

# *Systematic evaluation and meta-analysis of randomized controlled trial of TCM facial mask in the treatment of acne*

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**Abstract: Objective:** To systematically evaluate the clinical efficacy and safety of traditional Chinese medicine masks in the auxiliary treatment of acne, and provide evidence-based reference for clinical practice. **Methods:** Computer search of PubMed, China Knowledge Network (CNKI), WanFang, VIP (VIP) and other databases, collect randomized controlled trials of traditional Chinese medicine mask alone or in combination with conventional therapies to treat acne, and extract data from clinical studies that meet the inclusion criteria. Cochrane review Handbook 5.1 was used for quality evaluation, and stata 15.1 was used for meta-analysis. **Results:** A total of 13 articles were included, and a total of 945 patients with acne were included. Meta results showed that the clinical cure rate of acne treated with traditional Chinese medicine mask was significantly higher than that of the control group, which was statistically significant ( $P=0.000$ ). The RR value and 95% CI were 1.71 ( 1.40, 2.10); Compared with non-TCM facial mask treatment, the total clinical effective RR value and 95% CI for acne treatment with TCM facial mask is 1.22 (1.15, 1.29); TCM facial mask is better than acne comprehensive grading system score (GAGS) The control group, with statistical significance ( $P=0.000$ ), the estimated SMD point and 95% CI was -0.92 (-1.18, -0.65); there was no statistical difference between the treatment group and the control group in adverse reactions ( $P=0.344$ ), RR value and 95% CI were 0.73 (0.38, 1.40). **Discussion:** Traditional Chinese medicine masks have a definite clinical effect and good safety in the auxiliary treatment of acne. Commonly used Chinese medicines include heat-clearing medicines and blood-activating medicines for removing blood stasis. However, limited by the quality of the included studies, this conclusion still needs more large-sample, multi-center, high-quality RCTs for verification.

## 1. Introduction

Acne is a chronic inflammatory skin disease that occurs commonly in the hair follicles and sebaceous glands. It is most common in adolescents and has recurrent episodes of acne, papules, pustules, cysts, and nodules as its main clinical features, which seriously affect the appearance and physical and mental health of patients [1]. The pathogenesis of acne is complex and not yet fully

understood, and is generally considered to be related to sebaceous gland overproduction, abnormal keratinization of follicular sebaceous glands, microbial infections (e.g., *Propionibacterium acnes*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, etc.), inflammation, and immune factors [2] [3]. Traditional Chinese medicine has a unique understanding of acne and advocates a combination of internal and external treatment. In addition to oral Chinese medicine treatment, external treatments such as acupuncture, gua sha, and herbal mask application can be used [4], among which herbal mask application is a safe, simple, and easily accepted treatment by patients, but the currently reported studies on herbal mask treatment for acne have a small sample size and unreasonable design, which cannot effectively guide clinical practice. However, the present study aims to conduct a systematic evaluation study on the clinical efficacy and safety of herbal masks in the treatment of acne, and to investigate the drug composition of herbal masks, to explore the drug use pattern, and to provide evidence-based medical evidence for the treatment of acne with herbal masks.

## **2. Data and methods**

### **2.1 Literature search**

The literature on acne treatment with Chinese medicine mask published externally was searched from the English literature database Pubmed and the Chinese literature databases China Knowledge Network (CNKI), WanFang, and Vipers (VIP). The search was conducted by searching for acne, acne, Chinese medicine mask, clinical study, clinical observation, randomized controlled trial, efficacy observation, etc.; the English search was conducted for Chinese medicine mask, acne, etc. The search was adjusted accordingly according to different databases, and the search time was built until December 2021.

### **2.2 Inclusion criteria**

(1) Type of study: randomized controlled trial (RCT). (2) Research subjects: acne patients who were diagnosed to meet the diagnostic criteria of acne such as the Clinical Diagnosis and Treatment Guideline - Dermatology and Venereal Diseases Branch, Chinese Clinical Dermatology, and the Guidelines for Clinical Research on New Chinese Medicines. (3) Interventions: the control group was treated with oral Chinese medicine, alone or combined with conventional western medicine treatment, including tanshinone capsules, retinoids, and antibiotic drugs, which were unified as conventional western medicine treatment for the convenience of analyzing the data; the treatment group was treated with a combination of traditional Chinese medicine mask on the basis of the control group. (4) Outcome indicators: acne comprehensive grading system (GAGS) score, adverse reactions. The language of the literature was Chinese or English.

