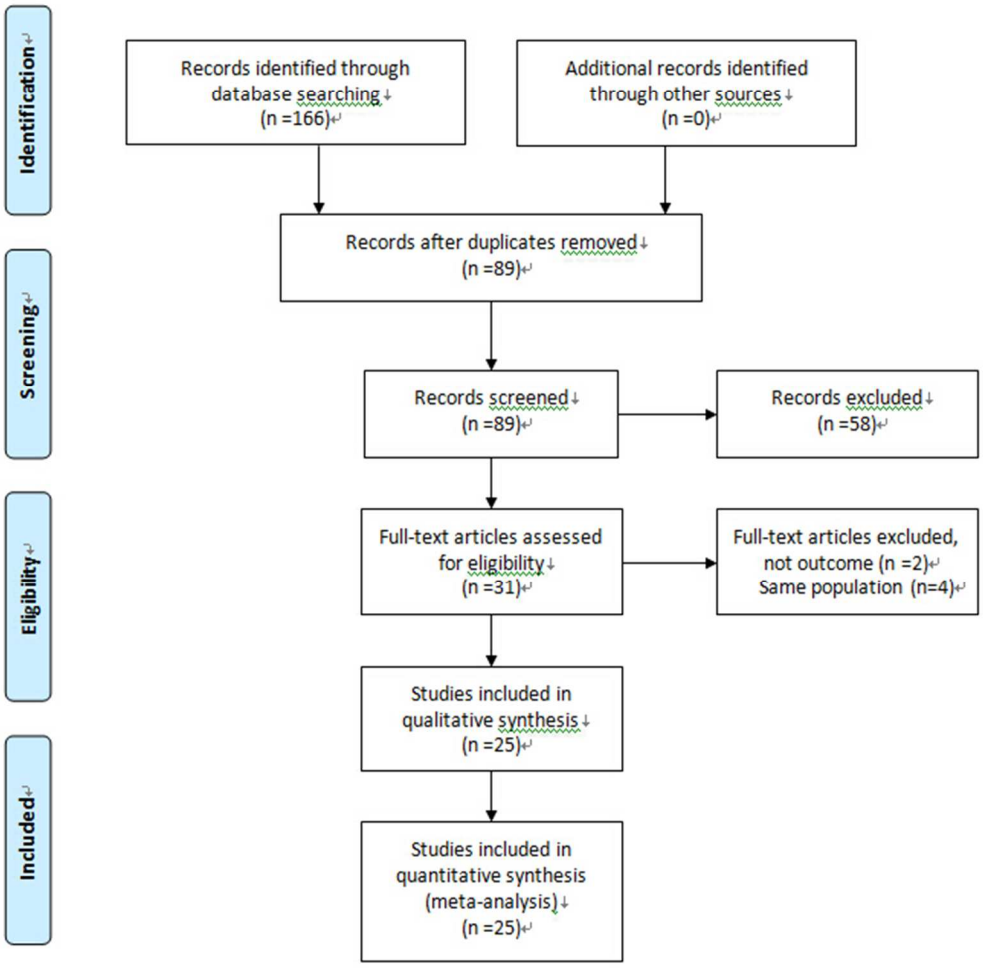
Name	Sampling scheme	Population characteristics	Prevalence definition	Diagnostic criteria	Response rate %	Score
Zhang feng	Random stratified sample	adequate	clear	clear	95	4
Liu lijuan	Random stratified sample	adequate	clear	clear	N/A	3
Liu qing	Cluster sampling	adequate	clear	clear	48.5	3
Li shengjie	Random stratified sample	adequate	clear	clear	100	4
Zhang zhiyong	Cluster sampling	adequate	clear	clear	97.75	4
Cai xinduan	Random stratified sample	adequate	clear	clear	98.05	4
Zhangjian	Random stratified sample	adequate	clear	clear	N/A	3
Wang renli	Random stratified sample	adequate	clear	clear	N/A	3
Pei guangde	Random stratified sample	adequate	clear	clear	53.4	3
Chenying	Random stratified sample	adequate	clear	clear	90.8	4
Zhang hong	Cross-sectional	adequate	clear	clear	N/A	3
Deng bin	Random stratified sample	adequate	clear	clear	N/A	3
Cui jianping	Random stratified sample	adequate	clear	clear	98.1	4
Min li	Random stratified sample	adequate	clear	clear	N/A	3
Feng jieying	Random stratified sample	adequate	clear	clear	98.24	4
Gao aili	Cross-sectional	adequate	clear	clear	96.2	4
Wu tieqiang	Cross-sectional	adequate	clear	clear	98.84	4
Sun zhenxiu	Random stratified sample	adequate	clear	clear	N/A	3
Liu zhaorui	Random stratified sample	adequate	clear	clear	N/A	3
Zhang aihua	Random stratified sample	adequate	clear	clear	N/A	3
Fu rui	Cross-sectional	adequate	clear	clear	99.06	4
Li bing	Random stratified sample	adequate	clear	clear	95.2	4
Yiwei Shen	Community-based study	adequate	clear	clear	86.84	4
Law MP	Cross-sectional	adequate	no	clear	99.3	4
Wu TQ	Cross-sectional	adequate	clear	clear	98.8	4

N/A= not available.

Table 3. Adjusted odds ratios for acne obtained by logistic meta-regression analysis

Factor	Number of studies	OR (95% CI)	P-value
Age of range			
undergraduate	11	1.00	
primary and secondary school students	10	3.127 (0.001-3.838)	0.012
Gender			
female	24	1.00	
male	24	1.217 (0.109-14.681)	0.024
Location			
north	10	1.00	
south	14	1.184 (0.002-3.833)	0.028

OR= odds ratio. CI=confidence interval



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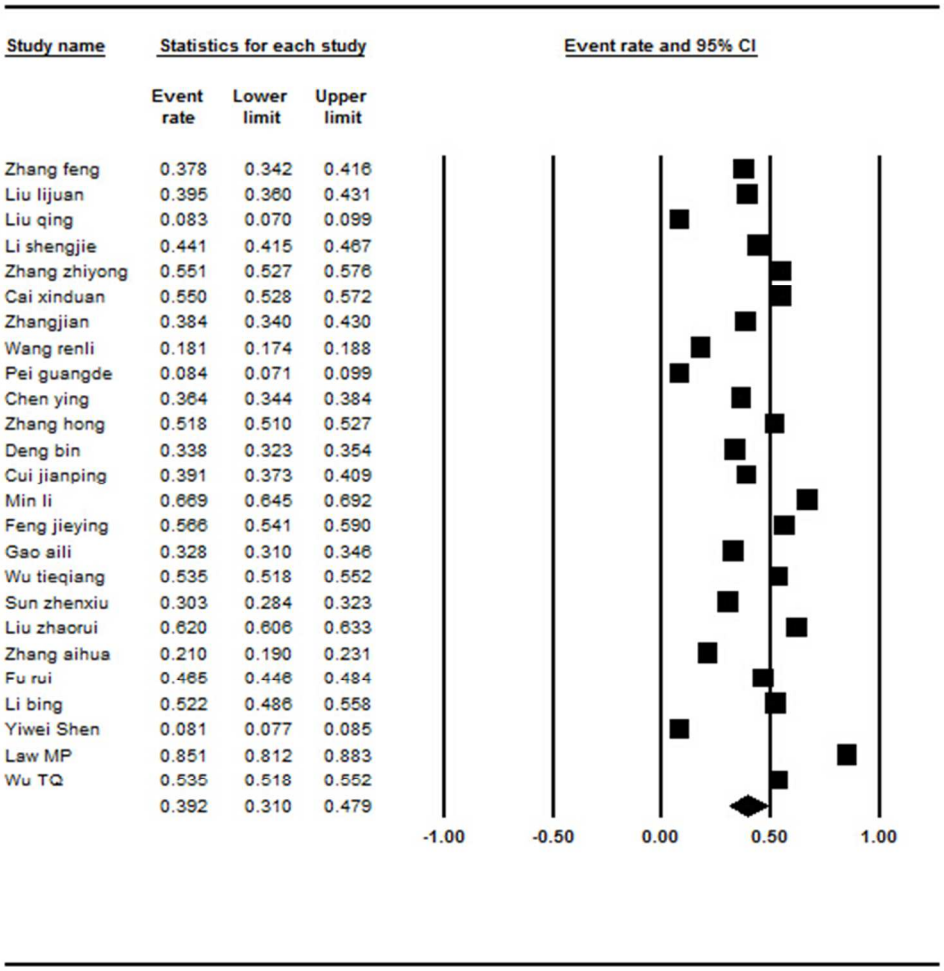

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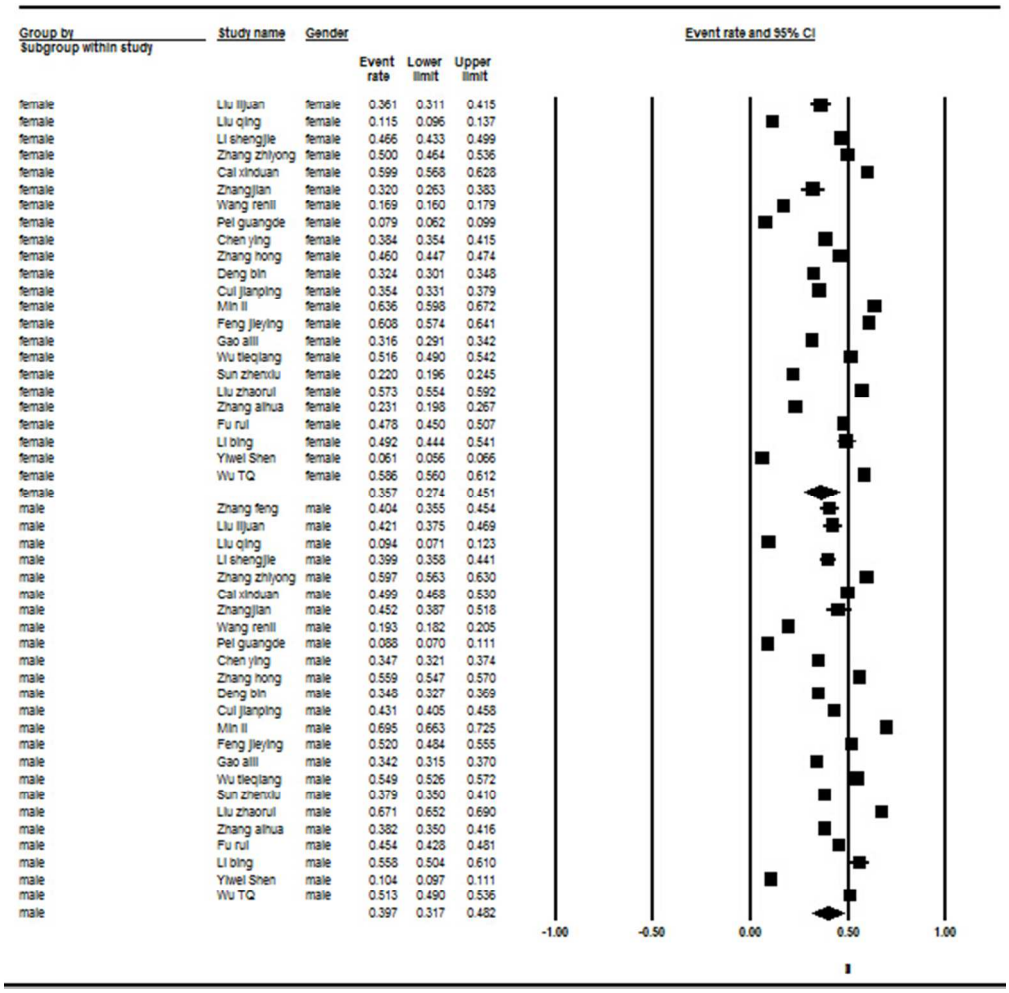

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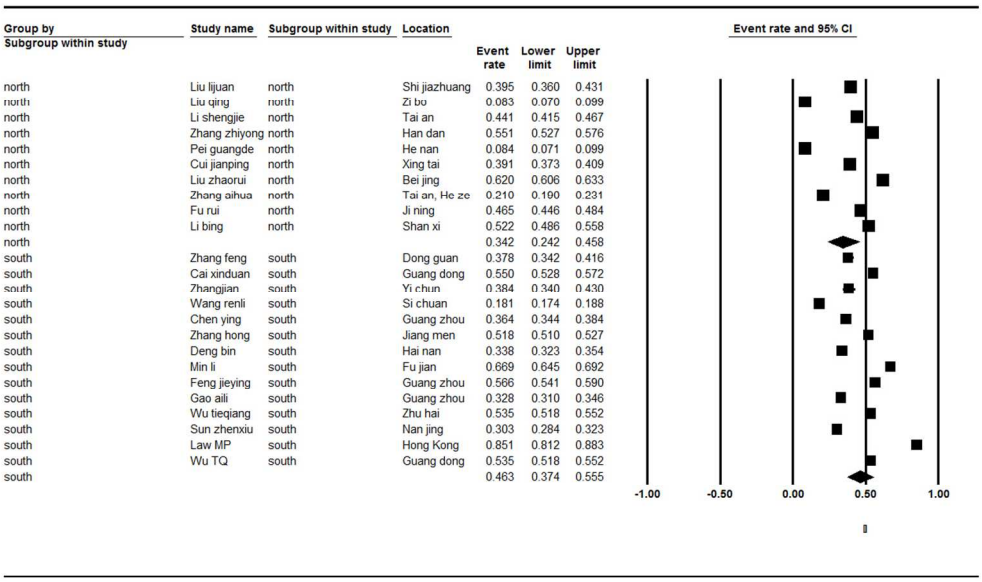

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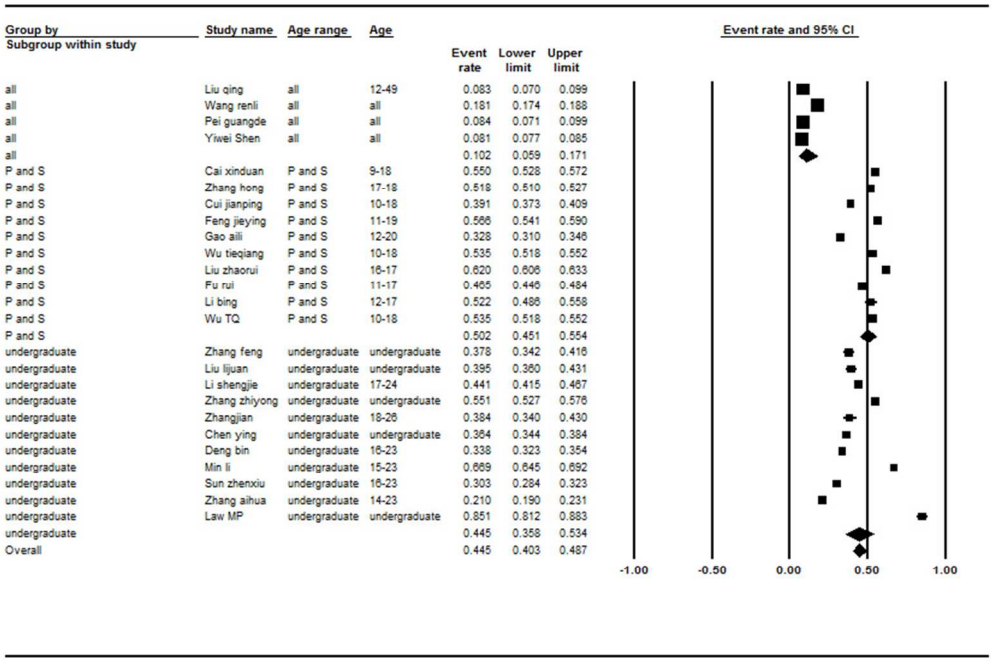

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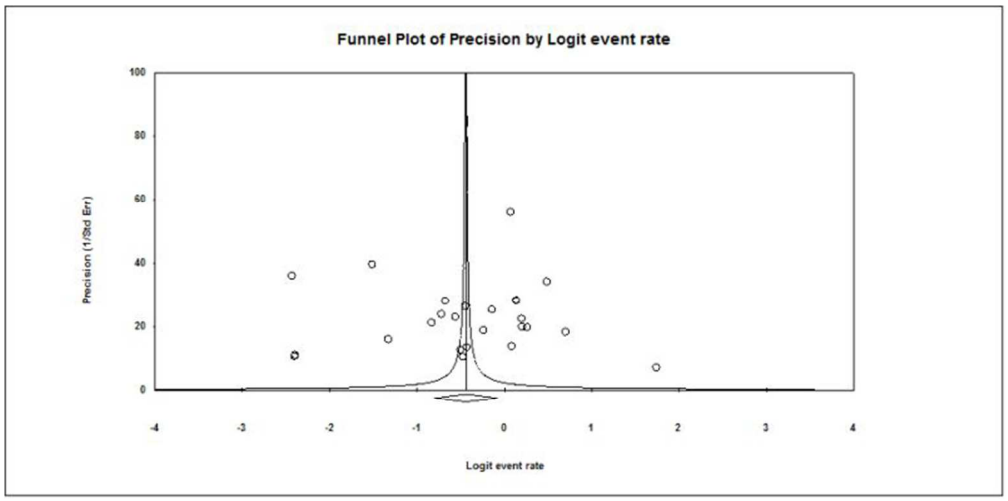

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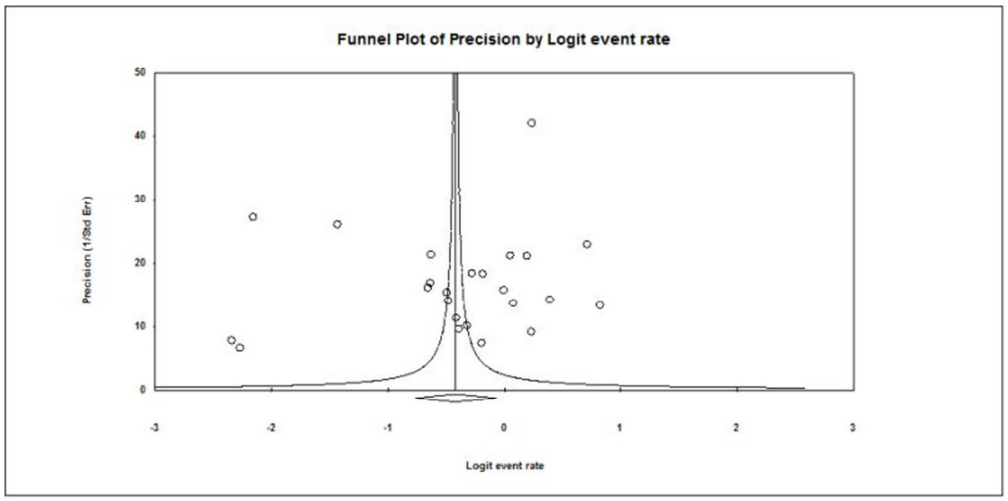

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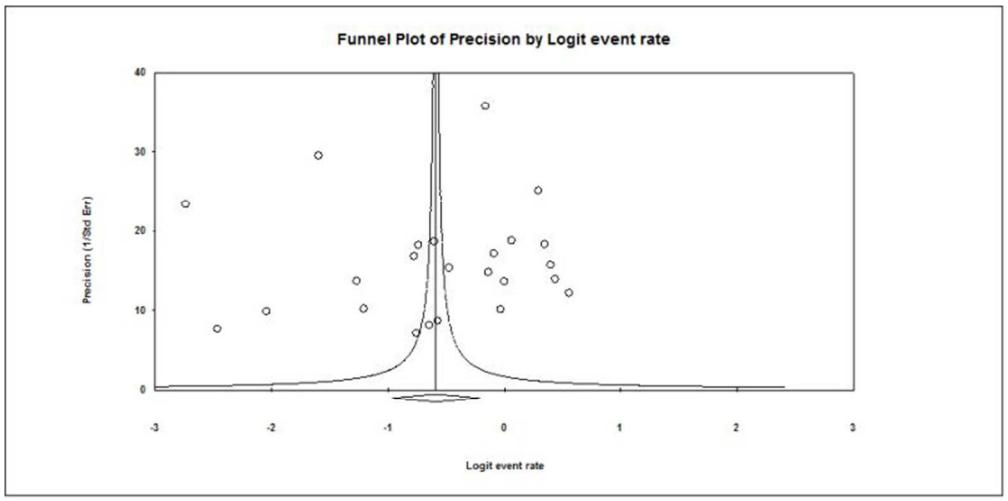

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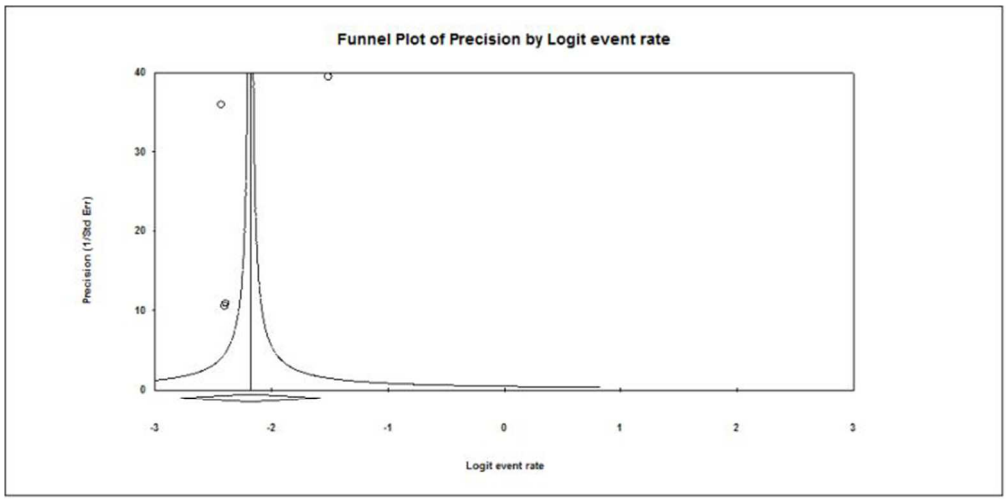

