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Rehabilitation and Covid-19: the Cochrane Rehabilitation 2020 rapid living systematic review

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Abstract

Introduction. This paper improves the methodology of the first edition of the rapid living systematic review started in April 2020, with the aim to gather and present the current evidence informing rehabilitation of patients with COVID-19 and/or describing the consequences due to the disease and its treatment.

Methods. The Cochrane methodology for a rapid living systematic review was applied. Primary research papers, published from January 1st to June 30th, 2020, reporting patients' data, with no limits of study design were included. Studies were categorized for study design, research question, COVID-19 phase, limitations of functioning (disability) of rehabilitation interest and type of rehabilitation service involved. Methodological quality assessment was based on the Cochrane Risk of Bias tools, and the level of evidence table (OCEBM 2011) for all the other studies.

Results. Thirty-six, out of 3703 papers, were included. One paper was of level 2 (RCT), 7 were of level 3 (2 cohort studies, 2 cross-sectional studies and 3 case-control studies), and 28 papers of level 4 (descriptive studies); 61% of papers reported epidemiological data on clinical presentations, 5 investigated natural history/determining factors, 1 searched prevalence, 2 studies reported on intervention efficacy (though not on harms), and 5 studies looked at health service organization.

Discussion. Main issues emerging from the review: it is advised to test for COVID-19 people with neurological disorders presenting with symptom changes; dysphagia is a frequent complication after oro-tracheal intubation in COVID-19 patients admitted to the ICU; after discharge, COVID-19 survivors may report persistent restrictive ventilatory deficits regardless of disease severity; there is only sparse and low quality evidence concerning the efficacy of any rehabilitation intervention to promote functional recovery; a substantial increase in resource (staff and equipment) is needed for rehabilitation.

Introduction

COVID-19 pandemic is constantly growing throughout the world, and while some countries have been able to control it, others are hardly suffering from the disease; no country can claim to be free from the infection. The general interest of the scientific community is still focused on the acute phase but concerns on the short- and long-term disease sequelae are growing[1].

Cochrane Rehabilitation in agreement with the European Journal of Physical and Rehabilitation Medicine started in April 2020 a rapid living systematic review[2], that was updated monthly[3,4]. During this period, the methodology was improved gradually[4]. Moreover, new initiatives by Cochrane Rehabilitation like the launch of the REH-COVER action[5], the establishment of its Steering Committee[6], the publication of the interactive living evidence mapping[7], and the definition of the COVID-19 rehabilitation research questions in collaboration with the WHO rehabilitation programme (WHO-RP)[8] are informing the methodology of this series of papers. Accordingly, the authors decided to produce a second Edition to be updated monthly up to the end of the year.

The aim of this paper is to gather and present the current evidence informing rehabilitation of patients with COVID-19 and/or the consequences due to the disease and its treatment. In doing so, we will exploit a more rigorous methodology than in the first edition of this same work[2–4]. For this reason, in this paper we extend the systematic search to the whole period elapsed from the start of epidemics. The paper will hence include the results published in the rapid living systematic review first edition (e.g. Liu et al. [9]), reformatted according to the new methodology, and new evidence that has emerged up until June 2020.

Methods

Study design

A rapid living systematic review on rehabilitation and COVID-19 has been carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines[10] and the Interim Guidance from the Cochrane Rapid Reviews Methods Group[11]. A rapid review is a form of knowledge synthesis that accelerates the process of conducting a traditional systematic review through streamlining or omitting specific methods to produce evidence for stakeholders in a resource-efficient manner[12]. A living review is a form of knowledge synthesis that is constantly updated as soon as new evidence is available: in this case, the review is updated each month. This review updates the 1st Edition published in April 2020[2] and its subsequent monthly updates[3,4].

The protocol has been submitted for registration in PROSPERO (awaiting approval).

Search strategy and screening process

The search strategy was updated from the previous rapid reviews[2–4]. Consequently, it was performed from 1st January 2020 to 30th June 2020 in PubMed, Embase, CINAHL, Scopus, and Web of Science. The databases were searched for "rehabilitation" and "COVID-19" and the search strategies were adapted according to each database-specific thesaurus. Moreover, PEDro database was also searched with the following keywords: "COVID-19 and rehabilitation", "COVID-19 and exercise", "COVID-19 and physical therapy", "COVID-19 and physiotherapy", "COVID-19 and weaning", "COVID-19 and recovery" and "COVID-19 and complications". See **Appendix 1** for the complete search strategy.

Selection criteria

Due to the heterogeneity of the studies published during the pandemic period[13–15], a comprehensive approach was applied, considering all types of studies relevant to rehabilitation.

