

# BMJ Open Effects of respiratory rehabilitation on patients with novel coronavirus (COVID-19) pneumonia in the rehabilitation phase: protocol for a systematic review and meta-analysis

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## ABSTRACT

**Introduction** The recent viral pneumonia caused by the COVID-19 has gained the attention of the people all over the world. We aim to investigate the effects of respiratory rehabilitation therapy on patients infected with the novel coronavirus by conducting a systematic review and meta-analysis.

**Methods and analysis** This systematic review and meta-analysis have been registered in the International Prospective Register of Systematic Reviews (PROSPERO). The PubMed, Embase, Web of Science, the Cochrane Central Register of Controlled Trials, Chinese Biomedical Literature Database, China National Knowledge Infrastructure, Wanfang Data and Viper information databases will be searched from inception time to date without restricting research types to find relevant studies. We will also look into reference lists of relevant trials and reviews, and manually search grey literature, such as trial registries. Two reviewers will independently extract data and perform quality assessment of included studies. Review Manager V.5.3 (Cochrane Collaboration) and Stata V.16.0 software will be used to conduct this meta-analysis. The mean difference or standardised mean difference with 95% CIs is used in the computation of continuous variables to synthesise data.

**Ethics and dissemination** Ethical approval is not required due to the nature of this meta-analysis, which is based on published papers. The results of this systematic review and meta-analysis will be published in a peer-reviewed journal once we finish this study.

**PROSPERO registration number** CRD42020180214.

## INTRODUCTION

Towards the end of December 2019, patients with viral pneumonia subsequently infected by the COVID-19 were reported in Wuhan, China.<sup>1</sup> COVID-19 has sparked a pandemic around the world, and millions of people have been infected.<sup>2</sup> The management and control of COVID-19 infection remain a challenge for countries around the world.<sup>3</sup> Patients who suffered from the 2019 novel

## Strengths and limitations of this study

- This will be the first systematic review and meta-analysis investigating the effects of respiratory rehabilitation therapy on patients with novel coronavirus pneumonia.
- To avoid errors, data extraction and bias assessment will be independently performed by two reviewers.
- Egger's and Begg's tests will be conducted for the assessment of the publication bias under the use of Stata V.16.0 software.
- The absence of sufficient randomised controlled trials may be a limitation for this meta-analysis.

coronavirus had clinical manifestations of cough, shortness of breath, chest pain and so on.<sup>4</sup> COVID-19 is a highly contagious respiratory infection disease that can cause physical, respiratory and psychological disorders.<sup>5</sup> Pulmonary rehabilitation methods are important for patients with viral pneumonia due to by COVID-19.<sup>6</sup> Respiratory rehabilitation is crucial to the recovery of patients during clinical treatment and rehabilitation phase.<sup>7</sup> Early rehabilitation services can improve distressing physical and psychological symptoms with lung diseases.<sup>8</sup> Previously, pulmonary rehabilitation and chest physical therapy have been proven to provide the most positive effects for chronic obstructive pulmonary disease or other chronic respiratory diseases.<sup>9 10</sup> It was safe and feasible to perform early pulmonary rehabilitation in patients with acute exacerbation of lung diseases, which could effectively improve physical performance and quality of life.<sup>11 12</sup> Respiratory rehabilitation played a vital role in the non-invasive support management.<sup>13–17</sup> However, it is unclear whether respiratory rehabilitation therapy could improve lung

function in patients with coronavirus pneumonia. Additionally, up to now, there is no systematic review and meta-analysis investigating the association between respiratory rehabilitation therapy and COVID-19. Therefore, we will qualitatively and quantitatively examine the effects of respiratory rehabilitation therapy on patients with novel coronavirus in this systematic review and meta-analysis.

## METHODS

### Registration

The protocol followed the guideline of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P).<sup>18</sup>

### Patient and public involvement

No patient involved.