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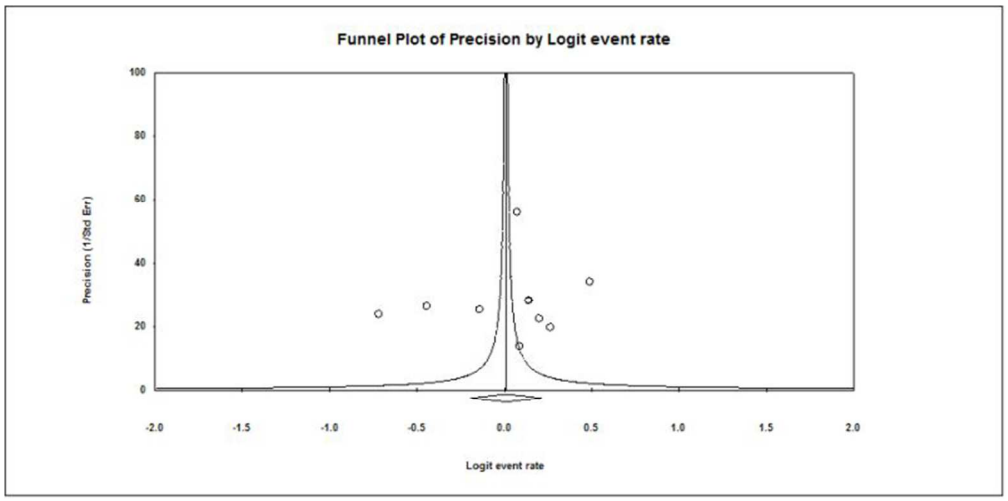

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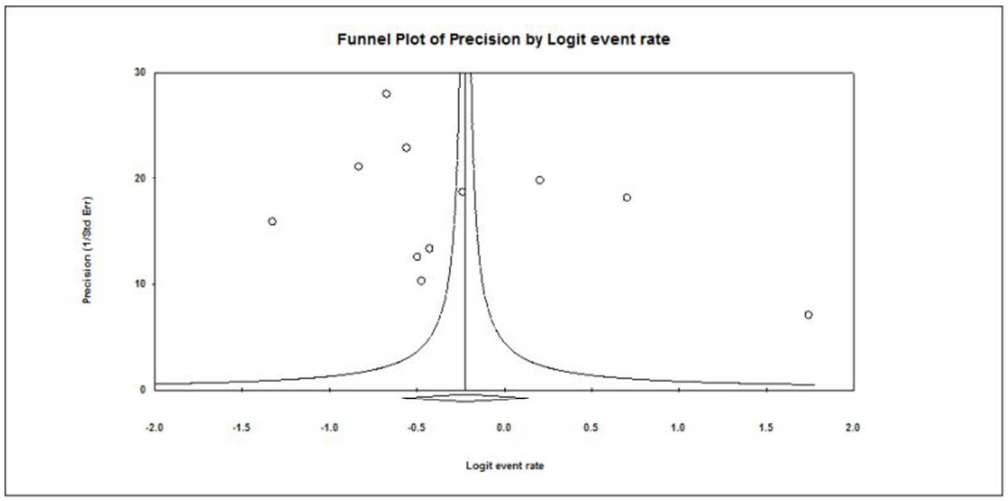

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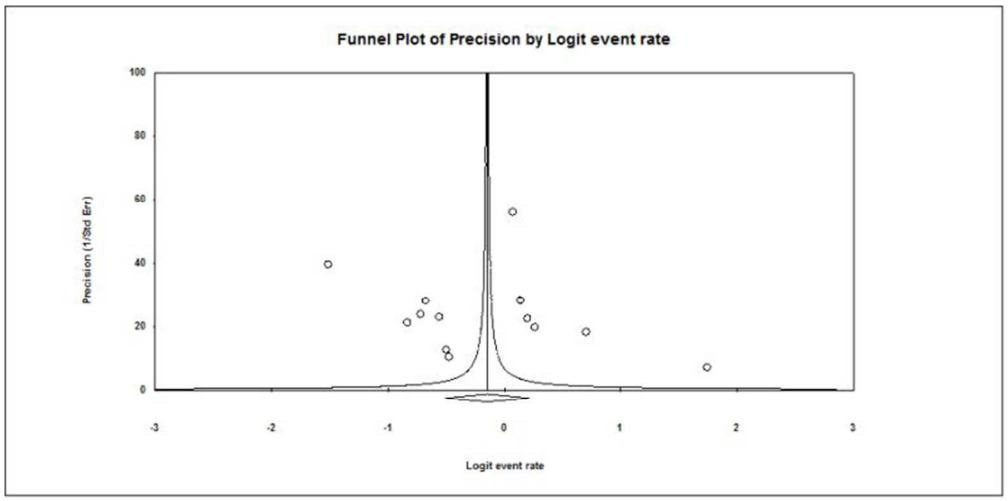

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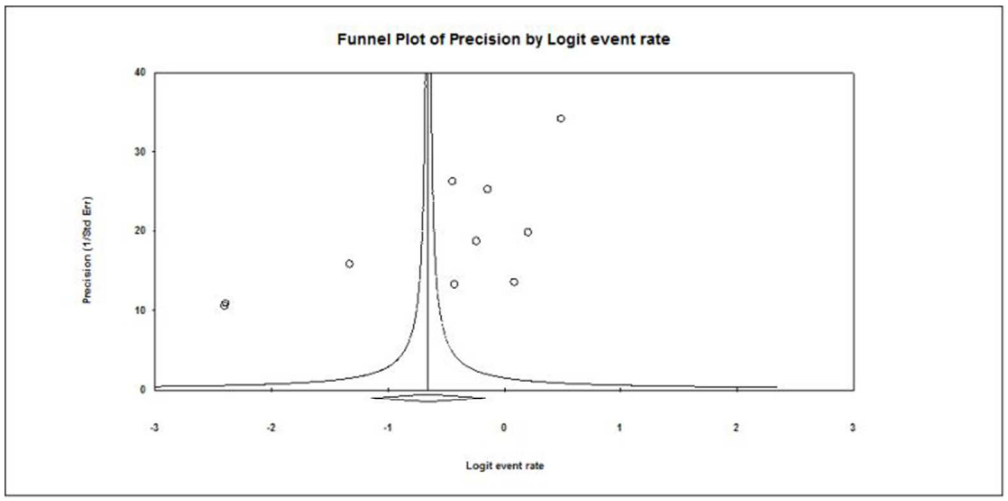

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Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	A Systematic Review of the Prevalence of Acne in Mainland China	1
ABSTRACT			
Structured summary	2	**Background and Objectives:** Acne, a very common skin disease, can result in psychological distress and sustained impairment in quality of life. Data on the prevalence of acne and their difference in gender, region and age is sketchy. The aim of this review is to estimate the prevalence of acne in mainland China comprehensively and to quantify its association with gender, region and age. **Methods and analysis:** We searched electronic databases with predetermined search terms to identify relevant studies published between January 1, 1996 and September 30, 2016. We pointed out repeated results using Note Express software and evaluated the studies for inclusion. Two independent reviewers extracted data. Then statistical analyses were performed using Comprehensive Meta-Analysis version 2.0. A random-effects model was adopted to calculate the overall pooled prevalence and to merge categories, including gender, region and age for subgroup analyses. Logistic meta-regression analysis was used to clarify the associations between acne and the predictors age, gender, and region using odds ratios and their associated 95% confidence intervals.**Results:** 25 relevant studies were included in this meta-analysis. The overall pooled prevalence rates of acne were 39.2% (95% CI=0.310-0.479). The prevalence rates in different age groups were 10.2% overall (95% CI=0.059-0.171), 50.2% for primary and secondary students (95% CI=0.451-0.554), and 44.5% for undergraduates (95% CI=0.358-0.534); by gender, the prevalence rates were 35.7% for females (95% CI=0.274-0.451) and 39.7% for males (95% CI=0.317-0.482); and by region, the prevalence rates were 34.2% for northern China (95% CI=0.242-0.458) and 46.3% for southern China (95% CI=0.374-0.555). The associations between acne and the predictors age, gender, and region were statistically significant.**Conclusions:** In mainland	2,3

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		China, primary and secondary students exhibited higher prevalence rates than undergraduate students, males had higher prevalence rates of acne than females, and the prevalence rates of acne in southern China was higher than northern China. **Ethics and dissemination:** This systematic review does not require ethical approval. The results of this review will be submitted for peer-reviewed publication regardless of outcome and will be presented at relevant conferences. **Strengths and limitations:** (1)To our knowledge, this was the first and largest meta-analysis of its scope which will give us a detailed understanding of the prevalence of acne in mainland China and its associations with age, gender, and region and a sound basis for the future provision of health services.(2)This systematic review of acne in mainland China, covering 12 different provinces, represents near-complete capture of the demographic for more than 80 thousand people over a 41-year period.(3)Some limitations should be considered: First, the diagnostic criteria for acne differed among included studies. Second, the age of the survey population could not be subdivided, for example, the intervals 5-9, 10-14 and15-19 years of age.	
INTRODUCTION			
Rationale	3	Acne, a very common skin disease among adolescents, was the fourth most common reason for patients aged 11–21 years to visit a doctor in the USA1. The clinical features of acne include papules, pustules, cysts, comedos, and nodules. Several studies have shown that the estimated prevalence rate of acne varies from 8.1% to 85.1% in China2-4, depending on the region, subjects' ages, and the nationality studied. Acne occurs primarily on the face, neck, and upper trunk and can lead to scar formation if treated improperly. Thus, acne can result in psychological distress, including anxiety, depression, diminished self-confidence, and communication difficulties, among other outcomes 5, 6. To date, many large population-based studies have been conducted to estimate the prevalence rates of acne in regional populations. Because China comprises 34 province-level administrative regions, with 56 nations and a population of 1.3 billion people, a country-wide,	3,4

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		population-based study of the prevalence rates of acne in China was needed.	
Objectives	4	In this review, we examined the prevalence of acne in mainland China and to analyse the effects of gender, region and age on it.	4
METHODS			
Protocol and registration	5	We have no original protocol and registration, so this item isn't applicable.	
Eligibility criteria	6	Studies that met all of the following criteria were included in the meta-analysis, (1) the study was a population-based survey; (2) the study evaluated the prevalence/incidence of acne; (3) the investigation involved random sampling or cluster sampling; (4) the sample size was >300; A flow chart illustrating the article search process is presented in Figure 1.	5,6
Information sources	7	Studies were aggregated from six databases between January 1, 1996 and September 30, 2016, including PubMed, EMBASE, the Web of Science, the China National Knowledge Infrastructure, the VIP Database for Chinese Technical Periodicals, and the Wan Fang Database for Chinese Periodicals.	4
Search	8	The following search terms were used to retrieve relevant studies, (acne), (prevalence or incidence) AND (China or Chinese).	4
Study selection	9	Figure1	Figure1
Data collection process	10	The data in this study were extractd independently and checked after independent extraction by two investigators.	5
Data items	11	The following information was collected for each study, (1) the name of the first author; (2) the location of the investigation area; (3) the year in which the investigation occurred; (4) the age range of the subjects; (5) the sample size (male, female, and overall); (6) the prevalence rates obtained for males, females, and overall; (7) the method used to sample subjects; (8) the criteria used to diagnose acne; and (9) the response rate.	5
Risk of bias in individual studies	12	Quality assessment and analysis of the publication bias	5
Summary measures	13	odds ratios (ORs) and their associated 95% confidence intervals (CIs)	6
Synthesis of results	14	The heterogeneity of the pooled prevalence was estimated using the χ2-based Q statistic. Meanwhile, I2 metrics were calculated to quantify heterogeneity. A random-effects model was used if heterogeneity was observed ($p<0.05$); otherwise, a fixed-effects model was applied. All studies were classified into one of two groups (north versus south) according to the geographical regions in which the studies were conducted. Similarly, the studies were classified into	6

PRISMA 2009 Checklist

		three groups based upon the age of the participants in the samples, overall, undergraduate, and primary and secondary students ("p and s"). Subjects were also classified as male and female. The associations of age, gender, and region with the prevalence of acne were evaluated using a logistic meta-regression model. The associations between age, gender, region and risk of acne were expressed as ORs and 95% CIs. A value of p<0.05 was considered statistically significant.	

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Four key criteria7, 8 were used by two independent investigators (Qiang Chen and Danhui Li) to estimate study quality, (1) the sampling scheme (random or consecutive); (2) whether the study included an adequate description of the characteristics of the study population; (3) whether a clear definition of the prevalence rate was provided; and (4) whether the response rate exceeded 75%. The scoring rule used was the following, for each quality item, “clear or adequate” was scored as 1 point, whereas “no” was scored as 0 points. The study was considered to be of adequate quality if the quality score was greater than or equal to 3. We did not exclude studies on the basis of inadequate quality, but we accounted for inadequate quality in the statistical analysis. The two reviewers carefully assessed the included studies independently and agree on the final grading. Any disagreement will be resolved by a third reviewer.(Table2)	Table2
Additional analyses	16	All studies were classified into one of two groups (north versus south) according to the geographical regions in which the studies were conducted. Similarly, the studies were classified into three groups based upon the age of the participants in the samples, overall, undergraduate, and primary and secondary students ("p and s"). Subjects were also classified as male and female. The associations of age, gender, and region with the prevalence of acne were evaluated using a logistic meta-regression model. The associations between age, gender, region and risk of acne were expressed as ORs and 95% CIs. A value of p<0.05 was considered statistically significant.	6
RESULTS			
Study selection	17	Using the initial search strategy, 166 studies were identified, and 141 studies were subsequently excluded (Figure 1). A total of 25 studies 2-4, 9-30 involving 83,008 Chinese individuals were included in this meta-analysis.	6,7
Study characteristics	18	Detailed characteristics of each included study were presented in Table 1.	Table 1
Risk of bias within studies	19	The overall quality of all included studies was found to be adequate (Table 2).	Table 2
Results of individual studies	20	Figure2-5	Figure2-5
Synthesis of results	21	Figure2-5	Figure2-5
Risk of bias across studies	22	Table 2	Table 2

PRISMA 2009 Checklist

Additional analysis	23	logistic meta-regression model, subgroup analysis	8
DISCUSSION			
Summary of evidence	24	Our results showed that the overall pooled prevalence of acne was 39.2% for all ages. The prevalence rates in different age groups were 10.2% overall (95% CI=0.059-0.171), 50.2% for primary and secondary students (95% CI=0.451-0.554), and 44.5% for undergraduates (95% CI=0.358-0.534); by gender, the prevalence rates were 35.7% for females (95% CI=0.274-0.451) and 39.7% for males (95% CI=0.317-0.482); and by region, the prevalence rates were 34.2% northern China (95% CI=0.242-0.458) and 46.3% for southern China (95% CI=0.374-0.555).	9
Limitations	25	The diagnostic criteria for acne differed across studies and the age of the survey population could not be subdivided.	3
Conclusions	26	In conclusion, the overall pooled prevalence of acne was 39.2% in mainland China; acne occurred mainly among primary students, secondary students, and undergraduate students; the prevalence of acne in males was greater than that in females; and acne was more common in northern China than in southern China. This meta-analysis of the prevalence of acne may provide a sound basis for the future provision of health services.	9
FUNDING			
Funding	27	Issue of Tai'an Science and Technology Development Plan（201440774-05）	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	a protocol of a systematic review
Update	1b	
Registration	2	We didn't have a registration number.
Authors:		
Contact	3a	1.Danhui Li. Key Laboratory of Environment and Genes Related to Diseases, Ministry of Education, Medical School, Xi'an Jiaotong University, Xi'an, Shaanxi, China. E-mail:danhuili1002@sina.com 2.Qiang Chen. School of Public Health, Taishan Medical university, Tai'an, Shandong Province, China. E-mail:tychenqiang@126.com 3.Yi Liu. Department of Dermatology, Affiliated Hospital of Jining Medical University, Jining, Shandong province, China. E-mail: liuyx94@sohu.com 4.Ting-ting Liu. The school hospital of Taishan Medical university, Tai'an, Shandong Province, China. E-mail: tyliuting@yeah.net 5.Wenhui Tang Department of Biomedical Engineering, Maternal and Child Health Care of Laiwu City in Shandong Province, Laiwu, Shandong Province, China. E-mail: lwsfybjytwh@163.com 6.Sheng-jie Li. Department of Clinical Laboratory, Eye & ENT Hospital, Shanghai Medical College, Fudan University, China.* Corresponding author. Email: lishengjie6363020@163.com. Address: No.83 Fenyang Road, Shanghai, China, 200031
Contributions	3b	Shengjie Li and Danhui Li conceived the study, participated in drafting the final manuscript. Qiang Chen and Yi Liu analyzed the data and completed the final draft of the manuscript. TingTing Liu and Wenhui Tang prepared all the figures. All authors reviewed the manuscript.
Amendments	4	We searched electronic databases with predetermined search terms to identify relevant studies published between January 1, 1996 and September 30, 2016. We pointed out repeated results using Note Express software and evaluated the studies for inclusion. Two independent reviewers extracted data. Then statistical analyses were performed using Comprehensive Meta-Analysis version 2.0. A random-effects model was adopted to calculate the overall pooled prevalence and to merge categories, including gender, region and age for subgroup analyses. Logistic meta-regression analysis was used to clarify the associations between acne and the predictors age, gender, and region using odds ratios and their associated 95% confidence intervals.
Support:		

Sources	5a	This work was supported by Issue of Tai'an Science and Technology Development Plan grant number 201440774-05.
Sponsor	5b	Tai'an Municipal Science and Technology Bureau
Role of sponsor or funder	5c	

INTRODUCTION

Rationale	6	Acne, a very common skin disease among adolescents, was the fourth most common reason for patients aged 11–21 years to visit a doctor in the USA1. The clinical features of acne include papules, pustules, cysts, comedos, and nodules. Several studies have shown that the estimated prevalence rate of acne varies from 8.1% to 85.1% in China2-4, depending on the region, subjects' ages, and the nationality studied. Acne occurs primarily on the face, neck, and upper trunk and can lead to scar formation if treated improperly. Thus, acne can result in psychological distress, including anxiety, depression, diminished self-confidence, and communication difficulties, among other outcomes 5, 6. To date, many large population-based studies have been conducted to estimate the prevalence rates of acne in regional populations. Because China comprises 34 province-level administrative regions, with 56 nations and a population of 1.3 billion people, a country-wide, population-based study of the prevalence rates of acne in China was needed.
Objectives	7	In this review, we examined the prevalence of acne in mainland China and to analyse the effects of gender, region and age on it.

METHODS

Eligibility criteria	8	Studies that met all of the following criteria were included in the meta-analysis, (1) the study was a population-based survey; (2) the study evaluated the prevalence/incidence of acne; (3) the investigation involved random sampling or cluster sampling; (4) the sample size was >300; A flow chart illustrating the article search process is presented in Figure 1.
Information sources	9	Studies were aggregated from six databases between January 1, 1996 and September 30, 2016, including PubMed, EMBASE, the Web of Science, the China National Knowledge Infrastructure, the VIP Database for Chinese Technical Periodicals, and the Wan Fang Database for Chinese Periodicals.
Search strategy	10	The following search terms were used to retrieve relevant studies, (acne), (prevalence or incidence) AND (China or Chinese).
Study records:		
Data management	11a	Any duplicate studies was removed by Note Express. Two reviewers(Qiang Chen and Danhui Li) independently evaluated the title and abstract of all studies identified through the search against the inclusion and exclusion criteria. The full text of all eligible studies will then be retrieved. Any disagreement will be resolved by a third reviewer. Excluded studies and the reasons for exclusion will be recorded.

