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

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Keywords:	Rehabilitation medicine < INTERNAL MEDICINE, Respiratory infections < THORACIC MEDICINE, Public health < INFECTIOUS DISEASES

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4 1 **Effects of respiratory rehabilitation for patients with novel coronavirus**
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6 2 **(COVID-19) pneumonia in the rehabilitation phase: Protocol for a**
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8 3 **systematic review and meta-analysis**
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14 5 Feilong Zhu,¹ Ming Zhang,^{1,2} Wei Chen,^{1,2, *} Cheng Zeng,³ Dan Wang,¹
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20

21 **Word count**

22 2000 words

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4 23 **ABSTRACT**

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6 24 **Introduction:** Recent viral pneumonia infected by Coronavirus Disease 2019
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9 25 (COVID-19) has attracted the attention of people all over the world. We aim to
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11 26 investigate the effects of respiratory rehabilitation therapy on patients with novel
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13
14 27 coronavirus by conducting this systematic review and meta-analysis.

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17 28 **Methods and analysis:** Ethics approval is not required because this is a
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19 29 protocol for a systematic review and meta-analysis. This systematic review and
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21 30 meta-analysis has been registered in the PROSPERO. The PubMed, Embase,
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24 31 Web of Science, the Cochrane Central Register of Controlled Trials
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27 32 (CENTRAL), Chinese Biomedical Literature Database (CBM), China National
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29 33 Knowledge Infrastructure (CNKI), Wanfang and VIP information databases will
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31 34 be searched from their inception time to April 15, 2020 without restricting
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34 35 research types to find relevant studies. Two reviewers will independently extract
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37 36 data and perform quality assessment of included studies. Review Manager 5.3
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40 37 software (Cochrane Collaboration) and Stata 16.0 software will be used to
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43 38 conduct this meta-analysis. Mean difference (MD) or standardized mean
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46 39 difference (SMD) with 95% confidence intervals (CI) is used for calculating
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49 40 continuous variables to synthesize data.

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51 41 **Ethics and dissemination:** Ethical approval is not required because this meta-
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53 42 analysis is based on published papers. The results of this systematic review
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56 43 and meta-analysis will be published in a peer-reviewed journal once we have
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59 44 finished this study.

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4 45 **PROSPERO registration number:** CRD42020180214.
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6 46 **Keywords:** novel coronavirus pneumonia, lung function, respiratory
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9 47 rehabilitation, physical therapy
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12 13 14 49 **Strengths and limitations of this study**

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16
17 50 This will be the first systematic review and meta-analysis to investigate the
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19 51 effects of respiratory rehabilitation therapy on patients with novel coronavirus
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22 52 pneumonia.

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25 53 To avoid errors, data extraction and bias assessment will be carried out by two
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27 54 reviewers independently.

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30 55 Egger's test and Begg's test will be conducted to assess the publication bias
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32 56 with Stata 16.0 software.

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35 57 Absent of sufficient randomized controlled trials may be a limitation for this
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37 58 meta-analysis.

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41 42 43 60 **INTRODUCTION**

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45 61 In the late of December 2019, patients with viral pneumonia infected by
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48 62 subsequently named Coronavirus Disease 2019 (COVID-19) were reported in
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51 63 Wuhan, China.¹ COVID-19 virus has sparked a pandemic around the world and
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53 64 millions of people have been infected.² It is still remain difficult to manage and
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55 65 control COVID-19 for countries around the world.³ Patients who suffered from
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58 66 2019 novel coronavirus had clinical manifestations of cough, shortness of
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4 67 breath, chest pain and so forth.⁴ COVID-19 is a highly contagious respiratory
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6 68 infection disease that can cause physical, respiratory and psychological
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9 69 disorders.⁵ It is of great importance to provide the pulmonary rehabilitation
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11 70 methods for patients with viral pneumonia caused by COVID-19.⁶ Respiratory
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14 71 rehabilitation is crucial to the recovery of patients during clinical treatment and
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17 72 in the rehabilitation phase.⁷ Early rehabilitation services can improve
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20 73 distressing physical and psychological symptoms with lung diseases.⁸
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22 74 Previously, pulmonary rehabilitation and chest physical therapy have been
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25 75 proved that can provide greatest positive effects for chronic obstructive
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28 76 pulmonary disease (COPD) or other chronic respiratory diseases.^{9 10} However,
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31 77 it is unclear whether respiratory rehabilitation therapy could improve the lung
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34 78 function in patients with coronavirus pneumonia. Additionally, up to now, there
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37 79 is no systematic review and meta-analysis which investigates the association
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40 80 between respiratory rehabilitation therapy and COVID-19. Therefore, we will
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43 81 qualitatively and quantitatively investigate the effects of respiratory
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46 82 rehabilitation therapy on patients with novel coronavirus in this systematic
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49 83 review and meta-analysis.
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85 **METHODS**