The inclusion criteria were: 1) inpatients or outpatients with a confirmed diagnosis of COVID-19 with or without comorbidities or disability; 2) no age, gender or ethnicity restrictions; 3) all type of health conditions relevant to rehabilitation; 4) all type of rehabilitation interventions compared with any other interventions; 5) all type of diagnostic test or type of evaluation to determine the presence of COVID-19 associated with health conditions related to rehabilitation; 6) all type of outcome measures; and 7) English language. Studies addressing other coronavirus diseases (severe acute respiratory syndrome (SARS) or Middle East respiratory syndrome (MERS)) were excluded.

Differently from the first edition, and due to the increase of papers with original data, we excluded expert opinions and all papers not reporting patients' data; consequently, we also excluded secondary research papers (like systematic and scoping reviews) and expert literature interpretation (guidelines and consensus papers).

After removing duplicates and articles previously excluded in the first edition of the rapid review[2–4], each reviewer (FN, AdS and EA) screened articles for eligibility at the title/abstract stage and the full-text stage. In case of disagreement, a further reviewer was involved. A final check of the included studies was performed by two co-authors (MGC, SN) not involved in the screening process. The original articles already considered by the previous versions of the rapid review[2–4] have been also included in the analysis.

Data extraction

Three review authors (FN, AdS and EA) performed all data extraction, and one co-author (MGC) verified their accuracy. Two review authors (MP and SGL) assessed the studies included for the methodological quality and risk of bias, one author (CA) resolved any disagreement and another author (SN) verified their accuracy. The data extraction was performed using a customised data extraction form developed in Microsoft Excel and conducted according to Cochrane guidelines.

The following data were extracted from each paper: general information (author, publication date, country, experimental dates), and study characteristics (aim of the study, population, number of participants, clinical presentation, interventions, outcomes, adverse events, and main findings). Studies were categorized (through agreement, by MGC, CA and SN) for each of the following items: study design, research question, COVID-19 phase, limitations of functioning (disability) of rehabilitation interest (LFRI) and type of rehabilitation service involved, if any. These are explained as follows:

Study design classification

We followed the algorithm for the classification of types of clinical research[16] (**Figure 1**).

Research question classification

We used the list of research questions developed by the Cochrane Rehabilitation REH-COVER (REHabilitation – COVid-19 Evidence-based Response) International Multiprofessional Steering Committee in collaboration with the World Health Organization (WHO) rehabilitation programme (WHO-RP) in order to assign studies to the questions. The research questions should address the general term "Limitations of functioning (disability) of rehabilitation interest" (LFRI) including impairment(s), activity limitation(s) and participation restriction(s) as defined by the WHO International Classification of Functioning, disability and health – ICF[17].

The topics addressed in main research questions are: 1. epidemiology of LFRI due to COVID-19; 2. evidence on rehabilitation for LFRI due to COVID-19 at the individual level (micro-level); 3. evidence on rehabilitation for LFRI due to COVID-19 at service level (meso-level) and 4. evidence on rehabilitation for LFRI due to COVID-19 at system level (macro-level). The sub-questions have been synthesized in the categories reported in Table I.

COVID-19 phase classification

According to the proposal of REH-COVER and WHO-RP, we used the following categories:

1. Acute: during COVID-19 infection
2. Post-acute: continuing from the acute phase of COVID-19 and its treatment
3. Permanent: unresolved or not solvable, and causing a new health condition
4. Late-onset: appeared as a consequence of COVID-19 but after the end of the acute phase
5. Acute, post-acute, late-onset, or permanent on a pre-existing health condition: impact of COVID-19 on people with disability and/or experiencing disability at the time of infection

Limitations of functioning (disability) of rehabilitation interest (LFRI).

According to the proposal of REH-COVER and WHO-RP, we described the impact of COVID-19 on health, in terms of limitations of functioning (disability) of rehabilitation interest (LFRI). Based on the results of the previous edition of this rapid living systematic review and its updates[2–4], we classified the most prevalent LFRI addressed by each paper (in parenthesis the corresponding ICF codes), as follows:

Impairments in:

- Respiratory structures (s430) and related functions (b440-b455)
- Nervous system structures (s1) and related functions (b1, b2, b7)
- Cardiovascular functions (b410-b420)
- Digestive functions (b510)
- Any other body structure and function - generic (s/b)

Any activity limitation and participation restriction (d)

Barriers or facilitators in the following environmental factor categories:

- Products and technology (e110, e125)

- Health services, systems and policies (e580)
- Any other environmental factor- generic (e)

Type of rehabilitation service classification

We used the classification of the European Union of Medical Specialists (UEMS) Physical and Rehabilitation Medicine Section[18], including:

1. Rehabilitation in acute care
2. General postacute rehabilitation
3. Specialized postacute rehabilitation
4. General outpatient rehabilitation
5. Specialized outpatient rehabilitation
6. General Day rehabilitation
7. Specialized Day rehabilitation
8. Vocational rehabilitation
9. Rehabilitation in primary care
10. Rehabilitation services at home
11. Community-based rehabilitation (CBR)
12. Rehabilitation in health resorts
13. Rehabilitation in psychiatric care
14. Rehabilitation in social assistance
15. Rehabilitation in assistive service for specific disabled population groups

