Prevalence of long-term effects in individuals diagnosed with COVID-19: an updated living systematic review

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Abstract

Objective: Post COVID-19 condition refers to persisting or recurring symptoms weeks after acute COVID-19 illness which can significantly impact quality of life and health systems. It is important to understand the manifestation and magnitude of this condition. The objective of this living systematic review is to summarize the prevalence of symptoms and sequelae reported by people ≥4 weeks after COVID-19 diagnosis.

Design: Systematic review, meta-analysis and narrative synthesis.

Data sources: Embase, Medline, PsychInfo, Cochrane Central and select grey literature up to April 14, 2021.

Methods: We adapted a previous search strategy used by the U.K. National Institute for Health and Care Excellence and updated it to search for new literature. Two reviewers screened references independently; one extracted data and assessed risk of bias and certainty of the evidence while another verified them. Prevalence data from laboratory-confirmed populations were meta-analyzed using a random effects model and synthesized separately in the short-term (4-12 weeks) and long-term (>12 weeks) periods after diagnosis. Data from clinically-diagnosed populations were synthesized narratively.

Results: Of the 4444 unique citations, 84 observational studies met our inclusion criteria. Over 100 post COVID-19 symptoms and sequelae were reported. Sixty-one percent (95% CI: 44-76%, *low certainty*) and 53% (95% CI: 41-65%, *low certainty*) of laboratory-confirmed individuals reported persistence or presence of one or more symptoms in the short- and long-term periods, respectively. The most prevalent symptoms in both periods included: fatigue, general pain or discomfort, shortness of breath, cognitive impairment and mental health symptoms.

Conclusions: A substantial proportion of individuals reported a variety of symptoms ≥4 weeks after COVID-19 diagnosis. Due to gaps in the research base, and the low certainty of the evidence currently available, further research is needed to determine the true burden of post COVID-19 condition in the general population and in specific subgroups.

PROSPERO registration number: CRD42021231476.

Introduction

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) has resulted in over 230 million cases of COVID-19 and over 4 million deaths worldwide as of September 2021 (1). The typical duration of acute illness is two to six weeks, however, some patients have described debilitating symptoms persisting or recurring for weeks or months after acute illness(2). Affected patients are commonly referred to as post COVID or COVID long-haulers (3-5).

In this review, we used the term "post COVID-19 condition" to describe persistent or recurring symptoms. Other terms used in the literature have included long COVID, post-COVID conditions, chronic COVID syndrome and post-acute sequelae of SARS-CoV-2 infection (PASC) (2,6-9). Definitions of 'long-term' have varied from ≥4 to ≥12 weeks after COVID-19 diagnosis (10-13). On October 6, 2021, the World Health Organization published a clinical case definition for post COVID-19 condition, which was developed using a Delphi consensus process, noting that the definition may change as new information on the condition emerges(14). Post COVID-19 condition was defined as symptoms that usually appear three months from onset of COVID-19 symptoms and last for at least two months in individuals with a history of probable or confirmed SARS-CoV-2 infection.

Due, in part, to the lack of a standard case definition for post COVID-19 condition prior to October 2021(15), prevalence estimates have varied from 3% to as high as 80%(16-18). Given the millions of individuals who have been infected with COVID-19, serious ramifications on quality of life, health care utilization, and workforce productivity are anticipated even if the lowest prevalence estimates were found accurate. Improved understanding of the prevalence of post COVID-19 condition, the symptoms and sequelae observed, its effects on COVID-19 survivors, and its resolution over time is important to address this issue. Other reviews have also looked at estimating the prevalence of various symptoms related to post COVID-19 condition (13,19-26); however, none have assessed for certainty in the evidence body of evidence. The objective of this systematic review is to identify and summarize studies reporting the frequency of symptoms, sequelae, and difficulties in conducting usual activities experienced by individuals living with post COVID-19 condition at four weeks or more after initial COVID-19 diagnosis and provide certainty in the findings for select outcomes.

Methods

We conducted a systematic review that adhered to Cochrane methodology and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (27,28). Our multidisciplinary team included methodologists and subject matter experts currently treating patients with post COVID-19 condition. The review question and methodology were determined *a priori* (protocol registered in PROSPERO: CRD42021231476) (29). This living review will be periodically updated on a quarterly basis or as resources permit. Detailed methods are provided in Supplementary File 1 – Detailed methodology.

Information Sources and Search strategy

Our formative search identified a systematic review conducted by the National Institute for Health and Care Excellence (NICE) that examined post COVID-19 condition. We adapted the NICE review search strategy (NICE search dates were January 1st to October 21st, 2020) in consultation with a health librarian (12) (see Supplementary File 1 for the detailed search strategy). All studies included in the NICE review and any French articles they excluded were eligible for inclusion. We then updated the search (October 22, 2020 to January 15, 2021 and again from January 16, 2021 to April 14, 2021) using the following

databases: Embase, Medline, PsycINFO, and Cochrane Central. We conducted a complementary search for grey literature in January and again in April 2021 and included any relevant literature.

Eligibility Criteria

We included primary studies in English or French that included 50 or more participants of any age with laboratory-confirmed SARS-CoV-2 infection ("laboratory-confirmed") or with COVID-19 clinically-diagnosed by a health professional ("clinically-diagnosed"), and reported the prevalence of symptoms or sequelae four or more weeks after COVID-19 diagnosis. For participants who self-reported their laboratory diagnosis for COVID-19, and where proof of laboratory findings was not required for inclusion in the study, then we considered these participants as clinically-diagnosed. We excluded pre-prints, and non-peer reviewed articles and primary studies that recruited participants specifically because they reported experiencing such long-term effects.

"Time since COVID-19 diagnosis" was used synonymously with time since symptom onset, positive laboratory result, or diagnosis by a health professional. We defined short- and long-term outcomes as those measured between four and 12 weeks and those measured more than 12 weeks after COVID-19 diagnosis, respectively.