86 **Registration**

87 This systematic review and meta-analysis protocol has been registered in the
88 PROSPERO and the registration number is CRD42020180214. The protocol

89 will follow the guideline of the Preferred Reporting Items for Systematic Review
90 and Meta-Analyses (PRISMA-P).¹¹

91

92 **Patient and Public Involvement**

93 No patient involved.

94

95 **Search strategy**

96 The PubMed, Embase, Web of Science, the Cochrane Central Register of
97 Controlled Trials (CENTRAL), Chinese Biomedical Literature Database (CBM),
98 China National Knowledge Infrastructure (CNKI), Wanfang and VIP information
99 databases will be searched from their respective inception dates to April 15,
100 2020. Studies about the effects of respiratory rehabilitation programs for
101 patients with Coronavirus Disease 2019 in the rehabilitation phase will be
102 included in this meta-analysis, including randomized controlled trials (RCTs),
103 controlled clinical trials (CCTs), prospective and retrospective comparative
104 cohort studies, cluster trials, cross sectional studies and observational studies.

105 The detailed information of PubMed search strategy is shown (table 1).

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107 **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 "COVID 19"[Title/Abstract] OR "COVID19"[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]

5

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]

#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]

#4 #1 OR #2

#5 #3 AND #4

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109 Eligibility criteria

110 Study design

111 Relevant studies including randomized controlled trials (RCTs), controlled
 112 clinical trials (CCTs), prospective and retrospective comparative cohort studies,
 113 cluster trials, cross sectional studies and observational studies will be included
 114 in this meta-analysis. We attempt to search as many types of studies as
 115 possible because of absent original research about recently erupted COVID-
 116 19.

117

118 Participants

119 The patients who suffered from viral pneumonia affected by Coronavirus
 120 Disease 2019 and coordinated with respiratory rehabilitation treatments
 121 irrespective of gender and ethnicity will be involved in this meta-analysis.

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6 123 **Interventions**

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9 124 The interventions of respiratory rehabilitation therapy for viral pneumonia could
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11 125 be breathing exercises, respiratory muscle training, chest physiotherapy or
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14 126 other physical training programs.
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19 128 **Outcomes**

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22 129 The outcomes will be considered in this meta-analysis are as follows: forced
23
24 130 expiratory volume in one second (FEV₁), forced vital capacity (FVC), the ratio
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27 131 of forced expiratory volume in one second and forced vital capacity (FEV₁/FVC),
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30 132 Rated Perceived Exertion (RPE) scale scores, Borg scale scores, the ratio of
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32 133 ventilation and perfusion (V/Q), blood oxygen saturation and discharge time.
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37 135 **Study selection and data extraction**

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39 136 **Study selection**

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42 137 Two reviewers select studies independently and any different opinions between
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44 138 two reviewers should consult with a third reviewer to reach a consensus. We
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47 139 will remove repetitive articles at first and then exclude irrelevant studies through
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50 140 reading the title, abstract and the full text one by one. The study selection
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52 141 process is demonstrated in a PRISMA flow diagram (figure 1).
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58 143 **Data extraction**
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4 144 A standardized form will be used to extract data by two reviewers independently
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6 145 and disagreements between them should be solved with the help of the third
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9 146 reviewer. The detailed extraction information are as follows: the first author,
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11 147 year of publication, country of publication, study design, sample characteristics,
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14 148 number of participants, experimental and control interventions, intervention
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17 149 time, outcomes and results.
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21 22 151 **Quality assessment of included studies**

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24 152 The Cochrane risk of bias tool with items of random sequence generation,
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27 153 allocation concealment, blinding, incomplete outcome data, selective reporting
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30 154 and other bias will be used to assess the quality of included randomized
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33 155 controlled trials. Otherwise, the Newcastle-Ottawa Scale (NOS) which includes
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35 156 consideration of patient selection, study comparability and outcome
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38 157 assessment will be performed to evaluate non-randomized studies quality. We
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40 158 need to select the suitable scale according to the type of included studies.
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44 45 160 **Data synthesis and statistical analysis**

46 47 48 161 **Data synthesis**

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50 162 Review Manager 5.3 software (Cochrane Collaboration) and Stata 16.0
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53 163 software will be used to conduct this meta-analysis. Mean difference (MD) or
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56 164 standardized mean difference (SMD) with 95% confidence intervals (CI) is used
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59 165 for calculating continuous variables.
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6 167 **Assessment of heterogeneity**

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9 168 Statistical heterogeneity among included studies will be assessed by the chi-
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11 169 square test and I^2 test. We use a fixed-effect model for data analysis at first. If
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14 170 $I^2 > 0.5$ or $P < 0.1$, it is considered that there is a significant heterogeneity
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17 171 among studies and a random effects model will be used without finding suitable
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19 172 reasons for the high heterogeneity.

