

# Acupuncture for blepharospasm: a systematic review and meta-analysis protocol

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**Protocol**

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# Abstract

## Background

Blepharospasm is a disorder inducing bilateral eyelid closure due to irregular muscle contraction. Oral medications or surgical interventions currently still hardly achieve a great therapeutic effect. Acupuncture is indicated effective in improving blepharospasm, but its efficacy has not been comprehensively elucidated as a therapy, so a systematic evaluation on acupuncture for blepharospasm is desirable.

## Methods

All randomised controlled trials related to acupuncture for blepharospasm will be screened from 9 databases, including 5 English databases (Cochrane Central Register of Controlled Trials, Web of Science, PubMed, MEDLINE, Excerpta Medica Database) and 4 Chinese databases (CNKI, Chinese Biomedical Literature Database, China Wanfang Database, and VIP Database). The primary outcomes include degree of blepharospasm, scores of BFM, UDRS, JRC, BSS, BDS, and BSDI. The incidence of adverse events will be also considered. Two reviewers will screen studies, extract data and assess the quality. Review Manager software 5.4.1 (provided by Cochrane, London, United Kingdom) will be used to assess risk of bias and synthesize data synthesis.

## Discussion

Our study will investigate the efficacy and safety of acupuncture in treating blepharospasm, providing a summary to contribute to application of acupuncture.

## Systematic review registration:

CRD42020222489, registered on Dec 24, 2020.

## Background

Blepharospasm is a focal dystonia in which agonist and antagonist muscles contract simultaneously, followed by involuntary eyelid closure<sup>[1]</sup>. Blepharospasm affects approximately 20 to 133 cases per million individuals and is more common in women<sup>[2-4]</sup>. The etiology of blepharospasm is not well understood until now. It can be divided into two types, benign essential blepharospasm (BEB) and secondary blepharospasm. Study shows that a positive family history of BEB is found in 20–30% of cases, probably due to genetic susceptibility<sup>[5]</sup>. Developing BEB is also determined by non-inherited risk factors, including eye strain<sup>[6-7]</sup>, psychiatric conditions<sup>[8]</sup>, head trauma<sup>[9]</sup>, keratoconjunctivitis/blepharitis

and other ocular surface disease<sup>[10–11]</sup>. In ophthalmology, severe blepharospasm in patients with neurological symptoms is also known as Meige syndrome<sup>[12]</sup>.

Currently, there are already several treatment options available, including botulinum toxins injection<sup>[13]</sup>, oral medications such as benzodiazepines, anticholinergics, levodopa, baclofen, VMAT2 inhibitors (tetrabenazine), and surgical intervention<sup>[14]</sup>. However, there is no definitive cure for blepharospasm due to its complex mechanisms. In recent years, some investigators have managed to apply acupuncture in the treatment of blepharospasm in clinical practice and experimental study with few side effects<sup>[15–18]</sup>. Acupuncture is effective for blepharospasm in some researches, but its efficacy is still under controversy.

## Methods

### Objectives

This study aims to evaluate the efficacy and safety of acupuncture for blepharospasm using system valuation and meta-analysis. It also provides a safer and more effective treatment for patients with blepharospasm.

### Study registration

This protocol (registration number CRD42020222489) has been registered on the International Prospective Register of Systematic Reviews (PROSPERO). The protocol will strictly follow the guideline of Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocols (PRISMA-P)<sup>[19]</sup>. The PRISMA-P checklist for our study is displayed in **Additional file 1**. If necessary, the authors will update the protocol during our research.

### Inclusion criteria

#### Type of study

Randomized controlled trials (RCTs) of all acupuncture treatment for blepharospasm includes:

1. Traditional acupuncture
2. Warm-needle techniques
3. Electroacupuncture

No publication date was imposed on the initial search. Language restrictions are Chinese and English.