Study selection and data collection process

A priori, we developed multi-stage (title/abstract and full text) screening questions and data extraction forms that were piloted by all reviewers (Supplementary File 1). Two reviewers screened citations and full texts independently. At the title and abstract screening stage, citations passed to full text screening if they were included by at least one reviewer, but both reviewers had to agree on exclusions. At the full text stage, consensus was required for both inclusion and exclusion. For data extraction, one reviewer extracted data from included studies, which were verified by a second reviewer. At each stage, reviewers resolved conflicts through consensus or consultation with a third reviewer.

Outcomes

The main outcomes of interest were any symptom, sequelae or outcomes pertaining to difficulties conducting usual activities (i.e. functional outcomes) reported by individuals four or more weeks after a COVID-19 diagnosis. We identified the following key symptoms or sequelae: fatigue, shortness of breath, neurocognitive impairment, pain (in the joints, chest, or muscles), organ damage, dizziness, tachycardia, chest tightness or heaviness, mental health, olfactory and gustatory impairments, and sleeping disturbances. Additional outcomes, such as those from diagnostic imaging or pulmonary function tests, which may often provide abnormal results despite resolution of patient symptoms, were considered as outcomes of interest in the long-term period only.

Evidence synthesis

Our primary synthesis focused on outcomes in individuals who had laboratory-confirmed COVID-19 to reduce likelihood of including results due to unrelated conditions. We synthesized short- and long-term outcomes separately. When outcomes were reported at multiple time points within a study, we used results from the longest follow-up time point.

Where appropriate, we conducted meta-analyses for outcomes with two or more studies using a random effects model. To explore reasons for high heterogeneity across studies, we determined sub-group analyses *a priori* and considered these for key outcomes. We stratified results by level of care received during the acute stage of COVID-19 infection (i.e., admitted to ICU, hospitalized, non-hospitalized), which was used as a proxy for severity of COVID-19 (i.e., patients with more severe COVID-19 were more likely to require hospitalized care). We performed the analyses using R statistical software version 4.0.4 (30), with package metafor version 2.4-0 (31) and package meta version 4.18-0 (32). The pooled results with 95% confidence intervals are presented in forest plots. We conducted narrative syntheses for the outcomes in the clinically-diagnosed population and did not explore heterogeneity across these studies.

Assessing risk of bias and certainty in the evidence

We used a modified version of the Joanna Briggs Institute critical appraisal tool for prevalence studies (33) to assess risk of bias. After consulting with the authors of this tool, we omitted questions 3-5 to avoid duplication with the criteria on imprecision and indirectness used to assess the certainty of the evidence. We rated the risk of bias for each outcome separately for questions 6-8 and then categorized questions into three domains (participants [questions 1, 2 and 9], outcome measures [questions 6-7], and statistics [question 8]). Studies that met the criteria in these domains were rated as low risk of bias, those partially met were rated moderate, and those that did not meet the criteria were rated high risk of bias. The criteria and schema used to assess risk of bias are provided in Appendix 4 of Supplementary File 1. One reviewer assessed risk of bias, which was verified by a second reviewer. Reviewers resolved conflicts through consensus or consultation with a third reviewer.

We assessed certainty in the body of evidence for key symptoms or sequelae and the most prevalent outcomes using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (34). In the absence of a formal framework for prevalence and GRADE, and in consultation with GRADE experts, we adapted the GRADE framework for assessment of incidence estimates in the context of prognostic studies(35) as a basis to assess prevalence estimates similar to those used previously by Righy et al.(36)

In the context of prevalence, observational studies may provide robust estimates due to broad eligibility criteria and enrollment of representative populations (35). Thus, the quality of the evidence from observational studies were initially assigned as “high” for all outcomes. The quality of the evidence was then downgraded (to “moderate”, “low”, or “very low”) if there were serious or very serious concerns over any of the following five domains that reduce certainty in the prevalence estimates: risk of bias, inconsistency, indirectness, imprecision, or publication bias. In instances where there were minor concerns with one of these domains, a decision was made to downgrade by half a point instead of a full point. Half-points were then combined across domains to yield a total score (e.g., downgrading by 1.5 points for risk of bias and 0.5 points for indirectness for a total of 2 points from “high” to “low”). In the event that the final rating included a half point (e.g., 1.5 points), we conservatively rounded up (i.e., in this case to downgrade by 2). Due to the nature of prevalence outcomes and design of the application of GRADE criteria to these outcomes, no criteria for upgrading were considered applicable. The specific

decision rules that we applied for judgments in relation to the five GRADE domains are described in detail in Appendix 5 of Supplementary File 1.

After piloting the tool, one reviewer assessed risk of bias and graded the evidence while a second verified the assessments. Reviewers resolved conflicts through consensus or consultation with a third reviewer.

Patient and Public Involvement

We did not involve patients in the conduct of this review.

Results

Study Selection

Of the 4444 unique citations yielded in the search, 779 met criteria for full-text screening (Figure 1). The list of studies excluded in full-text screening by reason of exclusion are provided in Supplementary File 2. Eighty-four studies met our inclusion criteria, of which 62 included prevalence data for individuals with laboratory-confirmed COVID-19, 21 included prevalence data for individuals who were clinically-diagnosed with COVID-19, and one included prevalence data on both. (Table 1, Supplementary Table 1)

Prevalence in laboratory-confirmed COVID-19 population (all ages)

Study Characteristics

Study characteristics of 63 studies with data from participants with laboratory-confirmed COVID-19 are shown in Table 1. All studies were observational (cohort or cross-sectional) and included between 58 and 1733 individuals, with most studies (42/63) having less than 200 participants. The majority were conducted in Europe (38/63), with the remaining in Asia (8/63), North America (6/63) and others (11/63). More than half of the studies (37/63) only recruited adult participants, 24/63 did not restrict recruitment by age, and 2/63 studies focused on a pediatric sample. Almost half of the studies (27/63) only recruited participants who were hospitalized or admitted to the intensive care unit (ICU) due to COVID-19. Outcome data were reported with mean or median times from COVID-19 diagnosis occurring in the short-term for 56% (35/63), in the long-term for 36% (23/63) and in both the short- and long-term for 8% (5/63) of the studies.