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24 174 **Subgroup analysis**

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27 175 If the heterogeneity of the included studies is large, subgroup analyses will be
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29 176 carried out by types of respiratory rehabilitation programs.

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34 178 **Sensitivity analysis**

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37 179 Sensitivity analysis is conducted through excluding studies one by one so that
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39 180 we can seek out the source of heterogeneity.

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44 182 **Assessment of publication bias**

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47 183 Egger's test and Begg's test will be conducted to assess the publication bias
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49 184 with Stata 16.0 software.

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54 186 **Ethics and dissemination**

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57 187 Ethical approval is not required because this meta-analysis is based on
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4 188 published papers. The results of this systematic review and meta-analysis will
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6 189 be published in a peer-reviewed journal once we have finished this study
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11 191 **DISCUSSION**

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14 192 As far as we know, this is the first systematic review and meta-analysis to
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17 193 investigate the effects of respiratory rehabilitation therapy on patients with novel
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20 194 coronavirus pneumonia. Respiratory rehabilitation therapy has been widely
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23 195 applied to chronic respiratory diseases.¹² But, it is uncertain whether respiratory
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26 196 rehabilitation therapy could improve the lung function in patients with
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29 197 coronavirus pneumonia as a result of few original research. This is a problem
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32 198 that we and people from all over the world are worrying about. However, absent
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35 199 of sufficient randomized controlled trials may be a limitation for this meta-
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38 200 analysis.
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58 209 **Contributions**

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4 210 CW, ZM conceived and designed the study. ZF made the search strategy of
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6 211 databases. WD, HQ, and ZC will be involved in data extraction and the
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9 212 assessment of methodological quality. The protocol manuscripts were finished
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12 213 by ZF. All authors have checked manuscripts and approved the publication of
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14 214 the protocol.
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24 218 grant number [QNRC2016376] and [Xuzhou Medical Young Talents Projects]
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27 219 grant number [2016015].
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32 221 **Competing interests statement**

34 222 None
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39 224 **REFERENCES**

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17 259 rehabilitation in chronic obstructive pulmonary disease. *Lancet*
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19 260 1996;348(9035):1115-9.

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25 262 **Figure 1** Flow chart and descriptions of study selection. N, Number.