### Search strategy

The PubMed, Embase, Web of Science, the Cochrane Central Register of Controlled Trials, Chinese Biomedical Literature Database, China National Knowledge Infrastructure, Wanfang and VIP information databases will be searched from inception time to date. We will also search for reference lists of relevant trials and reviews, and manually search grey literature, such as trial registries. Studies concerning the effects of respiratory rehabilitation programmes for patients with COVID-19 in the rehabilitation phase will be included in this meta-analysis, as well as randomised controlled trials (RCTs), controlled clinical trials (CCTs), prospective and retrospective comparative cohort studies, cluster trials, cross-sectional studies and observational studies. The detailed information of PubMed search strategy is presented in [table 1](#).

## Eligibility criteria

### Study design

Relevant studies, including RCTs, CCTs, prospective and retrospective comparative cohort studies, cluster trials, cross-sectional studies and observational studies will be included in this meta-analysis. We attempt to search as many types of studies as possible due to the absence of original research on the recently emerging COVID-19.

### Participants

Patients who suffered from viral pneumonia caused by the COVID-19 and coordinated with respiratory rehabilitation treatments regardless of section, whether in the intensive care unit (ICU), intermediate respiratory unit, general ward or rehabilitation facility will be involved in this meta-analysis. There will be no restrictions with respect to gender, age or ethnicity.

### Interventions

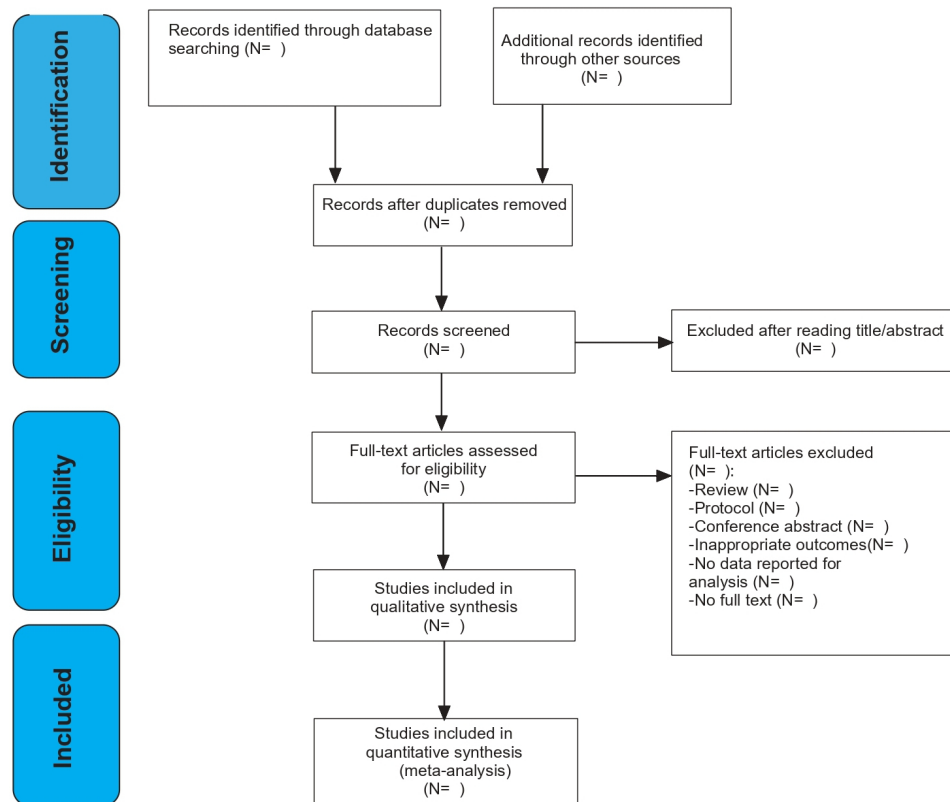
The interventions of respiratory rehabilitation therapy for viral pneumonia could be breathing exercises, respiratory muscle training, chest physiotherapy, active circular breathing technique, chest expansion exercises, forced exhalation technique, airway clearance techniques, positive expiratory pressure, using mechanical devices (eg, mechanical cough assist), exercise training (aerobic exercise or, resistance and endurance training) or other physical training programmes.

