

# BMJ Open Acupuncture for the treatment of chronic obstructive pulmonary disease: a protocol of a systematic review

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## ABSTRACT

**Introduction:** This review aims to evaluate the efficacy of acupuncture in the treatment of chronic obstructive pulmonary disease (COPD).

**Methods and analysis:** 14 databases will be searched from their inception. These include PubMed, AMED, EMBASE, the Cochrane Library, seven Korean medical databases (Korean Studies Information Service System, DBPIA, Oriental Medicine Advanced Searching Integrated System, Research Information Service System, KoreaMed, The Town Society of Science Technology and the Korean National Assembly Library), three Chinese Databases (China National Knowledge Infrastructure Database (CNKI), the Chongqing VIP Chinese Science and Technology Periodical Database (VIP), and the Wanfang Database). Only randomised clinical trials (RCTs) using acupuncture for COPD will be considered. The selection of the studies, data abstraction and validation will be performed independently by two researchers. Methodological quality will be assessed with the Cochrane risk of bias.

**Dissemination:** The systematic review will be published in a peer-reviewed journal. The review will also be disseminated electronically and in print. Updates of the review will be conducted to inform and guide the healthcare practice and policy.

**Trial registration number:** PROSPERO 2013: CRD42013004824.

## INTRODUCTION

### Description of the condition

Chronic obstructive pulmonary disease (COPD) is a slowly progressive disease characterised by airflow limitation and the gradual loss of lung function that is not fully reversible.<sup>1</sup> COPD includes emphysema and chronic bronchitis, and the main symptoms include cough and breathlessness.<sup>2</sup> This disease is predominantly caused by smoking.<sup>2</sup> COPD is a serious public health problem; according to the WHO, an estimated 64 million people worldwide currently suffer from moderate to severe COPD.<sup>3</sup> In fact, the WHO ranked COPD as the fifth leading cause

## Strengths and limitations of this study

- The strength of this systematic review is its extensive, unbiased search of various databases without a language restriction.
- The trial screening, data extraction and assessing risk of bias will be conducted independently by two of the authors.
- Our systematic review may pertain to the potential incompleteness of the evidence reviewed including publication and location bias, poor quality of the primary data and poor reporting of results.

of death worldwide, and it is estimated that COPD will be ranked as the third leading cause of death by 2030.<sup>4,5</sup> COPD also places a significant burden on healthcare systems, and a loss in health-related quality of life is observed in many patients.<sup>6</sup> Therefore, appropriate therapies are necessary to address this disease.

## Description of the intervention

In China, Traditional Chinese Medicine, as an auxiliary therapy to Western medicine, was extensively employed for the treatment of stable COPD.<sup>7</sup> Acupuncture is a popular treatment for COPD in China.<sup>8</sup> The most common treatment for pain in patients with COPD was acupuncture/transcutaneous electrical nerve stimulation compared with physiotherapy in the Norwegian general population.<sup>9</sup> Proponents argue that acupuncture is effective at relieving symptoms, reducing the incidence of COPD exacerbations and improving quality of life, and that it is associated with fewer adverse effects than conventional approaches to COPD.<sup>10</sup>

## How the intervention might work

Acupuncture may help relieve COPD by reducing bronchial immune-mediated inflammation<sup>11</sup> and reducing inflammation in general



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by promoting release of vascular and immunomodulatory factors.<sup>12</sup> However, the reliable evidence is unclear.<sup>13</sup>

### Why it is important to this review

Response to treatment may differ with the pathophysiological variation between stable and acute disease. Acute exacerbations of COPD (AECOPD) are defined by acute, excessive increases in dyspnoea, cough and/or sputum, and are often associated with bacterial infection, neutrophilic inflammation and specific immune responses.<sup>14</sup>

### Objectives

This review aims at systematically evaluating the evidence of acupuncture for treating AECOPD and stable COPD from RCTs.