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Identification

Screening

Eligibility

Included

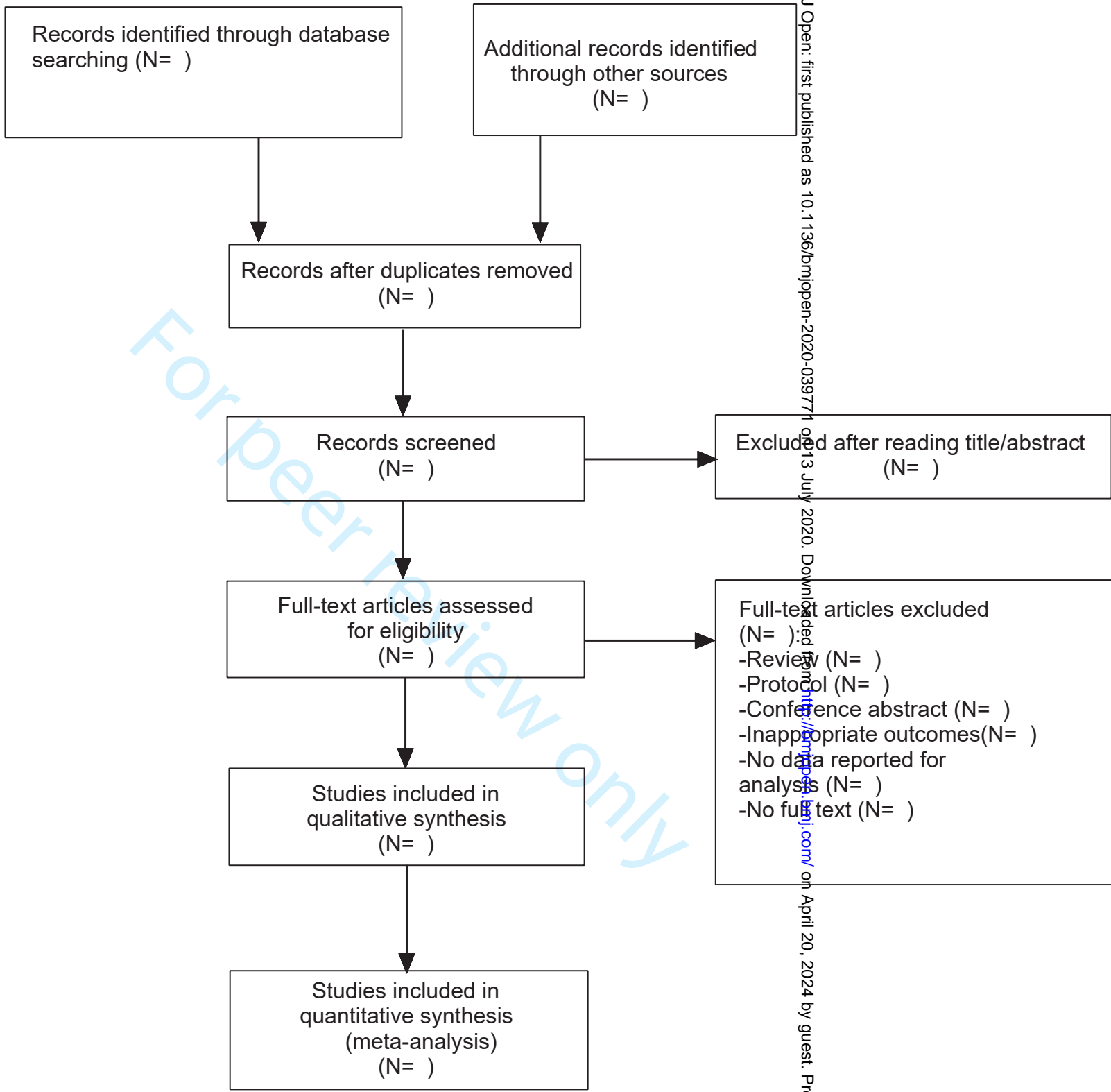


Figure 1 Flow chart and descriptions of study selection. N, Number.

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review (YES)
Update	1b	If the protocol is for an update of a previous systematic review, identify as such (YES)
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number (YES, PROSPERO, CRD42020180214)
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author (YES)
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review (YES)
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments (YES)
Support:		
Sources	5a	Indicate sources of financial or other support for the review (YES)
Sponsor	5b	Provide name for the review funder and/or sponsor (YES)
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol (YES)
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known (YES)
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) (YES)
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review (YES)
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage (YES)
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated (YES)
Study records:		

Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review (YES)
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis) (YES)
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators (YES)
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications (YES)
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale (YES)
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis (YES)
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised (YES)
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ) (YES)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) (YES)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned (YES)
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies) (YES)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE) (YES)

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Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Global health, Respiratory medicine
Keywords:	Rehabilitation medicine < INTERNAL MEDICINE, Public health < INFECTIOUS DISEASES, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Respiratory infections < THORACIC MEDICINE

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4 1 **Effects of respiratory rehabilitation on patients with novel coronavirus (COVID-**
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6 2 **19) pneumonia in the rehabilitation phase: protocol for a systematic review and**
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9 3 **meta-analysis**
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50 19 view these materials, please visit the BMJ Open journal online.
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55 21 **Word count**

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4 23 **ABSTRACT**

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6 24 **Introduction:** The recent viral pneumonia caused by the coronavirus disease 2019
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8
9 25 (COVID-19) has gained the attention of the people all over the world. We aim to
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11 26 investigate the effects of respiratory rehabilitation therapy on patients infected with the
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14 27 novel coronavirus by conducting a systematic review and meta-analysis.

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16
17 28 **Methods and analysis:** This systematic review and meta-analysis have been registered
18
19 29 in the International Prospective Register of Systematic Reviews (PROSPERO). The
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21 30 PubMed, Embase, Web of Science, the Cochrane Central Register of Controlled Trials
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24 31 (CENTRAL), Chinese Biomedical Literature Database (CBM), China National
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27 32 Knowledge Infrastructure (CNKI), Wanfang Data, and VIP information databases will
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30 33 be searched from inception time to date without restricting research types to find
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32 34 relevant studies. We will also look into reference lists of relevant trials and reviews,
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35 35 and manually search gray literature, such as trial registries. Two reviewers will
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38 36 independently extract data and perform quality assessment of included studies. Review
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40
41 37 Manager 5.3 (Cochrane Collaboration) and Stata 16.0 software will be utilized to
42
43 38 conduct this meta-analysis. The mean difference (MD) or standardized mean difference
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46 39 (SMD) with 95% confidence intervals (CI) is used in the computation of continuous
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48
49 40 variables to synthesize data.