Risk of bias and certainty of the evidence

Of the 63 studies, we assessed 45 to be at moderate risk of bias and 18 to be at high risk of bias [Supplementary Table 2]. The most common sources of potential biases were from participant selection (i.e. convenience samples or study population was not representative of the target population) and poor objectivity/validity of outcome measurement (i.e. many outcomes were self-reported or obtained using non-validated measures).

We assessed certainty (or confidence) of the body of evidence for 81 key outcomes and found moderate certainty in 6% (5/81), low certainty in 62% (50/81) and very low certainty in 32% (26/81) of these outcomes. (Table 2, Supplementary Table 3)

Prevalence of symptoms, sequelae, and difficulties conducting usual activities

Over 100 different outcomes were reported for which the prevalence estimates in the short- and long-term are provided in Table 2.

SHORT-TERM (4-12 WEEKS AFTER COVID-19 DIAGNOSIS)

Approximately 3 in 5 individuals (61%, 95% CI: 44-76%, *low certainty*) reported the persistence or presence of one or more symptoms in the short-term. The most prevalent symptoms were: fatigue (41%, 95% CI: 30-52%, *low certainty*), general pain or discomfort (40%, 95% CI: 24-58%, *low certainty*), shortness of breath (34%, 95% CI: 25-45%, *low certainty*), cognitive impairment (29%, 95% CI: 19-41%, *low certainty*), depression (23%, 95% CI: 14-34%, *low certainty*), post-traumatic stress disorder (PTSD) (23%, 95% CI: 14-35%, *low certainty*) and hyposmia (23%, 95% CI: 8-49%, *low certainty*). General functional impairment was reported in 35% of individuals (95% CI: 18-56%, *low certainty*) and 41% (95% CI: 28-55%, *low certainty*) reported feeling ill or not back to full health in the short-term.

LONG-TERM (>12 WEEKS AFTER COVID-19 DIAGNOSIS)

Approximately half of individuals (53%, 95% CI: 41-65%, *low certainty*) reported persistence or presence of one or more symptoms in the long-term. The most prevalent symptoms were: anxiety (32%, 95% CI: 22-43%, *very low certainty*), general pain or discomfort (28%, 95% CI: 23-34%, *moderate certainty*), fatigue (25%, 95% CI: 19-34%, *low certainty*), insomnia (22%, 95% CI: 17-28%, *moderate certainty*) and cognitive impairment (20%, 95% CI: 5-54%, *very low certainty*). The following symptoms had similar prevalence of 17%-18% (*low to very low certainty*): depression, PTSD and shortness of breath. General functional impairment was reported in 17% (95% CI: 5-44%, *very low certainty*) of individuals in the long-term.

PREVALENCE IN CHILDREN (≤18 YEARS OF AGE)

Only two studies specifically recruited children (≤18 years) to determine the prevalence of short- and long-term effects after COVID-19 infection (37,38). One study (37) reported 58% (95% CI: 50-67%, *low certainty*) of children experienced at least one symptom 162.5 ± 113.7 days after laboratory-confirmed COVID-19 diagnosis, which is similar to the proportion reported for the whole laboratory-confirmed population studied in this review. The most prevalent of these symptoms (ranging from 10-19%, *low certainty*) included: insomnia, nasal congestion or runny nose, fatigue, headache, concentration problems, muscle pain (Table 3). The other study (38) only reported on the prevalence of one outcome in children – hyposmia – and found that none (0%, n=72) experienced hyposmia 2 months after COVID-19 diagnosis.

Potential reasons for heterogeneity

Subgroup analyses by level of care received during the acute COVID-19 infection appeared to explain some of the heterogeneity in prevalence of outcomes such as fatigue and shortness of breath (Figure 2, Supplementary File 3). However, we still observed moderate to high heterogeneity within some of the subgroups, particularly among hospitalized populations. Differences in how outcomes were measured (i.e., self-reported versus validated tests) and the thresholds used in each study to indicate an adverse outcome (e.g. binary versus a multi-point scale) may have contributed to differences in prevalence estimates across studies (analyses not shown). In addition, measurement of outcomes at different

points or periods of follow-up within the short- or long-term (e.g. outcomes measured at 4, 8 and 12 weeks reported together in the short-term) may have contributed to differences in prevalence estimates across studies; however, there were insufficient data to conduct subgroup analyses at each separate time point.

Prevalence in clinically-diagnosed COVID-19 population (all ages)

Characteristics of the 22 included studies with prevalence data for individuals (all ages) who were clinically-diagnosed with COVID-19 are presented in Supplementary Table 1. About half of the studies (12/22) recruited participants who were hospitalized for COVID-19, 64% (14/22) included adult participants only and 55% (12/22) were conducted in Europe. Outcome data were reported with mean or median times from COVID-19 diagnosis occurring in the short-term for 6/22 studies, in the long-term for 13/22 studies and in both the short- and long-term for 3/22 studies. Seventeen of 22 studies were assessed to be at moderate risk of bias while 5/22 were at high risk of bias. [Supplementary Table 2]

The prevalence of various symptoms, sequelae, and complications from COVID-19 in the short- and long-term in the clinically-diagnosed population are presented in Supplementary Table 4.

Interpretation

Based on data from this systematic review, most laboratory-confirmed COVID-19 patients experienced one or more symptoms in the short- (61%) and long-term (53%) after diagnosis. The most commonly reported symptoms included fatigue, general pain or discomfort, sleep disturbances, shortness of breath, cognitive impairment and mental health symptoms. A large proportion of convalescent COVID-19 patients experienced other mild to severe and debilitating symptoms as well. Consequently, roughly 30% and 10% of individuals were unable to return to work in the short- and long-term following COVID-19 diagnosis, respectively. Because a large proportion of population included in our review represent those who experienced moderate to severe COVID-19 during their acute phase, it is possible that the kinds of symptoms or the frequencies of symptoms reported in those who experienced a milder COVID-19 infection may be different from those reported in our review. In addition, due to limited data available, and low certainty in the existing evidence, clarity around the burden of post COVID-19 condition will require additional research to untangle the sequelae caused directly by COVID-19 infection from those arising from related factors such as extensive hospitalization due to severe illness. The prevalence and complex nature of this condition will require multi-disciplinary approaches in developing appropriate diagnostic models and tools, patient care pathways, and support structures to address the needs of those suffering from post COVID-19 condition.