Selection process	11b	The data in this study were extractd independently and checked after independent extraction by two investigators.
Data collection process	11c	Customised data information was extracted independently by two investigators. The two pieces of final results were re-checked.
Data items	12	The following information was collected for each study, (1) the name of the first author; (2) the location of the investigation area; (3) the year in which the investigation occurred; (4) the age range of the subjects; (5) the sample size (male, female, and overall); (6) the prevalence rates obtained for males, females, and overall; (7) the method used to sample subjects; (8) the criteria used to diagnose acne; and (9) the response rate.
Outcomes and prioritization	13	We calculated the pooled prevalence estimates as proportions and 95% CIs for the subgroup categories weighted by the sample sizes of the individual studies and then pooled these data to derive an overall proportion and its associated 95% CI. The heterogeneity of the pooled prevalence was estimated using the $\chi 2$-based Q statistic. Meanwhile, I2 metrics were calculated to quantify heterogeneity. A random-effects model was used if heterogeneity was observed ($p<0.05$); otherwise, a fixed-effects model was applied. All studies were classified into one of two groups (north versus south) according to the geographical regions in which the studies were conducted. Similarly, the studies were classified into three groups based upon the age of the participants in the samples, overall, undergraduate, and primary and secondary students ("p and s"). Subjects were also classified as male and female. The associations of age, gender, and region with the prevalence of acne were evaluated using a logistic meta-regression model. The associations between age, gender, region and risk of acne were expressed as ORs and 95% CIs. A value of $p<0.05$ was considered statistically significant.
Risk of bias in individual studies	14	Quality assessment and analysis of the publication bias
Data synthesis	15a	The heterogeneity of the pooled prevalence was estimated using the $\chi 2$-based Q statistic. Meanwhile, I2 metrics were calculated to quantify heterogeneity. A random-effects model was used if heterogeneity was observed ($p<0.05$); otherwise, a fixed-effects model was applied. All studies were classified into one of two groups (north versus south) according to the geographical regions in which the studies were conducted. Similarly, the studies were classified into three groups based upon the age of the participants in the samples, overall, undergraduate, and primary and secondary students ("p and s"). Subjects were also classified as male and female. The associations of age, gender, and region with the prevalence of acne were evaluated using a logistic meta-regression model. The associations between age, gender, region and risk of acne were expressed as ORs and 95% CIs. A value of $p<0.05$ was considered statistically significant.;
	15b	odds ratios (ORs) and their associated 95% confidence intervals (CIs)
	15c	Logistic meta-regression analysis a
	15d	
Meta-bias(es)	16	Analysis of the publication bias
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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The Prevalence of Acne in Mainland China: a systematic review and meta-analysis

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Abstract

Introduction Acne, a very common skin disease, can result in psychological distress and sustained impairment in quality of life. Data on the prevalence of acne and their difference in gender, region and age is sketchy. The aim of this review is to estimate the prevalence of acne in mainland China comprehensively and to quantify its association with gender, region and age.

Methods We searched electronic databases with predetermined search terms to identify relevant studies published between January 1, 1996 and September 30, 2016. We pointed out repeated results using Note Express software and evaluated the studies for inclusion. Two independent reviewers extracted data. Then statistical analyses were performed using Comprehensive Meta-Analysis version 2.0. A random-effects model was adopted to calculate the overall pooled prevalence and to merge categories, including gender (males and females), region (Northern China and Southern China) and age (primary and secondary students: 7-17 years old; undergraduates: 18-23 years old; overall: no limits of age) for subgroup analyses. Logistic meta-regression analysis was used to clarify the associations between acne and the predictors age, gender, and region using odds ratios and their associated 95% confidence intervals.

Results 25 relevant studies were included in this meta-analysis. The overall pooled prevalence rates of acne were 39.2% (95% CI=0.310-0.479). The prevalence rates in different age groups were 10.2% overall (95% CI=0.059-0.171), 50.2% for primary and secondary students (95% CI=0.451-0.554), and 44.5% for undergraduates (95% CI=0.358-0.534); by gender, the prevalence rates were 35.7% for females (95% CI=0.274-0.451) and 39.7% for males (95% CI=0.317-0.482); and by region, the prevalence rates were 34.2% for Northern China (95% CI=0.242-0.458) and 46.3%

for Southern China (95% CI=0.374-0.555). The associations between acne and the predictors age, gender, and region were statistically significant.

Conclusions In mainland China, primary and secondary students exhibited higher prevalence rates than undergraduate students; males had higher prevalence rates of acne than females; and the prevalence rates of acne in Southern China was higher than Northern China.

Strengths and limitations

To our knowledge, this was the first systemic review evaluating the overall acne prevalence in mainland China and analyzing its associations with age, gender, and region.

This systematic review, covering 12 different provinces, was composed of 25 studies, 80 thousand people over a 41-year period.

Some limitations should be considered: the diagnostic criteria for acne differed among the included studies; the age of the survey population could not be subdivided. Moreover due to heterogeneity among papers, sample changed from variable to variable.

Introduction

Acne, a very common skin disease among adolescents, was the fourth most common reason for patients aged 11–21 years to visit a doctor in the USA[1]. Acne is estimated to affect 9.4% of the world's population with the highest prevalence in adolescents[2]. Acne vulgaris-associated disease burden exhibits global distribution and has continued to grow in prevalence over time within this population[3]. In addition, a group of increasing epidemiological data suggest that acne also affects a considerable number of adults[4] and women are more frequently affected by adult acne than

men[5]. The incidence of acne is different from various countries and ethnic groups. In Northern Tanzania, the prevalence of acne is reported to be 0.1%[6]. The prevalence of acne is 3.9% in the German population aged between 16 and 70 years[7]. The prevalence of acne is reported to be low in developing countries of Africa[8,9]. Whereas a comprehensive systemic review of the prevalence of acne in the Chinese population is still lacking. Several studies have shown that the estimated prevalence rate of acne varies from 8.1% to 85.1% in China[10-12] depending on the region, subjects' ages, and the nationality studied.

Acne is a chronic inflammatory disease of the pilosebaceous unit resulting from androgen-induced increased sebum production, altered keratinization, inflammation, and bacterial colonisation of hair follicles by propionibacterium acnes[13]. Acne vulgar alters the normal skin physiology, impairing stratum corneum and transepidermal water loss[14]. The clinical features of acne include papules, pustules, cysts, comedos, and nodules. Acne occurs primarily on the face, neck, and upper trunk and can lead to scar formation if treated improperly. Acne scarring is a frequent complication of acne and patients are often lack of effective and safe methods of managing this condition[15] . Then resulting scars may negatively impact on an affected person's psychosocial and physical well-being. It is reported that acne can result in psychological distress and have profound effects on patients' self-esteem, which may lead to anxiety, depression, diminished self-confidence, and communication difficulties[16,17].

Many large population-based studies have been conducted to estimate the prevalence rates of acne in regional populations, but a comprehensive statistical analysis of the prevalence of Chinese acne has not emerged so far. China being a vast region, comprises of 34 province-level administrative regions, with 56 nations and a population of 1.3 billion people. Therefore a country-wide, population-based study of

the prevalence rates of acne in China was needed. In this review, we examined the prevalence of acne in mainland China systematically and analysed the effects of gender, region and age on acne.

Methods

Search strategy

Studies were aggregated from six databases between January 1, 1996 and September 30, 2016, including PubMed, EMBASE, the Web of Science, the China National Knowledge Infrastructure, the VIP Database for Chinese Technical Periodicals, and the Wan Fang Database for Chinese Periodicals. The following search terms were used to retrieve relevant studies, (acne), (prevalence or incidence) AND (China or Chinese). The combination of acne, prevalence, incidence, China and Chinese were used in varying combinations to identify relevant literature. Search strategies were customised to suit each database. The search strategy is presented in supplementary table 1. In addition, a manual search was performed by checking the reference lists of eligible articles and relevant reviews.

Inclusion criteria

Studies that met all of the following criteria were included in the meta-analysis,

(1) the study was a population-based survey;

(2) the study evaluated the prevalence/incidence of acne;

(3) the investigation involved random sampling or cluster sampling;

(4) the sample size was >300;

A flow chart illustrating the article search process is presented in Figure 1.

Data management

Any duplicate studies was removed by Note Express. Two reviewers (Qiang Chen and Danhui Li) independently evaluated the title and abstract of all studies identified

through the search against the inclusion and exclusion criteria. The full text of all eligible studies were then retrieved. Any disagreement were resolved by a third reviewer. Excluded studies and the reasons for exclusion were recorded.

Data extraction

Customised data information was extracted independently by two investigators. The following information was collected for each study: (1) the name of the first author; (2) the location of the investigation area; (3) the year in which the investigation occurred; (4) the age range of the subjects; (5) the sample size (male, female, and overall); (6) the prevalence rates obtained for males, females, and overall; (7) the method used to sample subjects; (8) the criteria used to diagnose acne; and (9) the response rate.

Risk of bias (quality) assessment

Four key criteria[18, 19] were used by two independent investigators (Qiang Chen and Danhui Li) to estimate study quality: (1) the sampling scheme (random or consecutive); (2) whether the study included an adequate description of the characteristics of the study population; (3) whether a clear definition of the prevalence rate was provided; and (4) whether the response rate exceeded 75%. The scoring rule used was the following, for each quality item, “clear or adequate” was scored as 1 point, whereas “no” was scored as 0 points. The study was considered to be of adequate quality if the quality score was greater than or equal to 3. The two reviewers carefully assessed the included studies independently and agree on the final grading. An additional reviewer was consulted should there be any uncertainty or disagreement.

Ethics and dissemination

Since primary data was not collected, formal ethical approval was not required. The results will be disseminated through peer-reviewed publications, conference

presentations and the media.

Statistical analysis

The statistical analyses were performed using Comprehensive Meta-Analysis version 2.0 (Biostat, Englewood Cliffs, NJ, USA; http,//www.meta-analysis.com). We calculated the pooled prevalence estimates as proportions and 95% CIs for the subgroup categories weighted by the sample sizes of the individual studies and then pooled these data to derive an overall proportion and its associated 95% CI. The heterogeneity of the pooled prevalence was estimated using the χ^2-based Q statistic. Meanwhile, I^2 metrics were calculated to quantify heterogeneity. A random-effects model was used if heterogeneity was observed ($p<0.05$); otherwise, a fixed-effects model was applied. All studies were classified into one of two groups (north versus south) according to the geographical regions in which the studies were conducted. Similarly, the studies were classified into three groups based upon the age of the participants in the samples, overall (no limits of age), undergraduate (18-23 years old), and primary and secondary students ("p and s", 7-17 years old). Subjects were also classified as male and female. The associations of age, gender, and region with the prevalence of acne were evaluated using a logistic meta-regression model. The associations between age, gender, region and risk of acne were expressed as ORs and 95% CIs. A value of $p<0.05$ was considered statistically significant.

Analysis of the publication bias

To examine the authenticity of data, Egger test and Funnel plots were made by Comprehensive Meta-Analysis version 2.0. No publication bias exists if the studies arranged symmetrically around the central line with a p value of >0.05.

Results

Characteristics of the studies

Using the initial search strategy, 166 studies were identified, and 141 studies were subsequently excluded (Figure 1). A total of 25 studies[10-12,20-41] involving 83,008 Chinese individuals were included in this meta-analysis. Detailed characteristics of each included study were presented in Table 1. The overall quality of all included studies was found to be adequate (Table 2).

The overall prevalence rates of acne in mainland China

A total of 25 studies involving 83,008 Chinese people were included in this meta-analysis. However, there was significant heterogeneity in this meta-analysis (I^2=99.797%, Q=11823.369, P<0.001). Thus, a random-effects model was selected for the analysis. The overall pooled prevalence of acne was 39.2% (95% CI=0.310-0.479; Figure 2).

The prevalence rates of acne in mainland China by gender

A total of 24 studies involving 40,712 males and 41,907 females were included in this subgroup meta-analysis. However, there was significant heterogeneity among both the males (I^2=99.582%, Q=5508.959, P<0.001) and females (I^2=99.614%, Q=5957.125, P<0.001) in this meta-analysis. Thus, a random-effects model was selected for the analysis. Males (39.7%, 95% CI=0.317-0.482) exhibited a higher prevalence of acne than females (35.7%, 95% CI=0.274-0.451, Z=3.903, p<0.001) in the subgroup analysis (Figure 3).

The prevalence rates of acne in mainland China by region

A total of 24 studies involving 65,663 Chinese were included in this subgroup meta-analysis. 10 of these studies were conducted in Northern China (19,377 Chinese), and 14 studies were conducted in Southern China (46,286 Chinese). However, significant heterogeneity was found both in the North (I^2=99.573%, Q=2109.204, P<0.001) and in the South (I^2=99.689%, Q=4176.791, P<0.001) in this

meta-analysis. Thus, a random-effects model was selected for the analysis. The South (46.3%, 95% CI=0.374-0.555) had a higher prevalence of acne than did the North (34.2%, 95% CI=0.242-0.458, Z=2.498, p=0.012) in the subgroup analysis (Figure 4).

The prevalence rates of acne in mainland China by age

A total of 25 studies, consisting of 4 studies that examined the overall population, 10 p-and-s studies, and 11 undergraduate studies, were included in this subgroup meta-analysis. However, significant heterogeneity was found overall (I^2=99.534%, Q=643.149, P<0.001), for the p and s subgroup (I^2=98.860%, Q=789.719, P<0.001), and for the undergraduates (I^2=99.130%, Q=1149.658, P<0.001) in this meta-analysis. Thus, a random-effects model was selected for the analysis. The prevalence of acne over all ages was 10.2% (95% CI=0.059-0.171). The primary and secondary students (50.2%, 95% CI=0.451-0.554) had a higher prevalence of acne than did the undergraduates (44.5%, 95% CI=0.358-0.534, Z=2.411, p=0.016) in the subgroup analysis (Figure 5).

Logistic meta-regression analysis of the associations between age, gender, and region and the prevalence of acne

The associations between acne and the predictors age, gender, and region were statistically significant (Table 3) as measured by the corresponding ORs and their associated 95% CIs. The OR of acne prevalence was 1.217 (95%CI=0.109-14.681, p=0.024) between male and female. Chinese males might be more susceptible to acne than females. The OR between Southern China and Northern China were 1.184 (95%CI=0.002-3.833, p=0.028) for acne. The geographical factors of Southern China might be a risk factor for acne. The OR between primary and secondary school students and undergraduate were 3.127 (95%CI=0.001-3.838, p=0.012) for acne. Age might play a vital role in the development of acne.

Analysis of the publication bias

There were no obvious asymmetries in the Funnel plots and the value of p>0.05 for the following groups: the overall pooled studies (t=0.030, p=0.976, 95% CI=-0.215~0.222) (Supplementary Figure 1), male subgroup (t=0.346, p=0.733, 95% CI=-0.185~0.132) (Supplementary Figure 2), female subgroup (t=0.143, p=0.887, 95% CI=-0.164~0.188) (Supplementary Figure 3), subgroup of all age layers (t=0.501, p=0.666, 95% CI=-0.831~0.658) (Supplementary Figure 4), subgroup of primary and secondary school students (t=0.580, p=0.578, 95% CI=-0.246~0.147) (Supplementary Figure 5), subgroup of undergraduates (t=1.061, p=0.316, 95% CI=-0.121~0.335) (Supplementary Figure 6) and Southern China subgroup (t=0.441, p=0.667, 95% CI=-0.194~0.293) (Supplementary Figure 7). Only the studies of the Northern China subgroup had publication bias (t=3.369, p=0.01, 95% CI=-0.520~-0.974) (Supplementary Figure 8).

Discussion

This meta-analysis, based on 83,008 subjects, derived from 25 studies, covering 12 provinces and municipalities in China, enable us to assess reliable prevalence of acne at the national level. Our results showed that the overall pooled prevalence of acne was 39.2%. The acne prevalence was estimated to be 3.9% in the German population aged between 16 and 70 years[7] and 61.5% in the population aged from 20 to 60 years old in Portugal[42]. The difference in age range, ethnic background and regions might explain the difference in the incidence of acne. Males (39.7%) exhibited a higher prevalence of acne than females (35.7%, Z=3.903, p<0.001) in the subgroup analysis of gender. Meanwhile, the South (46.3%) had a higher prevalence of acne than North (34.2%, Z=2.498, p=0.012) in the regional subgroup analysis. Moreover, the primary and secondary students (50.2%) had a higher prevalence of acne than undergraduates

(44.5%, Z=2.411, p=0.016) in the subgroup analysis of age. There was heterogeneity among the 25 included studies in this meta-analysis (I^2=99.797%, Q=11823.369, P<0.001) and the following reasons might explain the phenomenon. (1) Differences existed in the design of studies, such as non-unified age range, collection of data and research objects, explaining the deviation of the prevalence of acne. (2) Evidence for seasonality was observed, with lower lipid production and reduced barrier function during the winter[43]. A correlation between the incidence of acne and skin surface lipid[34,44] has been observed before, thus the included articles may have been conducted in different seasons[26,29,35,40], which resulted in different incidences of acne.

The age-related subgroup prevalence rates were also calculated in this study. The prevalence of primary and secondary students was 50.2%, which was consistent with the results of B Wei *et al*[45] (51.3%). This result was similar to those reported by Karciauskiene J *et al*'s[46] results among schoolchildren aged 7-19 years, which was 55.4% in Lithuania. However, these results are lower than a study conducted in Brazil, where a prevalence rate of 96% was found in adolescents aged 10-17[47]. This difference may also be attributed to the different age range, regions and ethnic backgrounds of the study subjects. Our results suggested that primary and secondary students (50.2%) had a higher prevalence of acne than undergraduates (44.5%, Z=2.411, p=0.016), which was in agreement with the findings of Shen *et al*[10]. Moreover, using Logistic meta-regression analysis, we found that the OR between primary and secondary school students and undergraduate were 3.127 (95% CI=0.001-3.838, p=0.012) for acne. Gustavo Nunes *et al*[48] and Yentzer BA *et al*[49] also reported that primary and secondary students (89.3%) had a higher prevalence of acne than the undergraduate subjects (61.9%) in the US population. Choi CW *et al*[50] reported that in patients with late onset acne, the number of comedones and total

number of acne lesions and the proportions of comedones were significantly less than in patients with early onset acne. The age of onset had a negative correlation with the number of comedones and the proportion of comedones in the T-zone and the entire face, namely, acne. The clinical differences in acne based on age appeared to be mainly a result of age of onset and not from the progression of the acne[51,52].

In the present study, males (39.7%) had a 1.112 times higher prevalence rate of acne than did females (35.7%, Z=3.903, p<0.001). This result was in agreement with the findings of T Schafer[53] that acne was more present in men (29.9%) than women (23.7%) in the city of Hamburg (Germany). Adityan B *et al*[54] showed that the male to female ratio was 1.25:1 in South India. In Auckland, Lello J[55] reported that males (91%) were more susceptible to acne compared with females (79%) and severe and moderately severe acne was significantly more common in males (OR = 2.6, 95% Cl: 1.73 < OR < 3.9) as well. What's more, moderate and severe acne (27.1% and 0.4l% of patients, respectively) were significantly (P < 0.01) were common in males (36.2% and 0.9%, respectively) than females (21.2% and 0.2%, respectively) in Egypt[56]. This indicated that males had a higher risk of occurrence and development of acne than females. (1) This difference might be related to lifestyle. It is well known to us that males accounted for a larger proportion than females in drinking and smoking[57-59]. (2) Males also tend to pay less attention to skin than females did in China. Inappropriate personal hygiene (use of abrasive soaps, harsh detergents, and excessive scrubbing) can contribute to the pathological process of acne[60,61]. (3) Androgen levels elevation are greater in males than females during adolescence and increased androgen levels are a risk factors of acne[62]. The interplay of growth hormone (GH), insulin, and insulin-like growth factor-1 (IGF-1) signaling during puberty may also have a causal role in the pathogenesis of acne by influencing adrenal and gonadal androgen

metabolism[63]. Adult women in different age categories have a lower prevalence of acne than adolescence. But recent researches have shown that acne is affecting an increasing number of adults, particularly females. Adult female acne should be considered as a specific acne subtype distinct from adolescent acne and a review on the topical and oral treatment options suitable for treating acne in adult females[5] are expected in the future.

The prevalence rates of acne was also different in different regions. The prevalence of acne among individuals in Southern China (46.3%) was higher than Northern China (34.2%, Z=2.498, p=0.012). This is consistent with Subramaniyan R[64], who considered that the prevalence of acne was different between the east of the Indian mainland and its Southern part. This difference may be due to several factors. (1) Ultraviolet radiation. Enhanced sebum excretion, colonization of the pilosebaceous duct with Propionibacterium acnes and resultant inflammation were thought to play a critical role in the pathogenesis of acne[65]. The function of the sebaceous gland as an endocrine skin organ, which is mainly composed of sebocytes, has an important role in the occurrence and development of acne[66]. Excessive sebum production and its abnormal lipid ingredients from the sebaceous gland contributed to the formation of primary acne lesions[67]. Sebocytes also produce inflammatory cytokines and they had a vital effect on formation and aggravation of acne lesions[68]. Southern China has longer hours of sunshine than Northern China. Solar radiation contains ultraviolet radiation, which is an external environmental factor causing many skin disease. Ultraviiolet radiation can affect the glands through direct or indirect pathways[69]. It is widely accepted that sebaceous gland hyperplasia and increased sebum secretion occur after irradiation of ultraviolet (UV)-B. The expression of inflammatory cytokines, especially IL-1b, IL-6, IL-8 and TNF-a are significantly increased in

cultured sebocytes after treatment with UV-B[70]. Meanwhile, correlational research showed that time-distinct gene induction of TNF-a, IL-1b and matrilysin in cultured HaCaT cells may be involved in UV-induced cellular responses[71]. Although, mRNA levels do not always correspond to protein level *in vivo*, mRNA levels of inflammatory cytokines such as IL-1, IL-6 and TNF-a are also identified to be increased through studies using whole mouse skin and human skin exposed to UV-B[72,73]. What's more, it has been known that epithelial keratinocytes contain a functional PPAR-c system and this system is a target for UV-B radiation[74]. The synthesis of free fatty acids by PPAR-c stimulates the production of pro-inflammatory cytokines, such as IL-1b and TNF-a, in sebaceous glands[70]. (2) Humidity. There is greater humidity in Southern parts of China than the Northern China. Subramaniyan R[64] reported that the prevalence of dermatoses, including acne, are much higher in humid regions than arid regions. (3) Diet. Chili is a popular food for Southern residents compared to the Northern residents, and is consumed in greater quantities than Northern residents, and spicy food has been identified as a risk factor for the development of acne[33]. In simple terms, both environmental factors (climate and humidity) and diet may lead to the different prevalence rates of acne between Northern and Southern China.

