



# Acupuncture for the treatment of chronic obstructive pulmonary disease (COPD): a protocol of a systematic review

Journal:	BMJ Open
Manuscript ID:	bmjopen-2013-004590
Article Type:	Protocol
Date Submitted by the Author:	01-Dec-2013
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<b>Primary Subject Heading</b>:	Complementary medicine
Secondary Subject Heading:	Complementary medicine, Respiratory medicine
Keywords:	COMPLEMENTARY MEDICINE, Chronic airways disease < THORACIC MEDICINE, RESPIRATORY MEDICINE (see Thoracic Medicine)

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**Acupuncture for the treatment of chronic obstructive pulmonary disease (COPD): a protocol of a systematic review**

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**Short title:** A protocol of systematic review of acupuncture for COPD

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**Article focus**

- The aim of the proposed systematic review is to analyse randomised trial of acupuncture for chronic obstructive pulmonary disease (COPD).

**Key messages**

- This systematic review will be performed using a comprehensive search strategy and will establish the current status of the evidence using unbiased methods.

**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.

## Abstract

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

**Methods and analysis:** Thirteen databases will be searched from their inception. These include PubMed, AMED, EMBASE, the Cochrane Library, six Korean medical databases (Korean Studies Information, DBPIA, the Korean Institute of Science and Technology Information, the Research Information Centre for Health Database, KoreaMed, and the Korean National Assembly Library), the 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 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.

**Keywords:** chronic obstructive pulmonary disease (COPD), acupuncture, systematic review, randomised controlled trials

**Introduction**

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. This disease is predominantly caused by smoking.<sup>2</sup> COPD is a serious public health problem; according to the World Health Organization (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 of death worldwide, and it is estimated that COPD will be ranked as 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.

Acupuncture is a popular treatment for COPD in China.<sup>7</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>8</sup> However, the reliable evidence is unclear.<sup>9</sup> Therefore, the current review aims at systematically evaluating the evidence from RCTs testing the effectiveness of acupuncture for COPD.

## Methods

### Study registration

The protocol of this systematic review has been registered on PROSPERO 2013 (registration number: CRD42013004824).<sup>10</sup> This systematic review protocol was conducted and reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines.<sup>11</sup>

### Data sources

The following databases were searched from their inception: PubMed, AMED, EMBASE, The Cochrane Library, six Korean Medical Databases (Korean Studies Information, DBPIA, the Korean Institute of Science and Technology Information, the Research Information Centre for Health Database, KoreaMed, 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' (Supplement 1). Study selection will be documented and summarized in a PRISMA compliant flowchart (Figure 1).

### Eligibility criteria

#### Population

We will include populations with a diagnosis of COPD. We only will include studies in which an external set of criteria had been used to screen participants for the condition (e.g., criteria from the Global Initiative for Obstructive Lung Disease (GOLD),<sup>1</sup> American

Thoracic Society (ATS),<sup>12</sup> British Thoracic Society (BTS),<sup>13</sup> or Group of Chronic Obstructive Pulmonary Diseases/the Branch of Respiratory Diseases/Chinese Medical Association<sup>14-16</sup>). Included patients will be those who are clinically stable and do not show evidence of an exacerbation one month prior to study entry. 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 (e.g., 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 (e.g., relaxation, physical therapies). We also will 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 (e.g., drugs, exercise, education, etc.). Because our objective is to evaluate the effects of acupuncture compared to non-acupuncture controls, we will exclude RCTs in which one form of acupuncture was compared to 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, e.g., St. George's Respiratory Questionnaire (SGRQ) <sup>17</sup>

#### Secondary outcomes

1. Pulmonary function: Change in forced expiratory volume in one second (FEV1) and change in forced ventilatory capacity (FVC) <sup>18</sup> (trough, peak and average) and other measures of pulmonary function
2. Dyspnoea using Borg scale score <sup>19</sup>
3. Anxiety on a 10 cm Visual analogue scale (VAS) <sup>20</sup>
4. Exercise tolerance: six-minute walk test <sup>21</sup>
5. Adverse events

### Study design

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

### 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

(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>22</sup> (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 (Supplement 4).<sup>23</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 judgments; 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), Version 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 (RRs), and continuous data will be assessed in terms of mean difference (MD). Both count data and continuous variables will be expressed as efficacy values with 95% confidence intervals

(CIs). In cases of outcome variables with different scales, the standard mean difference (SMD) will be used instead of the weighted MD (WMD). 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 Eggers' regression method<sup>24</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, the type of acupuncture, the design of the trial (acupuncture vs. conventional medication, acupuncture combined conventional medication vs. conventional medication), and treatment frequency. Sensitivity analysis will be performed to evaluate the robustness of the meta-analysis results. Consistent with other meta-analyses and meta-regressions,<sup>25</sup> the primary quality measure will be a binary measure of allocation concealment.<sup>26</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**

To date, 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.