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51 41 **Ethics and dissemination:** Ethical approval is not required due to the nature of this
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53 42 meta-analysis, which is based on published papers. The results of this systematic review
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56 43 and meta-analysis will be published in a peer-reviewed journal once we finish this study.

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58 44 **PROSPERO registration number:** CRD42020180214.
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4 45 **Keywords:** COVID-19, lung function, respiratory rehabilitation, physical therapy
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9 47 **Strengths and limitations of this study**
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11 48 This will be the first systematic review and meta-analysis investigating the effects of
12
13 49 respiratory rehabilitation therapy on patients with novel coronavirus pneumonia.
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16 50 To avoid errors, data extraction and bias assessment will be independently performed
17
18 51 by two reviewers.
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20
21 52 Egger's and Begg's tests will be conducted for the assessment of the publication bias
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23 53 under the use of Stata 16.0 software.
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26 54 The absence of sufficient randomized controlled trials may be a limitation for this meta-
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28 55 analysis.
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34 57 **INTRODUCTION**
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37 58 Toward the end of December 2019, patients with viral pneumonia subsequently
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39 59 infected by the coronavirus disease 2019 (COVID-19) were reported in Wuhan, China.¹
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42 60 COVID-19 has sparked a pandemic around the world, and millions of people have been
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44 61 infected.² The management and control of COVID-19 infection remains a challenge for
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47 62 countries around the world.³ Patients who suffered from the 2019 novel coronavirus
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49 63 had clinical manifestations of cough, shortness of breath, chest pain, and so on.⁴
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51
52 64 COVID-19 is a highly contagious respiratory infection disease that can cause physical,
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54 65 respiratory, and psychological disorders.⁵ Pulmonary rehabilitation methods are
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57 66 important for patients with viral pneumonia due to by COVID-19.⁶ Respiratory
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4 67 rehabilitation is crucial to the recovery of patients during clinical treatment and
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6 68 rehabilitation phase.⁷ Early rehabilitation services can improve distressing physical and
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9 69 psychological symptoms with lung diseases.⁸ Previously, pulmonary rehabilitation and
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11 70 chest physical therapy have been proven to provide the most positive effects for chronic
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14 71 obstructive pulmonary disease or other chronic respiratory diseases.^{9 10} It was safe and
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16
17 72 feasible to perform early pulmonary rehabilitation in patients with acute exacerbation
18
19
20 73 of lung diseases, which could effectively improve physical performance and quality of
21
22 74 life.^{11 12} Respiratory rehabilitation played a vital role in the non-invasive support
23
24
25 75 management.¹³⁻¹⁷ However, it is unclear whether respiratory rehabilitation therapy
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27 76 could improve lung function in patients with coronavirus pneumonia. Additionally, up
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29
30 77 to now, there is no systematic review and meta-analysis investigating the association
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33 78 between respiratory rehabilitation therapy and COVID-19. Therefore, we will
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35
36 79 qualitatively and quantitatively examine the effects of respiratory rehabilitation therapy
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38 80 on patients with novel coronavirus in this systematic review and meta-analysis.

81

82 **METHODS**

83 **Registration**

84 This systematic review and meta-analysis protocol have been registered in the
85 International Prospective Register of Systematic Reviews (PROSPERO), and the
86 registration number was CRD42020180214. The protocol followed the guideline of the
87 Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA-P).¹⁸

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4 **89 Patient and Public Involvement**

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7 90 No patient involved.

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12 **92 Search strategy**

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14 93 The PubMed, Embase, Web of Science, the Cochrane Central Register of Controlled
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17 94 Trials (CENTRAL), Chinese Biomedical Literature Database (CBM), China National
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20 95 Knowledge Infrastructure (CNKI), Wanfang, and VIP information databases will be
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22 96 searched from inception time to date. We will also search for reference lists of relevant
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25 97 trials and reviews, and manually search gray literature, such as trial registries. Studies
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28 98 concerning the effects of respiratory rehabilitation programs for COVID-19 patients in
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31 99 the rehabilitation phase will be included in this meta-analysis, as well as randomized
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33 100 controlled trials (RCTs), controlled clinical trials (CCTs), prospective and retrospective
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36 101 comparative cohort studies, cluster trials, cross-sectional studies, and observational
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38 102 studies. The detailed information of PubMed search strategy is presented in table 1.