### Outcomes

The primary outcomes of interest will be 6min walking distance, cardiopulmonary exercise test and quality of life. The secondary outcomes are as follows: body mass index, arterial partial pressure of oxygen/fraction of inspired

**Table 1** Search strategy of PubMed

Search	Query
#1	"COVID-19"[Mesh Terms]
#2	"2019 nCoV"[Title/Abstract] OR "2019nCoV"[Title/Abstract] OR "2019 novel coronavirus"[Title/Abstract] OR "COVID19"[Title/Abstract] OR "COVID 19"[Title/Abstract] OR "new coronavirus"[Title/Abstract] OR "novel coronavirus"[Title/Abstract] OR "SARS CoV-2"[Title/Abstract] OR "(Wuhan[Title/Abstract] AND coronavirus)[Title/Abstract]" OR "COVID-19"[Title/Abstract] OR "SARS-CoV"[Title/Abstract] OR "2019-nCoV"[Title/Abstract] OR "SARS-CoV-2"[Title/Abstract] OR "novel coronavirus pneumonia" [Title/Abstract] OR "COVID-19 pneumonia" [Title/Abstract] OR "corona-virus"[Title/Abstract] OR "coronavirus"[Title/Abstract] OR "NcovWuhan"[Title/Abstract] OR "NcovHubei"[Title/Abstract] OR "NcovChina"[Title/Abstract] OR "NcovChinese"[Title/Abstract]
#3	"Respiratory rehabilitation"[Title/Abstract] OR "pulmonary rehabilitation"[Title/Abstract] OR "Respiratory therapy"[Title/Abstract] OR "pulmonary recovery"[Title/Abstract] OR "pulmonary rehabilitation program"[Title/Abstract] OR "physiotherapy"[Title/Abstract] OR "physical therapy"[Title/Abstract] OR "physical intervention"[Title/Abstract] OR "physical rehabilitation"[Title/Abstract] OR "pulmonary Therapy"[Title/Abstract] OR "pulmonary intervention"[Title/Abstract] OR "respiratory intervention"[Title/Abstract] OR "breath"[Title/Abstract] OR "exercis"[Title/Abstract] OR "train"[Title/Abstract] OR "fitness"[Title/Abstract] OR "aerobic"[Title/Abstract] OR "resistanc"[Title/Abstract] OR "endurance"[Title/Abstract] OR "inspiratory muscle train"[Title/Abstract] OR "inspiratory muscle strength" [Title/Abstract] OR "respiratory muscle train"[Title/Abstract] OR "respiratory muscle strength"[Title/Abstract] OR "respiratory muscle endurance" [Title/Abstract] OR "muscle relaxation therapy" [Title/Abstract] OR "hydrotherapy" [Title/Abstract] OR "swim" [Title/Abstract] OR "bik"[Title/Abstract] OR "joy"[Title/Abstract] OR "walk"[Title/Abstract] OR "run"[Title/Abstract] OR "danc"[Title/Abstract] OR "sport"[Title/Abstract] OR "active circular breathing technique"[Title/Abstract] OR "ACBT" [Title/Abstract] OR "chest expansion"[Title/Abstract] OR "forced exhalation technique"[Title/Abstract] OR "airway clearance"[Title/Abstract] OR "mechanical cough assist" [Title/Abstract] OR "manual technique"[Title/Abstract] OR "mechanical device"[Title/Abstract] OR "positive expiratory pressure"[Title/Abstract] OR "power breath"[Title/Abstract]
#4	#1 OR #2
#5	#3 AND #4



**Figure 1** Flow chart and descriptions of study selection.

oxygen ( $\text{PaO}_2/\text{FiO}_2$ ) ratio, forced expiratory volume in one second (FEV<sub>1</sub>), forced vital capacity (FVC), FEV<sub>1</sub>/FVC, baseline dyspnoea index, rating of perceived exertion scale scores, Borg scale scores, blood oxygen saturation and discharge time.