## Acknowledgement

TYC, JHJ and MSL were supported by Korea Institute of Oriental Medicine (K13400 and K13281).

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

TYC and MSL conceived the study, developed the criteria and searched the literature, performed data analysis and wrote the protocol. JHJ assisted in searched the Chinese literature, extraction of data. JYC and JIK wrote the introduction of this protocol. EE advised on protocol design and revised the manuscript. All authors read and approved the final manuscript.

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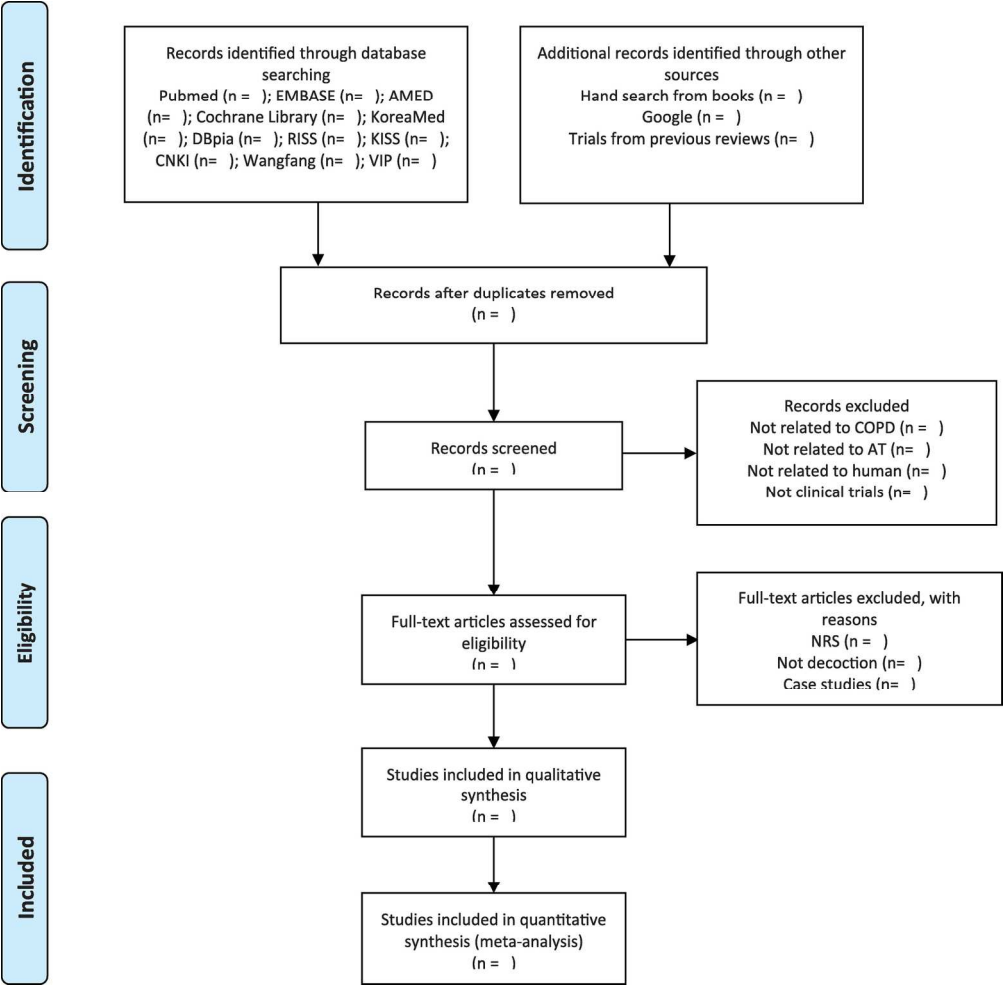
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172x169mm (300 x 300 DPI)

## Supplement 1. Search strategy

### MEDLINE search strategy

#### COPD search

1. Lung Diseases, Obstructive/
2. exp Pulmonary Disease, Chronic Obstructive/
3. emphysema\$.mp.
4. (chronic\$ adj3 bronchiti\$).mp.
5. (obstruct\$ adj3 (pulmonary or lung\$ or airway\$ or airflow\$ or bronch\$ or respirat\$)).mp.
6. COPD.mp.
7. COAD.mp.
8. COBD.mp.
9. AECEB.mp.
10. or/1-9

