

# Using Acupuncture Points Embedding to Treat Acne Vulgaris: A Meta-Analysis

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## ABSTRACT

**Objective:** To evaluate the clinical efficacy and safety of acupuncture points embedding in the treatment of Acne Vulgaris.

**Methods:** Randomized controlled trials on acupuncture points embedding for Acne Vulgaris were searched in English and Chinese, including China Knowledge Network, Wanfang database, Vipsop database, Pubmed, Embase, and the Cochrane Library, from the time of database construction to October 2022. 2 researchers independently read and screened the literature, extracted data, and evaluated the literature for risk of bias. Review Manager 5.3 software was used for Meta-analysis.

**Results:** Twelve randomized controlled trial studies involving 1456 patients were finally shown. Meta-analysis results showed that acupuncture points embedding alone or in combination with acupuncture points embedding improved the overall clinical efficiency (RR=3.81, 95%, 2.70 to 5.36, P<0.00001); reduced the recurrence rate (RR=0.28, 95%CI, 0.17 to 0.48, P<0.00001); significantly improved skin lesion score (MD=-2.91, 95%CI, -5.14 to -0.69, P=0.01); reduced incidence of adverse effects (RR=0.32, 95%CI, 0.22 to 0.47), P<0.00001 and in terms of hormone levels, when comparing the changes in hormone levels (serum testosterone and estradiol) before and after treatment between the two groups, there was no significant difference in serum testosterone levels (MD=-0.11, 95%CI, -0.55 to -0.33), P=0.62 and estradiol levels (MD=4.56, 95%CI, 59.12 to 68.23, P=0.89).

**Conclusion:** Acupuncture point embedding or combined acupuncture point embedding treatment for acne vulgaris can significantly improve the clinical efficacy, improve the lesion score and reduce the recurrence rate and the incidence of adverse reactions compared with conventional treatment with western medicine.

**Keywords:** Acupuncture points embedding; Acne vulgaris; Meta-analysis

## INTRODUCTION

Acne Vulgaris is the most common skin condition among adolescents, affecting 85% of the global population aged 12 to 24 years, usually starting before puberty and lasting into adulthood [1]. Acne itself has profoundly negative effects on mental health, including mood disorders, school absenteeism, unemployment, psychiatric hospitalization, and increased suicide rates [2], and the resulting post-inflammatory hyperpigmentation of acne has a negative impact on adolescents' self-perceptions, social interactions, and quality of life scores [3]. In contrast, standardized treatment can significantly improve these problems. In recent years, the treatment strategy for acne has largely remained unchanged, and in the context of increasing global drug resistance, acne treatment is also shifting from monotherapy to more rigorous regimens, including strict antibiotic use and

isotretinoin, which remains the treatment of choice for patients with moderate to severe acne. However, patient adherence to treatment remains poor due to a number of factors [4], including worsening of the local rash during treatment, concerns about drug side effects [5], development of drug resistance [6], cost [7], etc. Given the growing number and young age of adolescent acne patients, there is a clear need for new treatments to supplement existing ones.

Recent studies at the domestic and international level have shown that acupuncture, moxibustion, tui na and other Chinese medicine external treatment methods have unique advantages in disease treatment. Based on acupuncture, it is the inheritance and development of acupuncture. Under the guidance of the meridian theory and the basic theory of Chinese medicine, it relies on the action of the thread on a certain acupuncture point or area to achieve the purpose of disease prevention and treatment [8].

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Compared with ordinary acupuncture, the treatment interval is long and the treatment cost is low, which greatly improves the patient's compliance and makes it more suitable for the treatment of chronic diseases. It is now widely used in the treatment of skin diseases such as psoriasis, urticaria, acne, chloasma, and herpes zoster [9].

There are many studies on acupuncture point embedding for the treatment of acne, but due to small sample sizes, there is a lack of definitive evaluation of the effectiveness and safety of acupuncture point embedding for the treatment of acne. The aim of this paper is to systematically assess the evidence for the effectiveness of acupuncture point embedding in acne patients.

## MATERIALS AND METHODS

### Search of literature

The publicly available literature on acupuncture point embedding for acne was searched, including China Knowledge Network, Wanfang database, Vipshop database, Pubmed, Embase, and the Cochrane Library, with the search time frame from the establishment of the database to October 2022. The search strategy included subject phrases along with unrestricted words, using China Knowledge Network as an illustration: (Acupuncture points embedding or acupuncture points buried thread or buried thread) and (acne). English search terms: acupuncture point embedding or acupoint catgut embedding; acne; Acne Vulgaris.

### Inclusion and exclusion criteria

**Inclusion criteria:** Published literature of randomized controlled trials, including Chinese and English; interventions: acupuncture point embedding combined with other treatments for the treatment group and conventional Western medicine treatments for the control group; outcome indicators include total effective rate, recurrence rate, adverse effects, TCM symptom score, skin lesion score and hormone levels.