This systematic review is likely limited by the different diagnostic criteria for acne among the included studies. Due to the enormous number of Chinese people, unitive diagnostic criteria was difficult to implement. In addition, the age of the survey population could not be subdivided, which made further detailed analysis of age groups impossible. More research are needed on the national prevalence of acne in order to provide better baseline data and to monitor the effect of acne over time in China.

Conclusion

The overall pooled prevalence rate of acne was 39.2% in mainland China. Primary and secondary students exhibited higher prevalence rates than undergraduate students. Due to differences in lifestyle, skincare routines and androgen levels, males showed higher prevalence rates of acne than females. A possible eitiological factor for the difference in prevalence rates of acne between Southern China and Northern China may be due to the varying ultraviolet radiation, humidity and dietary habits between these two regions. The evidence generated from this paper may prove beneficial in terms of understanding the age and regional distribution and prevalence rates of acne amongst the Chinese population, which may help in identifying target prevention and treatment strategies for this cohort of patients.

Footnotes

Contributors Shengjie Li and Danhui Li conceived the study, participated in drafting the final manuscript. Qiang Chen and Yi Liu analyzed the data and completed the final draft of the manuscript. TingTing Liu and Wenhui Tang prepared all the figures. All authors reviewed the manuscript.

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Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The data used to conduct this study are secondarily held data available to the public in peer reviewed journals. As such we do not own the data and have access to the data publicly. We therefore needed no special permissions to use the data and wish to inform BMJ Open that all data used in this document are publicly held.

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Figure legends

Figure 1 Flow-chart illustrating the article search process

First, we obtained 166 records identified through database searching. No additional records identified through other sources. Second, 89 records left after duplicates removed. Third, 58 studies were excluded after records screening. Then the remainder 31 studies were full-text articles assessed for eligibility and 6 studies were excluded. Finally 25 studies were included in quantitative synthesis (meta-analysis).

Figure 2 Forest plot of the overall prevalence rates of acne. CI=confidence interval.

A total of 25 studies were included in this meta-analysis. Through analyzing in a random-effects model, the overall pooled prevalence of acne was calculated as 39.2% (95% CI=0.310-0.479) through analyzing in a random-effects model.

Figure 3 Forest plot of the prevalence rates of acne according to gender. CI=confidence interval.

A total of 24 studies were included in this subgroup meta-analysis. Through analyzing in a random-effects model, the prevalence rates of acne in males was 39.7% (95% CI=0.317-0.482) and 35.7% (95% CI=0.274-0.451) in females. Males (39.7%) exhibited a higher prevalence of acne than did females (35.7%) in the subgroup analysis (Z=3.903, p<0.001).

Figure 4 Forest plot of the prevalence rates of acne according to region. CI=confidence interval.

A total of 24 studies were included in this subgroup meta-analysis. 10 of these studies were conducted in Northern China and 14 studies were conducted in Southern China. Through analyzing in a random-effects model, the prevalence rates of acne in South was 46.3% (95% CI=0.374-0.555) and 34.2% in North (95% CI=0.242-0.458). The South (46.3%) had a higher prevalence of acne than did the North (34.2%) in the subgroup analysis (Z=2.498, p=0.012).

Figure 5 Forest plot of the prevalence rates of acne according to age. CI=confidence interval. All=overall age. P and s=primary and secondary students.

A total of 25 studies, consisting of 4 studies that examined the overall population, 10 p-and-s studies, and 11 undergraduate studies, were included in this subgroup meta-analysis. Through analyzing in a random-effects model, the prevalence of acne over all ages was 10.2% (95% CI=0.059-0.171). The prevalence of acne in the primary and secondary students was 50.2% (95% CI=0.451-0.554) and 44.5% (95% CI=0.358-0.534) in the undergraduates. The primary and secondary students (50.2%) had a higher prevalence of acne than did the undergraduates (44.5%) in the subgroup analysis (Z=2.411, p=0.016).

Supplementary Figure 1 Funnel plots for the overall pooled studies

The total studies arrange around the center line symmetrically, so there is no publication bia.

Supplementary Figure 2 Funnel plots for the male subgroup

A total of 24 studies involving 40,712 males were included in the male subgroup meta-analysis. The 24 studies arrange around the center line symmetrically, so there is no publication bia.

Supplementary Figure 3 Funnel plots for the female subgroup

A total of 24 studies involving 41,907 females were included in the female subgroup meta-analysis. The 24 studies arrange around the center line symmetrically, so there is no publication bia.

Supplementary Figure 4 Funnel plots for the all-age-layer subgroup

A total of 4 studies were included in the all-age-layer subgroup meta-analysis. The studies arrange around the center line symmetrically, so there is no publication bia.

Supplementary Figure 5 Funnel plots for the subgroup of primary and secondary school students

A total of 10 studies were included in the subgroup meta-analysis of primary and secondary school students. The studies arrange around the center line symmetrically, so there is no publication bia.

Supplementary Figure 6 Funnel plots for the subgroup of undergraduates

A total of 11 studies were included in the subgroup meta-analysis of undergraduates.The studies arrange around the center line symmetrically, so there is no publication bia.

Supplementary Figure 7 Funnel plots for the subgroup of Southern China

A total of 14 studies were included in the Southern subgroup meta-analysis. The studies arrange around the center line symmetrically, so there is no publication bia.

Supplementary Figure 8 Funnel plots for the subgroup of Northern China

A total of 10 studies were included in the Northern subgroup meta-analysis. The studies arrange around the center line nonsymmetrically, so there existed publication bia.

Tables

Table1. Characteristics of the populations examined in studies reporting the prevalence of acne in mainland China

Name	Region	Year	Age range	Sample size	Prevalence (%)		
					Male % (n)	Female % (n)	Total (%)
Zhang feng	Dong guan	2013	undergraduate	669	40.37 (379)	34.48 (290)	37.82
Liu lijuan	Shi jiazhuang	2013	undergraduate	742	42.11 (418)	36.11 (324)	39.49
Liu qing	Zi bo	2013	12-49	1455	9.4 (504)	11.5 (951)	8.32
Li shengjie	Tai an	2010	17-24	1416	39.85 (532)	46.61 (884)	44.07
Zhang zhiyong	Han dan	2010	undergraduate	1582	59.71 (834)	50.00 (748)	55.12
Cai xinduan	Guang dong	2010	9-18	2015	49.90 (986)	59.86 (1029)	54.99
Zhangjian	Yi chun	2011	18-26	448	45.16 (217)	32.03 (231)	38.39
Wang renli	Si chuan	2008-2009	all	10,503	19.3 (4319)	16.9 (6184)	18.1
Pei guangde	He nan	2008	all	1547	8.80 (742)	7.86 (805)	8.39
Chen ying	Guang zhou	2008	undergraduate	2252	34.7 (1253)	38.4 (999)	36.4
Zhang hong	Jiang men	2006-2008	17-18	12,450	55.9 (7134)	46.02 (5136)	51.83
Deng bin	Hai nan	2005	16-23	3500	34.8 (1990)	32.4 (1510)	33.8
Cui jianping	Xing tai	2007	10-18	2891	43.14 (1370)	35.44 (1521)	39.1
Min li	Fu jian	2007	15-23	1484	69.5 (836)	63.6 (648)	66.9
Feng jieying	Guang zhou	2004-2005	11-19	1561	51.95 (743)	60.76 (818)	56.57
Gao aili	Guang zhou	2004	12-20	2552	34.2 (1151)	31.6 (1305)	32.8
Wu tieqiang	Zhu hai	2004	10-18	3200	54.9 (1790)	51.6 (1410)	53.5
Sun zhenxiu	Nan jing	2005	16-23	2100	37.91 (1000)	22 (1100)	30.33
Liu zhaorui	Bei jing	2003	16-17	4933	67.1 (2364)	57.3 (2569)	62.0
Zhang aihua	Tai an, He ze	1996	14-23	1510	38.24 (829)	23.06 (581)	20.99
Fu rui	Ji ning	2012	11-17	2560	45.40 (1343)	47.80 (1177)	46.51
Li bing	Shan xi	2012	12-17	741	55.8 (335)	49.2 (406)	52.2
Yiwei Shen	China	2012	all	17,345	10.4 (7858)	6.1 (9487)	8.1
Law MP	Hong Kong	2010	undergraduate	389	N/A	N/A	85.1
Wu TQ	Guang dong	2007	10-18	3163	51.3 (1785)	58.6 (1378)	53.5

(n)= the number of participants, N/A= not available.

Table 2. Methodological quality of the studies reporting the prevalence of acne in mainland China

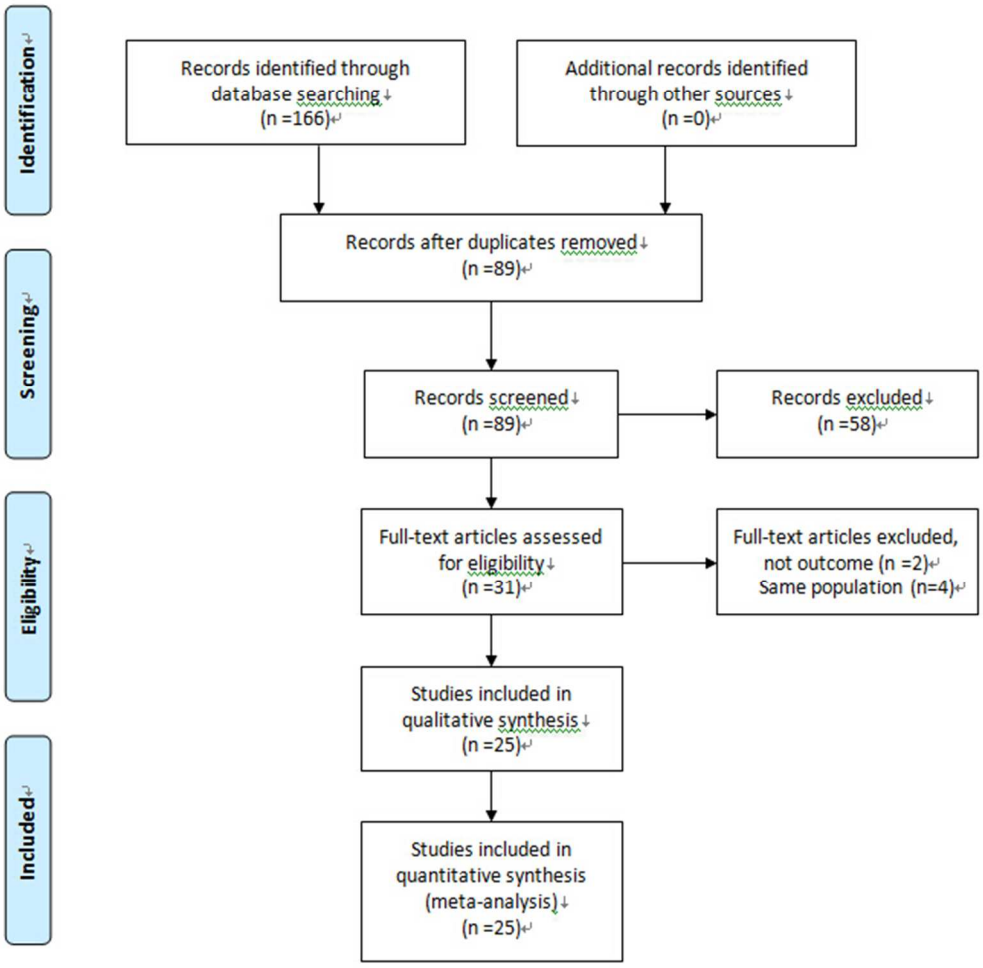
Name	Sampling scheme	Population characteristics	Prevalence definition	Diagnostic criteria	Response rate %	Score
Zhang feng	Random stratified sample	adequate	clear	clear	95	4
Liu lijuan	Random stratified sample	adequate	clear	clear	N/A	3
Liu qing	Cluster sampling	adequate	clear	clear	48.5	3
Li shengjie	Random stratified sample	adequate	clear	clear	100	4
Zhang zhiyong	Cluster sampling	adequate	clear	clear	97.75	4
Cai xinduan	Random stratified sample	adequate	clear	clear	98.05	4
Zhangjian	Random stratified sample	adequate	clear	clear	N/A	3
Wang renli	Random stratified sample	adequate	clear	clear	N/A	3
Pei guangde	Random stratified sample	adequate	clear	clear	53.4	3
Chenying	Random stratified sample	adequate	clear	clear	90.8	4
Zhang hong	Cross-sectional	adequate	clear	clear	N/A	3
Deng bin	Random stratified sample	adequate	clear	clear	N/A	3
Cui jianping	Random stratified sample	adequate	clear	clear	98.1	4
Min li	Random stratified sample	adequate	clear	clear	N/A	3
Feng jieying	Random stratified sample	adequate	clear	clear	98.24	4
Gao aili	Cross-sectional	adequate	clear	clear	96.2	4
Wu tieqiang	Cross-sectional	adequate	clear	clear	98.84	4
Sun zhenxiu	Random stratified sample	adequate	clear	clear	N/A	3
Liu zhaorui	Random stratified sample	adequate	clear	clear	N/A	3
Zhang aihua	Random stratified sample	adequate	clear	clear	N/A	3
Fu rui	Cross-sectional	adequate	clear	clear	99.06	4
Li bing	Random stratified sample	adequate	clear	clear	95.2	4
Yiwei Shen	Community-based study	adequate	clear	clear	86.84	4
Law MP	Cross-sectional	adequate	no	clear	99.3	4
Wu TQ	Cross-sectional	adequate	clear	clear	98.8	4

N/A= not available.

Table 3. Adjusted odds ratios for acne obtained by logistic meta-regression analysis

Factor	Number of studies	OR (95% CI)	P-value
Age of range			
undergraduate	11	1.00	
primary and secondary school students	10	3.127 (0.001-3.838)	0.012
Gender			
female	24	1.00	
male	24	1.217 (0.109-14.681)	0.024
Location			
north	10	1.00	
south	14	1.184 (0.002-3.833)	0.028

OR= odds ratio. CI=confidence interval



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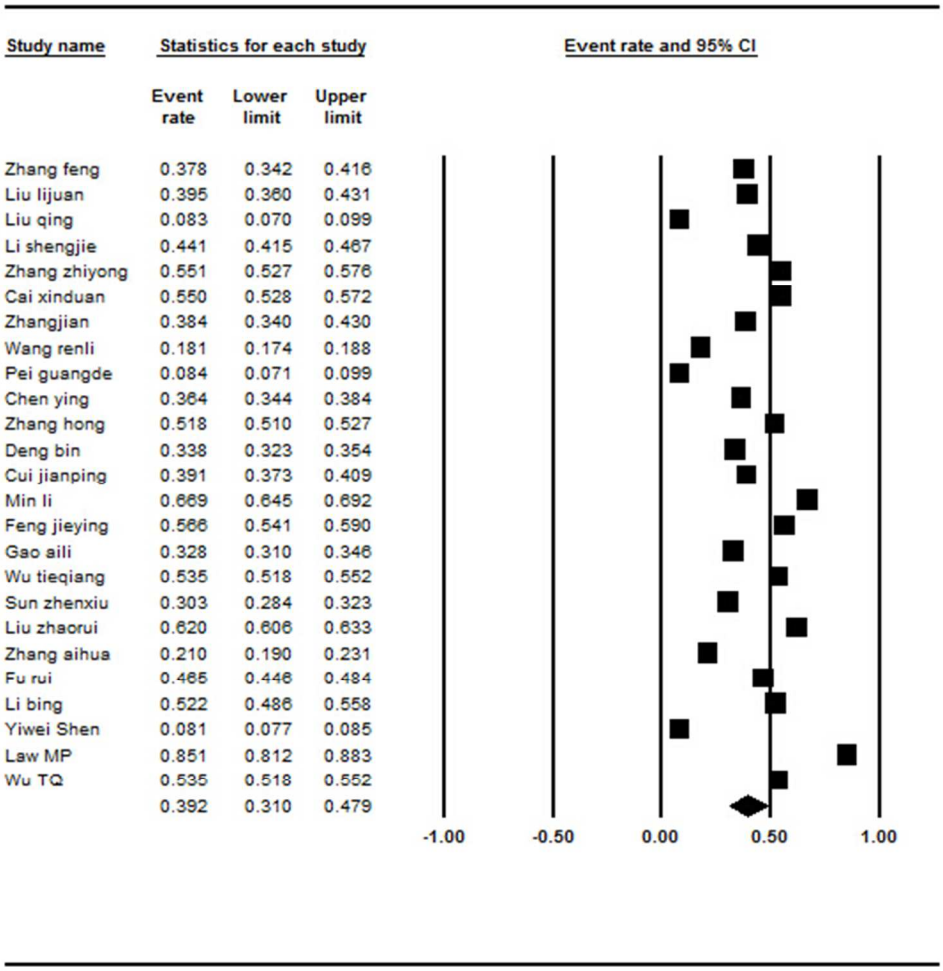

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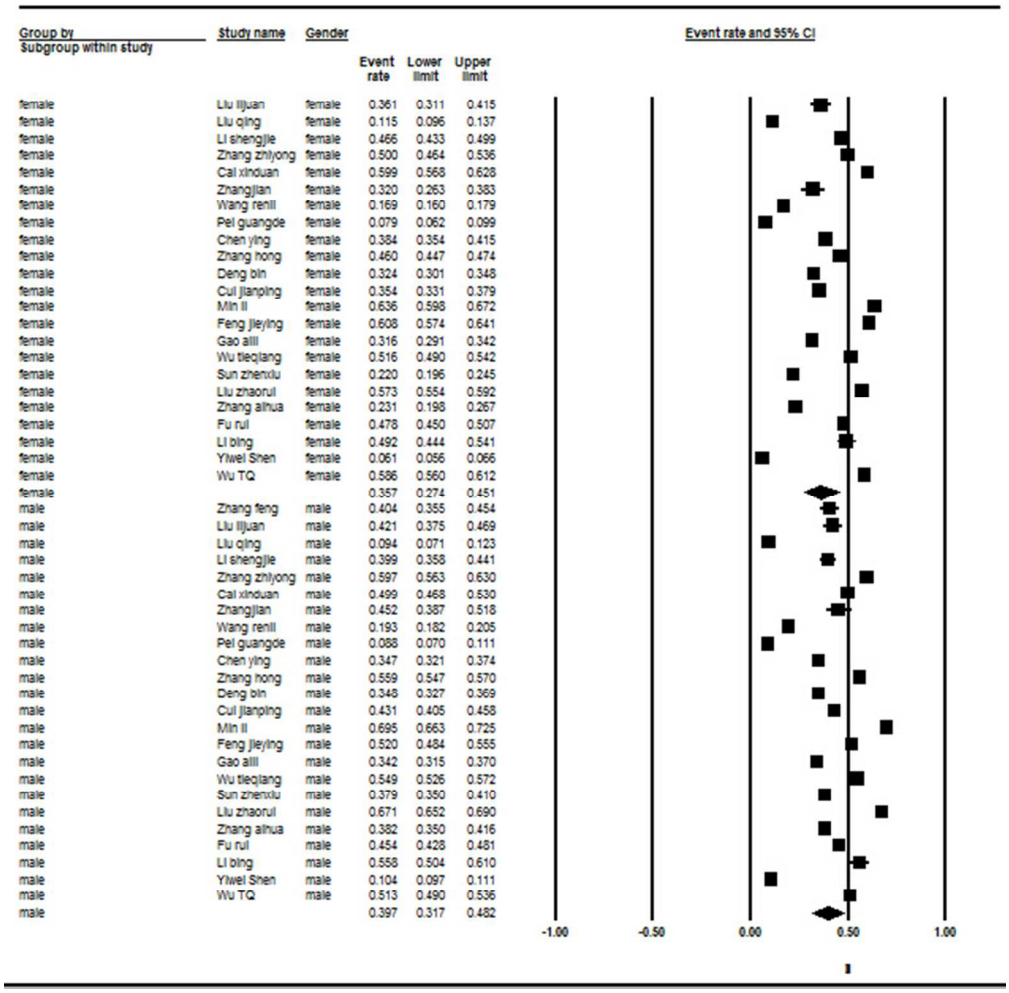

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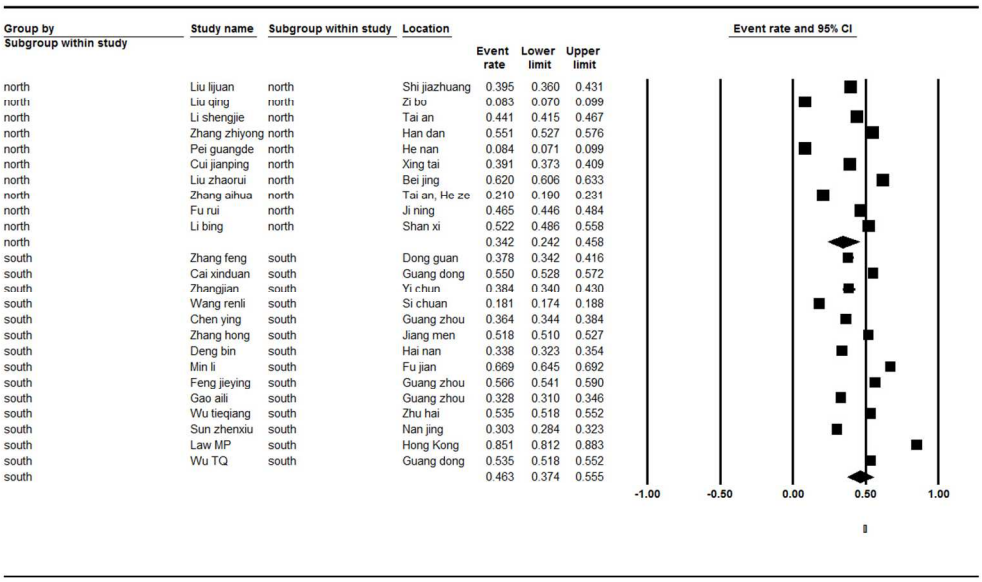