#### Types of participants

1. Blepharospasm patients (aged 18 years or older) regardless of gender and nationality.

2. Patients with Meige syndrome or blepharospasm.

3. Types of blepharospasm are not restricted.

### **Types of intervention**

Acupuncture therapies used in the observation group include body acupuncture, ear acupuncture, scalp acupuncture, fire acupuncture, warming acupuncture and electroacupuncture. There is no limit on the length or frequency of treatment.

Control interventions include no treatment/wait list, sham control, or no active treatment (such as physical therapy, oral medications, surgery, injections, or other traditional medication). Studies that compare the effects of blepharospasm to herbal remedies will be excluded. If participants in the blepharospasm group received another aggressive treatment, only studies that included all control group participants receiving the same aggressive treatment as the combined intervention would be selected.

### **Types of efficacy index**

#### **Primary outcomes**

1. Muscle motor function using dystonias scales (eg, BurkeFahn-Marsden dystonia rating scale(BFM), UDRS<sup>[20]</sup>), and the Blepharospasm Severity Scale (BSS), the Jankovic Rating Scale (JRC), the Blepharospasm Disability Scale (BDS), and Blepharospasm Disability Index (BSDI) <sup>[12,21]</sup>.

2. Change in level of consciousness.

3. Severe adverse events.

#### **Secondary outcomes**

1. Comprehensive assessment of participant improvement (eg, proportion of overall improvement and subjective improvement).

2. Adverse events associated with blepharospasm or any other treatments.

#### **Exclusion criteria**

1. Diagnostic criteria is unclear .

2. The data are duplicated, or the data information is incomplete.

3. The research is a type of Non-RCTs or Quasi-RCTs.

4. The studies are observational or retrospective.

5. The study subjects are non-human.

## Search methods for identification of studies

### Electronic data sources

We will screen eligible published studies from 9 databases up to December 2020, including 5 English databases (Cochrane Central Register of Controlled Trials, Web of Science, MEDLINE, PubMed, and Excerpta Medica Database) and 4 Chinese databases (China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database, China Wanfang Database, and VIP Database).

### Other resources

Searches will be also carried out on the Cochrane Central Register of Controlled Trials, the PROSPERO Register of Controlled Trials, and the Cochrane Complementary Medicine Field Specialized Register. If part of the data is incomplete, we will also obtain complete data information from the author by certain means.

### Search strategy

Acupuncture and randomized controlled trial/RCT will be search terms. Multiple retrieval methods in Chinese and English databases will be conducted without publication restriction. The search strategy in PubMed is presented in **Table 1**. Additionally, appropriate modifications will be conducted in accordance with requirements.

## The literature collection and data analysis

### Screening of literature

Two researchers (HH, QH) will screen the studies in accordance with the inclusion and exclusion standard independently. The final selection procedure will be demonstrated in **Figure 1** according to the PRISMA guidelines.

### Data extraction and management

The data will be extracted by QH and NG. Each study is evaluated in terms of the type of design, randomisation, inclusion or exclusion standard, the characteristics of participants, intervention measures, outcomes measures, and the quality of study. Encountering differences, they will turn to YLZ for verification.

### Quality assessment of the studies included

Two researchers (HH, RXL) will evaluate the included literature quality. According to Cochrane Handbook for Systematic Reviews of Interventions<sup>[22]</sup>, 7 aspects of bias risk will be assessed:

1. whether the sequence is randomly generated;

2. whether allocation concealment is adopted;
3. whether participants and personnel implement the blind method;
4. whether the blind method is used to evaluate the results;
5. whether the outcome data are complete;
6. whether the selective outcome has been reported;
7. other bias: follow-up, conflicts of interest, non-intention-to-treat or per-protocol analysis, etc.

The study quality will be described as “bias of low risk,” “bias of high risk,” and “uncertainty of bias risk.”

### **Measures of treatment effect**

The odds ratio (OR) is used as the effect size if the data type is binary, while the standardized mean difference (SMD) and its 95% confidence interval (CI) is adopted as the effect size if the data type is quantitative.