Several systematic reviews, most of which conducted meta-analyses to arrive at prevalence estimates for the long-term effects of COVID-19, similarly reported two or more of the following symptoms as the most frequently reported: fatigue, shortness of breath, mental health-related symptoms and cognitive impairment (13,19-26). Such similarities in findings across reviews helps advance our understanding of post COVID-19 condition and its burden, and substantiates the need for ongoing support for many COVID-19 survivors. Where prevalence estimates for specific symptoms or sequelae varied widely between the findings from our review and those of others', we believe that the variability may in part be explained by methodological differences across reviews. For example, the other reviews synthesized

both laboratory-confirmed and clinically-diagnosed populations, while we analyzed these populations separately in order to minimize bias in capturing symptoms that may be due to other causes. We wanted to identify all possible symptoms that may be associated with post COVID-19 condition, therefore we did not restrict inclusion of studies in our review, nor our syntheses of the findings, to only select symptoms, whereas other reviews did (21,24,26). Other reviews also excluded studies with less than 100 participants (23,25) while our review included relevant studies with a sample size of 50 or more; thereby increasing our likelihood of capturing additional relevant studies compared to others. Some reviews included studies with follow-up periods occurring between 2 and 3 weeks post-infection (19-21,25). We excluded such studies in our review in order to minimize the likelihood of capturing symptoms from acute COVID-19 infection. We also thought it was important to report prevalence separately for the short-term and long-term after COVID-19 infection, and to gain insight into any potential differences in what may be observed over time, whereas most reviews combined results from follow-up periods spanning both short and long-terms (13,20-22,24) or only reported on the long-term (23,26). Similar to the other reviews, we critically assessed studies for risk of bias. However, distinct from other reviews, we used the GRADE approach to provide certainty of the evidence for select outcomes. This information provides clinicians and policy-makers with an understanding of how confident we are in the findings given the limitations of the available data.

Some limitations should be considered including the possible omission of relevant studies. We adapted and updated our search based on the evidence review conducted by NICE in October 2020; the only studies that were eligible for inclusion in our review that were published prior to October 2020 were studies that were included in the NICE review, or French–language studies that were excluded from that review (12). To minimize the potential for missing relevant studies we supplemented with grey-literature searches. Another limitation is the inclusion of only English and French articles that may have introduced a language bias, but this was likely minimal (39). Finally, although we had consulted with GRADE experts on our modified process for assessing evidence on prevalence using the GRADE approach, this process has yet to be validated.

Evidence gaps and Research Priorities

There were limited data (i.e. estimates based on a single study) or no studies identified for many outcomes in this systematic review. The majority of studies in this review included adults only or individuals who were hospitalized or treated for moderate-to-severe COVID-19; therefore, the prevalence of long-term effects in children (particularly very young children between 0-5 years of age), and in individuals who were asymptomatic or who presented with mild COVID-19 symptoms in the acute stage may not be sufficiently represented in our results. Additionally, investigating how post COVID-19 condition may differ across specific populations (e.g., sex/gender, race, age, underlying conditions) will be important to inform equity considerations for future health program and policy decisions.

Just over half of our included studies (n=43) reported on long-term effects beyond 12 weeks post-diagnosis (laboratory-confirmed or clinically-diagnosed). However, only a few (n= 6) of these included mean follow-up periods beyond 6 months from initial COVID-19 diagnosis. Longer-term follow up is needed to help inform how post COVID-19 condition changes or resolves over time. Many of the included studies had small sample sizes (<200 participants) or were at moderate or high risk of bias due to the selection of participants and use of non-validated outcome measures. The Post-COVID Core Outcome Set (PC-COS) group, along with the World Health Organization, are in the process of creating a

core set of outcomes for use in research studies and clinical care for individuals with post COVID-19 condition (40). The use of a standardized approach, such as the one being developed by the PC-COS group for measuring symptoms and other outcomes in individuals with post COVID-19 condition, would help reduce heterogeneity and bias and subsequently increase confidence in the research findings. Given the lack of contemporaneous control groups, it was not possible to determine whether symptoms were due exclusively to COVID-19. Other possible contributing factors could include the presence of pre-existing symptoms or conditions prior to COVID-19 infection, effects of treatment received or effects of being hospitalized or admitted to the ICU, and effects due to the pandemic itself (e.g., barriers to seeking treatment, psychosocial impacts). However, the extensive list of symptoms reported in this review provide a good starting point for further detailed investigations as to which ones are more closely associated with post-infection sequelae versus those related to other factors.

Health policy implications

Understanding the burden and characteristics of post COVID-19 condition is important in the planning and development of mitigation strategies to support those in need of rehabilitation, medical care and other community resources for recovery after COVID-19 infection. This evidence is expected to support national and international health organizations who are in the process of planning for and developing supportive measures for patients with post COVID-19 condition. Such efforts include developing clinical practice and public health guidelines, innovative patient care pathways, education materials for patients and healthcare professionals, and creating appropriate services and social constructs to support COVID-19 survivors for a full recovery (41). Understanding the burden of post COVID-19 condition will also help inform broader public health measures to mitigate COVID-19 transmission.