**Excluded literature:** Case reports, experience summaries, own-controlled trials, reviews, and other non-randomised controlled trials; unclear diagnostic criteria and efficacy evaluation criteria; studies that did not concentrate on Acne Vulgaris patients; missing primary outcome indicators; duplication of published literature; literature with inaccurate or incomplete data.

### Literature screening and data extraction

The literature was independently screened by 2 researchers in strict accordance with the inclusion and exclusion criteria, and both parties cross-checked after the screening was completed. In case of disagreement, both parties will discuss and if still unable to decide, the decision will be made through third party discussion. Data were extracted from the literature that met the inclusion criteria, including title, author, year, sample size, intervention, duration of treatment, outcome indicators, recurrence, adverse effects, etc.

### Quality evaluation

The Cochrane Risk of Bias Tool was used to evaluate the quality of the included studies. The evaluation included seven evaluation items: Generation of randomised sequences, allocation concealment, blinding of investigators and study subjects, blinded evaluation of study outcomes, completeness of outcome data, selective reporting, and other biases. The evaluation results were classified as "low risk", "unclear" and "high risk".

### Statistical analysis

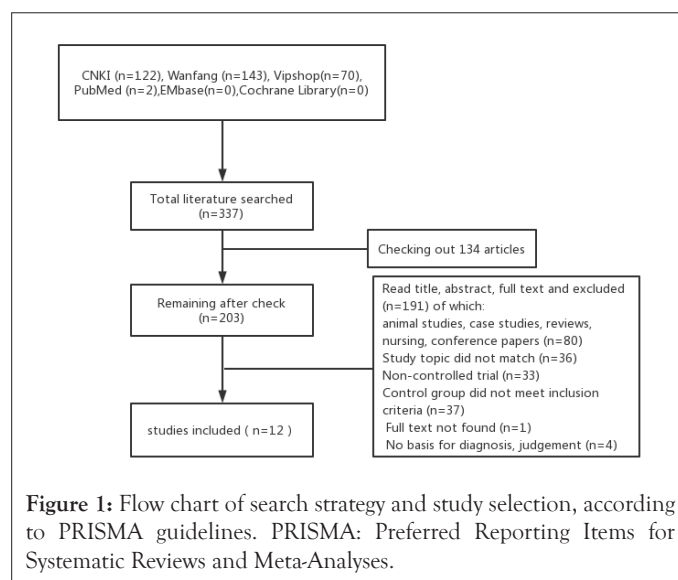
Statistical analyses were performed using Review Manager 5.3 software with a test level of  $\alpha=0.05$ . Relative risk RRs and

95% confidence intervals (95% CIs) were used to describe the combined effect sizes for dichotomous variables, and Weighted Mean Differences (WMDs) and their 95% Confidence Intervals (CIs) were used to describe the combined effect sizes for continuous variables. The presence of heterogeneity was determined by the I<sup>2</sup> test. If I<sup>2</sup>>50% indicated that there was significant statistical heterogeneity among the studies, sensitivity analysis was used to clarify the stability of the results, and a random-effects model was used for the combined analysis when clinical and methodological heterogeneity was excluded; if I<sup>2</sup><50% indicated that there was no significant statistical heterogeneity among the studies, a fixed-effects model was used for the combined analysis.

## RESULTS

### Literature screening process and results

According to the search strategy and data collection method, 335 Chinese and 2 English literatures were retrieved, and 12 studies were finally included. The comprehensive details of these trials are presented in Figure 1.



**Figure 1:** Flow chart of search strategy and study selection, according to PRISMA guidelines. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

### Basic characteristics of the included studies

The final 12 included papers had a total of 1456 patients, 697 in the treatment group and 659 in the control group [10-21]. All literature reported the total effective rate, six [1,3,6,8,11,12] reported the occurrence of adverse reactions, six reported relapse [1,2,4,6,11,12], three reported the skin lesion score and two reported hormone levels [2,3,5,8]. The basic characteristics of the included studies are shown in Table 1.

### Evaluation of the quality of the included literature

The included patients were comparable at baseline in terms of gender and age. Random sequence generation, three articles used software to generate random sequences and were low risk, one article used odd-even grouping [5] and one article used consultation order random grouping, both were high risk [3,6,9,11]. Allocation concealment, with 2 allocated in order of consultation, was high risk [5,9]. Implementation of bias blinding, 1 was single blinded [8], 1 was blinded by third party evaluation [5], 2 were unblinded but evaluated by objective indicators and were low risk [1,6], 1 was unblinded [11], but the author considered that outcome may be affected by missing blinding and was high risk, the rest were not mentioned. All data in the literature were free of missing data (Table 2 and Figure 2).

Table 1: Characteristics of included trials.

