

# INPLASY PROTOCOL

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**Conflicts of interest:**  
None declared.

## Does acupuncture improve lung function in chronic obstructive pulmonary disease animal model?: a systematic review and meta-analysis

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**Review question / Objective:** Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease characterized by persistent respiratory symptoms and progressive airflow obstruction documented on spirometry. Acupuncture, as a safe and economical non-pharmacology therapy, has pronounced therapeutic effects in COPD patients. Several systematic reviews draw the conclusion that acupuncture could improve patients' quality of life, exercise capacity and dyspnoea, however, the results about lung function were inconclusive. Recently, increasing number of animal studies has been published to illustrate the effects of acupuncture in improving lung function in COPD animal model. However, the efficacy of acupuncture for experimentally induced COPD have not been systematically investigated yet. A systematic review of animal experiments can benefit future experimental designs, promote the conduct and report of basic researches and provide some guidance to translate the achievements of basic researches to clinical application in acupuncture for COPD. Therefore, we will conduct this systematic review and meta-analysis to evaluate effects of acupuncture on COPD animal model.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 March 2022 and was last updated on 02 October 2022 (registration number INPLASY202230104).

### INTRODUCTION

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draw the conclusion that acupuncture could improve patients' quality of life, exercise capacity and dyspnoea, however, the results about lung function were inconclusive. Recently, increasing number of animal studies has been published to illustrate the effects of acupuncture in improving lung function in COPD animal model. However, the efficacy of acupuncture for experimentally induced COPD have not been systematically investigated yet. A systematic review of animal experiments can benefit future experimental designs, promote the conduct and report of basic researches and provide some guidance to translate the achievements of basic researches to clinical application in acupuncture for COPD. Therefore, we will conduct this systematic review and meta-analysis to evaluate effects of acupuncture on COPD animal model.

**Condition being studied:** Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease characterized by persistent respiratory symptoms and progressive airflow obstruction documented on spirometry. According to the World Health Organization (WHO), COPD is the third leading cause of death globally. Statistical projections state that by 2040, the annual death toll will reach 4.4 million, and 90% of COPD deaths will be more in both low-income and middle-income countries. Main pharmacotherapy in COPD accompanied with potential adverse effects (eg, tachycardia, tremor, palpitations, weight loss, skin bruising and et al). Acupuncture, as a safe and economical non-pharmacology therapy, has pronounced therapeutic effects in COPD patients. Several systematic reviews draw the conclusion that acupuncture could improve patients' quality of life, exercise capacity and dyspnoea, however, the results about lung function were inconclusive. Recently, increasing number of animal studies has been published to illustrate the effects of acupuncture in improving lung function in COPD animal model. However, the efficacy of acupuncture for experimentally induced COPD have not been systematically

investigated yet. A systematic review of animal experiments can benefit future experimental designs, promote the conduct and report of basic researches and provide some guidance to translate the achievements of basic researches to clinical application in acupuncture for COPD. Therefore, we will conduct this systematic review and meta-analysis to evaluate effects of acupuncture on COPD animal model.

## METHODS

**Participant or population:** Rats model of COPD which induced by cigarette smoke alone or cigarette smoke plus airway injection of lipopolysaccharide.

**Intervention:** Only manual acupuncture and electroacupuncture(EA) will be included.

**Comparator:** COPD model group or normal group.

**Study designs to be included:** We will include all controlled studies of the effect of acupuncture in rats model of COPD.

**Eligibility criteria:** Inclusion criteria(1) Types of Subjects. Rats model of COPD which induced by cigarette smoke alone or cigarette smoke plus airway injection of lipopolysaccharide.(2) Types of Interventions. Only manual acupuncture and electroacupuncture(EA) will be included.(3) Types of Controls. COPD model group or normal group.(4) Types of Outcomes. the lung function of COPD rats is reflected by results of the lung function test(outcome indicators such as forced expiratory volume in 0.1s(FEV0.1), forced expiratory volume in 0.3s(FEV0.3), forced vital capacity(FVC), the ratio of FEV 0.1 to FVC (FEV0.1/FVC), the ratio of FEV 0.3 to FVC (FEV0.3/FVC), dynamic lung compliance (C<sub>dyn</sub>), pulmonary resistance (RL),resistance of inspiration (RI), functional residual capacity(FRC))(5) Types of Studies Included. We will include all controlled studies of the effect of acupuncture in rats model of COPD.Exclusion criteria(1) Duplicate articles.(2) Studies that have no control