## METHODS

### Study registration

The protocol of this systematic review has been registered on PROSPERO 2013 (registration number: CRD42013004824).<sup>15</sup> This systematic review protocol was conducted and reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines.<sup>16</sup>

### Data sources

The following databases were searched from their inception: PubMed, AMED, EMBASE, The Cochrane Library, seven Korean Medical Databases (Korean Studies Information Service System, DBPIA, Oriental Medicine Advanced Searching Integrated System, Research Information Service System, KoreaMed, The Town Society of Science Technology and the Korean National Assembly Library), and the China National Knowledge Infrastructure Database (CNKI), the Chongqing VIP Chinese Science and Technology Periodical Database (VIP), and Wanfang Database. Articles identified through reference lists of included studies and relevant systematic reviews will be considered for inclusion based on their title. Our search strategy will include main keywords 'acupuncture' and 'chronic obstructive pulmonary disease' (see online supplement 1). Study selection will be documented and summarised in a PRISMA compliant flow chart (figure 1).

### Eligibility criteria

#### Population

We will include populations with a diagnosis of COPD. We will only include studies in which an external set of criteria had been used to screen participants for the condition (eg, criteria from the Global Initiative for Obstructive Lung Disease (GOLD),<sup>1</sup> American Thoracic Society (ATS),<sup>17</sup> British Thoracic Society (BTS)<sup>18</sup> or Group of Chronic Obstructive Pulmonary Diseases/the Branch of Respiratory Diseases/Chinese Medical Association<sup>19–21</sup>).

Patients who are clinically stable and do not show evidence of an exacerbation 1 month prior to study entry will be included. Patients at stable state and with exacerbations of COPD will be included. Patients with significant diseases other than COPD, including a diagnosis of asthma, cystic fibrosis, bronchiectasis or other lung diseases, will be excluded.

### Interventions

Studies that evaluated any type of invasive acupuncture will be included. The treatments considered have to involve needle insertion at acupuncture points, pain points or trigger points and had to be described as acupuncture. Studies investigating other methods of stimulating acupuncture points without needle insertion (eg, acupressure, pressed studs, laser stimulation or transcutaneous electrical stimulation) will be excluded. Control interventions in controlled studies may include treatments such as general care, sham treatment (interventions mimicking 'true' acupuncture/true treatment but deviating in at least one aspect considered important by acupuncture theory, such as skin penetration or correct point location), waiting list care or other treatment (eg, relaxation and physical therapies). We will also include trials that compared acupuncture plus another active treatment versus that other active treatment alone. Thus, we will include all pragmatic trials that compared acupuncture with any other treatments (eg, drugs, exercise, education, etc). Because our objective is to evaluate the effects of acupuncture compared with non-acupuncture controls, we will exclude RCTs in which one form of acupuncture was compared with another form of acupuncture.