Conclusion

A substantial proportion of individuals reported a variety of symptoms and sequelae more than four weeks after COVID-19 diagnosis. These physical and mental health symptoms have led to difficulties in conducting usual activities and resulted in diminished quality of life among COVID-19 survivors. This review provides a snapshot of symptoms presenting in COVID-19 survivors in the months after diagnosis. The data indicate that many are experiencing post COVID-19 condition, the range and impact of which are broad and will require a multidisciplinary approach to develop appropriate diagnostics, clinical practice and public health guidelines, and patient care pathways. Research on post COVID-19 condition is rapidly being produced and work is on-going to gather evidence which will lead to better and more refined estimates and understanding of the burden of post COVID-19 condition, the social and economic impacts, and resources needed to support a large number of survivors.

Ethics statements:

Ethics approval was not required to conduct this systematic review of previously published literature.

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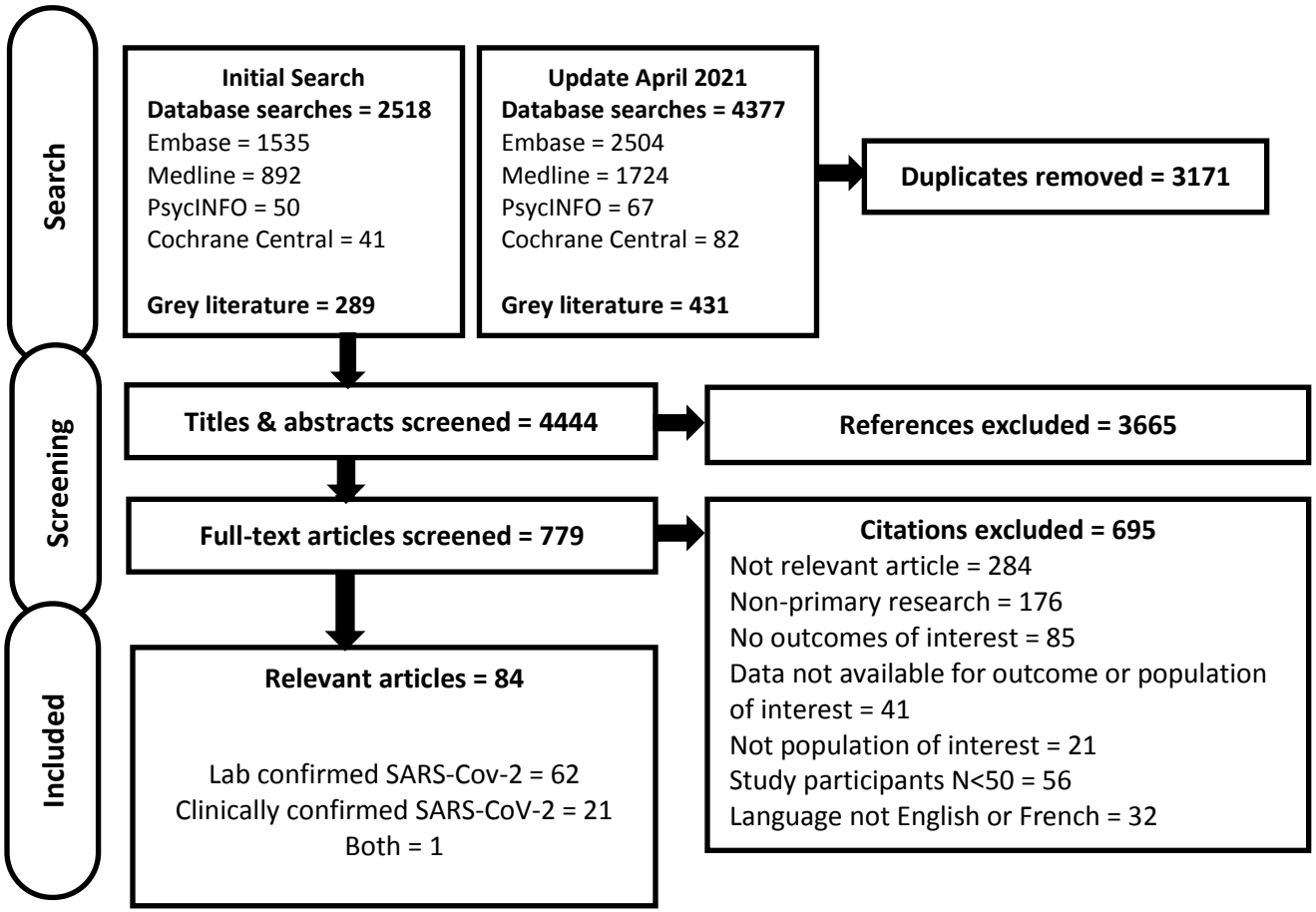
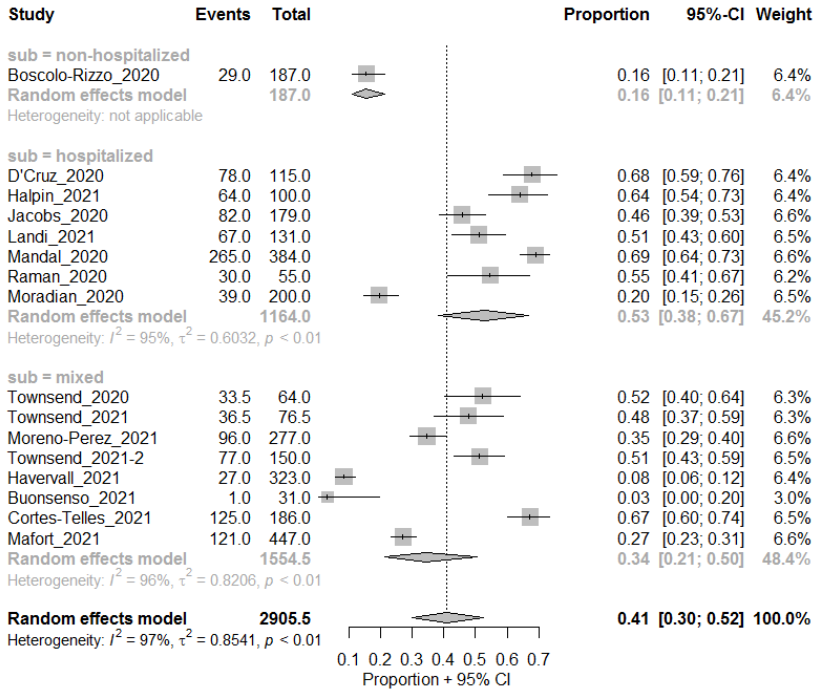