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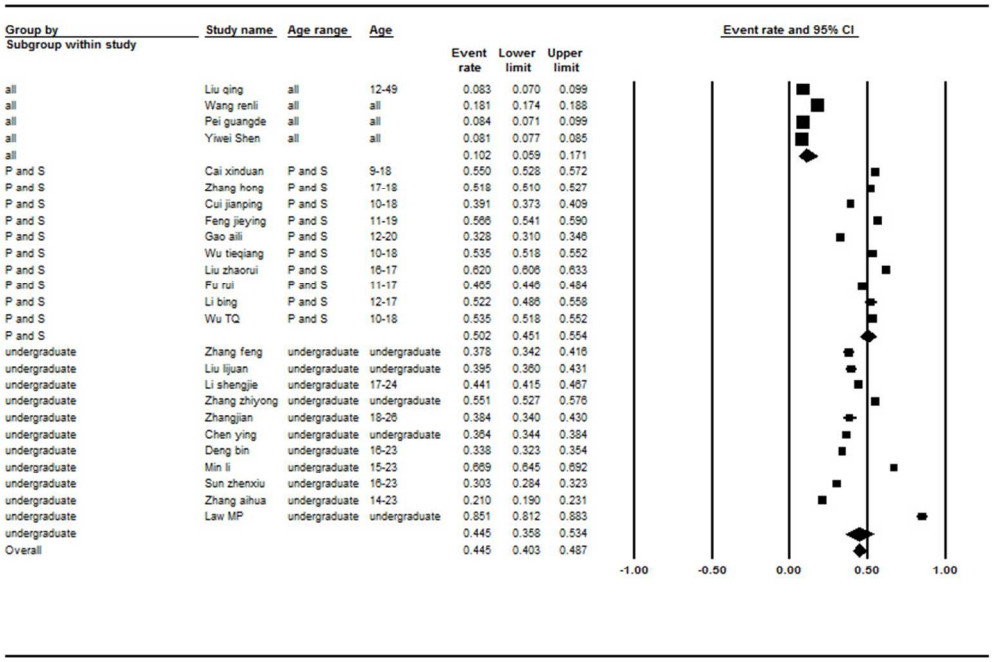

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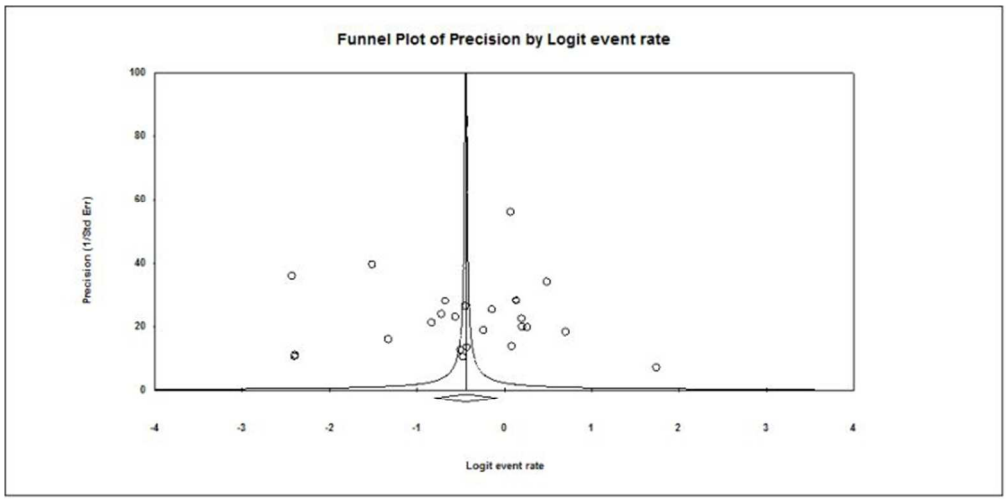
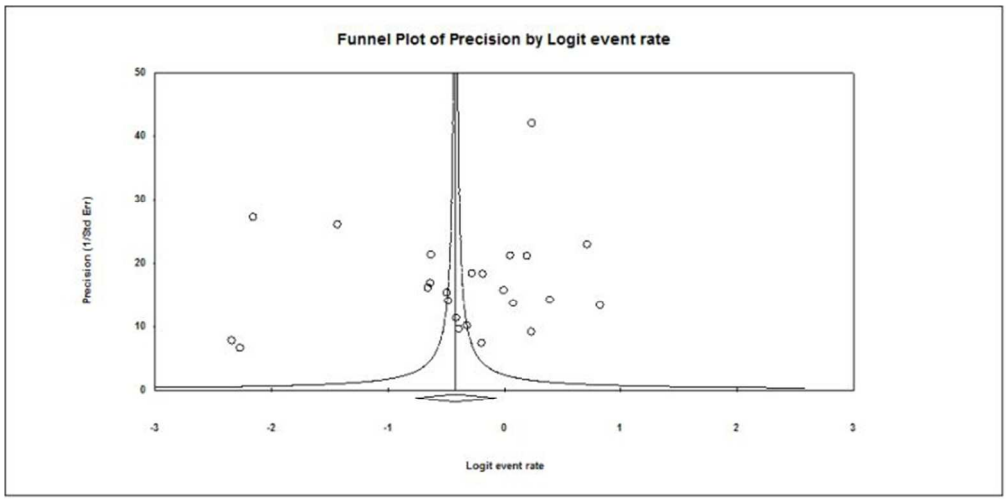
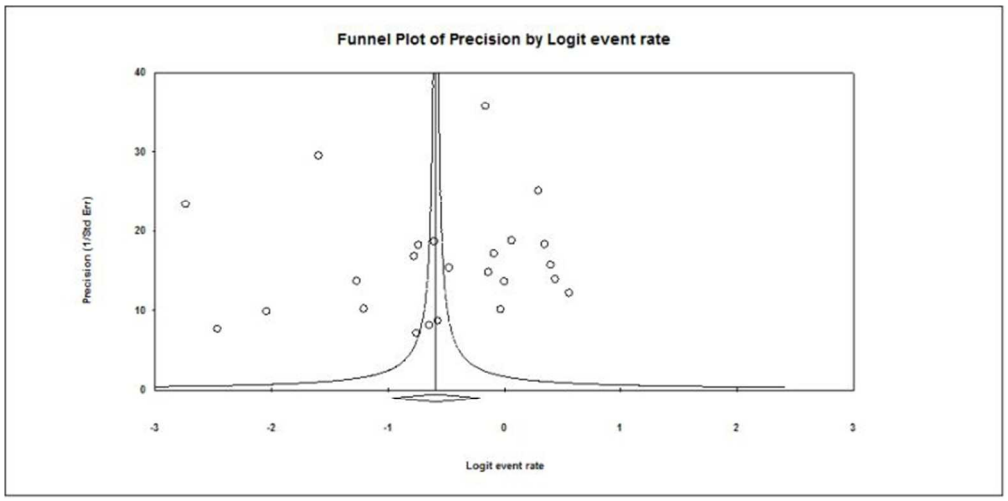
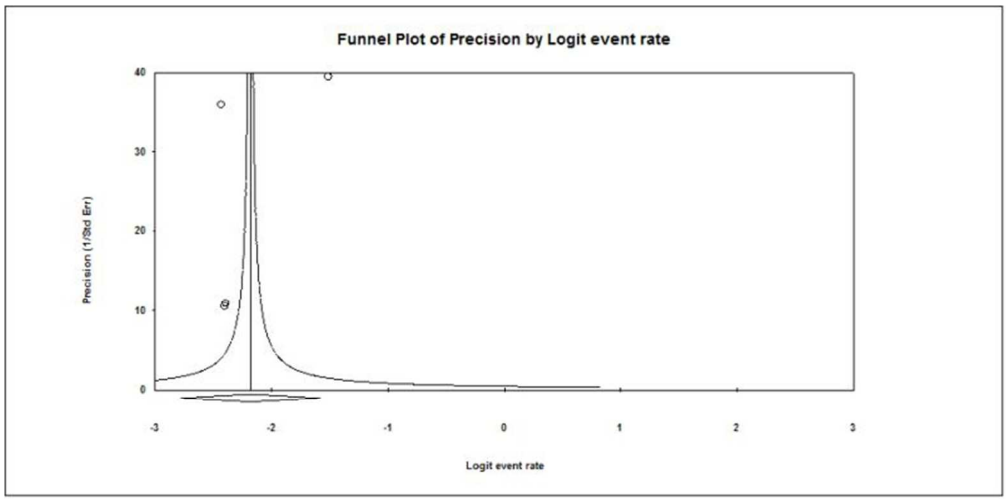
Supplementary table 1. Details of electronic bibliographic database search strategies

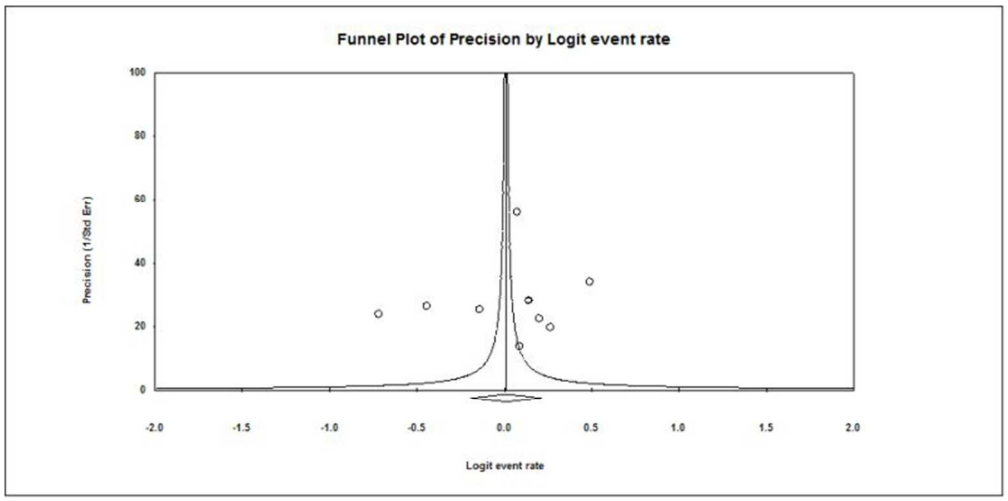
Database	Search strategies
Pubmed	((("acne vulgaris"[MeSH Terms] AND (("prevalence"[MeSH Terms]) OR "incidence"[MeSH Terms])) AND ("China"[MeSH Terms]) OR "Chinese"[MeSH Terms])
Embase	Title or Abstract acne AND Title or Abstract (china or chinese) AND Title or Abstract (prevalence or incidence or epidemiology)
Web of science	Title or Abstract:(acne) AND Title or Abstract: (prevalence or incidence or epidemiology) AND Title or Abstract: (china or Chinese)
China National Knowledge Infrastructure Periodicals	Keywords: acne AND Keywords: prevalence or incidence or epidemiology
The VIP Database for Chinese Technical	(1) Title or Keywords: acne; Property: dim AND Title or Keywords: prevalence; Property: dim (2) Title or Keywords: acne; Property: dim AND Title or Keywords: incidence; Property: dim
The Wan Fang Database for Chinese Periodicals	(1) Title or Keywords: acne; Property: dim AND Title or Keywords: prevalence; Property: dim (2) Title or Keywords: acne; Property: dim AND Title or Keywords: incidence; Property: dim

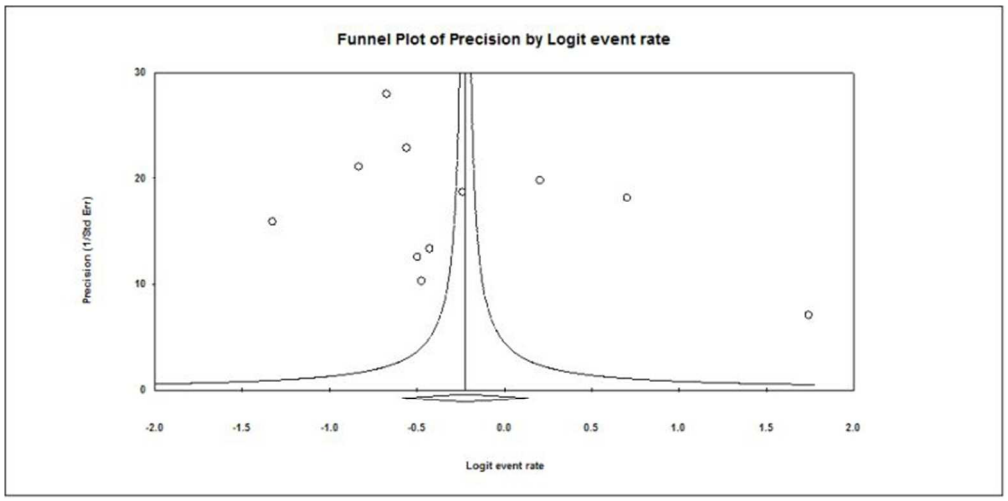


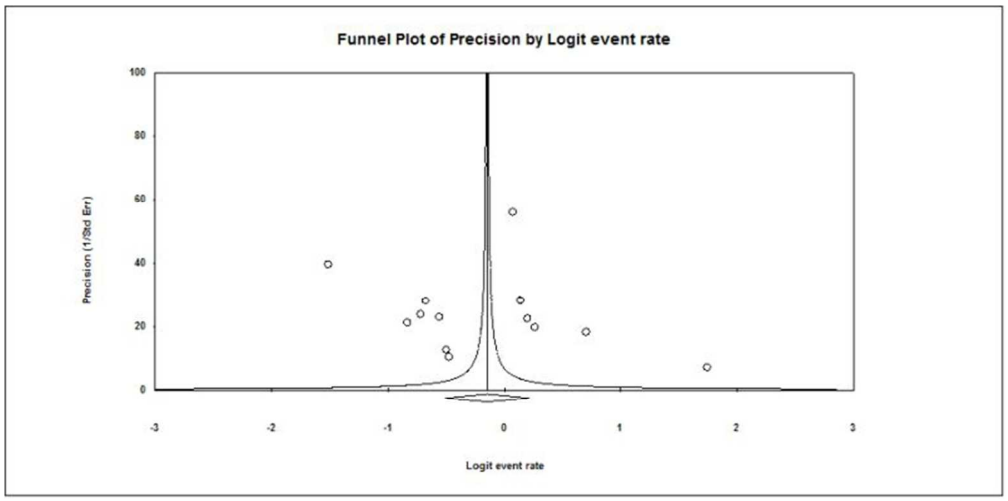


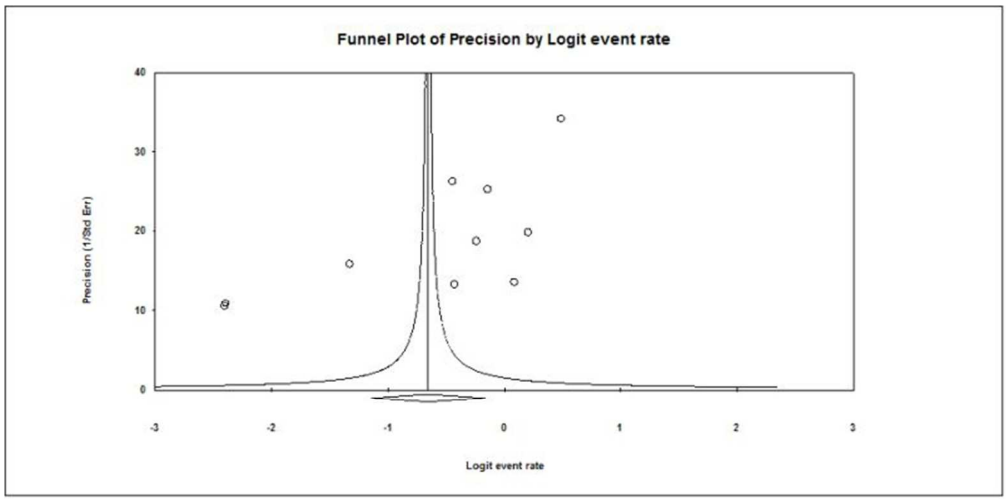












PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	The Prevalence of Acne in Mainland China: a systematic review and meta-analysis	1
ABSTRACT			
Structured summary	2	**Objectives:** The aim of this review is to estimate the prevalence of acne in mainland China comprehensively and to quantify its association with gender, region and age. **Methods and analysis:** We searched electronic databases with predetermined search terms to identify relevant studies published between January 1, 1996 and September 30, 2016. Note Express software, Comprehensive Meta-Analysis version 2.0, Logistic meta-regression analysis was used to dispose data and analyse. **Results:**The overall pooled prevalence rates of acne were 39.2%. In mainland China, primary and secondary students exhibited higher prevalence rates than undergraduate students; males had higher prevalence rates of acne than females; and the prevalence rates of acne in southern China was higher than northern China.	2,3
INTRODUCTION			
Rationale	3	Acne vulgaris burden exhibits global distribution and has continued to grow in prevalence over time within this population. Acne can result in psychological distress and have profound effects on patients' self-esteem. China comprises 34 province-level administrative regions, with 56 nations and a population of 1.3 billion people, a country-wide, population-based study of the prevalence rates of acne in China was needed.	3,4
Objectives	4	In this review, we examined the prevalence of acne in mainland China and to analyse the effects of gender, region and age on it.	4
METHODS			

PRISMA 2009 Checklist

Protocol and registration	5	We have no original protocol and registration, so this item isn't applicable.	
Eligibility criteria	6	Studies that met all of the following criteria were included in the meta-analysis, (1) the study was a population-based survey; (2) the study evaluated the prevalence/incidence of acne; (3) the investigation involved random sampling or cluster sampling; (4) the sample size was >300; A flow chart illustrating the article search process is presented in Figure 1.	5,6
Information sources	7	Studies were aggregated from six databases between January 1, 1996 and September 30, 2016, including PubMed, EMBASE, the Web of Science, the China National Knowledge Infrastructure, the VIP Database for Chinese Technical Periodicals, and the Wan Fang Database for Chinese Periodicals.	4
Search	8	The following search terms were used to retrieve relevant studies, (acne), (prevalence or incidence) AND (China or Chinese).	4
Study selection	9	Figure1	Figure1
Data collection process	10	The data in this study were extractd independently and checked after independent extraction by two investigators.	5
Data items	11	(1) the name of the first author; (2) the location of the investigation area; (3) the year in which the investigation occurred; (4) the age range of the subjects; (5) the sample size (male, female, and overall); (6) the prevalence rates obtained for males, females, and overall; (7) the method used to sample subjects; (8) the criteria used to diagnose acne; and (9) the response rate.	5
Risk of bias in individual studies	12	Quality assessment and analysis of the publication bias	5
Summary measures	13	odds ratios (ORs) and their associated 95% confidence intervals (CIs)	6
Synthesis of results	14	The heterogeneity of the pooled prevalence was estimated using the χ^2-based Q statistic and I^2 metrics. A random-effects model was used if heterogeneity was observed ($p<0.05$); otherwise, a fixed-effects model was applied. All studies were classified into subgroupsof regions, ages and gender. The associations of age, gender, and region with the prevalence of acne were evaluated using a logistic meta-regression model.	6

Section/topic	#	Checklist item	Reported

PRISMA 2009 Checklist

			on page #
Risk of bias across studies	15	Table 2	Table2
Additional analyses	16	Logistic meta-regression model, subgroup analysis	6
RESULTS			
Study selection	17	Using the initial search strategy, 166 studies were identified, and 141 studies were subsequently excluded (Figure 1). A total of 25 studies 2-4, 9-30 involving 83,008 Chinese individuals were included in this meta-analysis.	6,7
Study characteristics	18	Detailed characteristics of each included study were presented in Table 1.	Table 1
Risk of bias within studies	19	The overall quality of all included studies was found to be adequate (Table 2).	Table 2
Results of individual studies	20	Figure2-5	Figure2-5
Synthesis of results	21	Figure2-5	Figure2-5
Risk of bias across studies	22	Table 2	Table 2
Additional analysis	23	logistic meta-regression model, subgroup analysis	8
DISCUSSION			
Summary of evidence	24	Our results showed that the overall pooled prevalence of acne was 39.2% for all ages. The prevalence rates in different age groups were 10.2% overall (95% CI=0.059-0.171), 50.2% for primary and secondary students (95% CI=0.451-0.554), and 44.5% for undergraduates (95% CI=0.358-0.534); by gender, the prevalence rates were 35.7% for females (95% CI=0.274-0.451) and 39.7% for males (95% CI=0.317-0.482); and by region, the prevalence rates were 34.2% northern China (95% CI=0.242-0.458) and 46.3% for southern China (95% CI=0.374-0.555).	9
Limitations	25	The diagnostic criteria for acne differed across studies and the age of the survey population could not be subdivided.	3
Conclusions	26	The overall pooled prevalence of acne was 39.2% in mainland China; acne occurred highly in primary students and secondary students than undergraduate students; the prevalence of acne in males was greater than that in females; and acne was more common in northern China than in southern China. This meta-analysis of the prevalence of acne may provide a sound basis for the future provision of health services.	9
FUNDING			
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The Prevalence of Acne in Mainland China: a systematic review and meta-analysis

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Abstract

Introduction Acne, a very common skin disease, can result in psychological distress and sustain impairment in quality of life. Data on the prevalence of acne and the differences in gender, region and age is limited. The aim of this review is to estimate the prevalence of acne in mainland China comprehensively and to quantify its association with gender, region and age.