## Study selection and data extraction

### Study selection

Two reviewers independently select studies, and any disagreement between the two reviewers should be consulted by a third reviewer to reach a consensus. We will remove repetitive articles at first and exclude irrelevant studies based on the title, abstract and the full text. The study selection process is demonstrated in a PRISMA flow diagram (figure 1).

### Data extraction

A standardised form will be used by two reviewers to extract data independently, and disagreements between them should be solved with the help of a third reviewer. The detailed extraction information are as follows: the first author, year of publication, country of publication, study design, sample characteristics, number of participants, experimental and control interventions, intervention time, outcomes and results. We will try our best to contact the corresponding authors of the studies through email to deal with missing data.

### Quality assessment of included studies

The Cochrane risk-of-bias tool with items of random sequence generation, allocation concealment, blinding,

incomplete outcome data, selective reporting and other biases will be used to assess the quality of included RCTs. Otherwise, the Newcastle-Ottawa Scale, which includes consideration of patient selection, study comparability and outcome assessment will be used to evaluate the quality of non-randomised studies. We need to select a suitable scale according to the types of studies included.

## Data synthesis and statistical analysis

### Data synthesis

Review Manager V.5.3 (Cochrane Collaboration) and Stata V.16.0 software will be used to conduct this meta-analysis. The mean difference or standardised mean difference with 95% CIs is used to calculate continuous variables.

### Assessment of heterogeneity

Statistical heterogeneity among included studies will be assessed using the  $\chi^2$  test and  $I^2$  test. We use a fixed-effect model for data analysis at first. If  $I^2 > 0.5$  or  $p < 0.1$ , it is considered that there is a significant heterogeneity among the studies, and random-effect model will be used without examining the probable cause for the high heterogeneity.<sup>19</sup>

### Subgroup analysis

If there is a large heterogeneity in the included studies, subgroup analyses will be performed on different types of respiratory rehabilitation programmes and in different treatment locations, such as, ICU, intermediate respiratory unit, general ward or rehabilitation facility.

## Sensitivity analysis

Sensitivity analysis is conducted by excluding studies one by one, so that we can determine the source of heterogeneity.

## Assessment of publication bias

Publication bias will be examined according to the funnel plot method. Also, Egger's test and Begg's test will be conducted to quantitatively assess the publication bias using the Stata V.16.0 software.

## Quality of evidence

We will use the Grading of Recommendations Assessment, Development, and Evaluation guidelines for the assessment of the strength of evidence for each outcome. The result will be categorised as high, moderate, low and very low certainty of evidence.<sup>20</sup>

## Ethics and dissemination

Ethical approval is not required due to the nature of this meta-analysis, which is based on published papers. The results of this systematic review and meta-analysis will be published in a peer-reviewed journal once we finish this study.

## DISCUSSION

To the best of our knowledge, this is the first systematic review and meta-analysis to investigate the effects of respiratory rehabilitation therapy on patients with novel coronavirus pneumonia. Respiratory rehabilitation therapy has been widely applied to patients with chronic respiratory diseases.<sup>21</sup> However, it is uncertain whether respiratory rehabilitation therapy could improve lung function in patients with coronavirus pneumonia due to limited original research. This is a major concern for us and for everyone around the world. Nonetheless, the lack of sufficient RCTs may be a limitation for this meta-analysis.

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**Contributors** WC and MZ conceived and designed the study. FZ made the search strategy of databases. DW, QH, MG and CZ will be involved in data extraction and the assessment of methodological quality. The protocol manuscripts were finished by FZ. All authors have checked manuscripts and approved the publication of the protocol.

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**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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