#### Acupuncture search

1. exp Acupuncture Therapy/
2. exp Medicine, East Asian Traditional/
3. Acupuncture
4. (acupuncture or acupressure or acupoint\* or electroacupuncture or electro-acupuncture or meridian\* or moxibust\* or “traditional chinese medicine” or “traditional oriental medicine”).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
5. 4 or 1 or 3 or 2

#### Filter to identify RCTs

1. exp “clinical trial [publication type]”/
2. (randomised or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. Animals/
10. Humans/
11. 9 not (9 and 10)
12. 8 not 11

The MEDLINE strategy and RCT filter are adapted to identify trials in other electronic databases

**Index Terms**

**Medical Subject Headings (MeSH)**

Acupuncture Therapy [\*methods]; Pulmonary Disease, Chronic Obstructive [\*therapy];  
Randomized Controlled Trials as Topic

**MeSH check words**

Humans

**Supplement 2. Summary of randomized clinical studies of acupuncture for COPD.**

First author (year) Country	Patients No. (M/F); Age, mean (I/C); Diagnosis; Duration of diseases;	Intervention group (Regime)	Control group (Regime)	Duration of treatment (total times)	Main outcomes	Intergroup differences	Adverse events
Study 1							
Study 2							
Study 3							
.....							

COPD: chronic obstructive pulmonary disease

Supplement 3. Summarized acupuncture interventions in the included studies.

First author (year)	Acupuncture Method (Fixed/ Partially Individualized/ Individualized) <sup>1</sup>	Treatment Rationale	Regimen	Acupuncture Points <sup>2</sup>	Response Sought <sup>3</sup>	Co-interventions
Study 1						
Study 2						
Study 3						
.....						

1. Acupuncture method was classified into 3 categories on the basis of the levels of individualization: “fixed” means all patients receive the same treatment at all sessions, “partially individualized” means using a fixed set of points to be combined with a set of points to be used flexibly, and “individualized” means each patient receives a unique and evolving diagnosis and treatment.

2. Acupuncture point SI3 refers to 3rd point of small intestine meridian and extra points have different nomenclature (eg, Ex-UE7 means 7th extra point in upper extremity). Ashi points refer to local pain points.

3. De-qi means acupuncture-evoked specific sensations such as soreness, numbness, heaviness, and distention at the site of needle placement, and these sensations may spread to other parts of the body.

**Supplement 4. Risk of bias in included RCTs.**

First author (year) Country	Random allocation	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Study 1								
Study 2								
Study 3								
.....								

L<sup>2</sup> indicated a low risk of bias; 'U' indicated that the risk of bias is uncertain; 'H' indicated a high risk of bias

# BMJ Open

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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:** Thirteen databases will be searched from their inception. These include PubMed, AMED, EMBASE, the Cochrane Library, six Korean medical databases (Korean Studies Information, DBPIA, the Korean Institute of Science and Technology Information, the Research Information Centre for Health Database, KoreaMed, 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 Cochrane risk of bias.

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- The aim of the proposed systematic review is to analyse randomised trial of acupuncture for treating chronic obstructive pulmonary disease (COPD).

## Key messages

- This systematic review will be performed using a comprehensive search strategy and will establish the current status of the evidence using unbiased methods.

## 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.

**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. This disease is predominantly caused by smoking.<sup>2</sup> COPD is a serious public health problem; according to the World Health Organization (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 of death worldwide, and it is estimated that COPD will be ranked as 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 (TCM), 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 to 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 that reducing bronchial immune-mediated inflammation<sup>11</sup>, and reducing inflammation in general 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 dyspnea, 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>

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Patients who are clinically stable and do not show evidence of an exacerbation one month prior to study entry will be included. Patients with both stable state and 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 (e.g., 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 (e.g., relaxation, physical therapies). We also will 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 (e.g., drugs, exercise, education, etc.). Because our objective is to evaluate the effects of acupuncture compared to non-acupuncture controls, we will exclude RCTs in which one form of acupuncture was compared to 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, e.g., St. George's Respiratory Questionnaire (SGRQ)<sup>22</sup>, Chronic Respiratory Disease Questionnaire (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 one second (FEV1) and change in forced ventilatory capacity (FVC)<sup>25</sup> (trough, peak and average) and other measures of pulmonary function
2. Dyspnoea scores, e.g., Borg scale score<sup>26</sup>, a visual analogue scale (VAS)<sup>27</sup>, Medical Research Council dyspnoea scale (MRC)<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: e.g., six-minute walk test<sup>30</sup>, shuttle walk test<sup>31</sup>
5. Adverse events
6. Participant withdrawal

Study design

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

### ***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 (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> (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 (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 judgments; 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***

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## Discussion

To date, 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.