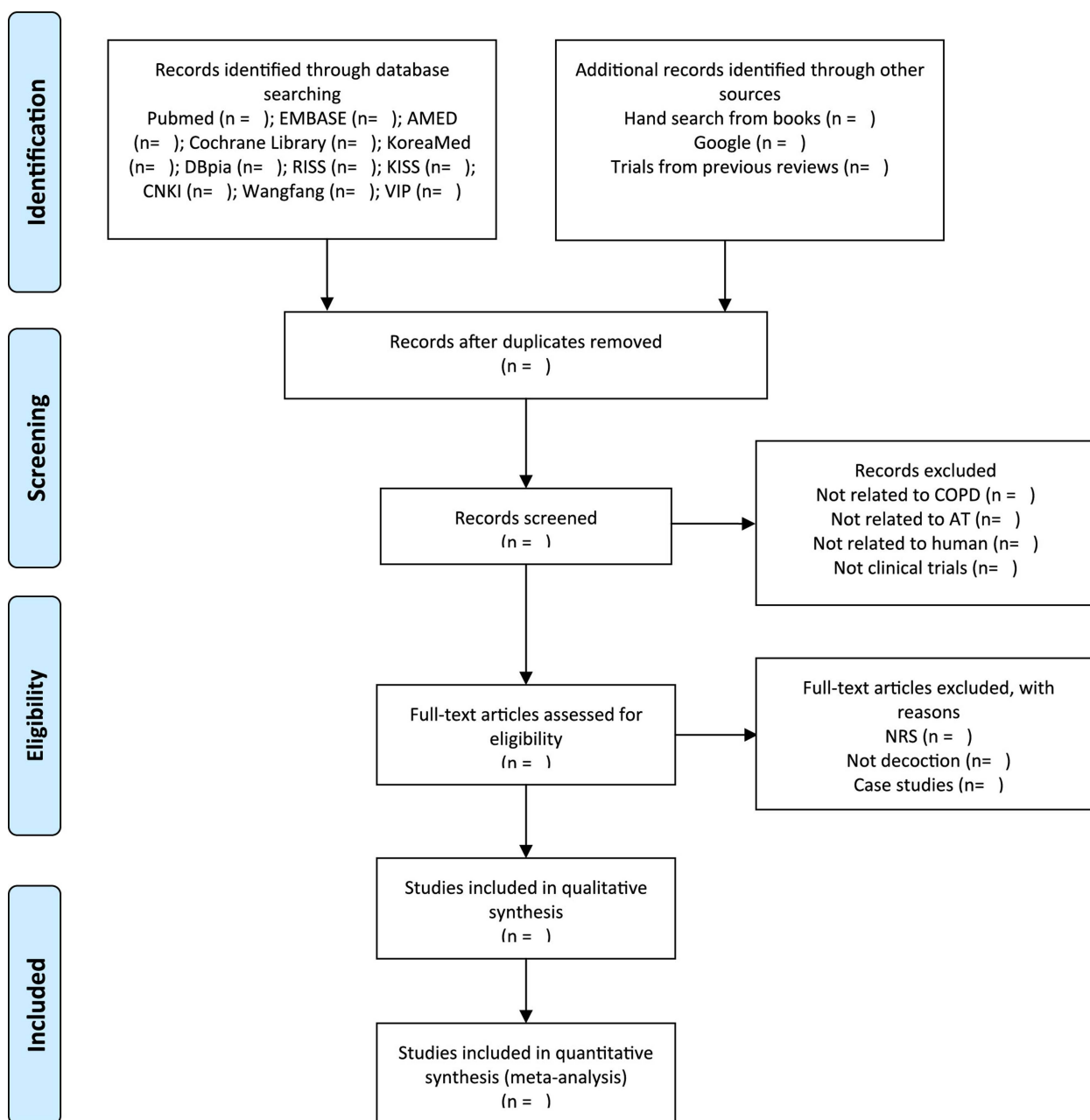
### Outcome measures

#### Primary outcomes

1. Treatment efficacy: the number of patients whose COPD symptoms improved.
2. Quality of life: measured using a validated questionnaire, for example, St. George's Respiratory Questionnaire (SGRQ)<sup>22</sup> or the Chronic Respiratory Disease Questionnaire (CRDQ or CRQ).<sup>23</sup>
3. Exacerbations<sup>24</sup>: frequency of exacerbations, time to first exacerbation, severity and duration of exacerbations.

#### Secondary outcomes

1. Pulmonary function: change in forced expiratory volume in 1 s and change in forced ventilatory capacity<sup>25</sup> (trough, peak and average) and other measures of pulmonary function.
2. Dyspnoea scores, for example, the Borg scale score,<sup>26</sup> the visual analogue scale (VAS),<sup>27</sup> the Medical Research Council (MRC) dyspnoea scale<sup>28</sup> components of the COPD assessment test (CAT).<sup>29</sup>
3. Anxiety on a 10 cm VAS.<sup>27</sup>
4. Exercise tolerance: for example, 6 min walk test,<sup>30</sup> shuttle walk test.<sup>31</sup>
5. Adverse events.
6. Participant withdrawal.



