



## REVIEW

# Rehabilitation and COVID-19: the Cochrane Rehabilitation 2020 rapid living systematic review. Update as of August 31<sup>st</sup>, 2020

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## ABSTRACT

**INTRODUCTION:** A monthly systematic review update is carried out to maintain the currency of scientific literature on rehabilitation of patients with COVID-19 and/or describing consequences due to the disease and its treatment, as they relate to limitations in functioning of rehabilitation interest. The aim of this study was to provide an updated summary of the available evidence published in August 2020.

**EVIDENCE ACQUISITION:** An extensive search on the main medical literature databases from August 1<sup>st</sup>, 2020 to August 31<sup>st</sup>, 2020 was performed, according to the methodology described in the second edition of the Cochrane Rehabilitation 2020 rapid living systematic review.

**EVIDENCE SYNTHESIS:** After removing duplicates, 1136 papers were identified, and 51 studies were finally included. According to OCEBM 2011 Levels of Evidence Table, they were Level 4 in most cases (76.5%) and Level 3 in the remaining (23.5%). Randomized controlled trials (RCTs) were not found. Thirty-two studies (62.7%) included COVID-19 patients who were assessed in the acute (20/32) or postacute phases (12/32). The other studies reported data on the impact of COVID-19 infection (7/19) or on the effect of lockdown restrictions (12/19) on subjects with pre-existing health conditions.

**CONCLUSIONS:** The scientific literature of August 2020 mainly focused on limitations in functioning of nervous system structure and related functions. Albeit the increased availability of data from analytical studies (both cohort and cross-sectional), there is still a lack of well-conducted Level 2 studies, to improve the knowledge on the effects of rehabilitation in COVID-19 patients.

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**KEY WORDS:** COVID-19; Severe acute respiratory syndrome coronavirus 2; Coronavirus; Rehabilitation; Physical and rehabilitation medicine.

## Introduction

Cochrane Rehabilitation has recently launched the REH-COVER – COVID-19 Evidence-based Response (REH-COVER) action aimed at focusing on the most recent evidence relating to COVID-19 (COVID-19) and rehabilitation.<sup>1</sup>

The first edition “Systematic rapid “living” review on rehabilitation needs due to COVID-19”<sup>2</sup> was monthly updated to April<sup>3</sup> and May<sup>4</sup> 2020. Then, on June 2020 started the second edition of the Cochrane Rehabilitation 2020 rapid living systematic review<sup>5</sup> that was updated to July 2020.<sup>6</sup>

In this second update to August 2020, we aim at show-

ing current evidence on rehabilitation needs of COVID-19 patients, describing the subsequent impairments related to limitations in functioning of rehabilitation interest (LFRI), and addressing specific rehabilitative approaches.

### Evidence acquisition

The present update was performed according to the same methodology as second edition of the Cochrane Rehabilitation 2020 rapid living systematic review.<sup>5</sup> We added all eligible papers available at the search databases performed on September 2<sup>nd</sup>, 2020 and August 31<sup>st</sup>, 2020. All results are also reported on the consolidated table of papers included in all editions of this rapid living systematic review on the Cochrane Rehabilitation REH-COVER action website ([https://tr.im/rr\\_dyn](https://tr.im/rr_dyn)).<sup>7</sup>

### Evidence synthesis

We identified 2594 publications. After deduplication, we retained 1136 unique records. Based on screening of title and abstract, 1133 publications were rejected, while 103 items were retained; eventually, full-text screening led to include 51 publications (Figure 1). A detailed overview of the new evidence is provided in the Supplementary Digital Material 1 (Supplementary Table I, available on Cochrane Rehabilitation website: <https://tr.im/rr08-20>).<sup>7</sup> Most studies (N.=23) were conducted in Europe, 8 in Italy,<sup>8-15</sup> 4 in UK,<sup>16-19</sup> 3 in France,<sup>20-22</sup> 2 in Germany,<sup>23, 24</sup> 2 in Switzerland,<sup>25, 26</sup> 1 in Spain,<sup>27</sup> 1 in Portugal,<sup>28</sup> while 2 were performed as International European collaborations;<sup>29, 30</sup> Fifteen researches were performed in Asia (N.=15), namely 3 in China,<sup>31-33</sup> 2 in Singapore,<sup>34, 35</sup> 2 in Japan,<sup>36</sup> 2 in Turkey,<sup>37, 38</sup> 2 in India,<sup>39, 40</sup> 1 Iran,<sup>41</sup> 1 Kuwait,<sup>42</sup> 1 Pakistan,<sup>43</sup> 1 Taiwan,<sup>44</sup> whereas 11 in Americas, of whom 10 in USA<sup>45-54</sup> and 1 in Chile.<sup>55</sup> Two studies were carried out by Intercontinental collaborations.<sup>56, 57</sup>