### **Management of missing data**

The missing data will be acquired through contacting first authors. The incomplete data will be deleted if they cannot be obtained. If necessary, the potential influence of missing data on the conclusions of the research would be clarified in the section of ‘Discussion’.

### **Heterogeneity analysis**

The Cochran Q statistic and the  $I^2$  statistic will be used to evaluate the heterogeneity across studies. If  $I^2 > 50\%$ , heterogeneity existing, a random-effects model (REM) will be selected. If  $I^2 < 50\%$ , indicating no significant heterogeneity, a fixed-effects model (FEM) will be adopted.

### **Assessment of publication biases**

Egger’s and Beg’s tests will be conducted to assess publication bias in a meta-analysis through funnel plot asymmetry. P value  $< .05$  refers to significant publication bias.

### **Subgroup analysis**

In case of sufficient studies ( $>10$ ), the the heterogeneity source will be clarified by the method of subgroup analysis based on acupoint therapy combined with other treatments. The study with low quality will be excluded to assure the reliability of the funding.

### **Sensitivity analysis**

Sensitivity analysis will be performed to assess the reliability of the conclusions and indicate the impact of the protocol deviations on results. If the stability is poor, the analysis model, inclusion and exclusion criteria will be adjusted to increase stability.

### **Data synthesis**

The RevMan 5.4.1 software will be used to analyse the data. The  $\chi^2$  test and  $I^2$  test will indicate the application of a FEM or a REM. Substantial statistical heterogeneity not found, a systematic narrative synthesis will be performed to summarize and analyse the findings of the studies included.

### **Grading of quality of evidence**

The evidence quality will be conducted according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system<sup>[23]</sup> in terms of inconsistency, limitation, imprecision, indirectness, and the publication bias. The system classifies evidence into high, moderate, low, and very low.

### **Ethics and dissemination**

We will publish this review in peer-reviewed journals, or address it in meetings. The individual participant data will be excluded, so it is not necessary to acquire the ethical approval or informed consent.

## **Discussion**

At present, the mainstream treatment for blepharospasm is botulinum toxins injection, which has many side effects, such as the presence of apraxia of eyelid opening and dose-dependent effects<sup>[24-25]</sup>. Consequently, it is urgent to look for a feasible, safe and effective treatment for blepharospasm. In traditional Chinese medicine, blepharospasm is usually caused by the deficiency of blood in the liver and spleen or the deficiency of both the heart and spleen. The treatment should be based on heart, liver and spleen, and acupuncture is often used to tonify Qi and blood<sup>[26-27]</sup>. A considerable number of studies have shown the efficacy of acupuncture in the treatment of blepharospasm.

This systematic review elucidates the function of acupuncture for blepharospasm. Conclusions may benefit patients clinicians and policy makers. This review comprises identification, the inclusion of study, the extraction of the data, and the synthesis of the data. It has some limitations such as considerable heterogeneity caused by various forms of acupuncture and the poor quality of included studies.

## **List Of Abbreviations**

**EMBASE:** Excerpta Medica Database

**CNKI:** China National Knowledge Infrastructure

**PRISMA-P:** Preferred reporting items for systematic reviews and meta-analysis protocols

**RCT:** Randomised controlled trial

**BEB:** Benign essential blepharospasm

**BFM:** BurkeFahn-Marsden dystonia rating scale(

**JRC:** Jankovic Rating Scale

**BSS:** The Blepharospasm Severity Scale

**BDS:** The Blepharospasm Disability Scale

**BSDI:** Blepharospasm Disability Index

**OR:** odds ratio

**SMD:** standardized mean difference

**GRADE:** Grading of recommendations assessment, development, and evaluation

## **Declarations**

### **Ethics and dissemination**

Ethics approval is not required because individual data are not included. The findings of this systematic review will be disseminated through peer-reviewed publication or conference presentations.