Assessment of methodological quality

We planned to divide the quality evaluation according to the methodology of the studies included using three different tools. If RCT data were available, we used the Cochrane Risk of Bias 2.0 (RoB

2) tool to analyse the risk of bias in the underlying study results[19]. For non-randomised studies of interventions (NRSIs), we used the Cochrane Risk Of Bias in Non-randomised Studies - of Interventions (ROBINS-I) tool[20]. For all the other designs, we evaluated the level of evidence using OCEBM 2011 Levels of Evidence table[21], to find the likely best evidence of all types of studies included. The level of evidence has been graded down based on study quality, imprecision, indirectness (study PICO does not match PICO questions), because of inconsistency between studies, or because the absolute effect size was very small. It has been also graded up if there was a large or very large effect size. For uncontrolled studies we did not carry out any risk of bias assessment.

One reviewer (CA) assessed eligible studies' designs. Two review authors (MP, SGL) performed quality assessments individually and resolved any disagreements by discussion; in case of persistent disagreement a third review author was consulted (CA or SN).

Data synthesis and reporting

We described the characteristics of included studies and synthesized the main findings according to the study design, the type of rehabilitation service, the research questions, LFRI classification and COVID-19 phases, with reference to the level of evidence of included studies. We grouped our synthesised evidence using the OCEBM 2011 Levels of Evidence table.

To keep rehabilitation stakeholders constantly updated on the last evidence on COVID-19 and rehabilitation, the selected studies will also be included in the Interactive Living Evidence Map of Cochrane Rehabilitation[7].

Results

Thirty-six studies out of 3703 search results were considered eligible for inclusion in this rapid living systematic review (Figure 2). Among the 346 full-text articles assessed for eligibility, 118 were excluded because the content did not address any relevant research question, being of no rehabilitation interest; the remainder 192 were excluded due to the lack of any original data, as they just conveyed expert opinions or were secondary research papers.

Evidence level of included studies

Due to the heterogeneity of studies, a meta-analysis was not appropriate, and the results have been narratively described and presented in tables. For the quality of methodology evaluation, we used the OCEBM 2011 Levels of Evidence table to identify the likely best evidence related to the research question (Table II).

Only one paper was of level 2 (RCT)[9], 7 studies were of level 3 (2 cohort studies[22,23] , 2 cross-sectional studies[24,25] and 3 case-control studies[26–28]), whereas the remainder 28 papers were of level 4 (6 historical cohort studies[29–34] and 22 case report/case series[35–56]).

Considering the topics addressed by the research question, 61% of papers (1 cross-sectional[25], 1 case-control study[26], 2 historical cohort studies[30,31], and 18 case reports/series[35–44,46,48,50–54,56]) reported epidemiological data on the clinical presentation of COVID-19 infection, 1 cohort study[23], 1 case-control[28] and 1 historical cohort study[29] investigated disease natural history/determining factors, whereas 1 historical cohort study[33] and 1 cross-sectional study[24] informed about disease prevalence; 2 papers reported on intervention efficacy (though not on harms) at the individual level (1 RCT[9], 1 cohort study[22]) and 5 on health service organization (1 case-control study[27] , 2 historical cohort studies[32,34] and 2 case reports[45,49]). Finally, 2 case reports described disease course under rehabilitation intervention[47,55].

Main content of included studies

Table III (Supplementary material) details the publication data, methodological aspects (e.g., study design, research question, sample features, time and geographical area of experimental data collection, intervention and outcome measures), and the main results of the 36 included studies.

The majority of studies report data collected up to the end of April 2020. One exception is represented by one cross-sectional investigation of COVID-19 incidence in the state of New York, presenting information updated to the end of May. In one-third of papers, there is no information about the study dates. Seventeen studies are based in Europe (mostly Italy and France, one from Spain), 12 in Asia (mostly China, 2 in Japan, 2 Turkey and 1 Thailand) and 7 in America (mostly USA, one from Brazil).

Twenty-one studies describe COVID-19 patients in the acute phase, 13 in the post-acute phase, whereas in two cases the disease phase is not disclosed. Overall, the studies present data on up to 1200 cases.

Matching the disease phase with the health domain of interest (LFRI), the main findings can be summarized, as follows.

Results in the acute phase

Most studies reporting about COVID-19 patients in the acute phase concern the clinical presentation of the disease, while two address the efficacy of interventions on symptom recovery.

Impairment in respiratory structures and related functions

One case report[50] describes the clinical presentation of COVID-19 with subtle respiratory symptoms in a person affected by tetraplegia, due to spinal cord injury.