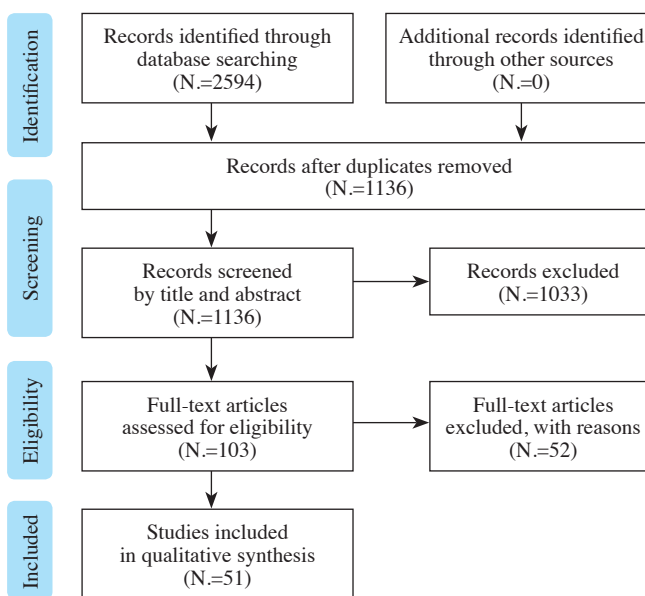


Figure 1.—PRISMA flow diagram.

### Evidence level of included studies

Due to the heterogeneity of published studies, a meta-analysis was not appropriate, so the results were qualitatively described. Based on the OCEBM 2011 Levels of Evidence table<sup>58</sup> the majority (76.5%) were level 4 (20 case report,<sup>8, 16, 18, 19, 21, 23, 27-30, 36, 37, 39, 42-44, 47, 49, 51, 53</sup> 10 case series,<sup>17, 20, 22, 26, 32, 34, 35, 41, 48, 59</sup> and 9 historical cohort<sup>9-11,13,15,24,55-57</sup>), whereas the remainder 12 papers (23.5%) were of level 3 (6 cohort<sup>12, 25, 33, 40, 46, 50</sup> and 6 cross sectional studies)<sup>14, 31, 38, 45, 52, 54</sup> (Table I). No RCT was found.

According to the research question, the majority of studies (43.1%) investigated disease natural history/determining factors (1 cohort study,<sup>40</sup> 2 cross-sectional,<sup>52, 54</sup> and 19 descriptive studies<sup>8-10, 19, 20, 27, 29, 30, 32, 34-36, 41, 44, 48, 49, 51, 57, 59</sup>); 14 descriptive papers reported epidemiological data on the clinical presentation of COVID-19 infection,<sup>16-18, 21-23, 26, 28, 37, 39, 42, 43, 47, 53</sup> and 8 described disease prevalence (cohort study,<sup>46</sup> cross sectional,<sup>14, 31, 38, 45</sup> his-

TABLE I.—Level of evidence of the studies included in the present rapid living systematic review.

	Level 1	Level 2	Level 3	Level 4	Total
Epidemiology - clinical presentation	0	0	0	14 (27.5%)	14 (27.5%)
Epidemiology - prevalence	0	0	5 (9.8%)	3 (5.9%)	8 (15.7%)
Epidemiology - natural history / determining and modifying factors	0	0	3 (5.9%)	19 (37.2%)	22 (43.1%)
Micro - Interventions (efficacy/harms)	0	0	2 (3.9%)	0	2 (3.9%)
Meso level	0	0	2 (3.9%)	3 (5.9%)	5 (9.8%)
Macro level	0	0	0	0	0
Total	0	0	12 (23.5%)	39 (76.5%)	51 (100%)

torical cohort<sup>15, 24, 56</sup>). Finally, 5 papers described data on health service organization (2 cohort studies<sup>12, 50</sup> and 3 historical cohort studies<sup>11, 13, 55</sup>) and only 2-cohort studies speculated about intervention efficacy (though not informing about harms).<sup>25, 33</sup>