## Authors' contributions

TYC and MSL conceived the study, developed the criteria and searched the literature, performed data analysis and wrote the protocol. JHJ assisted in searched the Chinese literature, extraction of data. JYC and JIK wrote the introduction of this protocol. EE advised on protocol design and revised the manuscript. All authors read and approved the final manuscript.

## Competing interests

The authors declare that they have no competing interests.

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# Acupuncture for the treatment of chronic obstructive pulmonary disease (COPD): a protocol of a systematic review

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**Short title:** A protocol of systematic review of acupuncture for COPD

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## Article focus

- The aim of the proposed systematic review is to analyse randomised trial of acupuncture for **treating** chronic obstructive pulmonary disease (COPD).

## Key messages

- This systematic review will be performed using a comprehensive search strategy and will establish the current status of the evidence using unbiased methods.

## 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.

**Abstract**

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

**Methods and analysis:** Thirteen databases will be searched from their inception. These include PubMed, AMED, EMBASE, the Cochrane Library, six Korean medical databases (Korean Studies Information, DBPIA, the Korean Institute of Science and Technology Information, the Research Information Centre for Health Database, KoreaMed, 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 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.

**Keywords:** chronic obstructive pulmonary disease (COPD), acupuncture, systematic review, randomised controlled trials

## 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. This disease is predominantly caused by smoking.<sup>2</sup> COPD is a serious public health problem; according to the World Health Organization (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 of death worldwide, and it is estimated that COPD will be ranked as 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 (TCM), 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 to 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 that reducing bronchial immune-mediated inflammation<sup>11</sup>, and reducing inflammation in general 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 dyspnea, 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, six Korean Medical Databases (Korean Studies Information, DBPIA, the Korean Institute of Science and Technology Information, the Research Information Centre for Health Database, KoreaMed, 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' (Supplement 1). Study selection will be documented and summarized in a PRISMA compliant flowchart (Figure 1).

### *Eligibility criteria*

#### Population

We will include populations with a diagnosis of COPD. We only will include studies in which an external set of criteria had been used to screen participants for the condition (e.g., 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 one month prior to study entry will be included. Patients with both stable state and 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.

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

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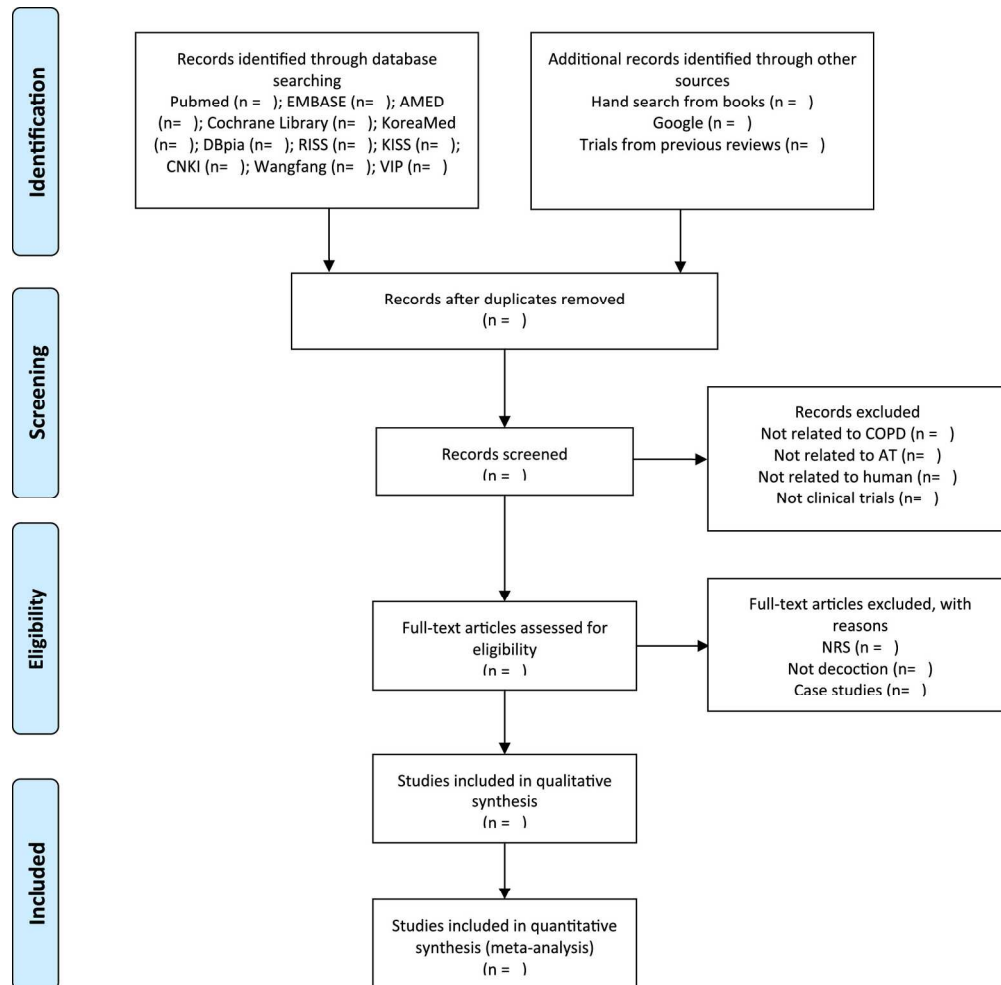