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41 104 **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]

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2
3 #3 “Respiratory rehabilitation”[Title/Abstract] OR “pulmonary
4 rehabilitation”[Title/Abstract] OR “Respiratory therapy”[Title/Abstract]
5 OR “pulmonary recovery”[Title/Abstract] OR “pulmonary
6 rehabilitation program”[Title/Abstract] OR
7 “physiotherapy”[Title/Abstract] OR “physical therapy”[Title/Abstract]
8 OR “physical intervention”[Title/Abstract] OR “physical
9 rehabilitation”[Title/Abstract] OR “pulmonary Therapy”[Title/Abstract]
10 OR “pulmonary intervention”[Title/Abstract] OR “respiratory
11 intervention”[Title/Abstract] OR “breath*”[Title/Abstract] OR
12 “exercis*”[Title/Abstract] OR “train*”[Title/Abstract] OR “fitness*”
13 [Title/Abstract] OR “aerobic”[Title/Abstract] OR “resistanc*”
14 [Title/Abstract] OR “endurance”[Title/Abstract] OR “inspiratory
15 muscle train*”[Title/Abstract] OR “inspiratory muscle strength”
16 [Title/Abstract] OR “respiratory muscle train*”[Title/Abstract] OR
17 “respiratory muscle strength”[Title/Abstract] OR “respiratory muscle
18 endurance” [Title/Abstract] OR “muscle relaxation therapy”
19 [Title/Abstract] OR “hydrotherapy” [Title/Abstract] OR “swim*”
20 [Title/Abstract] OR “bik*”[Title/Abstract] OR “joy*”[Title/Abstract]
21 OR “walk*”[Title/Abstract] OR “run*”[Title/Abstract] OR “danc*”
22 [Title/Abstract] OR “sport*”[Title/Abstract] OR “active circular
23 breathing technique”[Title/Abstract] OR “ACBT” [Title/Abstract] OR
24 “chest expansion”[Title/Abstract] OR “forced exhalation
25 technique”[Title/Abstract] OR “airway clearance”[Title/Abstract] OR
26 “mechanical cough assist” [Title/Abstract] OR “manual
27 technique”[Title/Abstract] OR “mechanical device”[Title/Abstract] OR
28 “positive expiratory pressure”[Title/Abstract] OR “power
29 breath”[Title/Abstract]

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38 #4 #1 OR #2
39 #5 #3 AND #4
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44 106 **Eligibility criteria**

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46 107 **Study design**

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49 108 Relevant studies, including randomized controlled trials (RCTs), controlled clinical
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52 109 trials (CCTs), prospective and retrospective comparative cohort studies, cluster trials,
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55 110 cross-sectional studies, and observational studies will be included in this meta-analysis.

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57 111 We attempt to search as many types of studies as possible due to the absence of original
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4 112 research on the recently emerging COVID-19.
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9 114 **Participants**
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11 115 Patients who suffered from viral pneumonia caused by the coronavirus disease 2019
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13 116 and coordinated with respiratory rehabilitation treatments regardless of section,
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15 117 whether in the intensive care unit (ICU), intermediate respiratory unit, general ward, or
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17 118 rehabilitation facility will be involved in this meta-analysis. There will be no
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19 119 restrictions with respect to gender, age, or ethnicity.
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27 121 **Interventions**
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30 122 The interventions of respiratory rehabilitation therapy for viral pneumonia could be
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32 123 breathing exercises, respiratory muscle training, chest physiotherapy, active circular
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34 124 breathing technique, chest expansion exercises, forced exhalation technique, airway
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36 125 clearance techniques, positive expiratory pressure, using mechanical devices (e.g.
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38 126 mechanical cough assist), exercise training (aerobic exercise or, resistance and
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40 127 endurance training), or other physical training programs.
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48 129 **Outcomes**
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50 130 The primary outcomes of interest will be 6-minute walking distance (6MWD),
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52 131 cardiopulmonary exercise test (CPET), quality of life. The secondary outcomes are as
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54 132 follows: body mass index, arterial partial pressure of oxygen/fraction of inspired
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56 133 oxygen (PaO₂/FiO₂) ratio, forced expiratory volume in one second (FEV₁), forced vital
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4 134 capacity (FVC), ratio of forced expiratory volume in one second and forced vital
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6 135 capacity (FEV1/FVC), baseline dyspnea index (BDI), rating of perceived exertion scale
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9 136 scores, Borg scale scores, blood oxygen saturation, and discharge time.
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13 138 **Study selection and data extraction**

14 139 **Study selection**

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19 140 Two reviewers independently select studies, and any disagreement between the two
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22 141 reviewers should be consulted by a third reviewer to reach a consensus. We will remove
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24 142 repetitive articles at first and exclude irrelevant studies based on the title, abstract, and
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26
27 143 the full text. The study selection process is demonstrated in a PRISMA flow diagram
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30 144 (figure 1).
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34 146 **Data extraction**