References	Group	Intervention	Total sample	Age	Sex M/F	Duration of illness (months)	Condition score	Course of treatment	Duration of treatment (weeks)	Outcome indicators
[10]	T	Acupuncture point embedding+Fire needling	94	22.58 ± 3.71	36/58	13.25 ± 2.16	11.96 ± 1.77	Embedding, 1 in 3 weeks; fire needling, qw	6	①④, Indicators related to skin barrier function
	C	Isotretinoin	73	21.94 ± 3.65	31/42	13.18 ± 2.09	12.05 ± 1.82	Po, 0.5mg /kg/d		
[17]	T	Acupuncture point embedding	120	26.53 ± 4.39	-	5.53 ± 1.92	5.33 ± 1.17	4 d before luteal phase, Acupuncture point embedding, 1 time per month, 3 times	12	①④⑤, Chinese Medicine Symptom Score
	C	Minocycline	120	27.62 ± 5.91	-	5.49 ± 1.29	5.43 ± 1.19	Frequency reduced from bid to qd and qod for three months		
[11]	T	Acupuncture point embedding+ Control group	21	23.1 ± 2.8	13/08	4.0 ± 2.4	15.0 ± 3.1	qw for the first 2 week, 1 every other week for the last 3	8	①②④
	C	Topical Clindamycin Phosphate+Adapalene	20	22.7 ± 2.8	12/08	3.9 ± 2.5	14.9 ± 3.1	Alternating morning and evening use		
[12]	T	Acupuncture point embedding+Isotretinoin	35	26.86 ± 5.87	12/23	20.67 ± 8.45	18.05 ± 2.14	1 time in 15 d, 2 times a course, 3 courses of treatment	12	①②③④-Chinese Medicine Symptom Score
	C	Isotretinoin	35	27.29 ± 5.36	17/18	19.54 ± 8.32	17.91 ± 3.14	Po, 10 mg, bid, 1 month; 10 mg, qod, 2 month		
[14]	T	Acupuncture Point Embedding (Body+Face)+Fire Acupuncture+Ear Acupuncture	50	31 ± 5	-	6.2 ± 3.4	12.64 ± 5.21	Embedding, qw for the first 2 w, 1 time every other week for the last 3; fire and ear acupuncture, qw	8	①④⑤
	C	Tanshinone capsules+topical Adapalene	48	31 ± 5	-	6.1 ± 3.4	12.63 ± 5.27	Po, 1 g, tid; topical, qn		
[15]	T	Acupuncture Point Embedding+General Acupuncture	47	27.1 ± 4.0	12/35	23.1 ± 15.6	-	Embedding, qw; general acupuncture, qod	8	①②③-Diagnostic grading
	C	Isotretinoin	48	26.8 ± 4.2	15/33	25.3 ± 17.1	-	Po, 10 mg, bid		

[20]	T	Acupuncture Point Embedding+Control group	31	20.3 ± 3.2	14/17	-	-	Embedding, 1 time in 15 d, 3 times a course, 2 courses of treatment	12	①②③
	C	Metronidazole+spironolactone+vitamin B6	31	20.4 ± 3.3	13/18	-	-	Metronidazole, 0.4-0.6 g tid; spironolactone, 40-120 mg 2-4 bid; vitamin B6, 1-2 tablets/day	6	
[18]	T	Acupuncture Point Embedding+blood cupping+fire acupuncture+thunderbolt moxibustion+Chinese herbs	59	28.5 ± 6.92	15/14	1.5 ± 0.8	-	Blood cupping+fire acupuncture once every 5 days, 3-5 times a course of 2 treatments; embedding, qw, 3 times a course of 3 treatments	7	①③
	C	Erythromycin Enteric tablets/ Isotretinoin+topical Tretinoin+Benzoil peroxide	59	29.5 ± 6.92	14/15	1.5 ± 0.7	-	Erythromycin enteric tablets, 0.5 g bid; isotretinoin, 20 mg, bid; peroxymethylphenidate, bid; retinoic acid, qn, 40 d		
[19]	T	Acupuncture Point Embedding+Back walking can	30	16-28	12/18	Mar-72	-	Walkingcan+Embedding, qw	6	①③
	C	Fusidic acid cream+Vincristine capsules	30	16-28	14/16	Mar-60	-	Fusidic acid cream, topica, bid; vincristine capsules, Po, 50 mg, bid		
[21]	T	Acupuncture Point Embedding+Control group	112	22.5±4.3	57/55	3.3 ± 2.1	-	Embedding,1 time in 2 weeks, 3 times for 1 course of treatment, 2 courses in total	12	①②③
	C	Fusidic acid cream+Vincristine capsules	98	21.3 ± 4.5	51/47	3.6 ± 2.3	-	Fusidic acid cream, bid; vincristine capsules, Po, 50 mg, bid, After 6 weeks change to 50mg qd		
[7]	T	Acupuncture Point Embedding+Fire acupuncture	50	21.38 ± 3.16	-	-	-	Embedding, 1 time in 15d; Fire acupuncture, unclear	8	①
	C	Doxycycline Enteric Tablets+Fusidic acid cream	50	22.02 ± 2.53	-	-	-	Doxycycline enteric tablets, Po, 0.1 g, bid; Fusidic acid cream, topica, bid		
[13]	T	Acupuncture Point Embedding+Isotretinoin	48	17-35	27/21	Mar-32	-	Embedding,1 time in 14d, 5 times a course, 2 courses of treatment	12	①③
	C	Isotretinoin	48	15-34	25/23	Mar-30	-	Po, 100 mg, qd		