Methods We searched electronic databases with predetermined search terms to identify relevant studies published between January 1st 1996 and September 30th 2016. We pointed out repeated results using Note Express software and evaluated the studies for inclusion. Two independent reviewers extracted the data, followed with statistical analyses using Comprehensive Meta-Analysis software version 2.0. A random-effects model was adopted to calculate the overall pooled prevalence and to merge categories, including gender (males and females), region (Northern China and Southern China) and age (primary and secondary students: 7-17 years old; undergraduates: 18-23 years old; overall: no limits of age) for subgroup analyses. Logistic meta-regression analysis was used to clarify the associations between acne and the predictors age, gender, and region using odds ratios and their associated 95% confidence intervals.

Results 25 relevant studies were included in this meta-analysis. The overall pooled prevalence rates of acne were 39.2% (95% CI=0.310-0.479). The prevalence rates in different age groups were 10.2% overall (95% CI=0.059-0.171), 50.2% for primary and secondary students (95% CI=0.451-0.554), and 44.5% for undergraduates (95% CI=0.358-0.534); by gender, the prevalence rates were 35.7% for females (95% CI=0.274-0.451) and 39.7% for males (95% CI=0.317-0.482); and by region, the prevalence rates were 34.2% for Northern China (95% CI=0.242-0.458) and 46.3%

for Southern China (95% CI=0.374-0.555). The associations between acne and the predictors age, gender, and region were statistically significant.

Conclusions In mainland China, primary and secondary students exhibited higher prevalence rates than undergraduate students; males had higher prevalence rates of acne than females; and the prevalence rates of acne in Southern China was higher than Northern China.

Strengths and limitations

To our knowledge, this was the first systemic review evaluating the overall acne prevalence in mainland China and analyzing its associations with age, gender, and region.

This systematic review, covering 12 different provinces, was composed of 25 studies, with 80 thousand people over a 41-year period.

Some limitations should be considered: the diagnostic criteria for acne differed among the included studies; the age of the survey population could not be subdivided. Moreover due to heterogeneity among papers, the samples changed from variable to variable.

Introduction

Acne, a very common skin disease among adolescents, is the fourth most common reason for patients aged 11–21 years to visit a doctor in the USA[1]. Acne is estimated to affect 9.4% of the world's population with the highest prevalence in adolescents[2]. Acne vulgaris-associated disease burden exhibits global distribution and has continued to grow in prevalence over time within this population[3]. In addition, a group of increasing epidemiological data suggest that acne also affects a considerable number of adults[4], and women are more frequently affected by adult acne than

men[5]. The incidence of acne is different from various countries and ethnic groups. The prevalence of acne is reported to be low in developing countries of Africa[6,7]. In Northern Tanzania, the prevalence of acne is reported to be 0.1%[8], whereas the prevalence of acne is 3.9% in the German population aged between 16 and 70 years[9]. However, a comprehensive systemic review of the prevalence of acne in the Chinese population is still lacking. Several studies have shown that the estimated prevalence rate of acne varies from 8.1% to 85.1% in China[10-12] depending on the region, subjects' ages, and nationality studied.

Acne is a chronic inflammatory disease of the pilosebaceous unit resulting from androgen-induced increased sebum production, altered keratinization, inflammation, and bacterial colonisation of hair follicles by *Propionibacterium acnes*[13]. Acne vulgaris alters the normal skin physiology, impairing stratum corneum and causing transepidermal water loss[14]. The clinical features of acne include papules, pustules, cysts, comedos, and nodules. Acne occurs primarily on the face, neck, and upper trunk and can lead to scar formation if treated improperly. Acne scarring is a frequent complication of acne and patients often lack effective and safe methods for managing this condition[15]. The resulting scars may negatively impact on an affected person's psychosocial and physical well-being. It has been reported that acne can result in psychological distress and have profound effects on the patients' self-esteem, which may lead to anxiety, depression, diminished self-confidence, and communication difficulties[16,17].

Many large population-based studies have been conducted to estimate the prevalence rates of acne in regional populations, but a comprehensive statistical analysis of the prevalence of Chinese acne has not emerged so far. China, being a vast region, comprises of 34 province-level administrative regions, with 56 ethnic groups and a

population of 1.3 billion people. Therefore a country-wide, population-based study of the prevalence rates of acne in China was needed. In this review, we examined the prevalence of acne in mainland China systematically and analysed the effects of gender, region and age on acne.

Methods

Search strategy

Studies were aggregated from six databases between January 1st 1996 and September 30th 2016, including PubMed, EMBASE, Web of Science, the China National Knowledge Infrastructure, the VIP Database for Chinese Technical Periodicals, and the Wan Fang Database for Chinese Periodicals. The following search terms were used to retrieve relevant studies, (acne), (prevalence or incidence) AND (China or Chinese). The combination of acne, prevalence, incidence, China and Chinese were used in varying combinations to identify relevant literature. Search strategies were customised to suit each database. The search strategy is presented in supplementary table 1. In addition, a manual search was performed by checking the reference lists of eligible articles and relevant reviews.

Inclusion criteria

Studies that met all of the following criteria were included in the meta-analysis,

(1) the study was a population-based survey;

(2) the study evaluated the prevalence/incidence of acne;

(3) the investigation involved random sampling or cluster sampling;

(4) the sample size was >300;

A flow chart illustrating the article search process is presented in Figure 1.

Data management

Any duplicate studies was removed by Note Express. Two reviewers (Qiang Chen and

Danhui Li) independently evaluated the title and abstract of all studies identified through the search against the inclusion and exclusion criteria. The full text of all eligible studies were then retrieved. Any disagreement were resolved by a third reviewer. Excluded studies and the reasons for exclusion were recorded.

Data extraction

Customised data information was extracted independently by two investigators. The following information was collected for each study: (1) the name of the first author; (2) the location of the investigation area; (3) the year in which the investigation occurred; (4) the age range of the subjects; (5) the sample size (male, female, and overall); (6) the prevalence rates obtained for males, females, and overall; (7) the method used to sample subjects; (8) the criteria used to diagnose acne; and (9) the response rate.

Risk of bias (quality) assessment

Four key criteria[18, 19] were used by two independent investigators (Yi Liu and Danhui Li) to estimate study quality: (1) the sampling scheme (random or consecutive); (2) whether the study included an adequate description of the characteristics of the study population; (3) whether a clear definition of the prevalence rate was provided; and (4) whether the response rate exceeded 75%. The scoring rule used was the following, for each quality item, “clear or adequate” was scored as 1 point, whereas “no” was scored as 0 points. The study was considered to be of adequate quality if the quality score was greater than or equal to 3. The two reviewers carefully assessed the included studies independently and agreed on the final grading. An additional reviewer was consulted should there be any uncertainty or disagreement.

Ethics and dissemination

Since primary data was not collected, formal ethical approval was not required. The results will be disseminated through peer-reviewed publications, conference

presentations and the media.

Statistical analysis

The statistical analyses were performed using Comprehensive Meta-Analysis software version 2.0 (Biostat, Englewood Cliffs, NJ, USA; http,//www.meta-analysis.com). We calculated the pooled prevalence estimates as proportions and 95% CIs for the subgroup categories weighted by the sample sizes of the individual studies and then pooled these data to derive an overall proportion and its associated 95% CI. The heterogeneity of the pooled prevalence was estimated using the χ^2-based Q statistic. Meanwhile, I^2 metrics were calculated to quantify heterogeneity. A random-effects model was used if heterogeneity was observed ($p<0.05$); otherwise, a fixed-effects model was applied. All studies were classified into one of two groups (North versus South) according to the geographical regions in which the studies were conducted. Similarly, the studies were classified into three groups based upon the age of the participants in the samples, overall (no limits of age), undergraduate (18-23 years old), and primary and secondary students ("p and s", 7-17 years old). Subjects were also classified as male and female. The associations of age, gender, and region with the prevalence of acne were evaluated using a logistic meta-regression model. The associations between age, gender, region and risk of acne were expressed as ORs and 95% CIs. A value of $p<0.05$ was considered statistically significant.

Analysis of the publication bias

To examine the authenticity of data, the Egger test and Funnel plots were produced using the Comprehensive Meta-Analysis software version 2.0. No publication bias exists if the studies arranged symmetrically around the central line with a p value of > 0.05.

Results

Characteristics of the studies

Using the initial search strategy, 166 studies were identified. 141 studies were subsequently excluded (Figure 1). A total of 25 studies[10-12,20-41] involving 83,008 Chinese individuals were included in this meta-analysis. Detailed characteristics of each included study are presented in Table 1. The overall quality of all included studies was found to be adequate (Table 2).

The overall prevalence rates of acne in mainland China

A total of 25 studies involving 83,008 Chinese people were included in this meta-analysis. However, there was significant heterogeneity in this meta-analysis (I^2=99.797%, Q=11823.369, P<0.001). Thus, a random-effects model was selected for the analysis. The overall pooled prevalence of acne was 39.2% (95% CI=0.310-0.479; Figure 2).

The prevalence rates of acne in mainland China by gender

A total of 24 studies involving 40,712 males and 41,907 females were included in this subgroup meta-analysis. However, there was significant heterogeneity among both the males (I^2=99.582%, Q=5508.959, P<0.001) and females (I^2=99.614%, Q=5957.125, P<0.001) in this meta-analysis. Thus, a random-effects model was selected for the analysis. Males (39.7%, 95% CI=0.317-0.482) exhibited a higher prevalence of acne than females (35.7%, 95% CI=0.274-0.451, Z=3.903, p<0.001) in the subgroup analysis (Figure 3).

The prevalence rates of acne in mainland China by region

A total of 24 studies involving 65,663 Chinese were included in this subgroup meta-analysis. 10 of these studies were conducted in Northern China (19,377 Chinese), and 14 studies were conducted in Southern China (46,286 Chinese). However, significant heterogeneity was found in both the North (I^2=99.573%,

Q=2109.204, P<0.001) and the South (I^2=99.689%, Q=4176.791, P<0.001) subgroups in this meta-analysis. Thus, a random-effects model was selected for the analysis. The South (46.3%, 95% CI=0.374-0.555) had a higher prevalence of acne than the North (34.2%, 95% CI=0.242-0.458, Z=2.498, p=0.012) in the subgroup analysis (Figure 4).

The prevalence rates of acne in mainland China by age

A total of 25 studies, consisting of 4 studies that examined the overall population, 10 p and s studies, and 11 undergraduate studies, were included in this subgroup meta-analysis. However, significant heterogeneity was found overall (I^2=99.534%, Q=643.149, P<0.001), for the p and s subgroup (I^2=98.860%, Q=789.719, P<0.001), and for the undergraduates (I^2=99.130%, Q=1149.658, P<0.001) in this meta-analysis. Thus, a random-effects model was selected for the analysis. The prevalence of acne over all ages was 10.2% (95% CI=0.059-0.171). The p and s students (50.2%, 95% CI=0.451-0.554) had a higher prevalence of acne than did the undergraduates (44.5%, 95% CI=0.358-0.534, Z=2.411, p=0.016) in the subgroup analysis (Figure 5).

Logistic meta-regression analysis of the associations between age, gender, and region and the prevalence of acne

The associations between acne and the predictors age, gender, and region were statistically significant (Table 3) as measured by the corresponding ORs and their associated 95% CIs. The OR of acne prevalence was 1.217 (95% CI=0.109-14.681, p=0.024) between male and female subgroups. Suggesting that Chinese males might be more susceptible to acne than females. The OR between Southern China and Northern China were 1.184 (95% CI=0.002-3.833, p=0.028) for acne. The geographical factors of Southern China might be a risk factor for acne. The OR between p and s students and undergraduate were 3.127 (95% CI=0.001-3.838, p=0.012) for acne, therefore age might have a vital role in the development of acne.

Analysis of the publication bias

There were no obvious asymmetries in the Funnel plots and the p value exceeded 0.05 for the following groups: the overall pooled studies (t=0.030, p=0.976, 95% CI=-0.215~0.222) (Supplementary Figure 1), male subgroup (t=0.346, p=0.733, 95% CI=-0.185~0.132) (Supplementary Figure 2), female subgroup (t=0.143, p=0.887, 95% CI=-0.164~0.188) (Supplementary Figure 3), subgroup of all age layers (t=0.501, p=0.666, 95% CI=-0.831~0.658) (Supplementary Figure 4), subgroup of p and s students (t=0.580, p=0.578, 95% CI=-0.246~0.147) (Supplementary Figure 5), subgroup of undergraduates (t=1.061, p=0.316, 95% CI=-0.121~0.335) (Supplementary Figure 6) and Southern China subgroup (t=0.441, p=0.667, 95% CI=-0.194~0.293) (Supplementary Figure 7). Only the studies of the Northern China subgroup had publication bias (t=3.369, p=0.01, 95% CI=-0.520~-0.974) (Supplementary Figure 8).

Discussion

This meta-analysis, based on 83,008 subjects, derived from 25 studies, covering 12 provinces and municipalities in China, enables us to assess reliable prevalence rates of acne at the national level. Our results showed that the overall pooled prevalence of acne was 39.2%. Other studies have reported a range of acne prevalence from different countries, such as 3.9% in the German population aged between 16 and 70 years[9] and 61.5% in the Portugal population between the ages of 20 to 60 years old[42]. The differences in age range, ethnic background, regions and pollution might explain the difference in the incidence of acne. Skin is the outermost barrier and various air pollutants such as oxides, particulate matter, ultraviolet radiation, polycyclic aromatic hydrocarbons and the ozone can all affect the skin. Puri[43] reported that air pollutants can cause damage to the skin by inducing oxidative stress, and prolonged or repetitive

exposure to high levels of these pollutants may have profound negative effects on the skin. The various degrees of air pollution in different countries over the years has had different effects on the human skin. Males (39.7%) exhibited a higher prevalence of acne than females (35.7%, Z=3.903, p<0.001) in the subgroup analysis of gender. Meanwhile, the South (46.3%) had a higher prevalence of acne than the North (34.2%, Z=2.498, p=0.012) in the regional subgroup analysis. Moreover, the primary and secondary students (50.2%) had a higher prevalence of acne than undergraduates (44.5%, Z=2.411, p=0.016) in the subgroup analysis of age. There was heterogeneity among the 25 included studies in this meta-analysis (I^2=99.797%, Q=11823.369, P<0.001) and the following reasons might explain the phenomenon. (1) Differences existed in the design of studies, such as non-unified age range, collection of data and research objects, explaining the deviation of the prevalence of acne. (2) Evidence for seasonality was observed, with lower lipid production and reduced barrier function during the winter[44]. A correlation between the incidence of acne and skin surface lipid[34,45] has been observed before, thus the included articles may have been conducted in different seasons[26,29,35,40], which resulted in different incidences of acne. The age-related subgroup prevalence rates were also calculated in this study. The prevalence of primary and secondary students was 50.2%, which was consistent with the results of Wei *et al*[46] (51.3%). This result was similar to those reported by Karciauskiene *et al*'s[47] results among schoolchildren aged 7-19 years, which was 55.4% in Lithuania. However, these results are lower than a study conducted in Brazil, where a prevalence rate of 96% was found in adolescents aged 10-17[48]. This difference may also be attributed to the different age range, regions and ethnic backgrounds of the study subjects. Our results suggest that primary and secondary students (50.2%) had a higher prevalence of acne than undergraduates (44.5%,

Z=2.411, p=0.016), which is in agreement with the findings of Shen *et al*[10]. Moreover, using Logistic meta-regression analysis, we found that the OR between primary and secondary school students and undergraduate were 3.127 (95% CI=0.001-3.838, p=0.012) for acne. Vilar *et al*[49] and Yentzer *et al*[50] also reported that primary and secondary students (89.3%) had a higher prevalence of acne than the undergraduate subjects (61.9%) in the US population. Choi *et al*[51] reported that in patients with late onset acne, the number of comedones and total number of acne lesions and the proportions of comedones were significantly less than in patients with early onset acne. The age of onset had a negative correlation with the number of comedones and the proportion of comedones in the T-zone and the entire face, namely, acne. The clinical differences in acne based on age appeared to be mainly a result of age of onset and not from the progression of the acne[52,53].

In the present study, males (39.7%) had a 1.112 times higher prevalence rate of acne than did females (35.7%, Z=3.903, p<0.001). This result is in agreement with the findings of Schafer *et al*[54] that acne was more present in men (29.9%) than women (23.7%) in the city of Hamburg (Germany). Adityan and Thappa[55] showed that the male to female ratio was 1.25:1 in South India. In Auckland, Lello *et al*[56] reported that males (91%) were more susceptible to acne compared with females (79%) and severe and moderately severe acne was significantly more common in males (OR = 2.6, 95% Cl: 1.73 < OR < 3.9) as well. Furthermore, moderate and severe acne (27.1% and 0.4l% of patients, respectively) were significantly (P < 0.01) were common in males (36.2% and 0.9%, respectively) than females (21.2% and 0.2%, respectively) in Egypt[57]. This indicated that males had a higher risk of occurrence and development of acne than females. (1) This difference might be related to lifestyle. It is well known to us that males accounted for a larger proportion than females in drinking and

smoking[58-60]. (2) Males also tend to pay less attention to skin health than females in China. Inappropriate personal hygiene (use of abrasive soaps, harsh detergents, and excessive scrubbing) can contribute to the pathological process of acne[61,62]. (3) Androgen levels elevation are greater in males than females during adolescence and increased androgen levels are a risk factor of acne[63]. The interplay of growth hormone (GH), insulin, and insulin-like growth factor-1 (IGF-1) signaling during puberty may also have a causal role in the pathogenesis of acne by influencing adrenal and gonadal androgen metabolism[64]. Adult women in different age categories have a lower prevalence of acne than adolescence. But recent research has shown that acne is affecting an increasing number of adults, particularly females. Adult female acne should be considered as a specific acne subtype distinct from adolescent acne and a review on the topical and oral treatment options suitable for treating acne in adult females[5] are expected in the future.

The prevalence rates of acne was also different in different regions. The prevalence of acne among individuals in Southern China (46.3%) was higher than Northern China (34.2%, $Z=2.498$, $p=0.012$). This is consistent with Subramaniyan[65], who considered that the prevalence of acne was different between the East of the Indian mainland and its Southern part. This difference may be due to several factors. (1) Ultraviolet radiation. Enhanced sebum excretion, colonization of the pilosebaceous duct with *Propionibacterium acnes* and resultant inflammation were thought to play a critical role in the pathogenesis of acne[66]. The function of the sebaceous gland as an endocrine skin organ, which is mainly composed of sebocytes, has an important role in the occurrence and development of acne[67]. Excessive sebum production and its abnormal lipid ingredients from the sebaceous gland contributed to the formation of primary acne lesions[68]. Sebocytes also produce inflammatory cytokines and they have

a vital effect on the formation and aggravation of acne lesions[69]. Southern China has longer hours of sunshine than Northern China. Solar radiation contains ultraviolet radiation, which is an external environmental factor causing many skin diseases. Ultraviolet radiation can affect the glands through direct or indirect pathways[70]. It is widely accepted that sebaceous gland hyperplasia and increased sebum secretion occur after irradiation of ultraviolet (UV)-B. The expression of inflammatory cytokines, especially IL-1b, IL-6, IL-8 and TNF-a are significantly increased in cultured sebocytes after treatment with UV-B[71]. Meanwhile, correlational research showed that time-distinct gene induction of TNF-a, IL-1b and matrilysin in cultured HaCaT cells may be involved in UV-induced cellular responses[72]. Although, mRNA levels do not always correspond to protein level *in vivo*, mRNA levels of inflammatory cytokines such as IL-1, IL-6 and TNF-a are also identified to be increased through studies using whole mouse skin and human skin exposed to UV-B[73,74]. Furthermore, it has been known that epithelial keratinocytes contain a functional PPAR-c system and this system is a target for UV-B radiation[75]. The synthesis of free fatty acids by PPAR-c stimulates the production of pro-inflammatory cytokines, such as IL-1b and TNF-a, in sebaceous glands[71]. (2) Humidity. There is greater humidity in Southern parts of China than Northern China. Subramaniyan[65] reported that the prevalence of dermatoses, including acne, are much higher in humid regions than arid regions. (3) Diet. Chili is a popular food for Southern residents compared to the Northern residents, and is consumed in greater quantities than Northern residents. Spicy food has been identified as a risk factor for the development of acne[33]. In simple terms, both environmental factors (climate and humidity) and diet may lead to the different prevalence rates of acne between Northern and Southern China.