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38 147 A standardized form will be used by two reviewers to extract data independently, and
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40 148 disagreements between them should be solved with the help of a third reviewer. The
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43 149 detailed extraction information are as follows: the first author, year of publication,
44
45
46 150 country of publication, study design, sample characteristics, number of participants,
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48 151 experimental and control interventions, intervention time, outcomes, and results. We
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51 152 will try our best to contact the corresponding authors of the studies through email to
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53 153 deal with missing data.
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57 58 155 **Quality assessment of included studies**

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4 156 The Cochrane risk of bias tool with items of random sequence generation, allocation
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6 157 concealment, blinding, incomplete outcome data, selective reporting, and other biases
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8
9 158 will be used to assess the quality of included randomized controlled trials. Otherwise,
10
11 159 the Newcastle-Ottawa Scale, which includes consideration of patient selection, study
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14 160 comparability, and outcome assessment will be used to evaluate the quality of non-
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17 161 randomized studies. We need to select a suitable scale according to the types of studies
18
19
20 162 included.

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23 24 164 **Data synthesis and statistical analysis**

25 26 165 **Data synthesis**

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30 166 Review Manager 5.3 (Cochrane Collaboration) and Stata 16.0 software will be used to
31
32 167 conduct this meta-analysis. The mean difference (MD) or standardized mean difference
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35 168 (SMD) with 95% confidence intervals (CI) is used to calculate continuous variables.
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39 40 170 **Assessment of heterogeneity**

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43 171 Statistical heterogeneity among included studies will be assessed using the chi-squared
44
45 172 test and I^2 test. We use a fixed-effect model for data analysis at first. If $I^2 > 0.5$ or $P <$
46
47
48 173 0.1 , it is considered that there is a significant heterogeneity among the studies, and
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51 174 random-effect model will be used without examining the probable cause for the high
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53 175 heterogeneity.¹⁹

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57 58 177 **Subgroup analysis**

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4 178 If there is a large heterogeneity in the included studies, subgroup analyses will be
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6 179 performed on different types of respiratory rehabilitation programs and in different
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9 180 treatment locations, such as, intensive care unit (ICU), intermediate respiratory unit,
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12 181 general ward, or rehabilitation facility.

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17 183 **Sensitivity analysis**

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19 184 Sensitivity analysis is conducted by excluding studies one by one, so that we can
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22 185 determine the source of heterogeneity.

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27 187 **Assessment of publication bias**

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29 188 Publication bias will be examined according to the funnel plot method. Also, Egger's
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32 189 test and Begg's test will be conducted to quantitatively assess the publication bias using
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34
35 190 the Stata 16.0 software.

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40 192 **Quality of evidence**

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42 193 We will use the Grading of Recommendations Assessment, Development, and
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45 194 Evaluation (GRADE) guidelines for the assessment of the strength of evidence for each
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48 195 outcome. The result will be categorized as high, moderate, low, and very low certainty
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51 196 of evidence.²⁰

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56 198 **Ethics and dissemination**

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58 199 Ethical approval is not required due to the nature of this meta-analysis, which is based
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4 200 on published papers. The results of this systematic review and meta-analysis will be
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7 201 published in a peer-reviewed journal once we finish this study.
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9 202

11 203 **DISCUSSION**

14 204 To the best of our knowledge, this is the first systematic review and meta-analysis to
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17 205 investigate the effects of respiratory rehabilitation therapy on patients with novel
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19
20 206 coronavirus pneumonia. Respiratory rehabilitation therapy has been widely applied to
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22 207 patients with chronic respiratory diseases.²¹ However, it is uncertain whether
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25 208 respiratory rehabilitation therapy could improve lung function in patients with
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27 209 coronavirus pneumonia due to limited original research. This is a major concern for us
28
29
30 210 and for everyone around the world. Nonetheless, the lack of sufficient randomized
31
32 211 controlled trials may be a limitation for this meta-analysis.
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35 212

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4 222 The authors acknowledge Emerald Publishing TSS Dept for help in revising this
5
6 223 protocol. We also particularly thank the reviewers and editors for their valuable
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9 224 comments, which helped considerably to improve the quality of the manuscript.
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14 226 **Contributions**

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16
17 227 CW, ZM conceived and designed the study. ZF made the search strategy of databases.
18
19 228 WD, HQ, GM, and ZC will be involved in data extraction and the assessment of
20
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22 229 methodological quality. The protocol manuscripts were finished by ZF. All authors
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25 230 have checked manuscripts and approved the publication of the protocol.
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38 235 [2016015].
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43 237 **Competing interests statement**

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45 238 None declared.
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310 **Table 1** Search strategy of PubMed

311 **Figure 1** Flow chart and descriptions of study selection. N, Number.