**Note:** T: Treatment group; C: Control group; qw1: Per week; po: Oral; bid: Twice daily; qd: Once daily; qod: Every other day; tid: 3 times daily; qn: Once a night; ①: Clinical efficacy; ②: Recurrence rate; ③: Adverse effects; ④: Lesion score; ⑤: Hormone level.

Table 2: Evaluation of the quality of the included literature.

References	Random sequence generation	Allocation concealment	Trial blinding of study participants and subjects	Blinded evaluation of study outcomes	Completeness of outcome data	Selective reporting of study results	Other bias
[10]	unclear	unclear	low risk	low risk	low risk	unclear	unclear
[16]	unclear	unclear	low risk	low risk	low risk	low risk	unclear
[22]	unclear	unclear	high risk	high risk	low risk	unclear	unclear
[12]	low risk	unclear	high risk	high risk	low risk	unclear	unclear
[14]	high risk	high risk	low risk	low risk	low risk	unclear	unclear
[15]	low risk	unclear	low risk	high risk	low risk	unclear	unclear
[20]	low risk	unclear	high risk	high risk	low risk	unclear	unclear
[18]	high risk	high risk	unclear	high risk	low risk	unclear	unclear
[19]	unclear	unclear	unclear	unclear	low risk	unclear	unclear
[21]	unclear	unclear	unclear	high risk	low risk	unclear	unclear
[16]	unclear	unclear	unclear	high risk	low risk	unclear	unclear
[12]	unclear	unclear	unclear	high risk	low risk	unclear	high risk

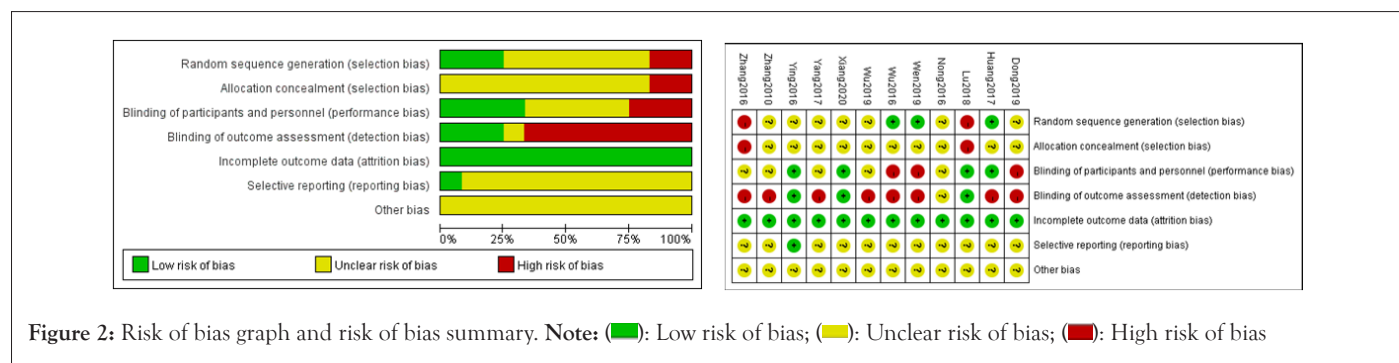


Figure 2: Risk of bias graph and risk of bias summary. Note: (Green): Low risk of bias; (Yellow): Unclear risk of bias; (Red): High risk of bias

**Total effective rate analysis**

The 12 included articles were observed for the outcome indicator of total effective rate. Heterogeneity tests using RerMan 5.4 forest plots showed homogeneity ( $P=0.85$ ,  $I^2=0$ ), so a fixed effects model was used to combine the statistics, and the results showed that the total effective rate of the test group was better than that of the control group, and the difference was statistically significant ( $RR=3.81$ , 95% (2.70,5.36),  $Z=7.67$ ,  $P<0.00001$ ) (Figure 3).

**Recurrence rate analysis**

The six papers included were observed for recurrence, and the results of the heterogeneity test showed homogeneity ( $P=0.28$ ,  $I^2=21\%$ ), so the fixed effects model was used to combine the statistics, and the results showed that the recurrence rate in the test group was lower than that in the control group, and the difference was statistically significant ( $RR=0.28$ , 95% (0.17, 0.48),  $Z=4.79$ ,  $P<0.00001$ ) (Figure 4) [11,2,4,6,11,12].