One case series[55] reports on two COVID-19 patients who underwent ozone therapy major autohemotherapy for seven days showing fast recovery of symptoms.

Impairment in nervous system structures and related functions

One cross-sectional study[25], one historical cohort study[30] and 12 case reports/series[35,37,38,40,42–44,46,51,52,54,56] present epidemiological data on the involvement of the nervous system in COVID-19 patients. The cross-sectional study describes neurologic disorders in 13/51 (26%) patients, also providing an estimate of case-fatality (11%), need for active post-resuscitation care (11%) and follow-up care (98%). The retrospective study reports on a large cohort of 214 hospitalized patients who displayed neurological signs or symptoms in approximately one-third of cases, including a small subset of patients for which stroke-like symptoms were the primary presentation of infection[30].

The case reports describe cases where COVID-19 infection presented with brain haemorrhage (3 cases)[43], or ischemic stroke (4 cases)[52]. One case presented with encephalitis mimicking a glial tumor[40], 2 with posterior reversible encephalopathy syndromes[44], one with acute disseminated encephalomyelitis[46], several with Guillain-Barré[35,51] or Miller-Fisher syndromes[42] or other polyneuropathies[38].

Impairment in cardiovascular functions

Grimaud[29] authored the only historical cohort study on children with COVID-19 infection, who presented to the ICU with hypotensive shock and fever associated with a major systemic inflammation and acute myocarditis. Nineteen of the 20 patients had identified SARS-CoV-2 infection on PCR (n= 12) and/or by serology (n= 15), 8 needed intubation. All children survived, recovering full left ventricular systolic function.

Impairment in digestive functions

A cohort study on 32 cases[22] described the efficacy of a three-step nutritional protocol at improving malnutrition in 32 out of 50 hospitalized patients (90% with dysphagia).

One case-control study on 101 COVID-19 patients admitted to the ICU[26], analysed the course of dysphagia resolution after removal of the oro-tracheal tube, compared to a control series of 150 critical (not COVID-19) ICU patients subjected to prolonged oro-tracheal intubation. Although patients with COVID-19 remained intubated longer, they exhibited milder degrees of swallowing impairment after extubation and needed fewer swallowing rehabilitation sessions to return to safe oral feeding.

Aoyagi described the case of a 70-year-old male who developed dysphagia and consequent aspiration pneumonia during recovery from severe COVID-19[36].

Products and technology

One case series describes a preliminary attempt to use a telerehabilitation system to deliver exercise opportunities to individuals who could not be managed with the traditional face-to-face approach due to contagiousness concerns[45].

Results in the post-acute phase

Thirteen studies focus on the post-acute phase of COVID-19

Impairment in respiratory structures and related functions

The only RCT[9] included in the review describes the efficacy of respiratory rehabilitation (2 sessions/week for 6 weeks, 10 minutes per session) compared to no treatment, at increasing pulmonary function, endurance, quality of life and well-being perception in 76 elderly COVID-19 patients, in the post-acute phase. One case report[47] proposes the efficacy of early rehabilitation care for a 51-year-old patient with acute respiratory distress syndrome (ARDS), who achieved autonomous walking within 1 week from intensive care unit (ICU) discharge.

One cohort study of 131 COVID-19 patients reported that 40% of cases still had symptomatology, on discharge, including cough (29.01%), fatigue (7.63%), expectoration (6.11%), chest tightness (6.11%), dyspnoea (3.82%), chest pain (3.05%), and palpitation (1.53%). At one month, only 18 patients had one or more symptoms, with 8 patients still testing positive for SARS-CoV-2[23].

Two historical cohort studies with a total of 128 cases alert on the risk that COVID-19 survivors after discharge may report persistent restrictive ventilatory deficits regardless of their disease severity[31,33].

One case control study reports that COVID-19 patients who are still dyspnoic one month after remission from fever may exhibit extended hypoperfused areas of lung parenchyma, despite the absence of residual pulmonary fibrous stripes[28], whereas one case report describes a patient developing delayed lung thromboembolic complications[41].

Nervous system structures and related functions

Vitale et al[53] investigated the association between sleep duration and functional recovery in 4 COVID-19 patients undergoing rehabilitation after acute ward discharge, concluding that functional recovery could not be considered as directly linked to sleep quality.

Aoyagi[36] described the case of a 70-year-old male who developed dysphagia and consequent aspiration pneumonia during recovery from severe COVID-19. They suggest that glossopharyngeal and vagal neuropathy might have elicited dysphagia following COVID-19.

A further case report[39] describes a 62-year-old patient who presented persistent dysphonia and swallowing difficulties one month after removal of orotracheal intubation, due to a lesion of left hypoglossal and vagus nerve.