### Clinical characteristics of included studies

Thirty-two studies (62.7%) included COVID-19 patients who were assessed in the acute (20 studies)<sup>16-19, 21-23, 26, 28, 32, 33, 35-37, 39, 42, 44, 47, 48, 57</sup> or postacute phases (12 studies)<sup>8, 9, 11, 20, 25, 27, 29, 34, 51, 52, 54, 59</sup> no studies described patients in the chronic phase. Seven studies (13.7%) reported data on the impact of COVID-19 infection on subjects with pre-existing health conditions, *i.e.* spinal cord injury (SCI),<sup>10, 49</sup> brain injury,<sup>31</sup> idiopathic pulmonary fibrosis,<sup>43</sup> multiple sclerosis (MS),<sup>30</sup> Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL),<sup>53</sup> and hip fractures.<sup>41</sup> Finally, 12 papers (23.5%) studied the effect of the pandemic lockdown restrictions on people with pre-existing diseases (laryngectomy patients with a voice prosthesis,<sup>12</sup> diabetes,<sup>40</sup> heart diseases,<sup>14, 46</sup> bone fractures,<sup>38</sup> spinal disorders,<sup>13</sup> breast cancer,<sup>55</sup> Parkinson's disease [PD],<sup>15, 50</sup> and stroke<sup>24, 45, 56</sup>).

Eighteen papers (35.3%) provided data about the type of rehabilitation service: 6 acute care,<sup>19, 32, 33, 35, 36, 48</sup> 4 general postacute,<sup>8, 11, 31, 59</sup> and 8 specialized postacute rehabilitation<sup>10, 12, 25, 34, 51, 55</sup> including outpatients.<sup>13, 50</sup>

According to the LFRI, most studies (N.=21; 41.2%)<sup>8, 10, 16-18, 20-23, 26-29, 31, 37, 39, 42, 44, 47, 53, 57</sup> concerned nervous system structure and related functions, 13 (25.5%) respiratory structures and related functions,<sup>11, 19, 25, 30, 32-36, 43, 48, 49, 51</sup> 3 (5.9%) activity limitation and participation restriction,<sup>9, 52, 59</sup> and 2 (3.9%) any other body structures and functions.<sup>41, 54</sup> Twelve papers<sup>12-15, 24, 38, 40, 45, 46, 50, 55, 56</sup> did not include people affected by COVID-19, so LFRI criteria were not applicable. The following summarizes the main evidence.

### Epidemiology. Impairment in respiratory structures and related functions

Ten case reports or series described the effect and the clinical manifestation of COVID-19 infection on people with or without pre-existing diseases. People with idiopathic pulmonary fibrosis<sup>43</sup> or SCI<sup>49</sup> seem to be at high risk of more severe pulmonary manifestations<sup>43</sup> or of complications like venous thromboembolism.<sup>49</sup> Conversely, Wurm *et al.*<sup>30</sup> excluded a higher risk of severe complications for a patient with MS in treatment with immunotherapy. Finally,

7 papers (13.7%), mostly case reports, described the clinical respiratory improvements of COVID-19 patients after specific rehabilitation treatments.<sup>19, 32, 34-36, 48, 51</sup>