**Skin lesion score**

Three [2,3,5] papers were conducted to compare the improvement in skin lesion score before and after treatment, and the two groups were tested for heterogeneity and the results showed homogeneity ( $P=0.01$ ,  $I^2=77\%$ ), so a random effects model was used to combine the statistics, and the results showed that the skin lesion score in the test group was significantly lower than that in the control group, and the difference was statistically significant [ $RR=-2.91$ , 95%(-5.14,- 0.69),  $Z=2.57$ ,  $P=0.01$ ] (Figure 5).

**Hormone level analysis**

There are 2 papers evaluating post-treatment hormone levels

(serum testosterone, estradiol) [5,8], but 1 only tested hormone levels before and after treatment due to subject funding [5]. Therefore, a meta-analysis could not be performed. However, 2 papers showed lower premenstrual oestrogen levels in acne patients compared to healthy normal individuals without acne; serum testosterone levels, which were not significantly different compared to normal individuals, and no improvement in testosterone levels after comprehensive acupuncture point embedding treatment (Table 3).

**Adverse reactions**

Six papers observed adverse reactions [1,3,6,8,11,12]. Adverse reactions in the experimental group included dryness of the mouth and lips [3,12], facial desquamation [3], fatigue [12], and local injection reactions (petechiae [8], sclerosis [8], subcutaneous haematoma [6], local swelling and pain [12]). Adverse reactions in the control group included gastrointestinal reactions [8], dryness of the mouth and lips [1,3,6,11,12], facial flaking [3,6], fatigue [11], dry skin [1], hand eczema [3], and menstrual irregularities [8]. There was a statistically significant difference in the incidence of adverse reactions between the two groups [ $RR=0.32$ , 95% (0.22,0.47),  $Z=5.84$ ,  $P<0.00001$ ] (Figure 6).

**Publication bias**

In the publication bias analysis of the total effective rate, the funnel plot was asymmetrically distributed, indicating some publication bias, which may be related to the poor quality of the included studies, small sample size or unpublished negative results (Figure 7).

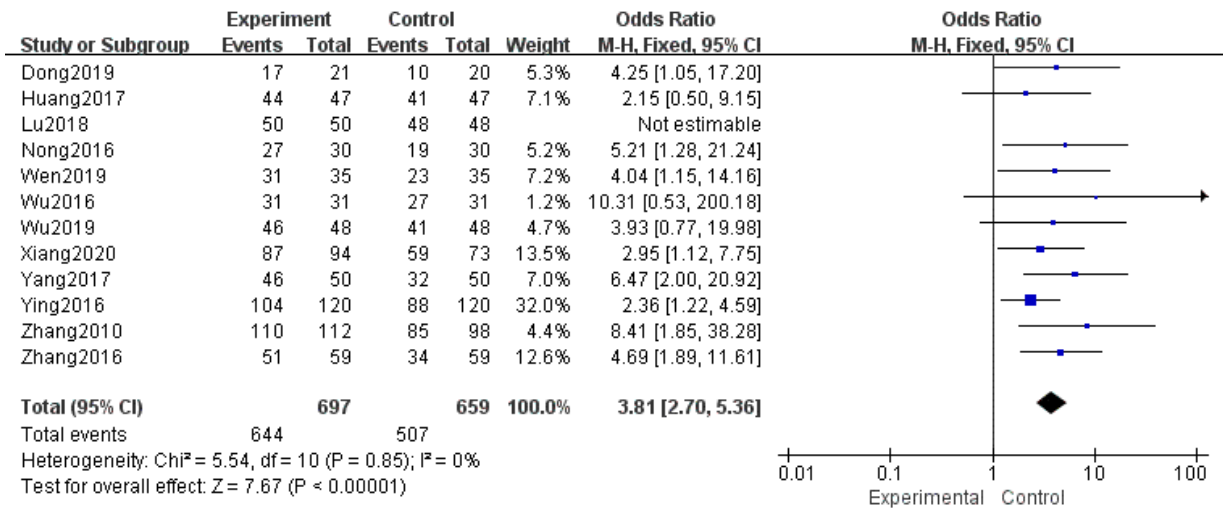


Figure 3: Forest plot of odds ratios and 95% CIs of total effective rate, experimental group include acupuncture point embedding combined with other treatments and control group include conventional Western medicine treatments.