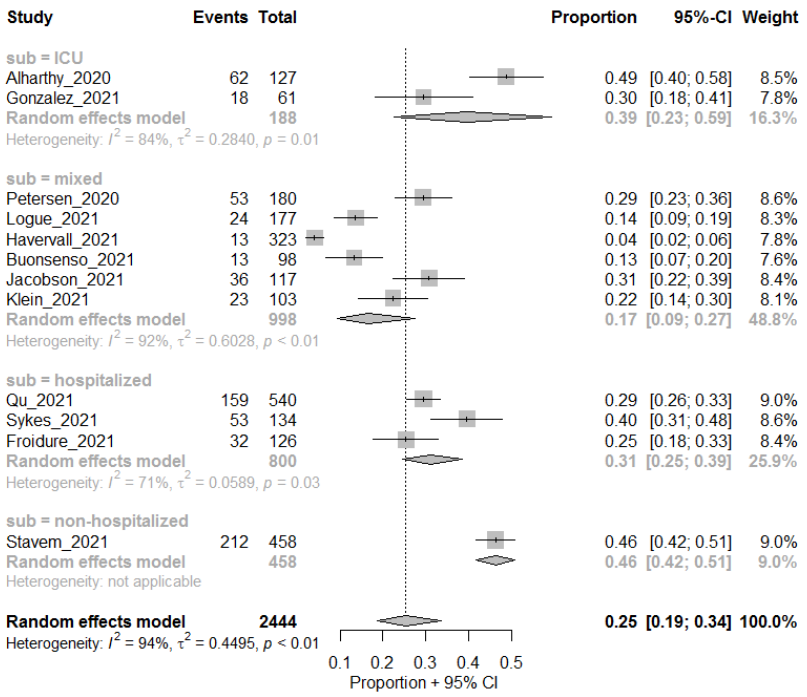
Figure 1: PRISMA flow diagram of articles through the systematic review process