group and studies that only compared different acupuncture techniques/acupoints or only compared the different intervention frequencies within the same acupuncture technique. (3) Studies that only compared acupuncture with TCM/western medication or only compared a combotherapy of acupuncture and TCM/western medication with either acupuncture or TCM/western medication. (4) Other acupuncture techniques including laser acupuncture, auricular acupuncture, acupoint injection and etc. Acupuncture therapies combined with other forms of acupuncture (such as auricular acupuncture, acupoint injection, moxibustion and etc), TCM or western medication.(5) Case reports, cross-over studies, reviews, meta-analyses or meeting abstracts.

**Information sources:** The following sources will be searched from February 2011 to March 2022: China National Knowledge Infrastructure(CNKI), VIP Database for Chinese Technical Periodicals(VIP), WANFANG Database (WF), Chinese biomedical literature service system(SinoMed), PubMed, Web of Science (WOS) and Embase. Reference lists of eligible studies and previous reviews will also be reviewed to identify further eligible studies.

**Main outcome(s):** Forced expiratory volume in 0.1s(FEV0.1), forced expiratory volume in 0.3s(FEV0.3), forced vital capacity(FVC), the ratio of FEV 0.1 to FVC (FEV0.1/FVC), the ratio of FEV 0.3 to FVC(FEV0.3/FVC).

**Additional outcome(s):** Dynamic lung compliance(Cdyn), pulmonary resistance(RL),resistance of inspiration (RI), functional residual capacity(FRC).

**Quality assessment / Risk of bias analysis:** Risk of bias assessment - The SYRCLE animal experiment bias risk assessment tool will be applied to evaluate the risk of bias in individual included studies. This tool contains 10 items about the selection, performance, detection, attrition, reporting bias, etc. Studies will be divided into low-bias risk, high-bias risk, and unclear-bias

risk. Each study could score ranging from zero to ten, with a high score represented a superior quality. Two investigators will independently read the included articles and assess the risk of bias. Discrepancies will be resolved through discussion, or by consulting a third investigator. Quality of evidence - Two investigators will independently evaluate the methodological quality of the included studies by using a checklist of the Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies (CAMARADES) with minor modifications. Ten items are as follows: (1) peer reviewed publication; (2) control of temperature; (3) random allocation to treatment group; (4) allocation concealment; (5) blinded assessment to outcome; (6) reporting of animals excluded from analysis; (7) precise animal species; (8) sample size calculation; (9) compliance with animal welfare regulations; (10) statement of potential conflict of interests. Each item of the ten-item scale is attributed to one point. Based on this, each study has a quality score from zero to ten. The higher the score is, the better the article's quality is. Any disagreement will be arbitrated by a third reviewer.

**Strategy of data synthesis:** Meta-analyses will be performed using Stata 17.0 software. Outcome measures (lung function indicators such as FEV0.1, FEV0.3, FEV0.1/FVC, FEV0.3/FVC, FVC, Cdyn, RL, RI and FRC) are considered as continuous data. The funnel plot and Egger's test will be applied to detect the publication bias. Heterogeneity will be detected by the I<sup>2</sup> statistic. If the I<sup>2</sup> statistic was higher than 50%, we consider that there's significant heterogeneity, and a random-effects model will be used to pool the data, otherwise, a fixed-effects model will be used.

**Subgroup analysis:** To explore the impact of factors potentially influencing the lung function, subgroup analyses will be conducted for the following factors: modeling method, frequency of disperse-dense waves, EA duration, EA sessions and frequency of EA treatment.

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**Sensitivity analysis:** We will evaluate the robustness of the results using leave-one-out sensitivity analyses.

**Country(ies) involved:** China.

**Keywords:** acupuncture; COPD; systematic review; meta-analysis.

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