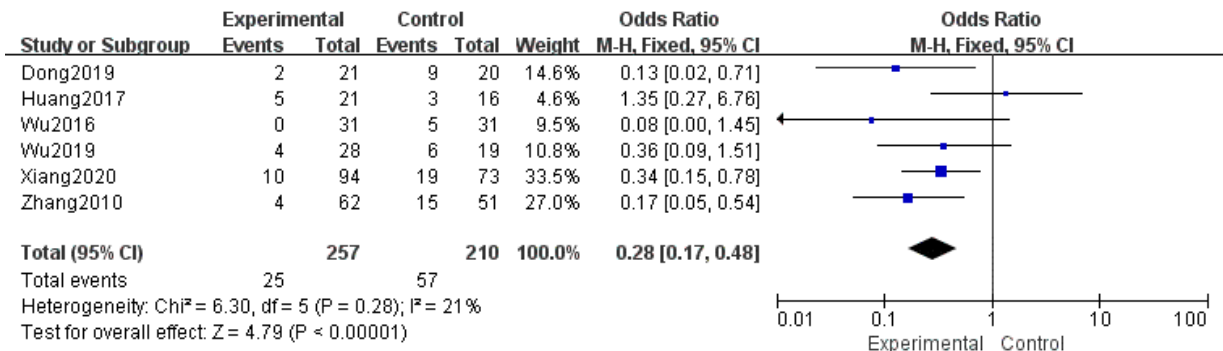


Figure 4: Forest plot of odds ratios and 95% CIs of recurrence rate, experimental group include acupuncture point embedding combined with other treatments and control group include conventional Western medicine treatments.

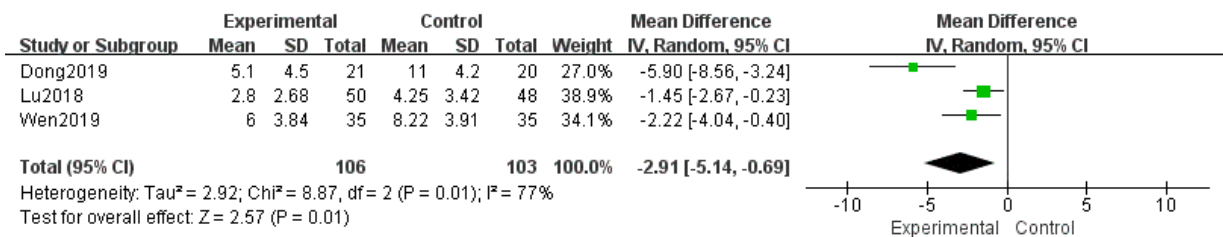


Figure 5: plot of mean difference and 95% CIs of skin lesion score; according to the "Guidelines for Clinical Research on New Chinese Medicines", the number, type, texture and colour of lesions in the 2 groups were scored.

Table 3: Hormone levels analysis of the included literature.

Reference	Group	Total	Before treatment		After treatment	
			T(nmol/L)	E2(pmol/L)	T(nmol/L)	E2(pmol/L)
[14]	T	21	1.25 ± 0.35	66.57 ± 29.40	1.38 ± 0.48	140.52 ± 43.56
	N	46	1.30 ± 0.41	160.67 ± 44.7	-	-
[16]	T	120	1.75 ± 0.52	137.71 ± 46.12	1.43 ± 0.54	272.4 ± 50.07 <sup>Δ</sup>
	C	120	1.57 ± 0.44	131.77 ± 51.49	1.58 ± 0.51	146.52 ± 50.15
	N	120	1.52 ± 0.53	265.81 ± 54.19	-	-

Note: T: Treatment group; N: Normal; C: Control group; <sup>Δ</sup>P<0.05.

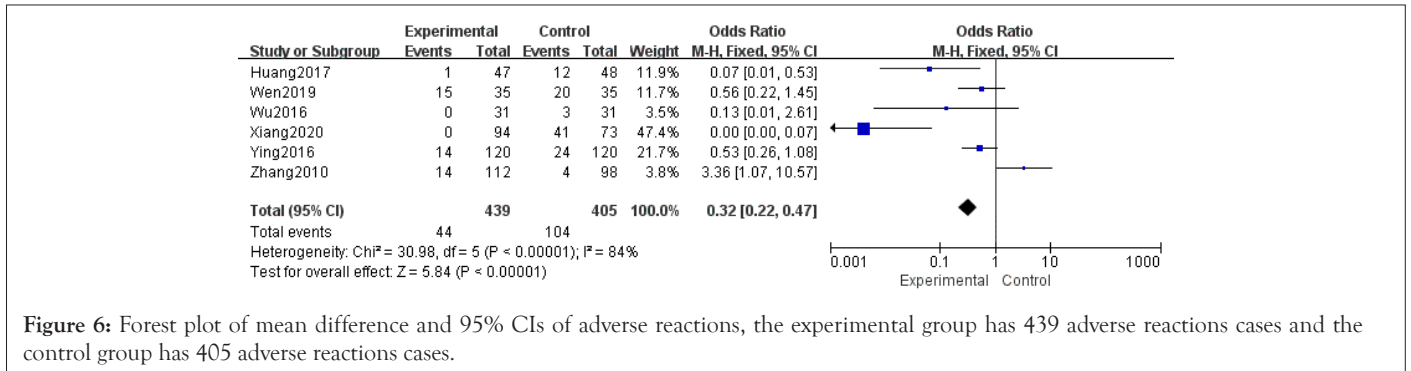


Figure 6: Forest plot of mean difference and 95% CIs of adverse reactions, the experimental group has 439 adverse reactions cases and the control group has 405 adverse reactions cases.