### **2.3 Exclusion criteria**

(1) Exclude literature that did not mention specific skin lesion scoring methods and did not refer to the acne comprehensive grading system (GAGS) scoring; (2) Exclude literature whose efficacy assessment was not assessed by reference to the Guidelines for Clinical Research on New Chinese Medicines; (3) Exclude literature with incomplete data; (4) Exclude literature with multiple drafts and suspected duplication.

## 2.4 Literature screening and data extraction

After the first round of computerized literature search, 2 researchers read the literature individually, and according to the inclusion and exclusion criteria, collated the literature that met the requirements and extracted the important information of the literature: authors, literature source, year of publication, sample size, intervention method, treatment period, and outcome indicators. At the end of the entry, the 2 researchers cross-checked, and if there was a dispute between the data collated by the 2 people, it was referred to a third party to assist in the resolution.

## 2.5 Statistical analysis and literature quality evaluation

The screened literature was organized in Excel and then analyzed by stata 15.1 for data processing. For continuous variables, the standardized mean squared deviation (SMD) and its 95% confidence interval (95% CI) were used as effect sizes, and for dichotomous variables, the relative risk ratio (RR) and its 95% confidence interval (95% CI) were used for treatment efficiency and adverse effects. CI) were used as effect sizes, and  $P < 0.05$  was considered a statistically significant difference. Heterogeneity was tested using  $I^2$ ; if  $I^2 \leq 50\%$  and  $P \geq 0.01$ , heterogeneity was considered small and the statistics were combined using a fixed-effects model; if  $I^2 > 50\%$  and  $P < 0.01$ , heterogeneity was considered large and a random-effects model was used with subgroup analysis or sensitivity analysis to clarify the source of heterogeneity; when heterogeneity was not statistically different ( $P < 0.05$ ), a fixed-effects model was analysis was performed.

The quality of the literature was evaluated through the Risk of Bias Assessment Tool in the Cochrane Handbook for the Systematic Evaluation of Interventions: where high risk of bias was recorded as no, low risk of bias as yes, and uncertain risk of bias as unclear. specific evaluations included: randomization methods, allocation concealment, blinded implementation bias, blinding of outcome evaluators, completeness of outcome data, selective reporting risk, and other sources of bias.

## 3. Results

### 3.1 Literature search

According to the search protocol and data collection methods, a total of 1124 relevant literature were searched in the initial review, and 98 remaining articles were removed after reading the titles and abstracts to remove duplicate publications and non-RCT studies, and the full text was further read and collated, and 13 articles were finally included in the literature for analysis, and all included literature were in Chinese. The flow chart of literature screening is detailed in Figure 1.

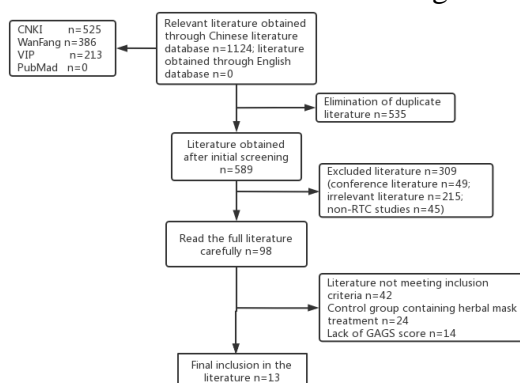


Figure 1: Flow chart of literature screening

### 3.2 Basic characteristics of the literature

A total of 945 patients with acne were included in 13 papers, 493 in the treatment group and 452 in the control group, including 225 males and 270 females in the treatment group and 226 males and 227 females in the control group. 3 did not count the mean age and mean duration of disease [10] [16] [17], the treatment course was 4 weeks-3 months, and the interventions were mainly: Chinese herbal masks, Chinese oral medications, Chinese topical treatments, Danshinone capsules, antibiotic drugs, and retinoids. The basic characteristics of the included literature are detailed in Table 1.