For peer review only

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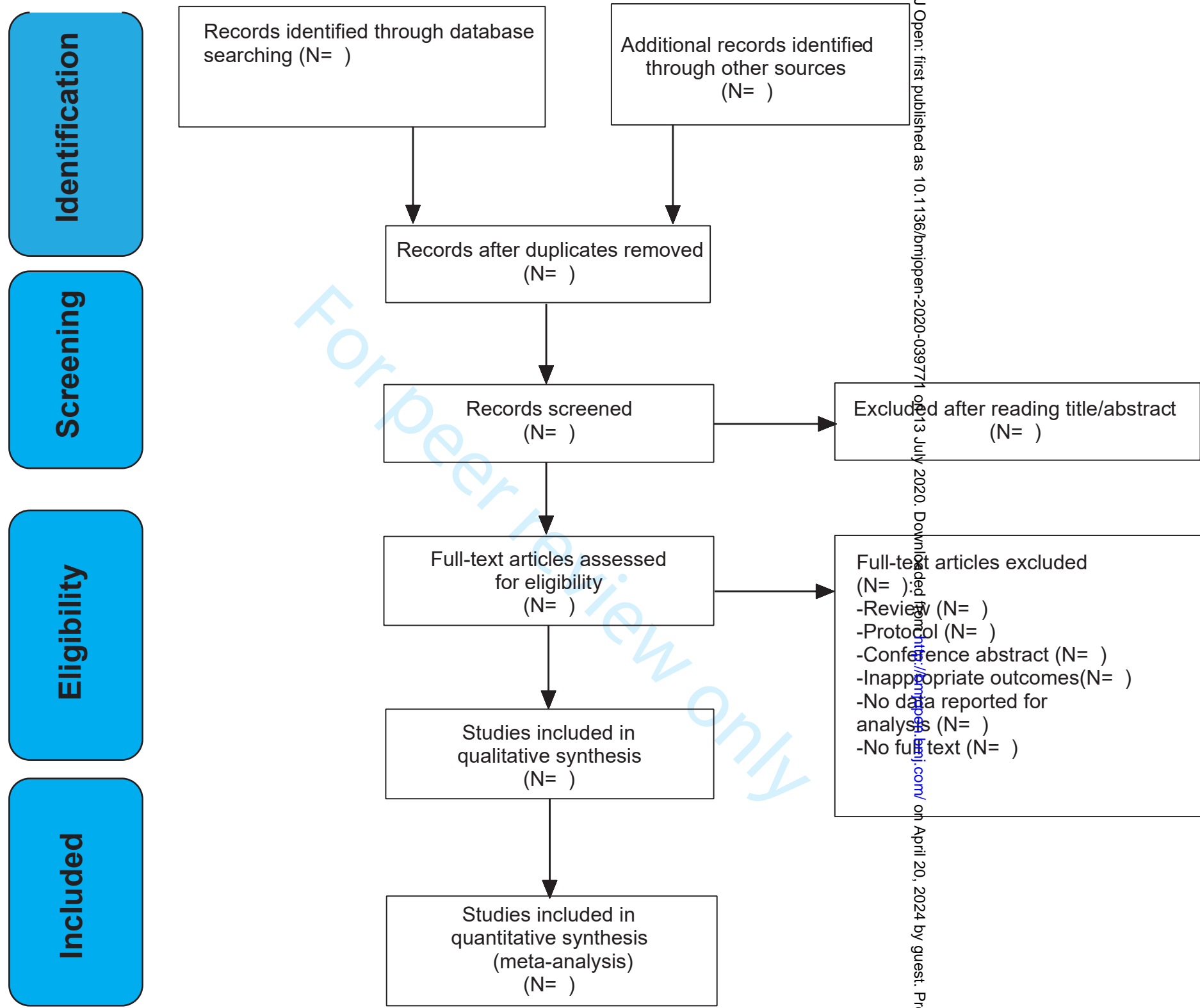


Figure 1 Flow chart and descriptions of study selection. N, Number.

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review (YES)
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number (YES, PROSPERO, CRD42020180214)
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author (YES)
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review (YES)
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments (YES)
Support:		
Sources	5a	Indicate sources of financial or other support for the review (YES)
Sponsor	5b	Provide name for the review funder and/or sponsor (YES)
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol (YES)
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known (YES)
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) (YES)
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review (YES)
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage (YES)
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated (YES)
Study records:		

Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review (YES)
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis) (YES)
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators (YES)
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications (YES)
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale (YES)
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis (YES)
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised (YES)
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ) (YES)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) (YES)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned (YES)
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies) (YES)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE) (YES)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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