(a) Fatigue

4-12 WEEKS

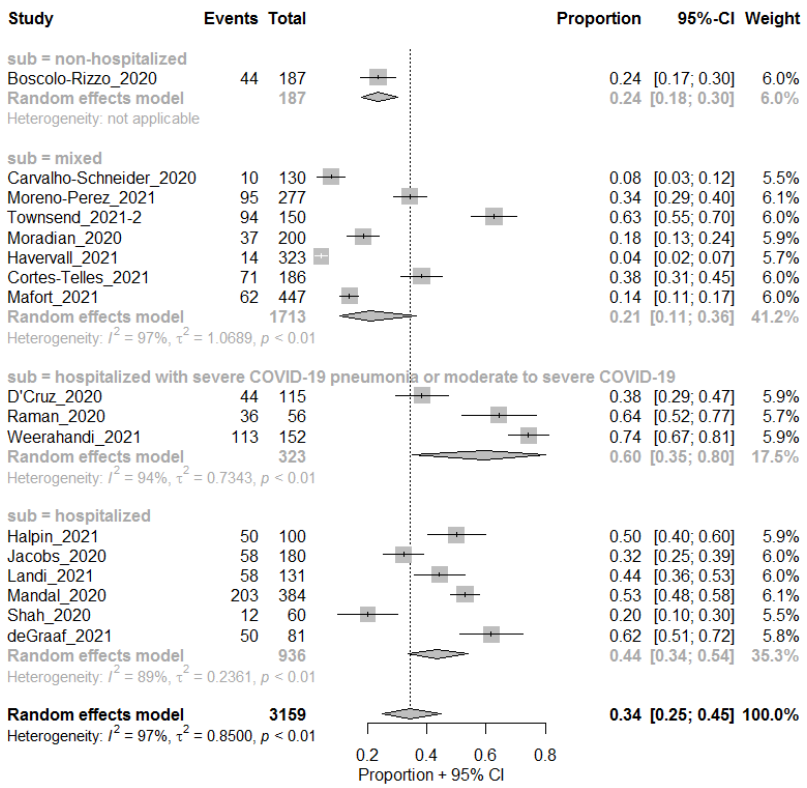


>12 WEEKS



(b) Shortness of breath

4-12 WEEKS



>12 WEEKS

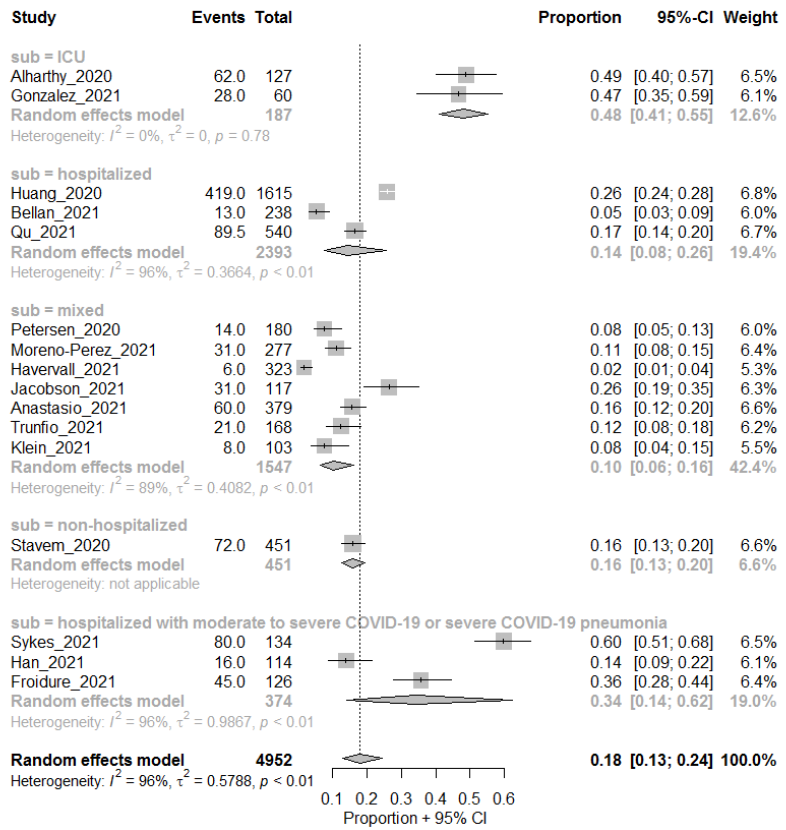


Figure 2. Prevalence (proportion of study sample) of (a) fatigue and (b) shortness of breath, at 4-12 weeks and >12 weeks after COVID-19 diagnosis and by level of care received at the acute stage of COVID-19 infection. Note that level of care may be considered a proxy for severity of COVID-19 (i.e., such that patients with more severe COVID-19 were more likely to require hospitalized care).

Table 1: Characteristics of Included Studies with Laboratory-Confirmed Participants

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
Akter, 2020 Clinical characteristics and short term outcomes after recovery from COVID-19 in patients with and without diabetes in Bangladesh	Bangladesh, Cross-Sectional Study, April 1- June 30, 2020	734 patients Age range: 0 to >60 years 24.0% female	n/a	4 weeks after recovery from COVID-19	Mobility issues Self care issues Pain/discomfort Anxiety/depression Sleep disturbances Panic attack Loss of concentration Memory loss Hair fall
Alemanno, 2021 COVID-19 cognitive deficits after respiratory assistance in the subacute phase: A COVID rehabilitation unit experience	Italy, Prospective Cohort Study, March 27-June 20, 2020	87 patients Mean age 67.23 ± 12.89 years 29.0% female	Patients admitted in the COVID-19 Rehabilitation Unit	1 month after home-discharge from COVID-19	cognitive deficit - MoCA test cognitive deficit - MMSE test depression PTSD symptoms
Alharthy, 2020 Residual Lung Injury in Patients Recovering From COVID-19 Critical Illness: A Prospective Longitudinal Point-of-Care Lung Ultrasound Study	Saudi Arabia, Prospective Cohort Study, April 2020	171 adults (≥18 years) Mean age (SD): 47.00 ± 11.38 years 21.1% female	Individuals diagnosed with severe COVID-19 pneumonia and admitted to ICU	4 month follow-up after hospital discharge	Pulmonary embolism Pulmonary hypertension Breathing difficulties Fatigue Walking difficulties Deep vein thrombosis Interstitial lung disease Symptomatic
AlShakhs, 2021 The Association of Smell and Taste Dysfunction with COVID19, And Their Functional Impacts; 7822753 CSR - Reports results	Saudi Arabia, Cross-Sectional Study, June 5-July 30, 2020	274 patients Age range: 18–50 years 55.0 % female	Mild to moderate	Unspecified	dysgeusia

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
Anastasio, 2021 Medium-term impact of COVID-19 on pulmonary funtion, functional capacity and quality of life	Italy, Prospective Cohort Study March 1, 2020 June 1, 2020	379 patients 20–80 years, median 56 (IQR 49–63) 54.1 % female	Any	4 months after SARS-COV-2 diagnosis	inactive breathlessness at least one symptom
Bellan, 2021 Respiratory and Psychophysical Sequelae Among Patients With COVID-19 Four Months After Hospital Discharge	Italy, Prospective Cohort Study, between March 1 and June 29, 2020	238 patients 61 (50-71) years 40.3 % female	Individuals hospitalized due to COVID-19	4 months after discharge from COVID-19	Fever Cough Dyspnea Ageusia Anosmia Diarrhea Arthralgia Myalgia Chest pain Sore throat Headache DLCO < expected Limited physical performance on SPPB test 2-minute walk test Some degree of functional impairment Tolerance to exercise Posttraumatic stress symptoms
Blair, 2021 The Clinical Course of COVID-19 in the Outpatient Setting: A Prospective Cohort Study	United States of America, Prospective Cohort Study,	118 patients 56.0 (50.0–63.0) years	Any	Median (IQR) of 20 (13–38) days from symptom onset	not returned to usual health not returned to doing usual activities any symptoms perception of health - poor

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
	April 21 and July 23, 2020	57.6 % female			effect of symptoms on activities weakness dry cough
Blanco, 2021 Pulmonary long-term consequences of COVID-19 infections after hospital discharge	Spain, Prospective Cohort Study, 45 days after discharge	100 patients 54.98 ± 10.72 36.0 % female	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)	Days after onset of symptoms 104 (IQR 89.25, 126.75)	Abnormal lung function 6MWT - Pathological Pathological CT
Boscolo-Rizzo, 2020 Evolution of altered sense of smell or taste in patients with mildly symptomatic COVID-19	Italy, Cross Sectional Study, March 2020	187 adults (≥18 years) Median age: 56 (range: 20-89) years 55.1% female	Mildly symptomatic individuals with no evidence of pneumonia and not requiring hospitalization	4 weeks after first swab test	Fever Dry cough or coughing up mucus Blocked nose Problems breathing Headache Sore throat Muscle or joint pains Chest pain Sinonasal pain Loss of appetite Felt tired Diarrhea Nausea Vomiting Abdominal pain Dizziness Altered sense of smell or taste
Brandao, 2021 Chemosensory Dysfunction in COVID-19: Prevalences, Recovery Rates, and Clinical	Brazil, Prospective Cohort Study, April 2020	655 patients Mean age 37.7 (SD 10.4) years	Any	36 to 119 days after symptom onset (median,	olfactory deficit taste dysfunction