**Figure 1** Flow diagram of the trial selection process. AT, acupuncture; COPD, chronic obstructive pulmonary disease; NRS, non-randomised studies.

### Study design

Only RCTs will be included. Observational, cohort, case-control, case series, qualitative studies, uncontrolled trials and laboratory studies were excluded.

### Data collection and analysis

#### Data extraction

All articles will be read by two independent reviewers who extract data from the articles according to predefined criteria. The extracted data will include the authors, year of publication, country, study size, age and gender of the participants, acupuncture intervention, control intervention, main outcomes and adverse effects. The extracted data will be tabulated (see online

supplement 2) for further analysis. Details regarding the acupuncture and control interventions will be extracted on the basis of the revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA)<sup>32</sup> (see online supplement 3).

#### Risk of bias assessment

Quality assessment will be performed using the tool for 'risk of bias' from the Cochrane Handbook for Systematic Reviews of Interventions (see online supplement 4).<sup>33</sup> The following characteristics will be assessed: (1) Was the allocation sequence adequately generated? (2) Was the allocation adequately concealed? (3) Was knowledge of the allocated interventions adequately

presented during the study? (4) Were incomplete outcome data adequately addressed? (5) Were the study reports free of the suggestion of selective outcome reporting? and (6) Was the study free of other problems that could introduce a risk of bias? This review used 'L, U and H' as keys for these judgements; where 'Low' (L) indicated a low risk of bias, 'Unclear' (U) indicated that the risk of bias was uncertain, and 'High' (H) indicated a high risk of bias. Disagreements will be resolved by discussion between all authors.

### Data synthesis

All statistical analyses will be conducted using the Cochrane Collaboration's software program, Review Manager (RevMan), V.5.1 for Windows (Copenhagen, The Nordic Cochrane Center). Differences between the intervention and control groups will be assessed. In the analysis of clinical efficacy, count data will be assessed in terms of risk ratios, and continuous data will be assessed in terms of mean difference (MD). Count data and continuous variables will be expressed as efficacy values with 95% CIs. In cases of outcome variables with different scales, the standard mean difference will be used instead of the weighted MD. If the meta-analyses exhibit heterogeneity (defined as results of tests of heterogeneity that indicate that  $p < 0.1$  and  $I^2 \geq 50\%$ ), then a random effects model will be used to assess combined efficacy values; otherwise, fixed effects models were used for these assessments. Publication bias will be assessed using funnel plots and Egger's regression method.<sup>34</sup> If missing data are detected, we will request any missing or incomplete information from the original study investigators. Subgroup analysis will be conducted according to different control interventions (sham acupuncture vs conventional medication), the type of acupuncture (Chinese vs Western; standardised acupuncture vs individually adapted acupuncture points), type of stimulation (manual vs electric), treatment frequency (less than 14 vs more than 14), the design of the trial (acupuncture vs sham acupuncture; acupuncture vs conventional medication; acupuncture combined conventional medication vs conventional medication). Sensitivity analysis will be performed to evaluate the robustness of the meta-analysis results. Consistent with other meta-analyses and meta-regressions,<sup>35</sup> the primary quality measure will be a binary measure of allocation concealment.<sup>36</sup> Therefore, the risk of bias assessment for included studies will be summarised in a table, and the results and implications will be critically discussed.

### DISCUSSION

Until now, no systematic reviews have examined the use of acupuncture in the treatment of COPD. This systematic review will provide a detailed summary of the current evidence related to the effectiveness of acupuncture in treating the symptoms of patients with COPD. This evidence will be useful to practitioners, patients

and health policy-makers regarding the use of acupuncture in COPD treatment.

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**Contributors** T-YC and MSL conceived the study, developed the criteria and searched the literature, performed data analysis and wrote the protocol. JHJ assisted in searching the Chinese literature and extracting data. J-YC and J-IK wrote the introduction of this protocol. EE advised on the protocol design and revised the manuscript. All authors read and approved the final manuscript.

**Competing interests** None.

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