Table 1: Basic characteristics of the included literature literature

First author Year of publication	Number		Gender				Average age		Average duration of illness		Treatment cycle	Interventions	
	T	C	T	T	C	C	T	C	T/Month	C/Month		T	C
TanLL2021 <small>错误!未找到引用源。</small>	72	70	3	3	3	3	22.30±8.2	21.90±8.4	35.9±11.3	36.1±11.2	8week	①②②⑤⑥	
LiR2020 <small>错误!未找到引用源。</small>	30	30	7	2	8	2	23.80±5.6	23.53±5.8	20.6±9.02	19.5±8.93	30day	①③⑥	
LiuL2019 <small>错误!未找到引用源。</small>	61	61	3	2	3	2	22.10±3.4	21.9±3.7	12.4±5.3	12.6±5.9	4week	①⑥⑥	
WangQ2018 <small>错误!未找到引用源。</small>	33	29	1	1	1	1	20.55±2.2	21.04±2.0	15	14	4week	①②④	
HanYB2017 <small>错误!未找到引用源。</small>	15	15	9	6	9	6	23.88±7.3	22.33±7.1	4.46±2.21Y	3.85±1.13Y	8week	①②②	
LiY2017 <small>错误!未找到引用源。</small>	30	30	1	1	1	1	/	/	/	/	8week	①③⑥	
WangYY2016-1 <small>错误!未找到引用源。</small>	35	35	1	1	1	1	22.98±7.3	23.73±7.2	4.46±2.31Y	4.35±2.53Y	6week	①②②	
WangYY2016-2 <small>错误!未找到引用源。</small>	35	35	1	1	2	1	22.63±7.8	25.37±7.6	4.53±2.52Y	4.37±2.30Y	6week	①②②	
ChenQ2016 <small>错误!未找到引用源。</small>	30	30	1	1	1	1	23.15±4.3	24.37±4.7	23.23±11.69	24.00±11.60	2month	①③⑥	
ChenQ2015 <small>错误!未找到引用源。</small>	40	11	9	3	3	8	22.63±2.3	23.27±2.4	2.89±3.29Y	3.50±3.72Y	30day	①/	
WangGW2014 <small>错误!未找到引用源。</small>	29	28	8	2	1	9	24.30±6.2	23.20±7.6	29.10±24.16	28.23±24.98	8week	①③⑥	
YunGJ2013 <small>错误!未找到引用源。</small>	53	50	2	3	2	2	/	/	/	/	8week	①②⑤⑥	
LiFY2011 <small>错误!未找到引用源。</small>	30	28	1	1	1	1	/	/	/	/	3month	①②②	

Note: T is the treatment group, C is the control group; M is male, F is female; interventions: ① herbal mask, ② herbal oral medication, ③ herbal external treatment, ④ Danshinone capsule, ⑤ antibiotics, ⑥ retinoids.

### 3.3 Evaluation of the quality of the included literature

According to the Cochrane Handbook for the Systematic Evaluation of Interventions, high risk of bias was recorded as NO, low risk of bias as YES, and uncertain risk of bias as unclear, and the quality of the literature was assessed as detailed in Figure 2.

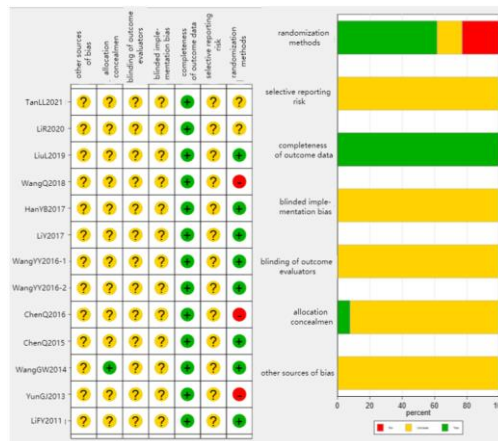


Figure 2: Evaluation of the quality of the included literature

### 3.4 Clinical cure rate of acne treated with herbal masks

Of the 13 included papers, the clinical cure rate of acne treated with herbal masks was tested for heterogeneity  $I^2=0.0\%$ ,  $p=0.997$ , which is small, and analyzed using a fixed effects model, and the Meta results showed that the RR value and 95% CI was 1.71 (1.40, 2.10), corresponding  $p=0.000$ ,  $p<0.05$ , and the clinical cure rate was significantly higher than that of the control group, which was statistically significant, as shown in Figure 3.