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176x172mm (300 x 300 DPI)

**Supplement 1. Search strategy**

**MEDLINE search strategy**

**COPD search**

1. Lung Diseases, Obstructive/
2. exp Pulmonary Disease, Chronic Obstructive/
3. emphysema\$.mp.
4. (chronic\$ adj3 bronchiti\$).mp.
5. (obstruct\$ adj3 (pulmonary or lung\$ or airway\$ or airflow\$ or bronch\$ or respirat\$)).mp.
6. COPD.mp.
7. COAD.mp.
8. COBD.mp.
9. AECEB.mp.
10. or/1-9

**Acupuncture search**

1. exp Acupuncture Therapy/
2. exp Medicine, East Asian Traditional/
3. Acupuncture
4. (acupuncture or acupressure or acupoint\* or electroacupuncture or electro-acupuncture or meridian\* or moxibust\* or “traditional chinese medicine” or “traditional oriental medicine”).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
5. 4 or 1 or 3 or 2

**Filter to identify RCTs**

1. exp “clinical trial [publication type]”/
2. (randomised or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. Animals/
10. Humans/
11. 9 not (9 and 10)
12. 8 not 11

The MEDLINE strategy and RCT filter are adapted to identify trials in other electronic databases

## Index Terms

### Medical Subject Headings (MeSH)

Acupuncture Therapy [\*methods]; Pulmonary Disease, Chronic Obstructive [\*therapy];  
Randomized Controlled Trials as Topic

### MeSH check words

Humans

**Supplement 2. Summary of randomized clinical studies of acupuncture for COPD.**

First author (year) Country	Patients No. (M/F); Age, mean (I/C); Diagnosis; Duration of diseases;	Intervention group (Regime)	Control group (Regime)	Duration of treatment (total times)	Main outcomes	Intergroup differences	Adverse events
Study 1							
Study 2							
Study 3							
.....							

COPD: chronic obstructive pulmonary disease

**Supplement 3. Summarized acupuncture interventions in the included studies.**

First author (year)	Acupuncture Method (Fixed/ Partially Individualized/ Individualized) <sup>1</sup>	Treatment Rationale	Regimen	Acupuncture Points <sup>2</sup>	Response Sought <sup>3</sup>	Co-interventions
Study 1						
Study 2						
Study 3						
.....						

1. Acupuncture method was classified into 3 categories on the basis of the levels of individualization: “fixed” means all patients receive the same treatment at all sessions, “partially individualized” means using a fixed set of points to be combined with a set of points to be used flexibly, and “individualized” means each patient receives a unique and evolving diagnosis and treatment.

2. Acupuncture point SI3 refers to 3rd point of small intestine meridian and extra points have different nomenclature (eg, Ex-UE7 means 7th extra point in upper extremity). Ashi points refer to local pain points.

3. De-qi means acupuncture-evoked specific sensations such as soreness, numbness, heaviness, and distention at the site of needle placement, and these sensations may spread to other parts of the body.



Supplement 4. Risk of bias in included RCTs.

First author (year) Country	Random allocation	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Study 1								
Study 2								
Study 3								
.....								

L<sup>2</sup> indicated a low risk of bias; ‘U’ indicated that the risk of bias is uncertain; ‘H’ indicated a high risk of bias

**BMJ Open**

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

Tae-Young Choi, Ji Hee Jun, Jun-Young Choi, Jong-In Kim, Myeong Soo Lee and Edzard Ernst

*BMJ Open* 2014 4:

doi: 10.1136/bmjopen-2013-004590

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