### **Consent for publication**

Not applicable

### **Availability of data and materials**

Data sharing is not applicable to this article as no datasets were generated or analysed during the current protocol.

### **Competing interests**

The sponsors are not involved in design, execution, or whiting the study. All authors involved in this work have no conflicts of interest.

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## Author contributions

HH, QH, NG contributed equally to this work and are cofirst authors. Contributors HH and YLZ contributed to the conception of the study. The manuscript protocol was drafted by HH, and was revised by YLZ, QH, NG. HH and QH developed the search strategies, and QH, NG will implement them. RXL, WWZ will extract data of included studies, assess the risk of bias and complete the data synthesis. YLZ will arbitrate the disagreements and ensure that no errors are introduced during the study. All authors approved the publication of the protocol.

## Acknowledgements

Not applicable

## References

1. Titi-Lartey OA, Patel BC. Benign Essential Blepharospasm. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing 2020. <https://www.ncbi.nlm.nih.gov/books/NBK560833/>. Accessed 15 Dec. 2020.
2. Duarte GS, Rodrigues FB, Marques RE, Castelão M, Ferreira J, Sampaio C, et al. Botulinum toxin type A therapy for blepharospasm. *Cochrane Database Syst Rev.* 2020; 11: CD004900.
3. Steeves TD, Day L, Dykeman J, Jette N, Pringsheim T. The prevalence of primary dystonia: a systematic review and meta-analysis. *Mov Disord.* 2012;27: 1789–96.
4. Anderson RL, Patel BC, Holds JB, Jordan DR. Blepharospasm: past, present, and future. *Ophthalmic Plast Reconstr Surg.* 1998;14:305–17.
5. Dong H, Luo Y, Fan S, Yin B, Weng C, Peng B. Screening Gene Mutations in Chinese Patients With Benign Essential Blepharospasm. *Front Neurol.* 2019;10:1387.
6. Bali J, Navin N, Thakur BR. Computer vision syndrome: a study of the knowledge, attitudes and practices in Indian ophthalmologists. *Indian J Ophthalmol.* 2007;55(4):289-94.
7. Sun Y, Tsai PJ, Chu CL, Huang WC, Bee YS. Epidemiology of benign essential blepharospasm: A nationwide population-based retrospective study in Taiwan. *PLoS One.* 2018;13(12):e0209558.
8. Kuyper DJ, Parra V, Aerts S, Okun MS, Kluger BM. Nonmotor manifestations of dystonia: a systematic review. *Mov Disord.* 2011;26(7):1206-17.
9. Peckham EL, Lopez G, Shamim EA, Richardson SP, Sanku S, Malkani R, et al. Clinical features of patients with blepharospasm: a report of 240 patients. *Eur J Neurol.* 2011;18:382–386.
10. Conte A, Berardelli I, Ferrazzano G, Pasquini M, Berardelli A, Fabbrini G. Non-motor symptoms in patients with adult-onset focal dystonia: Sensory and psychiatric disturbances. *Parkinsonism Relat Disord.* 2016;22 Suppl 1:S111-4.