Health services, systems and policies

One case-control study[27]estimated the resources (staff and instruments) needed by a COVID-19 rehabilitation unit compared to the Cardiac and Motor Rehabilitation Units having the same number of beds, showing that the first one required twice the amount of staff and instrumental equipment, leading to an increase in costs.

Out of two historical cohort studies, one[34] proposed a model to predict the length of stay of post-acute mild COVID-19 patients in an inpatient rehabilitation setting, based on laboratory findings. The other[32] described the organizational issues of developing a COVID-19 multidisciplinary team (including respiratory physiotherapists-RPT) to manage 90 beds for post-acute patients with COVID-19, and reported how RPTs managed oxygen therapy, reconditioning and initial and final functional motor capacity assessment.

Products and technology

Finally, one case report described the use of telemedicine to provide rehabilitation following tendon transfer surgery to a patient with Charcot-Marie-Tooth disease who developed COVID-19 without major respiratory symptoms[49].

Permanent sequelae or late onset complications

No study reported data concerning permanent sequelae or late onset complications of COVID-19.

Concerning the impact of COVID-19 on people with disability and/or experiencing disability at the time of infection, one cross-sectional study[24] described an increased COVID-19 case rate and case fatality in people with intellectual and developmental disabilities (IDD) living in residential group homes compared to people without IDD.

Discussion

This rapid living systematic review second edition represents an important advancement in the methodology of evidence extraction and reporting. This upgrade was unfortunately made possible by the relevance that COVID-19 pandemic gained, with its tremendous increase, affecting now most world countries with severe consequences at the individual and community level. Several initiatives were launched, worldwide, to support research and help governments to plan resources for the health systems. Some members of the Cochrane Rehabilitation REH-COVER (REHabilitation – COVid-19 Evidence-based Response) action Steering Committee co-authoring this paper are chairing a World Health Organization (WHO) Technical Working Group on "COVID-19 mid- and long-term follow up" (CK, MR), and developing a Cochrane Library Special Collection on expected consequences of COVID-19 (SN).

Compared to the first edition, this review is based on an upgraded list of research questions and a rigorous approach to the assessment of the levels of evidence of included studies. This is made possible by an increased availability of primary studies providing original information on the course and clinical characterization of COVID-19, both in the acute and post-acute phase, and some data on the efficacy of rehabilitation interventions.

The main clinical issues can be summarized as follows, according to the specific research questions:

Epidemiology – Clinical presentation – Prevalence - Natural history/Determining and modifying factors.

- Preliminary evidence suggest that neurological syndromes may be frequently associated with COVID-19 infection at onset or as a complication in the acute phase. The pathogenetic mechanisms of COVID-19 associated cerebrovascular disorders may include microvascular thrombosis or a cytokine storm resulting in platelet dysfunction. According to some reports

published after June 30 and not captured by the present search, leukoencephalopathy may occur in COVID-19 patients as a delayed response to the profound hypoxemia the patients experienced due to the infection[57], or as a nonspecific feature[58] .

An aberrant immune response to COVID-19 is the likely mechanism triggering a demyelinating damage and leading to acute disseminated encephalomyelitis or polyneuropathy syndromes.

- It is advised to test people presenting with neurological disorders for the presence of COVID-19 when they show any change in their clinical condition, as the infection may present with mild or unusual symptoms in these subjects.

- Dysphagia is reported to be a frequent complication after oro-tracheal intubation in COVID-19 patients admitted to the ICU, although its course seems to be more favourable than in people undergoing intubation for other pathologies. However, at least one case report alerts on the risk for COVID-19 patients to develop dysphagia as a consequence of glossopharyngeal and vagal neuropathy, eventually leading to an aspiration pneumonia that might be overlooked in severe respiratory infection during COVID-19.

- After discharge, COVID-19 survivors may report persistent restrictive ventilatory defect regardless of disease severity; they may even present lung hypoperfusion or develop delayed lung thromboembolic complications. A close follow-up after discharge is hence needed for patients with a higher risk of thromboembolism who may require anticoagulation for a long period;

moreover, a long-term follow-up of lung function is advised for patients with persistent respiratory symptoms, to provide a guideline for pulmonary rehabilitation.

Micro level – Outcomes

No study focused on the type of outcomes for limitation(s) of functioning

Micro level- Interventions

While most studies report an important risk for people with COVID-19 to present limitations of functioning of rehabilitation interest, that may persist after discharge for a still undefined period, there is only sparse and low-quality evidence concerning the efficacy of any rehabilitation intervention to promote functional recovery.

Meso Level- Services

The only analytical study providing information about the organizational issues linked with the provision of specialized rehabilitation care to COVID-19 patients highlights the need for a substantial increase in resources (staff and equipment).

Limitations

Even if a comprehensive approach was adopted, this systematic review is not free from limitations: papers of no English language were excluded, thus missing the opportunity to collect the experience coming from countries, like China, that first faced the epidemic in a massive way. Moreover, trial registers were not considered.