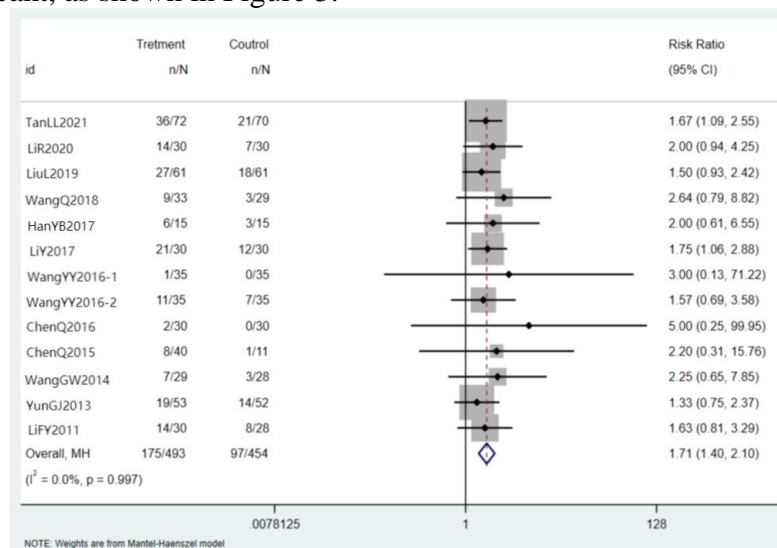


Figure 3: Forest plot of the cure rate of acne treated with herbal mask

### 3.5 Total clinical efficiency of herbal masks for acne

Of the 13 included papers, the total clinical effective rate (i.e., cured + significant + effective) of acne treated with herbal masks was tested for heterogeneity  $I^2=0.0\%$ ,  $p=0.721$ , which was less heterogeneous, and analyzed using a fixed effects model, and the Meta results showed that the RR value and 95% CI was 1.22 (1.15, 1.29), corresponding to  $p=0.000$ ,  $p<0.05$ , the total clinical efficiency of the herbal mask for acne was higher than that of the control group, and the difference was statistically significant, as shown in Figure 4.

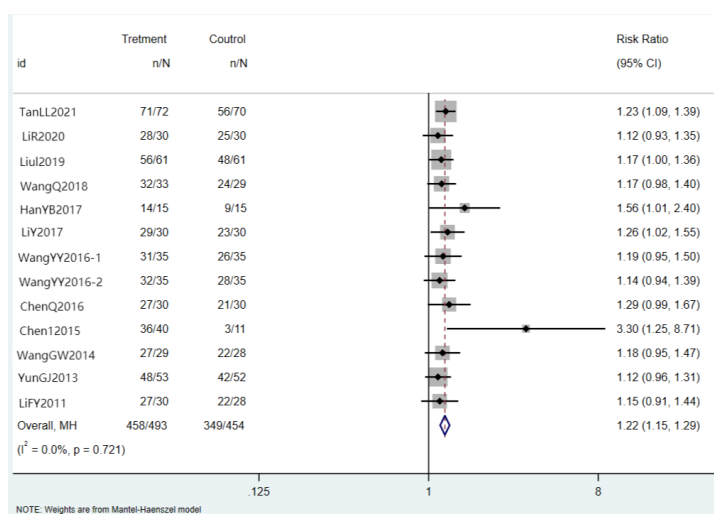


Figure 4: Forest plot of total clinical efficiency of Chinese herbal mask for acne

### 3.6 Effect of herbal masks on acne comprehensive grading system score (GAGS)

The included 13 literature GAGS score index before and after treatment, Meta results showed that the SMD point estimate and 95% C I was -0.92 (-1.18, -0.65), corresponding P=0.000, P<0.05, suggesting that the treatment group treated acne GAGS score is better than the control group, the difference is statistically significant, the treatment group than the control group GAGS score reduced by 0.92 points, see Figure 5.