11. Defazio G, Berardelli A, Abbruzzese G, Lepore V, Coviello V, Acquistapace D, et al. Possible risk factors for primary adult onset dystonia: a case-control investigation by the Italian Movement Disorders Study Group. *J Neurol Neurosurg Psychiatry*. 1998;64(1):25-32.
12. Hwang CJ, Eftekhari K. Benign Essential Blepharospasm: What We Know and What We Don't. *Int Ophthalmol Clin*. 2018;58(1):11-24.
13. Hellman A, Torres-Russotto D. Botulinum toxin in the management of blepharospasm: current evidence and recent developments. *Ther Adv Neurol Disord*. 2015;8(2):82-91.
14. Yen MT. Developments in the treatment of benign essential blepharospasm. *Curr Opin Ophthalmol*. 2018;29(5):440-444.
15. Chengyin W. Observations on the Efficacy of Acupuncture in Treating Idiopathic Blepharospasm 32 cases. *Clinical Journal of Chinese Medicine*. 2015;7(33):109-110.
16. Jian N, Hong X, Ren Z. Efficacy observation of acupuncture method of tonifying-qi and dredging-meridian for blepharospasm. *Chinese Acupuncture & Moxibustion*. 2014;34(1):37-40.
17. Xiaohong L. Effective observation on treating blepharospasm with the Buyang Huanwu decoction plus acupuncture. *Clinical Journal of Chinese Medicine*. 2016;8(28):98-99.
18. Donghong Y, Shuiyuan Y. Multiple needle shallow needling treatment of eye muscle spasm. *Jilin Journal of Traditional Chinese Medicine*. 2016;36(11):1166-1168.
19. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*. 2015; 4:1–9.
20. Defazio G, Hallett M, Jinnah HA, Stebbins GT, Gigante AF, Ferrazzano G, et al. Development and validation of a clinical scale for rating the severity of blepharospasm. *Mov Disord*. 2015;30(4):525-30.
21. Jankovic J, Kenney C, Grafe S, Goertelmeyer R, Comes G. Relationship between various clinical outcome assessments in patients with blepharospasm. *Mov Disord*. 2009;24(3), 407-13.
22. Chandler J, Cumpston M, Thomas J, Higgins JPT, Deeks JJ, Clarke MJ, et al. *Cochrane Handbook for Systematic Reviews of Interventions* version 6.1 (updated September 2020). Cochrane, 2020. Available from <https://www.training.cochrane.org/handbook>. Accessed 1 Feb. 2021.
23. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol*. 2011;64:401–6.
24. Ababneh OH, Cetinkaya A, Kulwin DR. Long-term efficacy and safety of botulinum toxin A injections to treat blepharospasm and hemifacial spasm. *Clin Exp Ophthalmol*. 2014;42(3):254-61.
25. Naumann M, Albanese A, Heinen F, Molenaers G, Relja M. Safety and efficacy of botulinum toxin type A following long-term use. *Eur J Neurol*. 2006;13 Suppl 4:35-40.
26. Fangfang B, Zhengyong Z, Xingru Z. Advances in treatment of blepharospasm by traditional Chinese medicine. *Chinese Journal of Chinese Ophthalmology*. 2015;25(5):374-376.
27. Shanshan Y, Shengzhi T, Xiaojuan C, Jun C. Advances in treatment of blepharospasm by traditional Chinese medicine. *Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine*.

## Table

Table 1.

Search strategy sample of PubMed	
number	searchs
#1	Blepharospasm (MeSh)
#2	Blepharospasm (ti,ab)
#3	Benign essential blepharospasm(MeSh)
#4	EBE (ti,ab)
#5	Meige Syndrome (MeSh)
#6	MS (ti,ab)
#7	or#1-6
#8	Medicine, Chinese Traditional(MeSh)
#9	Traditional Chinese Medicine(ti,ab)
#10	TCM(ti,ab)
#11	or#8-10
#12	Acupuncture (MeSh)
#13	Acupuncture (ti,ab)
#14	Body Acupuncture (ti,ab)
#15	Auricular Acupuncture (ti,ab)
#16	Scalp Acupuncture (ti,ab)
#17	Fire Needling(ti,ab)
#18	Warm Needling(ti,ab)
#19	Electroacupuncture(ti,ab)
#20	or#12-19
#21	Randomized Controlled Trial (MeSh)
#22	Randomized Controlled Trial(ti,ab)
#23	RCT(ti,ab)
#24	#7 and #11 and #20 and #24

MeSh = medical subject headings, RCT = randomized controlled trial.