This systematic review is likely limited by the different diagnostic criteria for acne among the included studies. Due to the enormous number of Chinese people, it was difficult to implement an unitive diagnostic criteria. In addition, the age of the survey population could not be subdivided, which made further detailed analysis of age groups impossible. More research are needed on the national prevalence of acne in order to provide better baseline data and to monitor the effect of acne over time in China.

Conclusion

The overall pooled prevalence rate of acne was 39.2% in mainland China. Primary and secondary students exhibited higher prevalence rates than undergraduate students. Due to differences in lifestyle, skincare routines and androgen levels, males showed higher prevalence rates of acne than females. Possible etiological factors for the difference in prevalence rates of acne between Southern China and Northern China may be due to the varying ultraviolet radiation, humidity and dietary habits between these two regions. The evidence generated from this paper may prove beneficial in terms of understanding the age and regional distribution and prevalence rates of acne amongst the Chinese population, which may help in identifying target prevention and treatment strategies for this cohort of patients.

Footnotes

Contributors Shengjie Li and Danhui Li conceived the study, participated in drafting the final manuscript. Qiang Chen and Yi Liu analyzed the data and completed the final draft of the manuscript. TingTing Liu and Wenhui Tang prepared all the figures. All authors reviewed the manuscript.

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Figure legends

Figure 1 Flow-chart illustrating the article search process

First, we obtained 166 records identified through database searching. No additional records identified through other sources. Second, 89 records remained after duplicates were removed. Third, 58 studies were excluded after records screening. Then the remainder 31 studies were full-text articles assessed for eligibility and 6 studies were excluded. Finally 25 studies were included in the quantitative synthesis (meta-analysis).

Figure 2 Forest plot of the overall prevalence rates of acne. CI=confidence interval.

A total of 25 studies were included in this meta-analysis. Through analyzing in a random-effects model, the overall pooled prevalence of acne was calculated as 39.2% (95% CI=0.310-0.479) through analyzing in a random-effects model.

Figure 3 Forest plot of the prevalence rates of acne according to gender. CI=confidence interval.

A total of 24 studies were included in this subgroup meta-analysis. Through analyzing in a random-effects model, the prevalence rates of acne in males was 39.7% (95% CI=0.317-0.482) and 35.7% (95% CI=0.274-0.451) in females. Males (39.7%) exhibited a higher prevalence of acne than did females (35.7%) in the subgroup analysis (Z=3.903, p<0.001).

Figure 4 Forest plot of the prevalence rates of acne according to region. CI=confidence interval.

A total of 24 studies were included in this subgroup meta-analysis. 10 of these studies were conducted in Northern China and 14 studies were conducted in Southern China. Through analyzing in a random-effects model, the prevalence rates of acne in South was 46.3% (95% CI=0.374-0.555) and 34.2% in North (95% CI=0.242-0.458). The South (46.3%) had a higher prevalence of acne than the North (34.2%) in the subgroup analysis (Z=2.498, p=0.012).

Figure 5 Forest plot of the prevalence rates of acne according to age. CI=confidence interval. All=overall age. P and s=primary and secondary students.

A total of 25 studies, consisting of 4 studies that examined the overall population, 10 p and s studies, and 11 undergraduate studies, were included in this subgroup meta-analysis. Through analyzing in a random-effects model, the prevalence of acne over all ages was 10.2% (95% CI=0.059-0.171). The prevalence of acne in the primary and secondary students was 50.2% (95% CI=0.451-0.554) and 44.5% (95% CI=0.358-0.534) in the undergraduates. The primary and secondary students (50.2%) had a higher prevalence of acne than the undergraduates (44.5%) in the subgroup analysis (Z=2.411, p=0.016).

Supplementary Figure 1 Funnel plots for the overall pooled studies

The studies arranged around the center line symmetrically, so there was no publication bias.

Supplementary Figure 2 Funnel plots for the male subgroup
A total of 24 studies involving 40,712 males were included in the male subgroup meta-analysis. The 24 studies arrange around the center line symmetrically, so there was no publication bia.

Supplementary Figure 3 Funnel plots for the female subgroup
A total of 24 studies involving 41,907 females were included in the female subgroup meta-analysis. The 24 studies arranged around the center line symmetrically, so there was no publication bias.

Supplementary Figure 4 Funnel plots for the all-age-layer subgroup
A total of 4 studies were included in the all-age-layer subgroup meta-analysis. The studies arranged around the center line symmetrically, so there was no publication bias.

Supplementary Figure 5 Funnel plots for the subgroup of primary and secondary school students
A total of 10 studies were included in the subgroup meta-analysis of primary and secondary school students. The studies arranged around the center line symmetrically, so there was no publication bias.

Supplementary Figure 6 Funnel plots for the subgroup of undergraduates
A total of 11 studies were included in the subgroup meta-analysis of undergraduates. The studies arranged around the center line symmetrically, so there was no publication bias.

Supplementary Figure 7 Funnel plots for the subgroup of Southern China
A total of 14 studies were included in the Southern subgroup meta-analysis. The studies arranged around the center line symmetrically, so there was no publication bias.

Supplementary Figure 8 Funnel plots for the subgroup of Northern China
A total of 10 studies were included in the Northern subgroup meta-analysis. The studies arranged around the center line nonsymmetrically, so there was publication bias.

Tables

Table1. Characteristics of the populations examined in studies reporting the prevalence of acne in mainland China

Name	Region	Year	Age range	Sample size	Prevalence (%)		
					Male % (n)	Female % (n)	Total (%)
Zhang feng	Dong guan	2013	undergraduate	669	40.37 (379)	34.48 (290)	37.82
Liu lijuan	Shi jiazhuang	2013	undergraduate	742	42.11 (418)	36.11 (324)	39.49
Liu qing	Zi bo	2013	12-49	1455	9.4 (504)	11.5 (951)	8.32
Li shengjie	Tai an	2010	17-24	1416	39.85 (532)	46.61 (884)	44.07
Zhang zhiyong	Han dan	2010	undergraduate	1582	59.71 (834)	50.00 (748)	55.12
Cai xinduan	Guang dong	2010	9-18	2015	49.90 (986)	59.86 (1029)	54.99
Zhangjian	Yi chun	2011	18-26	448	45.16 (217)	32.03 (231)	38.39
Wang renli	Si chuan	2008-2009	all	10,503	19.3 (4319)	16.9 (6184)	18.1
Pei guangde	He nan	2008	all	1547	8.80 (742)	7.86 (805)	8.39
Chen ying	Guang zhou	2008	undergraduate	2252	34.7 (1253)	38.4 (999)	36.4
Zhang hong	Jiang men	2006-2008	17-18	12,450	55.9 (7134)	46.02 (5136)	51.83
Deng bin	Hai nan	2005	16-23	3500	34.8 (1990)	32.4 (1510)	33.8
Cui jianping	Xing tai	2007	10-18	2891	43.14 (1370)	35.44 (1521)	39.1
Min li	Fu jian	2007	15-23	1484	69.5 (836)	63.6 (648)	66.9
Feng jieying	Guang zhou	2004-2005	11-19	1561	51.95 (743)	60.76 (818)	56.57
Gao aili	Guang zhou	2004	12-20	2552	34.2 (1151)	31.6 (1305)	32.8
Wu tieqiang	Zhu hai	2004	10-18	3200	54.9 (1790)	51.6 (1410)	53.5
Sun zhenxiu	Nan jing	2005	16-23	2100	37.91 (1000)	22 (1100)	30.33
Liu zhaorui	Bei jing	2003	16-17	4933	67.1 (2364)	57.3 (2569)	62.0
Zhang aihua	Tai an, He ze	1996	14-23	1510	38.24 (829)	23.06 (581)	20.99
Fu rui	Ji ning	2012	11-17	2560	45.40 (1343)	47.80 (1177)	46.51
Li bing	Shan xi	2012	12-17	741	55.8 (335)	49.2 (406)	52.2
Yiwei Shen	China	2012	all	17,345	10.4 (7858)	6.1 (9487)	8.1
Law MP	Hong Kong	2010	undergraduate	389	N/A	N/A	85.1
Wu TQ	Guang dong	2007	10-18	3163	51.3 (1785)	58.6 (1378)	53.5

(n)= the number of participants, N/A= not available.

Table 2. Methodological quality of the studies reporting the prevalence of acne in mainland China

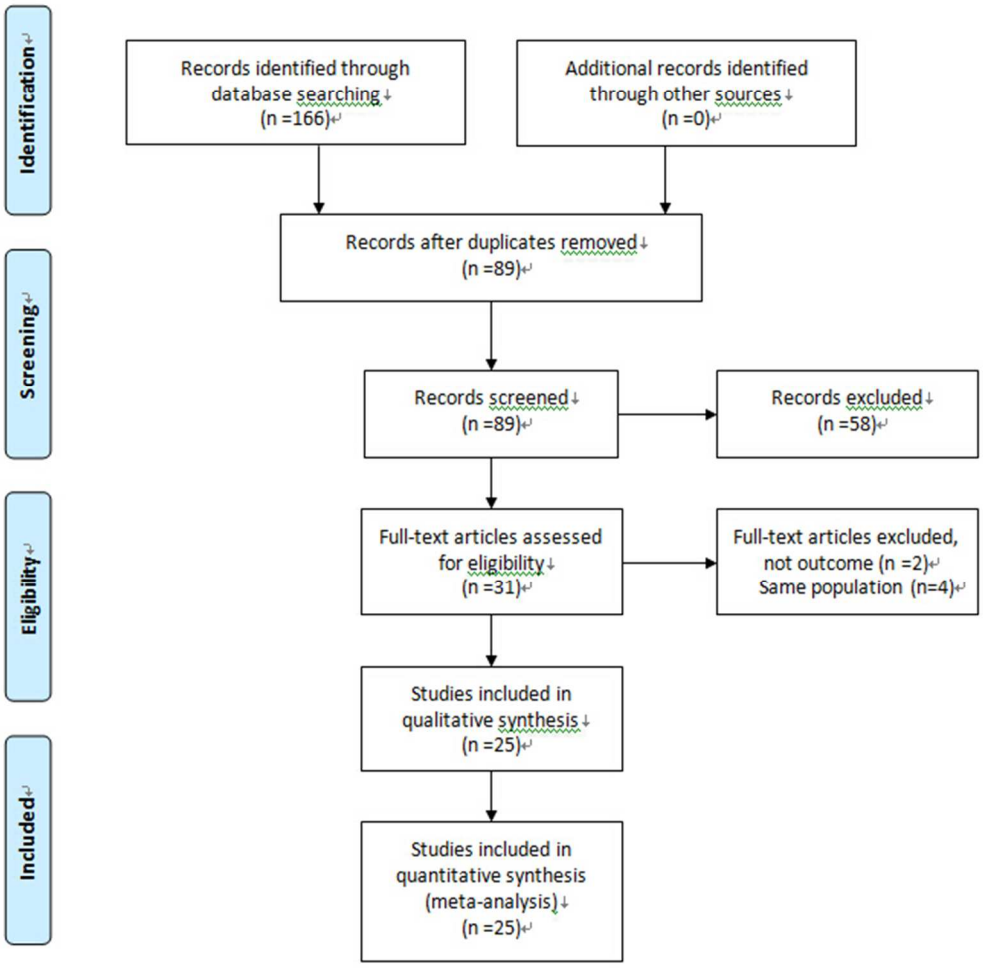
Name	Sampling scheme	Population characteristics	Prevalence definition	Diagnostic criteria	Response rate %	Score
Zhang feng	Random stratified sample	adequate	clear	clear	95	4
Liu lijuan	Random stratified sample	adequate	clear	clear	N/A	3
Liu qing	Cluster sampling	adequate	clear	clear	48.5	3
Li shengjie	Random stratified sample	adequate	clear	clear	100	4
Zhang zhiyong	Cluster sampling	adequate	clear	clear	97.75	4
Cai xinduan	Random stratified sample	adequate	clear	clear	98.05	4
Zhangjian	Random stratified sample	adequate	clear	clear	N/A	3
Wang renli	Random stratified sample	adequate	clear	clear	N/A	3
Pei guangde	Random stratified sample	adequate	clear	clear	53.4	3
Chenying	Random stratified sample	adequate	clear	clear	90.8	4
Zhang hong	Cross-sectional	adequate	clear	clear	N/A	3
Deng bin	Random stratified sample	adequate	clear	clear	N/A	3
Cui jianping	Random stratified sample	adequate	clear	clear	98.1	4
Min li	Random stratified sample	adequate	clear	clear	N/A	3
Feng jieying	Random stratified sample	adequate	clear	clear	98.24	4
Gao aili	Cross-sectional	adequate	clear	clear	96.2	4
Wu tieqiang	Cross-sectional	adequate	clear	clear	98.84	4
Sun zhenxiu	Random stratified sample	adequate	clear	clear	N/A	3
Liu zhaorui	Random stratified sample	adequate	clear	clear	N/A	3
Zhang aihua	Random stratified sample	adequate	clear	clear	N/A	3
Fu rui	Cross-sectional	adequate	clear	clear	99.06	4
Li bing	Random stratified sample	adequate	clear	clear	95.2	4
Yiwei Shen	Community-based study	adequate	clear	clear	86.84	4
Law MP	Cross-sectional	adequate	no	clear	99.3	4
Wu TQ	Cross-sectional	adequate	clear	clear	98.8	4

N/A= not available.

Table 3. Adjusted odds ratios for acne obtained by logistic meta-regression analysis

Factor	Number of studies	OR (95% CI)	P-value
Age of range			
undergraduate	11	1.00	
primary and secondary school students	10	3.127 (0.001-3.838)	0.012
Gender			
female	24	1.00	
male	24	1.217 (0.109-14.681)	0.024
Location			
north	10	1.00	
south	14	1.184 (0.002-3.833)	0.028

OR= odds ratio. CI=confidence interval



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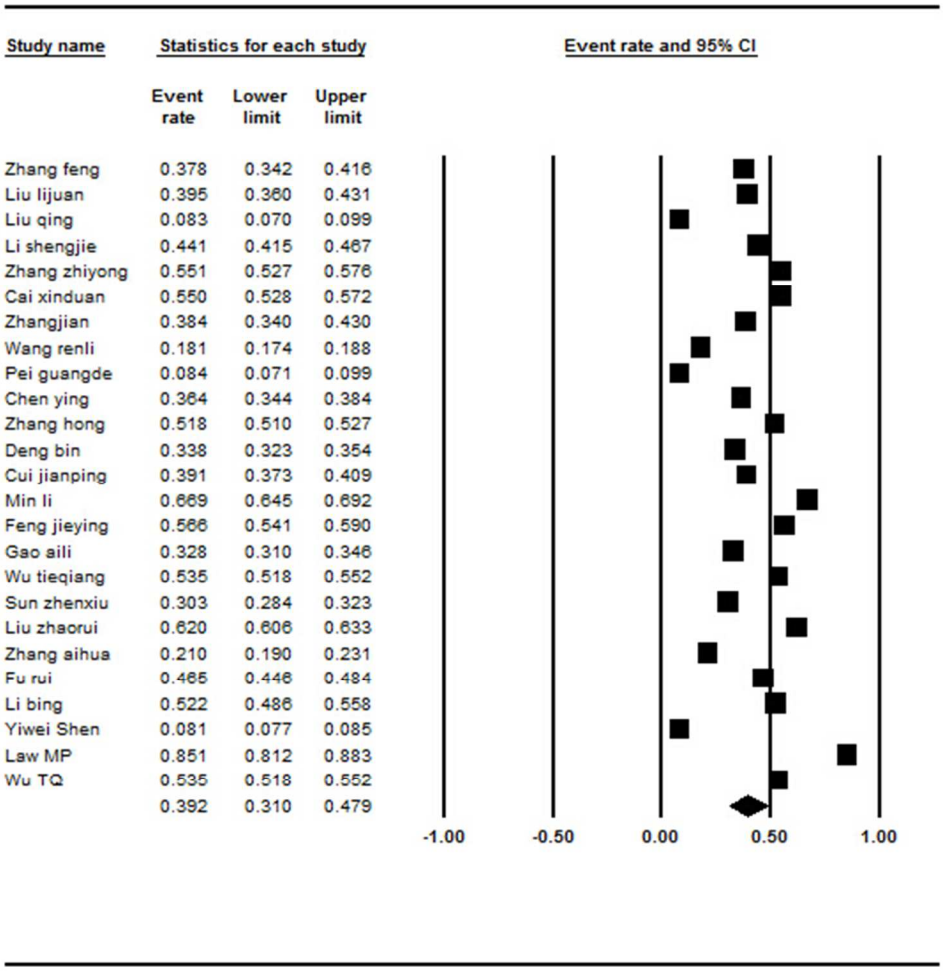

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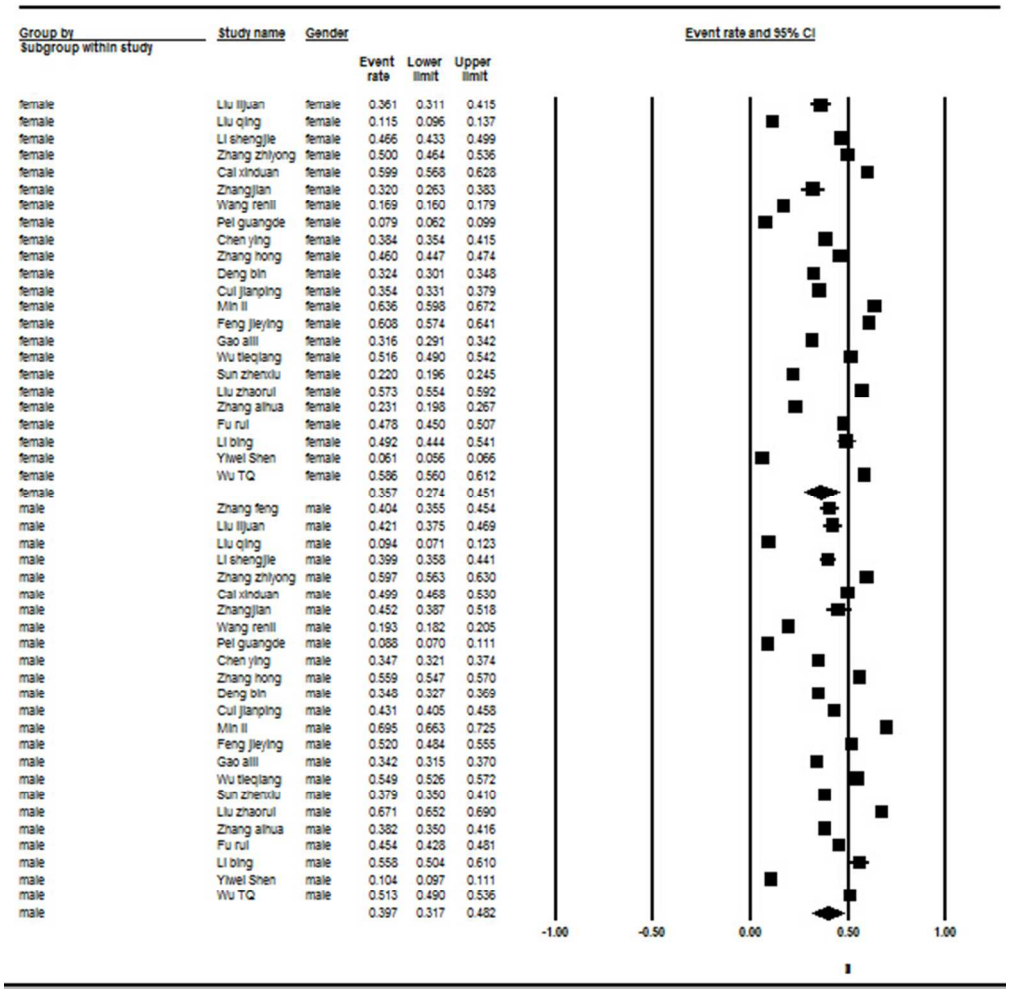

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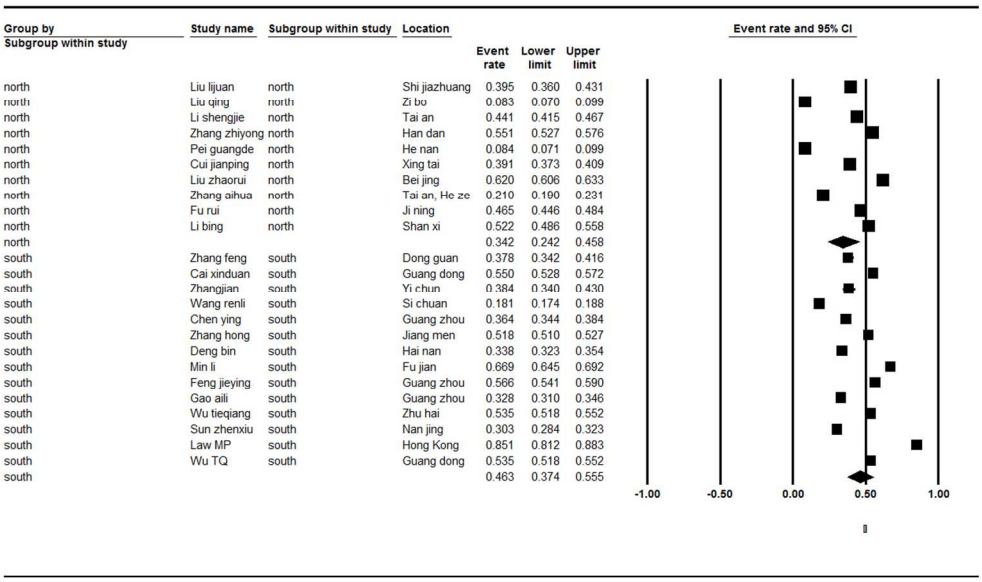