### Epidemiology. Impairment in nervous system structures and related functions

There is only one cross-sectional study<sup>45</sup> assessing the impact of COVID-19 on the volume of stroke patients that highlighted a delay in care and a significant decrease in transient ischemic attack (TIA) diagnosis. The majority of studies are descriptive ones, with 2 historical cohort studies<sup>10, 57</sup> and 19 case reports or case series. D'Andrea *et al.*<sup>10</sup> evaluated 15 SCI patients who developed COVID-19 with a favorable prognosis, while Ntaios *et al.*<sup>57</sup> reported a worse prognosis in stroke patients with COVID-19 compared to those without infection. The 19 case reports/series described: neurological diseases concurrent to the onset of COVID-19 (N.=13), such as status epilepticus,<sup>21, 42</sup> Guillain-Barré syndrome<sup>26</sup> and its variant,<sup>47</sup> ischemic<sup>16, 18, 53</sup> or haemorrhagic stroke,<sup>17, 23, 37</sup> transverse myelitis,<sup>39</sup> and facial palsy in a pregnant woman;<sup>28</sup> neurological disorders occurring during the infection course of COVID-19, such as critical illness myopathy,<sup>8</sup> abnormal movements,<sup>20, 27</sup> quadriplegia for a possible myopathy,<sup>44</sup> and axillary nerve palsy.<sup>29</sup>

### Epidemiology. Any activity limitation and participation restriction

In a cross-sectional study on 274 COVID-19 outpatients, Tenforde<sup>52</sup> showed that 2-3 weeks after tested positive for symptoms, 35% had not returned to their usual state of health with a good percentage of subjects including young adults with no chronic medical conditions, reporting symptom persistence. A historical cohort study<sup>9</sup> demonstrated that COVID-19 patients discharged home after hospitalization in an acute and subsequent postacute ward, had a severe disability (Barthel Index score with  $\leq 60$ ) with a clear need for rehabilitative interventions. Such treatment may be provided also remotely in an effective and safe modality.<sup>59</sup> Overall, the target population of telerehabilitation approaches seems to be younger with less severe symptoms than that treated with face-to-face rehabilitation.<sup>59</sup>

### Epidemiology. Impairment of any other body structure and function

The persistence of a general state of illness in the medium term is reported by Weerahandi *et al.*,<sup>54</sup> who describe pa-

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tients complaining for a worsening of general health and reduced ability to carry out social activities, one month after discharge for severe COVID-19.

Even greater care should be taken in subjects with pre-existing disease, like elderly patients with fragile lower extremity fractures who are at high risk of COVID-19 and can be re-hospitalized for recurrence of symptoms.<sup>41</sup>

### Epidemiology. Other papers

Ghanchi *et al.*<sup>45</sup> and Haidu *et al.*<sup>56</sup> conducted two studies on stroke patients showing a significant decrease in the final diagnosis of TIA, a delay in care, and a significant decrease in the mean number of endovascular therapies.

The home confinement with the resulting reduction of physical activity, well documented in cardiopathic subjects,<sup>14, 46</sup> led on the one hand to worsening of the health conditions of patients with pre-existing diseases such as diabetics<sup>40</sup> and PD patients,<sup>15</sup> on the other hand to a reduction in the frequency of new fractures.<sup>38</sup>

### Micro level. Interventions

Hermann *et al.*<sup>25</sup> and Zha *et al.*<sup>33</sup> designed two cohort studies in order to analyse respectively the effect of multimodal inpatient cardiopulmonary rehabilitation and modified rehabilitation exercise (full-body exercise retrieved from Chinese martial arts) on COVID-19 patients. Both studies described an improvement in outcome measures, which was independent of previous ventilation status.<sup>25</sup>

### Meso level. Services

This section includes 5 papers, 2 cohort studies,<sup>12, 50</sup> and 3 case historical cohort studies.<sup>11, 13, 55</sup> Of these, four studies showed a high level of acceptance and satisfaction of teleconsultations and telerehabilitation in people with pre-existing pathologies exposed to the effects of the lockdown restrictions.<sup>12, 13, 50, 55</sup> Moreover, Franco *et al.* investigated the feasibility and the effect of non-invasive respiratory support applied to 670 COVID-19 patients outside the ICU reporting favorable outcomes but with the risk of staff contamination.<sup>11</sup>

### Discussion

This Cochrane Rehabilitation 2020 rapid living systematic review update revealed the following key points:

- the higher number of studies (N.=51) included in this update shows that the knowledge on the rehabilitation needs of this new disease has been increasing in the last month;

- most studies (45.1%) were conducted in Europe, mainly in Italy<sup>8-15</sup> (N.=8), albeit USA is the country that performed the highest number of studies<sup>45-54</sup> (N.=10);

- there is still a high heterogeneity of published studies preventing the conduction of a meta-analysis.