## Figures

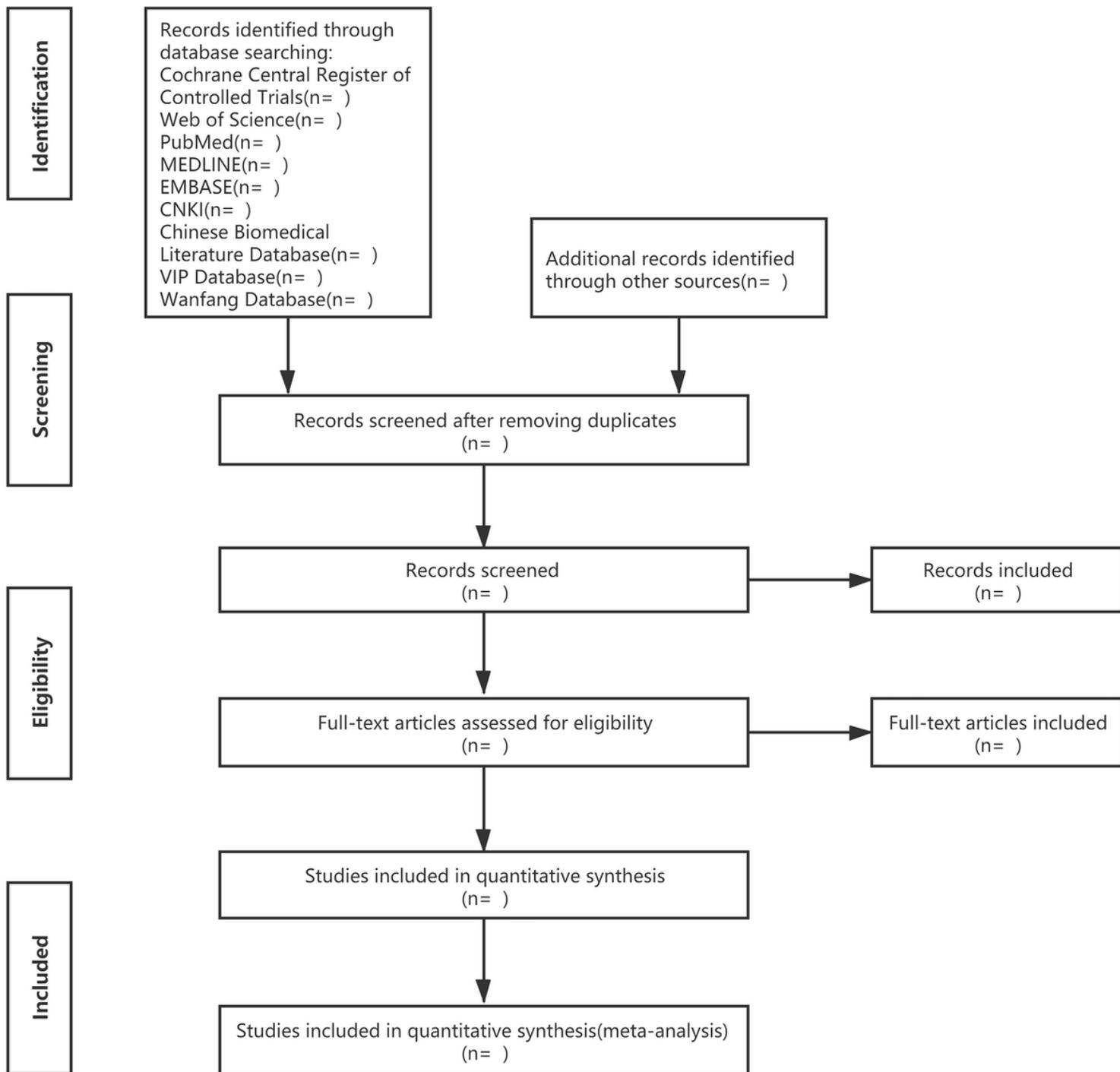


Figure 1

Flow diagram of the study selection process.

## Supplementary Files

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- [PRISMAPchecklist.docx](#)