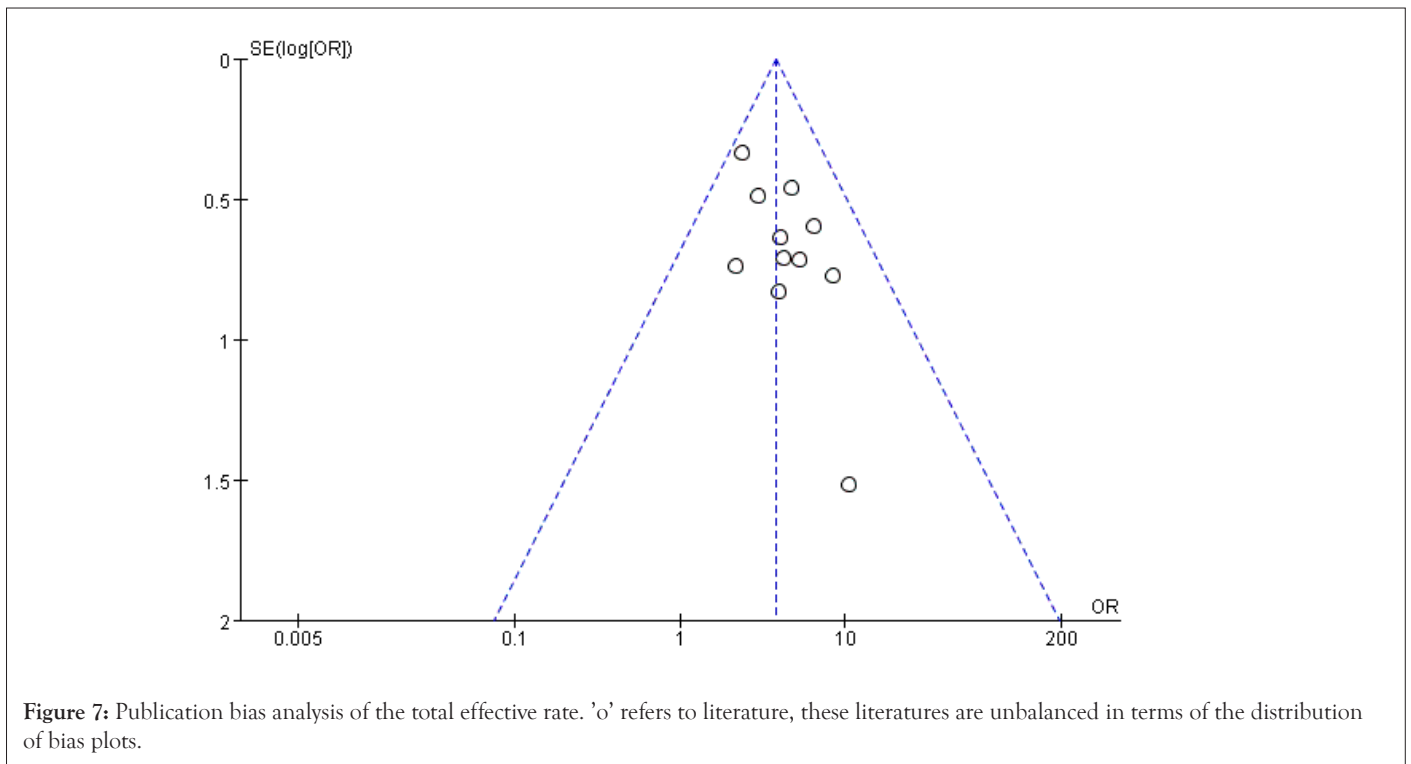


Figure 7: Publication bias analysis of the total effective rate. 'o' refers to literature, these literatures are unbalanced in terms of the distribution of bias plots.

## DISCUSSION

Acne Vulgaris is a chronic inflammatory skin disease with a complex pathogenesis. The key to its pathogenesis lies in the proliferation of Propionibacterium acnes, overproduction of sebum, increased affinity of the sebaceous glands for androgens, and abnormal keratinization of the hair follicle opening. Androgens, insulin, Insulin-like Growth Factor-1 (IGF-1), as well as corticotropin-releasing hormone, alpha-melanocyte stimulating hormone, and substance P, are hormones that contribute to the pathophysiology of acne. Sebocyte, keratinocyte, and inflammatory cell activity is regulated by the Wnt, PI3K/Akt, MAPK/ERK, and NF- $\kappa$ b pathways; among these, the IGF-1-induced PI3K/Akt/mTOR pathway is the most significant signaling route contributing to the pathogenesis of acne [22].