With only one RCT and seven analytical studies out of the total 36 papers, the methodological weakness of the available studies still represents the main limitation to fill the gap in current knowledge on LFRI due to COVID-19. Most studies focus on the clinical presentation or natural history of the disease, whereas none informs about the measures that might better capture functional outcome in COVID-19 survivors.

Available studies do not allow the generalizability of findings, also due to the fact that no meta-analysis was conducted, thus giving no possibility to establish cause-effect relationships. Nevertheless, these types of studies facilitate the identification of the novelties and the generation of hypotheses allowing emphasis on the narrative aspect with in-depth understanding and educational values[59].

Conclusions

This rapid living systematic review of limitations of functioning of rehabilitation interest suffered by COVID-19 patients confirms the severe impact of the disease in terms of rehabilitation needs. There is still an important information gap in scientific literature due to the low evidence level of the available studies, the lack of prospective studies describing the course of functional recovery after the resolution of infection symptoms, especially in people with neurological complications, and the lack of controlled studies looking into the efficacy of rehabilitation care.

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Figures and Tables legend

Table I Research questions outlined according to the definitions developed by the Cochrane Rehabilitation REH-COVER (REHabilitation – COVid-19 Evidence-based Response) international multiprofessional Steering Committee in collaboration with the World Health Organization (WHO) rehabilitation programme (WHO-RP).

Table II Level of evidence

Table III (Supplementary material) Description of the articles on rehabilitation needs due to COVID-19 included in the rapid living systematic review updated to 30th June 2020

Figure 1 Algorithm for classification of types of clinical research

Figure 2 PRISMA Flow diagram

Tables

Table I. Research questions outlined according to the definitions developed by the Cochrane Rehabilitation REH-COVER (REHabilitation – COVid-19 Evidence-based Response) international multi-professional Steering Committee in collaboration with the World Health Organization (WHO) rehabilitation programme (WHO-RP).

REH-COVER/WHO-RP	**Synthesis used in this paper**
1. Epidemiology of LFRI due to COVID-19	
1.1 What are the limitations of functioning at each stage?	Epidemiology - Clinical presentation
1.2 What is the prevalence of each limitation of functioning at each stage?	Epidemiology - Prevalence
1.3 What is the natural history of each limitation of functioning at each stage?	Epidemiology - Natural history/Determining and modifying factors
1.4 How are the limitations of functioning influenced by	
1.4.1 Demographics?	
1.4.2 Health (co-morbidities)?	
1.4.3. Virus (etiology)?	
1.4.4 Acute treatments?	
1.4.5 Clinical presentation (interaction between limitation(s) of functioning)?	
2. Evidence on rehabilitation for LFRI due to COVID-19 at the individual level (micro-level)	
2.1 What is the evidence on the type of outcomes for limitation(s) of functioning?	Micro - Outcome Measures
2.2 What is the evidence on effect of interventions for limitation(s) of functioning?	Micro - Interventions (efficacy/harms)
2.3 What is the evidence on side-effects/harms/disadvantages of interventions for limitation(s) of functioning?	
2.4 What is the evidence on cost-effectiveness of interventions for	

limitation(s) of functioning?	
3. Evidence on rehabilitation for LFRI due to COVID-19 at service level (meso-level)	
3.1 What is the evidence on accessibility (availability, access, utilization) to services?	Meso Level
3.2 What is the evidence on workforce and/or technology requirements?	
3.3 What is the evidence on accessibility (availability, access, utilization) to services?	
3.4 What is the evidence on workforce and/or technology requirements?	
4. Evidence on rehabilitation for LFRI due to COVID-19 at system level (macro-level)	
4.1 What is the evidence on the need of services?	Macro level
4.2 What is the evidence on financing of services?	
4.3 What is the evidence on health systems requirements?	
4.4 What is the evidence on regulation of delivery of services?	

Table II. Level of evidence

	Level 1	**Level 2**	**Level 3**	**Level 4**	**Level 5**	**Total**
Epidemiology - Clinical presentation	0 (0%)	0 (0%)	2 (6%)	20 (56%)	0 (0%)	**22 (61%)**
Epidemiology – Prevalence	0 (0%)	0 (0%)	1 (3%)	1 (3%)	0 (0%)	**2 (6%)**
Epidemiology - Natural history / Determining and modifying factors	0 (0%)	0 (0%)	2 (6%)	1 (3%)	0 (0%)	**3 (8%)**
Micro - Interventions (efficacy/harms)	0 (0%)	1 (3%)	1 (3%)	2 (6%)	0 (0%)	**4 (11%)**
Meso Level	0 (0%)	0 (0%)	1 (3%)	4 (11%)	0 (0%	**5 (14%)**
Macro Level	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
TOTAL	**0 (0%)**	**1 (3%)**	**7 (19%)**	**28 (78%)**	0 (0%)	**36 (100%)**