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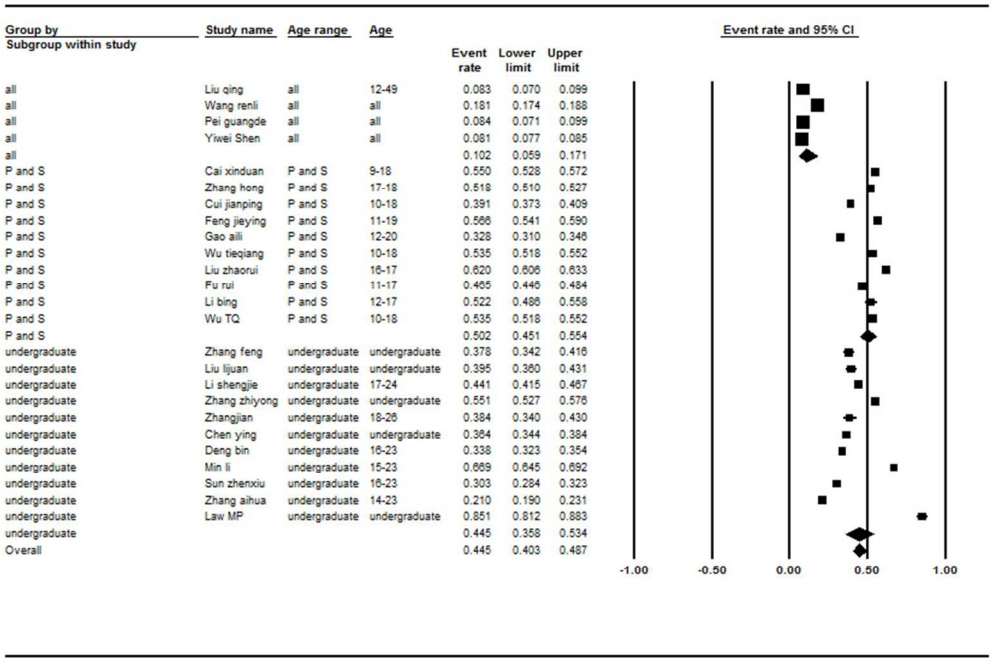
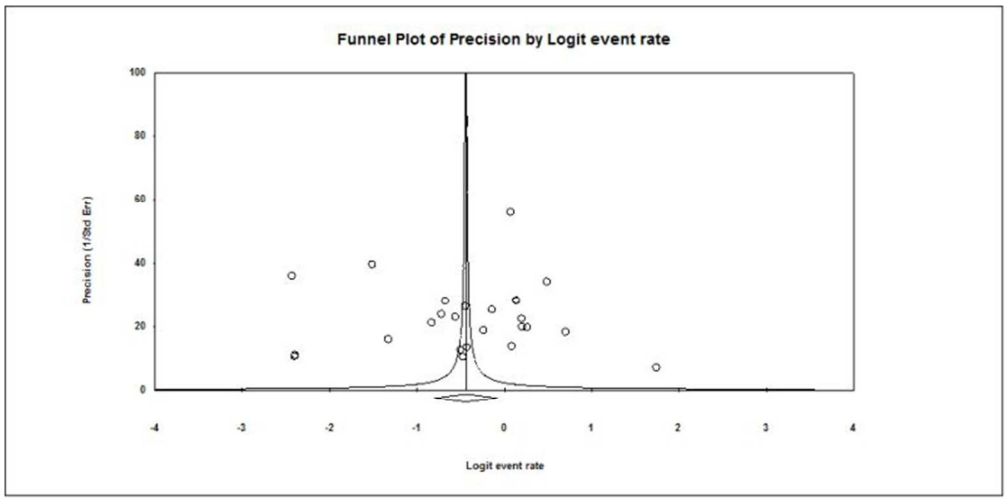
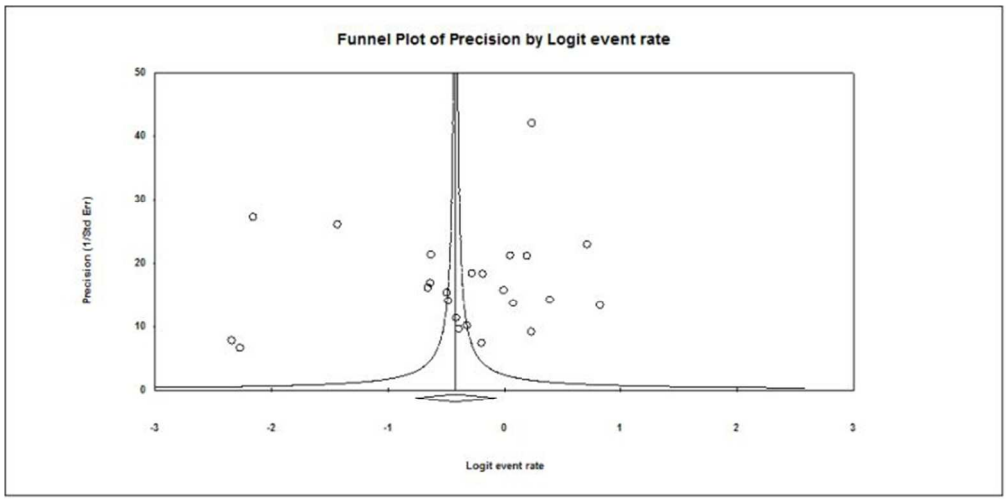


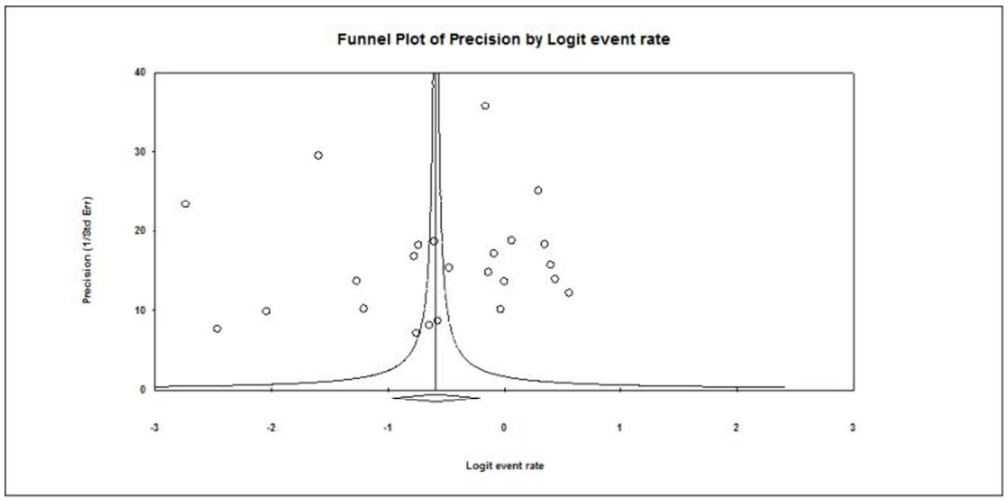
70x46mm (300 x 300 DPI)

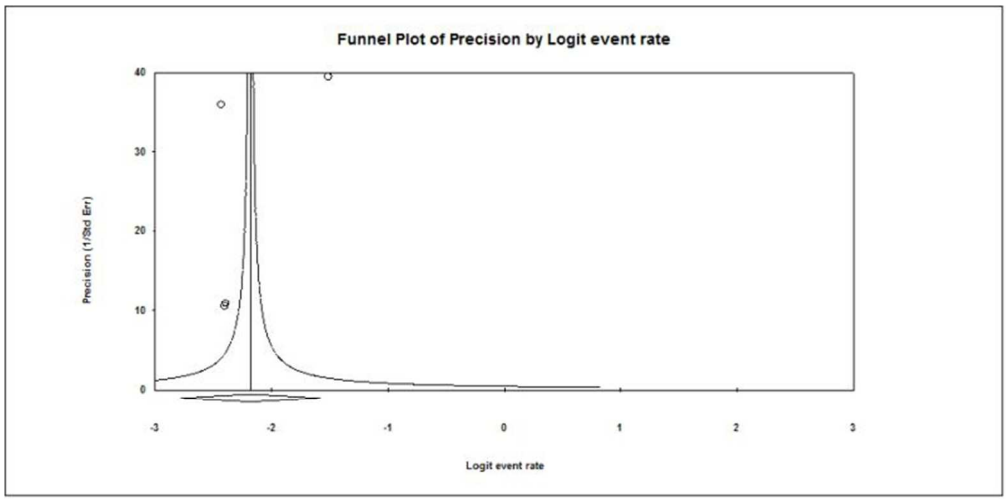
Supplementary table 1. Details of electronic bibliographic database search strategies

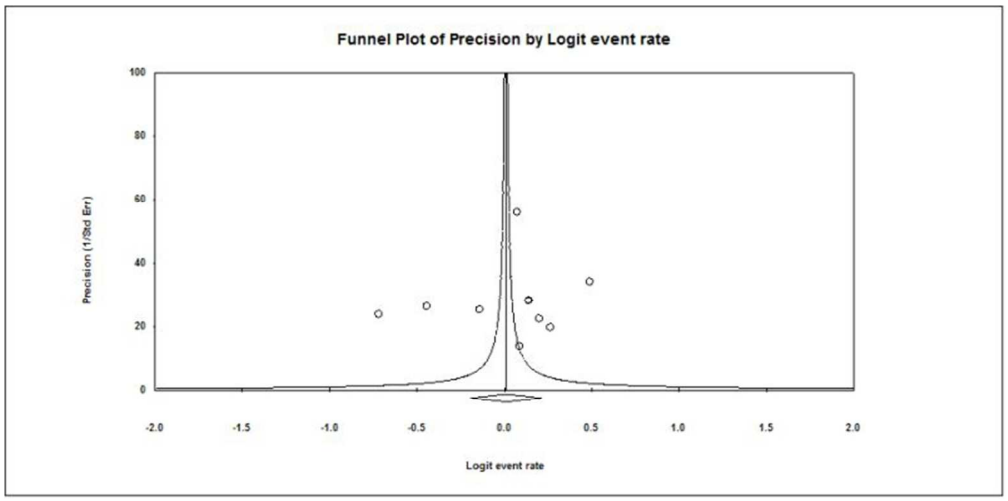
Database	Search strategies
Pubmed	((("acne vulgaris"[MeSH Terms] AND (("prevalence"[MeSH Terms]) OR "incidence"[MeSH Terms])) AND ("China"[MeSH Terms]) OR "Chinese"[MeSH Terms])
Embase	Title or Abstract acne AND Title or Abstract (china or chinese) AND Title or Abstract (prevalence or incidence or epidemiology)
Web of science	Title or Abstract:(acne) AND Title or Abstract: (prevalence or incidence or epidemiology) AND Title or Abstract: (china or Chinese)
China National Knowledge Infrastructure Periodicals	Keywords: acne AND Keywords: prevalence or incidence or epidemiology
The VIP Database for Chinese Technical	(1) Title or Keywords: acne; Property: dim AND Title or Keywords: prevalence; Property: dim (2) Title or Keywords: acne; Property: dim AND Title or Keywords: incidence; Property: dim
The Wan Fang Database for Chinese Periodicals	(1) Title or Keywords: acne; Property: dim AND Title or Keywords: prevalence; Property: dim (2) Title or Keywords: acne; Property: dim AND Title or Keywords: incidence; Property: dim

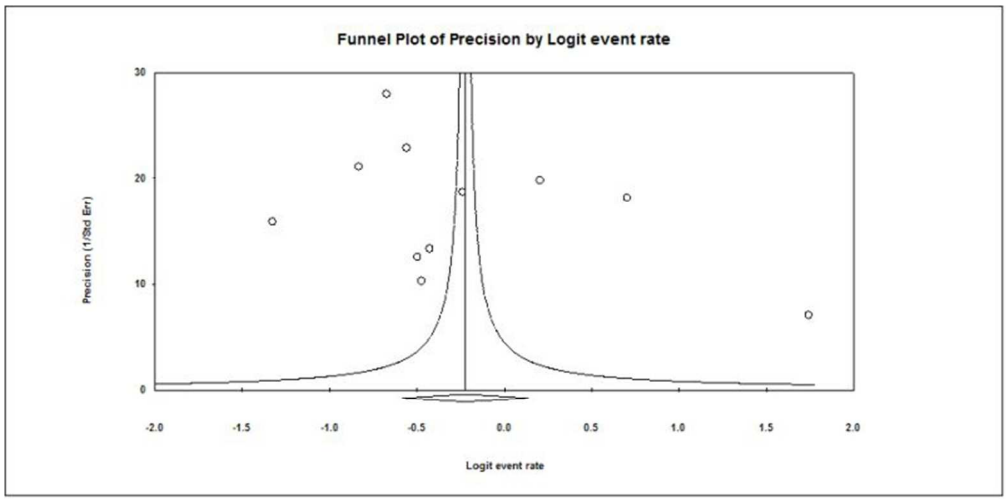


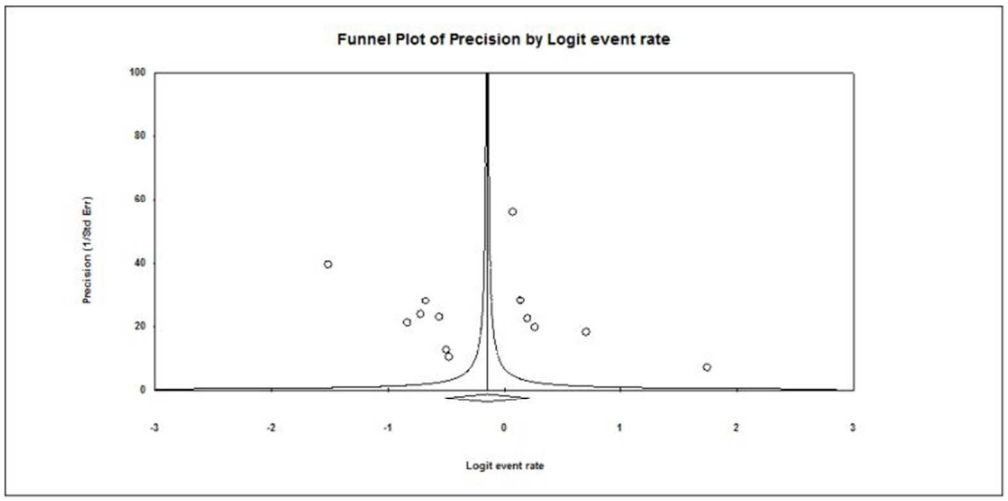


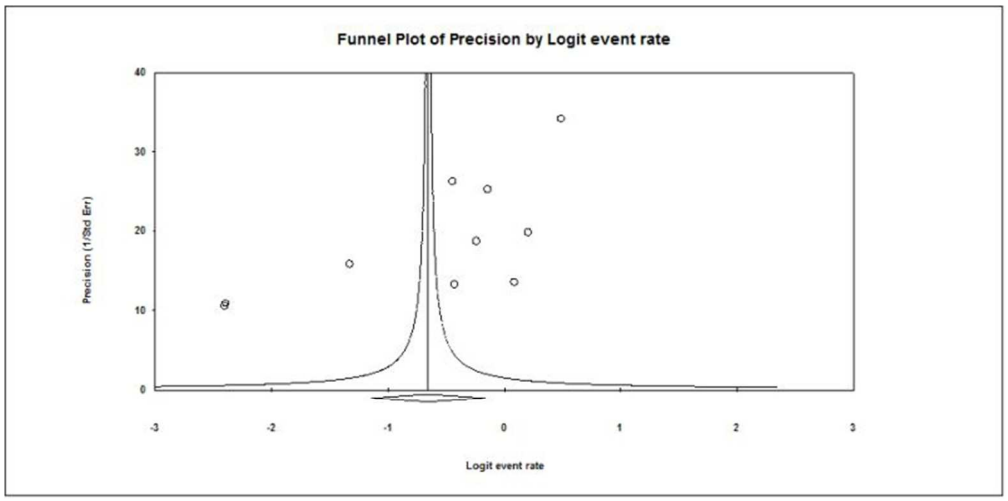












PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	The Prevalence of Acne in Mainland China: a systematic review and meta-analysis	1
ABSTRACT			
Structured summary	2	**Objectives:** The aim of this review is to estimate the prevalence of acne in mainland China comprehensively and to quantify its association with gender, region and age. **Methods and analysis:** We searched electronic databases with predetermined search terms to identify relevant studies published between January 1, 1996 and September 30, 2016. Note Express software, Comprehensive Meta-Analysis version 2.0, Logistic meta-regression analysis was used to dispose data and analyse. **Results:**The overall pooled prevalence rates of acne were 39.2%. In mainland China, primary and secondary students exhibited higher prevalence rates than undergraduate students; males had higher prevalence rates of acne than females; and the prevalence rates of acne in southern China was higher than northern China.	2,3
INTRODUCTION			
Rationale	3	Acne vulgaris burden exhibits global distribution and has continued to grow in prevalence over time within this population. Acne can result in psychological distress and have profound effects on patients' self-esteem. China comprises 34 province-level administrative regions, with 56 nations and a population of 1.3 billion people, a country-wide, population-based study of the prevalence rates of acne in China was needed.	3,4
Objectives	4	In this review, we examined the prevalence of acne in mainland China and to analyse the effects of gender, region and age on it.	4
METHODS			

PRISMA 2009 Checklist

Protocol and registration	5	We have no original protocol and registration, so this item isn't applicable.	
Eligibility criteria	6	Studies that met all of the following criteria were included in the meta-analysis, (1) the study was a population-based survey; (2) the study evaluated the prevalence/incidence of acne; (3) the investigation involved random sampling or cluster sampling; (4) the sample size was >300; A flow chart illustrating the article search process is presented in Figure 1.	5,6
Information sources	7	Studies were aggregated from six databases between January 1, 1996 and September 30, 2016, including PubMed, EMBASE, the Web of Science, the China National Knowledge Infrastructure, the VIP Database for Chinese Technical Periodicals, and the Wan Fang Database for Chinese Periodicals.	4
Search	8	The following search terms were used to retrieve relevant studies, (acne), (prevalence or incidence) AND (China or Chinese).	4
Study selection	9	Figure1	Figure1
Data collection process	10	The data in this study were extractd independently and checked after independent extraction by two investigators.	5
Data items	11	(1) the name of the first author; (2) the location of the investigation area; (3) the year in which the investigation occurred; (4) the age range of the subjects; (5) the sample size (male, female, and overall); (6) the prevalence rates obtained for males, females, and overall; (7) the method used to sample subjects; (8) the criteria used to diagnose acne; and (9) the response rate.	5
Risk of bias in individual studies	12	Quality assessment and analysis of the publication bias	5
Summary measures	13	odds ratios (ORs) and their associated 95% confidence intervals (CIs)	6
Synthesis of results	14	The heterogeneity of the pooled prevalence was estimated using the χ^2-based Q statistic and I^2 metrics. A random-effects model was used if heterogeneity was observed ($p<0.05$); otherwise, a fixed-effects model was applied. All studies were classified into subgroupsof regions, ages and gender. The associations of age, gender, and region with the prevalence of acne were evaluated using a logistic meta-regression model.	6

Section/topic	#	Checklist item	Reported

PRISMA 2009 Checklist

			on page #
Risk of bias across studies	15	Table 2	Table2
Additional analyses	16	Logistic meta-regression model, subgroup analysis	6
RESULTS			
Study selection	17	Using the initial search strategy, 166 studies were identified, and 141 studies were subsequently excluded (Figure 1). A total of 25 studies 2-4, 9-30 involving 83,008 Chinese individuals were included in this meta-analysis.	6,7
Study characteristics	18	Detailed characteristics of each included study were presented in Table 1.	Table 1
Risk of bias within studies	19	The overall quality of all included studies was found to be adequate (Table 2).	Table 2
Results of individual studies	20	Figure2-5	Figure2-5
Synthesis of results	21	Figure2-5	Figure2-5
Risk of bias across studies	22	Table 2	Table 2
Additional analysis	23	logistic meta-regression model, subgroup analysis	8
DISCUSSION			
Summary of evidence	24	Our results showed that the overall pooled prevalence of acne was 39.2% for all ages. The prevalence rates in different age groups were 10.2% overall (95% CI=0.059-0.171), 50.2% for primary and secondary students (95% CI=0.451-0.554), and 44.5% for undergraduates (95% CI=0.358-0.534); by gender, the prevalence rates were 35.7% for females (95% CI=0.274-0.451) and 39.7% for males (95% CI=0.317-0.482); and by region, the prevalence rates were 34.2% northern China (95% CI=0.242-0.458) and 46.3% for southern China (95% CI=0.374-0.555).	9
Limitations	25	The diagnostic criteria for acne differed across studies and the age of the survey population could not be subdivided.	3
Conclusions	26	The overall pooled prevalence of acne was 39.2% in mainland China; acne occurred highly in primary students and secondary students than undergraduate students; the prevalence of acne in males was greater than that in females; and acne was more common in northern China than in southern China. This meta-analysis of the prevalence of acne may provide a sound basis for the future provision of health services.	9
FUNDING			
Funding	27	Issue of Tai'an Science and Technology Development Plan（201440774-05）	

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