

# INPLASY PROTOCOL

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None declared.

## Systematic review and meta-analysis of rehabilitation effects of exercise therapy on COVID-19 patients

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**Review question / Objective:** To systematically evaluate the rehabilitation effect of exercise therapy on COVID-19 patients. **Condition being studied:** (1) The study subjects were patients with COVID-19; (2) The intervention methods were exercise therapy and exercise therapy combined with other training; (3) The type of study was experimental study; (4) The outcome measures included respiratory function, anxiety and depression, and motor function. Respiratory function included: Position DyspNOEA-12 (MD12), The Wisconsin Upper Respiratory Symptom Survey (WURSS), Dyspnoea Index Scale (modified Medical) Research Council (mMRC), oxygen deprivation support SpO<sub>2</sub> value, KBILD questionnaire-respiratory function; Anxiety and depression: Self-rating Depression Scale (SDS), Self-rating Anxiety Scale (SAS), Hamilton depression scale (Hamilton depression scale) HAMD and Hamilton Self-rating anxiety scale (HAMA); Motor function: 6 Minute Walk Test (6MWT), 30 seconds of continuous sitting, static squatting, and Time Up and Go Test (TUG).

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 October 2022 and was last updated on 09 October 2022 (registration number INPLASY2022100037).

### INTRODUCTION

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Survey (WURSS), Dyspnoea Index Scale (modified Medical) Research Council (mMRC), oxygen deprivation support SpO<sub>2</sub> value, KBILD questionnaire-respiratory function; Anxiety and depression: Self-rating Depression Scale (SDS), Self-rating Anxiety Scale (SAS), Hamilton depression scale (Hamilton depression scale) HAMD and Hamilton Self-rating anxiety scale (HAMA); Motor function: 6 Minute Walk Test (6MWT), 30 seconds of continuous sitting, static squatting, and Time Up and Go Test (TUG).

## METHODS

### Search strategy:

- #1 COVID-19[Mesh]
- #2 COVID-19 Patients[Title/Abstract] OR novel coronavirus pneumonia patients[Title/Abstract] OR Patients with COVID-19[Title/Abstract]
- #3 Exercise[Mesh]
- #4 aerobic exercise[Title/Abstract] OR resistance training[Title/Abstract] OR Strength training[Title/Abstract] OR baduanjin[Title/Abstract] OR wuqinxi[Title/Abstract] OR qigong[Title/Abstract] OR Tai Chi[Title/Abstract] OR yoga[Title/Abstract] OR respiratory training[Title/Abstract] OR breath training[Title/Abstract]
- #5 Randomized controlled trial[Publication Type]
- #6 Clinical trials[Publication Type]
- #7 #1 OR #2
- #8 #3 OR #4
- #9 #5 OR #6
- #10 #7 AND #8 AND #9.

**Participant or population:** COVID-19 patients.

**Intervention:** Exercise.

**Comparator:** Non exercise intervention.

**Study designs to be included:** Randomized Controlled Trial (RCT).

**Eligibility criteria:** (1) Non-Chinese and English documents; (2) Literature data could not be extracted; (3) Case studies, reviews, conference papers, etc.

**Information sources:** China National Knowledge Infrastructure, Wanfang, VIP, PubMed, Embase, The Cochrane Library and Web of Science<sup>7</sup> databases.

**Main outcome(s):** A total of 16 literatures were included, including 897 patients. Exercise therapy could improve the respiratory function of patients (SMD=0.84,  $P < 0.01$ ). The heterogeneity may be attributed to the type of patients, age, intervention content and intervention cycle. Exercise therapy could improve anxiety (SMD= -1.08,  $P < 0.001$ ) and depression (SMD=-0.95,  $P=0.0002$ ), and the sources of heterogeneity might be age and intervention content. Exercise therapy could improve patients' motor function (SMD=0.44,  $P < 0.001$ ).

**Quality assessment / Risk of bias analysis:** The PEDro score of the 16 studies was 5-9, with an average score of 7.06, indicating good quality of the included literature.