Appendix 1. Search strategy

Database	Search strategy
Pubmed	1. "Rehabilitation"[Mesh] OR "Exercise"[Mesh] OR "Physical Therapy Modalities"[Mesh] OR "Occupational Therapy"[Mesh] OR "Speech Therapy"[Mesh] OR "Breathing Exercises"[Mesh] OR "Ventilator Weaning"[Mesh] OR "Resistance Training"[Mesh] OR "Recovery of Function"[Mesh] OR "Telerehabilitation"[Mesh] 2. “Rehabilitat*” OR “physiotherap*” OR “physical therapy” OR “recovery” OR “exercise” OR “telerehabilitat*” OR “telecare” OR “telehealthcare” OR ((“respiratory” OR “pulmonary” OR “lung”) AND (“training” OR “exercise” OR “rehabilitat*”)) OR “ventilator weaning” OR “respiratory weaning” OR “strength training” OR “occupational therapy” OR ((“speech” OR “language” OR “swallow*”) AND (“therapy” OR “training” OR “exercise”)) 3. #1 OR #2 4. "coronavirus"[MeSH Terms] OR "COVID-19" [Supplementary Concept] 5. “covid-19” OR “sars-cov-2” 6. #4 OR #5 7. #3 AND #6
Embase	1. 'rehabilitat*' OR 'physiotherap*' OR 'physical therapy'/exp OR 'physical therapy' OR 'recovery'/exp OR 'recovery' OR 'exercise'/exp OR 'exercise' OR 'telerehabilitat*' OR 'telecare'/exp OR 'telecare' OR 'telehealthcare' OR (('respiratory' OR 'pulmonary' OR 'lung') NEAR/5 ('training' OR 'exercise' OR 'rehabilitat*')) OR 'ventilator weaning'/exp OR 'ventilator weaning' OR 'respiratory weaning' OR 'strength training'/exp OR 'strength training' OR 'occupational therapy'/exp OR 'occupational therapy' OR (('speech' OR 'language' OR 'swallow*') NEAR/5 ('therapy' OR 'training' OR 'exercise')) 2. 'covid-19' OR 'sars-cov-2' 3. #1 AND #2
CINAHL	1. “Rehabilitat*” OR “physiotherap*” OR “physical therapy” OR “recovery” OR “exercise” OR “telerehabilitat*” OR “telecare” OR “telehealthcare” OR ((“respiratory” OR “pulmonary” OR “lung”) AND (“training” OR “exercise” OR “rehabilitat*”)) OR “ventilator weaning” OR “respiratory weaning” OR “strength training” OR “occupational therapy” OR ((“speech” OR “language” OR “swallow*”) AND (“therapy” OR “training” OR “exercise”)) 2. “covid-19” OR “sars-cov-2” 3. #1 AND #2

SCOPUS	1. TITLE-ABS-KEY("Rehabilitat*" OR "physiotherap*" OR "physical therapy" OR "recovery" OR "exercise" OR "telerehabilitat*" OR "telecare" OR "telehealthcare" OR (("respiratory" OR "pulmonary" OR "lung") W/5 ("training" OR "exercise" OR "rehabilitat*")) OR "ventilator weaning" OR "respiratory weaning" OR "strength training" OR "occupational therapy" OR (("speech" OR "language" OR "swallow*") W/5 ("therapy" OR "training" OR "exercise"))) 2. TITLE-ABS-KEY("covid-19" OR "sars-cov-2") 3. #1 AND #2
Web of Science	1. TS=("Rehabilitat*" OR "physiotherap*" OR "physical therapy" OR "recovery" OR "exercise" OR "telerehabilitat*" OR "telecare" OR "telehealthcare" OR (("respiratory" OR "pulmonary" OR "lung") NEAR ("training" OR "exercise" OR "rehabilitat*")) OR "ventilator weaning" OR "respiratory weaning" OR "strength training" OR "occupational therapy" OR (("speech" OR "language" OR "swallow*") NEAR ("therapy" OR "training" OR "exercise"))) 2. TS=("covid-19" OR "sars-cov-2") 3. #1 AND #2
PEDro	1. "COVID-19 and rehabilitation" 2. "COVID-19 and exercise" 3. "COVID-19 and physical therapy" 4. "COVID-19 and physiotherapy" 5. "COVID-19 and weaning" 6. "COVID-19 and recovery" 7. "COVID-19 and complications" 8. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7

Supplementary material

Table III (Supplementary material) Description of the articles on rehabilitation needs due to COVID-19 included in the rapid living systematic review updated to 30th June 2020.

