1. Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable common lung disease.[1–4] It often manifests as dyspnea, chronic cough, and sputum production.[5,6] It is characterized by persistent respiratory symptoms and airflow limitation.[7–10] It is reported that about 90% deaths related to COPD occur in Asia and Africa,[11] and more than 0.9 million deaths are related to COPD.[12] Thus, effective treatment for COPD is very important.

Benralizumab is a humanized, afucosylated monoclonal antibody, which is utilized for reduction of sputum and blood eosinophil counts.[13–17] Previous studies have found that it can effectively treat patients with COPD.[18–20] However, no systematic review has been conducted to examine the efficacy and safety of benralizumab for COPD. Thus, this systematic review will assess the efficacy and safety of benralizumab for the treatment of COPD.
Table 1

Search strategy for Cochrane Library.

| Number | Search terms |
|--------|--------------|
| 1      | MeSH descriptor: (pulmonary disease, chronic obstructive) explode all trees |
| 2      | ([lung disease'] or [chronic obstructive pulmonary disease'] or [chronic inflammatory lung disease'] or [COPD']) or [obstructed airflow']);ti, ab, kw |
| 3      | Or 1-2 |
| 4      | [benralizumab] explode all trees |
| 5      | ([Fasenra'] or [monoclonal antibody']) or [benralizumab']) |
| 6      | Or 4-5 |
| 7      | MeSH descriptor: (randomized controlled trials) explode all trees |
| 8      | ([random'] or [randomly'] or [blind'] or [allocation'] or [placebo'] or [control'] or [comparison'] or [clinical trials'] or [controlled trials']);ti, ab, kw |
| 9      | Or 7-8 |
| 10     | 3 and 6 and 9 |

COPD = chronic obstructive pulmonary disease, MeSH = Medical Subject Headings.

2.2.2. Types of participants. Any patient who was diagnosed as COPD will be included irrespective of sex, age, and severity of COPD.

2.2.3. Types of interventions. In the experimental group, all patients who received benralizumab treatment will be included. In the control group, all patients received any management without restrictions. However, if we identified any study that involved any forms of benralizumab as their comparator, we will exclude it.

2.2.4. Type of outcome measurements. Primary outcome is lung function, which was measured by forced vital capacity or forced expiratory volume in 1 second or other relevant tools. Secondary outcomes are proportion of participants who had COPD exacerbation, rescue medication use, 6-minute walk test, dyspnea levels, quality of life (as measured by Saint George Respiratory Questionnaire or other tools), and adverse events.

2.3. Search methods for the identification of studies

2.3.1. Electronic database records searches. Electronic searches will be performed systematically and comprehensively for relevant studies in MEDLINE, EMBASE, Cochrane Library, Global health, PsycINFO, Scopus, WANGFANG, and CNKI. All these databases will be conducted from inception to the present regardless of their language and publication time. A search strategy sample of Cochrane Library is created (Table 1). Similar search strategies will be adapted and applied to other electronic databases.

2.3.2. Searching other records source. To avoid missing potential studies, other record sources will be identified, such as conference abstracts, dissertations, and reference lists of included studies.

2.4. Data collection and analysis

2.4.1. Study selection. Two reviewers will independently carry out study selection according to the previously designed eligibility criteria. Any disagreement will be solved by a third reviewer through discussion. Titles/abstracts of searched literatures will be identified to remove any irrelevant studies and duplicates. Then, we will read full text of remaining trials to further determine whether they meet all inclusion criteria. The whole process of study selection will be presented in a PRISMA flowchart.

2.4.2. Data collection. Two reviewers will independently extract data based on the predefined data extraction sheet. A third reviewer will help to solve any discrepancies through discussion. We will collect data of title, first author, year of publication, region, race, gender, diagnostic criteria, eligibility criteria, trial setting, trial methods, details of interventions and controls, outcome indicators, results, findings, adverse events, follow-up information, and conflict of interest.

2.4.3. Methodological quality assessment. Two reviewers will independently appraise study quality of all included trials using Cochrane Risk of Bias Tool, which covers 7 items, and each one is rated as low, unclear, and high risk of bias. We will invite a third reviewer to solve any different opinions by discussion.

2.4.4. Dealing with missing data. Any unclear or missing data will be obtained from primary authors if possible. If we cannot request such data, we will analyze available data by intention-to-treat analysis.

2.4.5. Data synthesis. RevMan 5.3 software will be utilized for performing statistical analysis. All discontinuous outcome variations will be estimated using risk ratio and 95% confidence intervals (CIs), and all continuous outcome variations will be calculated using weighted mean difference or standardized mean difference and 95% CI. Statistical heterogeneity among included trials will be checked using $I^2$ test: $I^2 \leq 50\%$ means minor heterogeneity, while $I^2 > 50\%$ suggests considerable heterogeneity. A fixed-effects model will be applied to pool the data if $I^2 \leq 50\%$. On the other hand, a random-effects model will be used to synthesize the data if $I^2 > 50\%$. When necessary, we will conduct a meta-analysis based on the similarity in characteristics of study and patient, interventions and controls, and outcome indicators. If obvious heterogeneity is identified, we will undertake a subgroup analysis to investigate possible sources of heterogeneity. In addition, we will report study results using narrative summary descriptions.

2.4.6. Reporting bias. We will examine reporting bias using Funnel plot and Egger regression test if more than 10 RCTs are included.[12,24]

2.4.7. Subgroup analysis. A subgroup analysis will be investigated to explore the possible sources of heterogeneity according to the different study characteristics, interventions, controls, and outcomes.

2.4.8. Sensitivity analysis. A sensitivity analysis will be conducted to check robustness and stability of study findings by eliminating low-quality studies.
2.5. Dissemination and ethics
We expect to publish this study in a peer-reviewed journal. Ethical approval is not needed because no privacy patient data will be obtained.

3. Discussion
Although published studies have reported that benralizumab has been used for the treatment of COPD,[18–20] there are still inconsistent results. In addition, no systematic review has been conducted to assess the efficacy and safety of benralizumab for the treatment of COPD. Therefore, this study will systematically investigate the efficacy and safety of benralizumab for the treatment of COPD. The findings of this study may provide evidence for clinical practice and health-related policy maker to improve COPD treatment approach.

Author contributions
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