The level of evidence is still low, as showed by the lack Level 2 studies; 23.5% of included studies were Level 3 and 76.5% Level 4. It is interesting to notice that almost 60% of papers included were case reports or case series, testifying researchers are publishing several interesting cases that might provide further insight on the multifaceted features of this novel disease.

The 62.7% of papers reported data on acute or postacute COVID-19 patients,<sup>8,9,11,16-23,25-29,32-37,39,42,44,47,48,51,52,54,57,59</sup> the 23.5% showed the effects of the lockdown restrictions on people with pre-existing diseases of rehabilitative interest,<sup>12-15, 24, 38, 40, 45, 46, 50, 55, 56</sup> and the 13.7% described the impact of COVID-19 on subjects with pre-existing diseases of rehabilitative interest (SCI,<sup>10, 49</sup> brain injury,<sup>31</sup> idiopathic pulmonary fibrosis,<sup>43</sup> MS,<sup>30</sup> CADASIL,<sup>53</sup> and hip fractures<sup>41</sup>).

Only the 35.3% of papers were performed in a rehabilitation service: 6 in acute care,<sup>19, 32, 33, 35, 36, 48</sup> 4 general post-acute,<sup>8, 11, 31, 59</sup> and 8 in specialized postacute rehabilitation units,<sup>10, 12, 13, 25, 34, 50, 51, 55</sup> thus showing the lack of evidence from specialized COVID-19 Rehabilitation Units that are warranted in the future months.

This update showed that the most common LFRI (41.2%) was nervous system structure and related functions,<sup>8, 10, 16-18, 20-23, 26-29, 31, 37, 39, 42, 44, 47, 53, 57</sup> followed by respiratory structures and related functions (25.5%);<sup>11, 19, 25, 30, 32-36, 43, 48, 49, 51</sup> however, in 12 papers LFRI criteria were not applicable because not including people affected by COVID-19.

The lower physical activity due to pandemic lockdown restrictions and home confinement might lead to a worsening of pre-existing diseases (*e.g.* diabetes,<sup>40</sup> PD<sup>15</sup>) but seemed to reduce incident fractures.<sup>38</sup>

The rehabilitation effects on functional outcome COVID-19 patients was described by two micro-level cohort studies: Hermann *et al.*<sup>25</sup> showed that a multimodal inpatient cardiopulmonary rehabilitation intervention is safe, feasible, and effective in 28 postacute COVID-19 patients, independently from their previous ventilation status; Zha *et al.*<sup>33</sup> demonstrated that a modified rehabilitation exercise (full-body exercise retrieved from Chinese martial arts) might reduce self-reported respiratory symptoms (dry cough, productive cough, difficulty in expectoration, dyspnea) in 60 acute COVID-19 patients.

Moreover, it is crucial to highlight that a patient-tailored rehabilitation intervention might improve respiratory outcome in COVID-19 patients.,<sup>19, 32, 34-36, 48, 51</sup>

A cross-sectional study<sup>52</sup> performed on large sample of COVID-19 outpatients (N.=274) reported that 35% of them had not returned to their usual state of health at 2-3 weeks after tested positive for symptoms; this aspect was confirmed by a historical cohort study<sup>9</sup> reporting a severe disability in COVID-19 patients discharged home after hospitalization (acute and postacute COVID-19 ward). Therefore, these studies pointed out that COVID-19 patients might have sequelae that need for rehabilitative interventions, also in outpatient clinic or through tele-rehabilitation.

In this context, four meso-level studies<sup>12, 13, 50, 55</sup> investigated the level of acceptance and satisfaction of tele-rehabilitation in patients with pre-existing diseases of rehabilitative interest limited to access to services due to pandemic lockdown restrictions and home confinement; the promising results might improve the role of tele-monitoring and tele-rehabilitation in the context of COVID-19 pandemic.

## Conclusions

Taken together, the findings of this rapid living systematic review pointed out that limitations in functioning of nervous system structure and related functions are an important source of disability in patients suffering from COVID-19. There is a persistent increasing interest on the role of tele-rehabilitation that might be beneficial in the COVID-19 scenario. Albeit the improvement of knowledge on the effects of rehabilitation against COVID-19, as showed by several descriptive studies, RCTs are still warranted to provide useful recommendations for COVID-19 patients to handle this disease from a rehabilitation perspective.

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