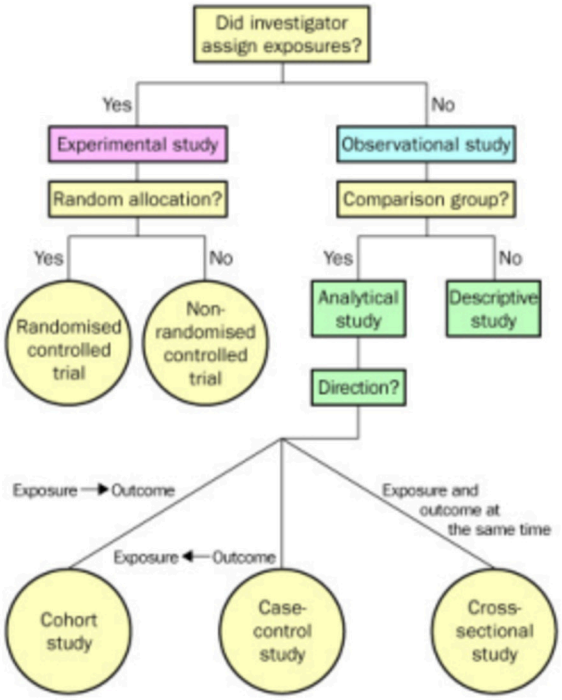
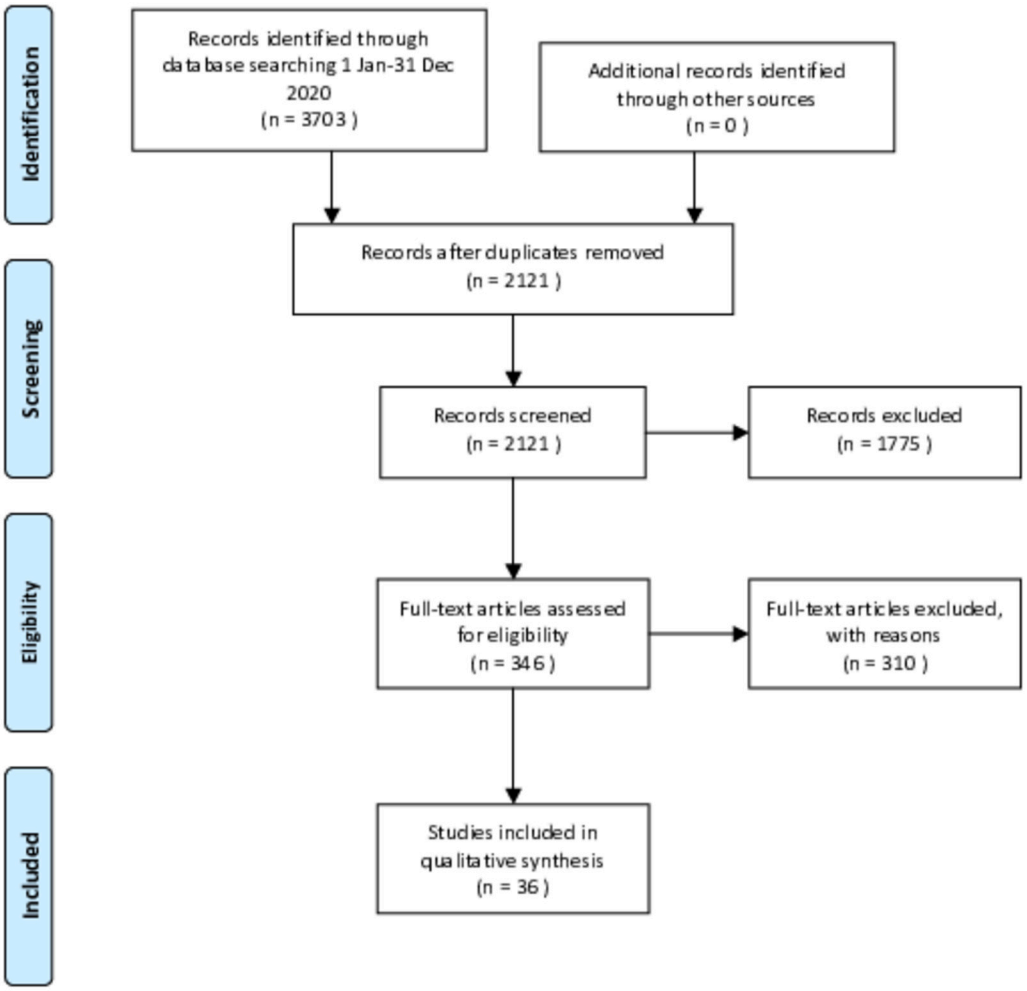


Figure 1. Algorithm for classification of types of clinical research

(From: David A Grimes, Kenneth F Schulz. An Overview of Clinical Research: The Lay of the Land. Lancet 2002, Jan 5;359(9300):57-61)

Figure2. PRISMA Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement.* PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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