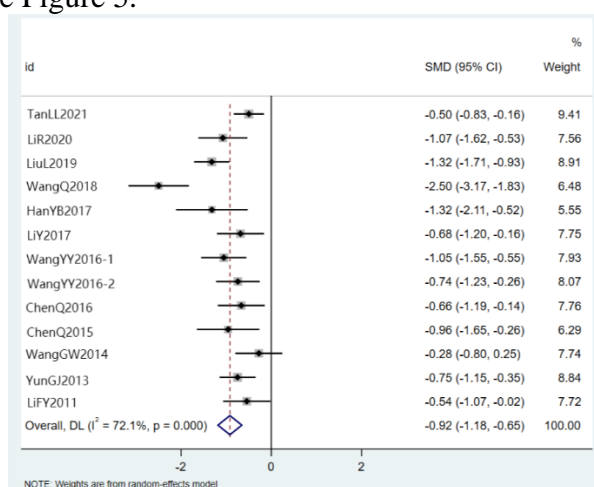


Figure 5: Forest plot of GAGS heterogeneity test for Chinese herbal masks

### 3.7 Adverse reactions

Of the 13 included papers, three mentioned follow-up and recurrence rates [1][7][15]; four did not mention adverse reactions [1][6][13][17]; nine reported adverse reactions, two of which did not occur [8][10]; and seven experienced adverse reactions [7][9][11][12][14][15][16]. There were 16 cases of adverse reactions in the treatment group, including 5 cases of digestive symptoms (2 cases of epigastric discomfort, 2 cases of increased stool frequency, 1 case of slightly diluted stool), 11 cases of skin symptoms (2 cases of allergic dermatitis, 3 cases of dry and itchy skin, 4 cases of skin redness, 2 cases of subcutaneous bruising); 20 cases of adverse reactions in the control group, including 3 cases of digestive symptoms (3 cases of increased stool frequency), 14 cases of skin

symptoms (14 cases of skin (14 cases of dry and itchy skin), and 3 cases of dizziness and headache. Heterogeneity test was performed for adverse reactions,  $I^2=0.0\%$ ,  $p=0.496$ , which is small heterogeneity, and using fixed effect model, Meta results showed that the RR value and 95% CI was 0.73 (0.38, 1.40), corresponding  $p=0.344$ ,  $p>0.05$ , and there was no statistical difference between the treatment and control groups, see Figure 6.

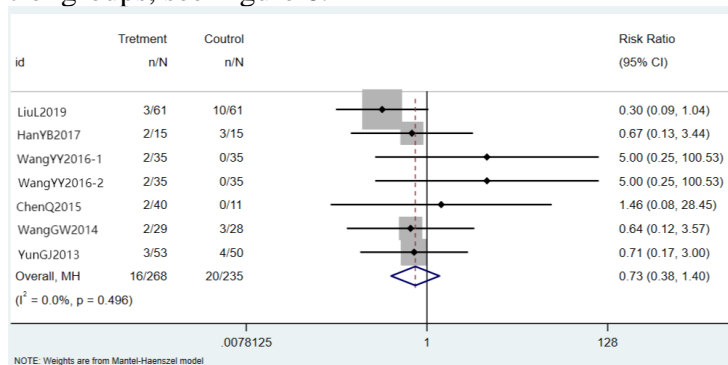


Figure 6: Forest plot of adverse reactions

### 3.8 Publication bias

The additional contour line funnel plot significance (0.01,0.05,0.1) identifies the points on the plotted funnel plot visible in 12 papers in the  $>10\%$  region and 1 in the  $<1\%$  region, the results suggest a symmetrical funnel plot and no significant publication bias in this study. For details, see Figure 7.