**Strategy of data synthesis:** Exercise Review Manager5.3 for Meta-analysis. The data extracted in this study were all measurement data. The difference between the final value and baseline measurement after intervention (difference score) was used as the main effect parameter, and was calculated by using equations 1 and 2.

Formula 1:  $M = (M1 - M2)$

Formula 2:  $S2 = S12 + S22 - 2 * R * S1 * S2$

R is the constant 0.5.

The effect sizes were large (0.8), medium (0.5) and small (0.2), respectively. Point estimates and 95% Confidence intervals (CI) were given for each effect size. When  $p < 0.05$ , When  $P < 0.05$ , there was a significant difference between the intervention group and the control group, which proved that the results of meta-analysis were statistically significant. Q value and I<sup>2</sup> were used to test for heterogeneity, which were divided into high (75%) medium (50%) and low (25%) heterogeneity. If heterogeneity existed in the study, subgroup analysis or sensitivity analysis was performed to explore the source of heterogeneity. In addition, Stata16.0 was used for publication bias test and sensitivity analysis.

**Subgroup analysis:** Subgroup analysis was conducted according to the type of patients, moderate heterogeneity was found in the isolated group ( $I^2=70\%$ ), and the effect sizes were pooled by the random effect model, and the difference was significant ( $P=0.004$ ), indicating that exercise therapy could improve the respiratory function of patients in isolation. There was no heterogeneity in the non-isolated group ( $I^2=0\%$ ), and the effect size was pooled by the fixed effect model, and the difference was significant ( $P < 0.001$ ), indicating that exercise therapy could improve the respiratory function of patients in the non-isolated group. Subgroup analysis according to the intervention content showed that there was no heterogeneity in the exercise alone group ( $I^2=0\%$ ), and the effect size was pooled by the fixed effect model, and the difference was significant ( $P < 0.001$ ), indicating that exercise alone could improve the respiratory function of patients. There was moderate heterogeneity ( $I^2=70\%$ ) in the exercise group combined with other therapies group, and the effect sizes were pooled by the random effect model, and the difference was significant ( $P=0.004$ ), indicating that exercise combined with other therapies could improve the respiratory function of patients. The subgroup analysis according to the intervention period showed moderate heterogeneity ( $I^2=64\%$ ) in the  $< 2$  weeks group, and the effect size was pooled by the random effect model, and the difference was significant ( $P=0.02$ ), indicating that the exercise therapy  $< 2$  weeks could improve the respiratory function of patients. In the  $\geq 2$  weeks group, there was low heterogeneity, and the effect sizes were pooled by the fixed effect model ( $I^2=39\%$ ), and the difference was significant ( $P < 0.001$ ), indicating that exercise therapy for  $\geq 2$  weeks could improve the respiratory function of patients. The subgroup analysis according to age showed low heterogeneity ( $I^2=39\%$ ) in the  $< 50$  years old group, and the effect size was pooled by the fixed effect model, and the difference was significant ( $P < 0.001$ ), indicating that exercise therapy could improve the respiratory function of patients

$< 50$  years old. There was moderate heterogeneity ( $I^2=62\%$ ) in the  $\geq 50$  year old group, and the effect sizes were pooled by the random effect model, and the difference was significant ( $P = 0.02$ ), indicating that exercise therapy could improve respiratory function in patients  $\geq 50$  years old.

**Sensitivity analysis:** To investigate whether the source of heterogeneity was caused by a single study, sensitivity analysis was performed using Stata16.0. The effect size did not change significantly when the single study was phased out, indicating that the results were stable.

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

**Keywords:** Exercise Therapy; COVID - 19 patients; Rehabilitation; Systematic review.

**Contributions of each author:**

Author 1 - Cong Liu.

Author 2 - Rao Chen.

Author 3 - Xing Wang.

Author 4 - Xinhu Zheng.

Author 5 - Xiaojing Zhou.