Acupuncture therapy is an important part of traditional medicine in China and has definite clinical efficacy for a variety of indications. An important mechanism for acupuncture's effectiveness is its anti-inflammatory effects. According to some research, acupuncture can reduce inflammatory mediators at the site of the lesion and prevent tissue damage. Additionally, the anti-inflammatory effect is implicated in the process of healing for a number of disorders, including: Acupuncture can reduce the severity of acne lesions, anxiety, and depression by lowering

IGF-1 and Dehydroepiandrosterone (DHEA) levels. Electroacupuncture increases the release of interleukin-10 and promotes inflammatory repair [23]. The electroacupuncture zu san li point activates the vagus nerve that projects to the adrenal medulla through signal transmission to the central core [24]. Acupuncture also has immunomodulatory effects that regulate the amount of T cells and stimulate T cell activity [25]. It can also influence the quantity of immune cells (NK cells, neutrophils, macrophages, etc.), as well as decrease the levels of inflammatory cytokines that are associated to these cells [26].

Acupuncture Point Embedding is the result of the development of needle retention and buried needle therapy. The composite effect of the buried threads and needles consists of the restricted effect of acupuncture points, the acupuncture effect, the pricking effect, the post-injury effect of tissues, the needle retention, and the buried needle effect [27], thus having contributed to the Yin and Yang of the inner and dredging the meridians of Qi and blood. Its theoretical foundation comes from HuangDiNeiJing, which claims that "in those who have been ill for a long time, the evil qi enters deeply and stays deep inside for a long time," and that the pattern of acupuncture points is typically the same as that of acupuncture but more streamlined with the purpose of reducing pain and discomfort. Studies have shown that in terms of acupuncture point selection, apart from the localized A'shi

acupoint, FeiShu (BL14), He Gu (LI4) and Qu Chi (IL11) are the most commonly used acupuncture points for acne, FeiShu (BL14), a dorsal point of the lung meridian, has the effect of regulating the Qi, Blood, Yin and Yang of the lung meridian; since acne typically affects the head and face, where the Yang Ming Stomach meridian travels, He Gu (LI4) and Qu Chi (IL11) are both acupuncture points on the Yang Ming Stomach meridian that have the effect of clearing heat and relieving pain. The meridian runs through the acupuncture sites on the head and face, and "where the meridian passes through, the main treatment reaches". The acupuncture point correlation study reveals that the combination of DaZhui (BL13)-FeiShu (BL14)-GeShu (BL17) points shares certain similarities in the selection of acupuncture points for the treatment of acne because the three work together to clear heat and cool blood [28].

This analysis comprised a total of 1456 patients from 12 randomised controlled trials. Acupuncture Point Embedding was used in the experimental intervention together with other acupuncture therapies and with treatments from traditional western medicine. As compared to conventional western medicine treatment, the combined acupoint embedding treatment group significantly increased clinical efficacy, improved skin lesion score, decreased recurrence rate, and reduced adverse reaction.

This Meta-analysis has certain limitations: Negative results that were intended for publication were excluded, and there may be publication bias. The quality of the literature's inclusion was moderate; some of them were not mentioned on random allocation methods, allocation blinding, and implementation blinding; and there may have been selection bias. The literature covers different research protocols and there is potential for confounding bias in the analysis process; Bias can be present across the literatures depending on the acupuncture point protocol, positioning, practitioner, material used for embedding, needles, etc. Additionally, the study methodology did not take into consideration the severity of the Acne Vulgaris included patients, which may have resulted in increased heterogeneity when analyzing the same data.

## CONCLUSION

In conclusion, this article suggests that combining acupuncture Point Embedding in the treatment of Acne Vulgaris has some advantages and can achieve good clinical outcomes, but further studies are needed for further studies that addressed detailed the selection of acupoint, the needles, the frequency. Further studies should be aimed to design multicentre, randomised, double-blind controlled research programmes to provide a more informed basis for clinical decision-making.

## DECLARATIONS

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### Conflict of interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this

article.

### Author's contributions

This study was proposed and designed by Ma Xueting and Zhou Yu.

Ma Xueting and Ma Fuchang obtained funding.

Data acquisition and extraction were conducted by Ma Xueting, Ma Fuchang, Cui Guimin, Guo Hong.

Ma Xueting and Zhou Yu performed the statistical analysis of all data.

Ma Xueting and Ma Fuchang drafted the article, and Zhou Yu, Cui Guimin, Guo Hong critically revised it.

### Ethical approval and consent to participate

This study was based on previously published studies; therefore, ethical approval and patient consent are not relevant.

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