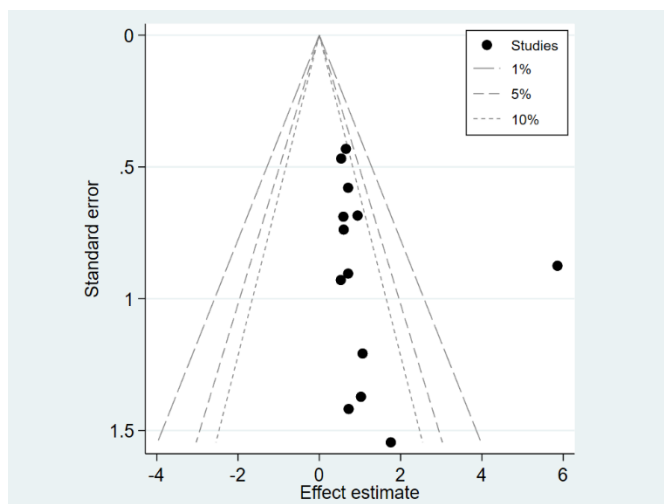


Figure 7: Funnel plot of GAGS heterogeneity test for Chinese herbal masks

## 4. Discussion

Acne, the disease belongs to the category of "acne" in Chinese medicine, and its earliest record is found in Su Wen - Anger Tong Tian Lun [18]: "Sweating and seeing wet, it is acne prickly... When the sweat is windy, the cold is thin and lousy, and the pimples are acne." In the Qing dynasty, the "Golden Guide to Medicine" [19] pointed out that "pulmonary wind acne, this disease is caused by blood heat in the lung meridian. Every occurrence in the face and nose, the start of broken pimples, shaped like millet crumbs, red swelling pain, broken out of the white powder juice ... It is advisable to take loquat clear lung drink internally and apply upside-down powder externally, slowly from the

work also." After a lot of research, Chinese medicine has increasingly improved its understanding of the etiology and pathogenesis of acne [20] [21] [22]. The pathogenesis of acne is mainly based on the lung and spleen meridians, and the nature of the disease is real, and the etiology and pathogenesis are mainly wind-heat in the lung meridians, damp-heat accumulation, blood stasis and phlegm condensation. According to the "Reasons for External Treatment" [23], "The reason for external treatment is the reason for internal treatment, and the medicine for external treatment is the medicine for internal treatment, the only difference is the method. Chen Shigong's "The Authentic Book of Surgery" [24]: "The lung wind, acne, and wine sickness are the same species. Pimples belong to the lungs and spleen to the sullen nose, and all of them have blood heat stagnation. The so-called have all the internal, the shape of all the external, it is appropriate to true Jun Miao sticker powder plus white sophora compresses, internal consumption of loquat leaf pill, baicalin Qing lung drink." As an easy-to-use and safer external Chinese medicine treatment, Chinese herbal masks are more easily accepted by acne patients. In the continuous practice and demonstration of medical practitioners, herbal masks have achieved certain efficacy in the treatment of acne. After the study, there was no significant publication bias in the included 13 papers, and meta-analysis of the herbal mask applied alone or in combination to treat acne versus other therapies for acne showed that the clinical cure rate, total clinical efficiency, and acne comprehensive grading system score (GAGS) of the herbal mask for acne were higher than those of the control group, with statistically significant differences ( $P < 0.05$ ), suggesting that the herbal mask application The clinical efficacy of acne treatment was encouraging. There was no statistically significant difference in the adverse reactions between the treatment group and the control group, and there was no significant difference in the occurrence of adverse reactions between the two groups, and no impact such as termination of the trial, suggesting that the herbal mask has good safety in the treatment of acne.

In conclusion, the results of this study adequately demonstrate that the adjuvant treatment of acne with herbal masks can reduce the acne comprehensive grading system score (GAGS) with good safety, which is worthy of vigorous clinical promotion and application. However, due to the low quality of some of the literature included in this study department, positive results were commonly reported and the lack of assessment of disease recurrence led to some bias in the results of this study. Future randomized controlled trials for the treatment of acne with herbal masks should be designed and implemented following the methods and principles of evidence-based medicine, so as to make a scientific and objective evaluation of the clinical efficacy and safety of herbal masks in the treatment of acne, and to better utilize the characteristics and advantages of herbal masks in the treatment of acne.

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