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Associations on a Large Brazilian Sample		64.7 % female		76; interquartile range, 66-88)	
Bulgurcu, 2020 Assessment of Smell and Taste Disorders in COVID-19: A Cross-sectional Study	Turkey Cross-Sectional Study March- May 2020	418 patients mean age of 46.50 ± 15.20 (18–85 years' old) 47% female	n/a	4th week after recovery	Non-recovery of smell loss Non-recovery of taste loss
Buonsenso, 2021 Preliminary Evidence on Long Covid in children	Italy, Cross-Sectional Study, March and November, 2020	129 patients mean age of 11 ± 4.4 years 48.1 % female	Individuals hospitalised & non-hospitalised	Patients were assessed on average 162.5 ± 113.7 days after COVID-19 microbiological diagnosis	fatigue Insomnia Nasal congestion/rhinorrea Persistent muscle pain Headache Lack of concentration Weight loss Joint pain or swelling Skin rashes Chest tightness Constipation Persistent cough Altered smell Palpitations Chest pain Altered taste Hypersomnia Stomach/abdominal pain Diarrhoea Change in menstruation Number of persisting symptoms Symptoms distress child

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					Hair loss Skin peeling
Carvalho-Schneider, 2020 Follow-up of adults with noncritical COVID-19 two months after symptom onset	France, Prospective Cohort Study), March-June 2020	150 adults (≥18 years) Mean age (SD): 49 ±15 years 56% female	Individuals not requiring admission to ICU	Up to 2 months after symptom onset	fever Dyspnea Chest pain Flulike symptoms Digestive disorders Weight loss >5% anosmia/ageusia palpitations arthralgia Cutaneous signs Sick leave presence of one or more symptoms at follow-up # of patients who still felt ill or were in worse clinical condition that at COVID-19 onset
Chiesa-Estomba, 2020 Patterns of smell recovery in 751 patients affected by the COVID-19 outbreak	Unclear, Prospective Cohort Study	751 adults (>18 years old) The mean age of patients was 41 ± 13 (range: 18 – 60) 63.5% female	n/a	47 ± 7 days (range 30-71) from the first consultation, All patients had at least 30 days of follow-up after their last negative COVID-19 test	Persistent subjective smell loss Partial recovery of smell loss
Cortes-Telles, 2021 Pulmonary function and functional capacity in	Mexico, Prospective Cohort Study,	186 patients 47.0 ± 13	Mild/moderate/severe symptoms	30 and 90 days following the onset of acute	fatigue on effort dyspnoea myalgias

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
COVID-19 survivors with persistent dyspnoea	prior to December, 2020	39.0 % female		COVID-19 symptoms	cough chest pain sore throat sputum production diaphoresis headache rhinitis telogen effluvium anosmia/ageusia dermatological symptoms wheezing conjunctivitis diarrhea
D'Cruz, 2020 Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia	UK, Prospective Cohort Study, June-July 2020	119 adults (⩾18 years old) mean±SD age 58.7±14.4 years 38% female	Hospitalized with severe COVID-19 pneumonia	61 (51–67) days post-discharge	Persistent symptoms Disease-specific functional impairment Burdensome breathlessness Persistent cough Burdensome cough Fatigue Sleep disturbance Pain Depression Anxiety Cognitive impairment Post-Traumatic Stress Disorder
de Graaf, 2021 Short-term outpatient follow-up of COVID-19 patients: A multidisciplinary approach	United States of America, Prospective Cohort Study, March 23 2020 and June 23 2020	81 patients 60·8 ± 13 37.0 % female	High/severe symptoms	6 weeks after discharge	Post COVID functional status score chest pain dyspnea palpitations Anxiety

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					Depression PTSD Psychiatric morbidities Cognitive functioning Cognitive functioning by partners
Einvik, 2021 Prevalence and Determinants of Fatigue after COVID-19 in Non-Hospitalized Subjects: a Population-Based Study; 7921928 CSR - Reports results	Norway, Cross-Sectional Study, end of June, 2020	458 patients 49.6 (17.7 to 87.9) 56.0 % female	Non-hospitalized	1.5–6 months after COVID-19	PTSD
Froidure, 2021 Integrative respiratory follow-up of severe COVID-19 reveals common functional and lung imaging sequelae	Belgium, Prospective Cohort Study March 10 and June 30, 2020	134 patients 60 (IQR 53–68) 41.0 % female	Severe and critical COVID-19 patients	Three-month follow-up	fatigue dyspnea requiring oxygen supplementation at exercise chronic dry cough chest oppression FEF <2 SD impaired FVC (forced vital capacity) impaired FEV1 (forced expired volume in 1) impaired FEF25-75 (forced expiratory flow at 25–75% of forced vital capacity) impaired DLCO (lung diffusion capacity) ground glass opacities consolidations isolated reticulations

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					signs of fibrosis lung parenchyma lesions
Gambini, 2020 Ocular Surface Impairment After Coronavirus Disease 2019: A Cohort Study	Italy, Prospective, Cohort Study, April 2020, to May 2020	64 individuals The mean age in the post-COVID-19 group was 56.2 ± 14.2 years 34.4% female	Hospitalized with COVID-19	Days since symptoms onset: 60.3 ±6 13.6	Eye irritations Dry eye disease
Gonzalez, 2021 PULMONARY FUNCTION AND RADIOLOGICAL FEATURES IN SURVIVORS OF CRITICAL COVID-19: A 3-MONTH PROSPECTIVE COHORT	Spain, Prospective Cohort Study, February 2020 to April 2020	62 patients 60 (48-65) 25.8 % female	all critical COVID-19 survivors 3 months after discharge	3 months after hospitalization discharge	symptomatic Dry cough Wet cough Dyspnea Muscular fatigue Depression Anxiety fever wheeze abdominal pain receiving supplemental oxygen incidental pulmonary thromboembolism Density ground glass Density mixed ground glass Density consolidation Internal structures interlobular septal thickening Internal structures bronchiectasis Internal structures atelectasis Internal structures solid nodule

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					Nonsolid nodule Lesions reticular Lesions fibrotic DLCO - abnormal TLC - altered Severe decrease of oxygen saturation after 6MWT
Halpin, 2020 Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation	UK, Cross-Sectional Study, May-June 2020	100 adults (≥18 years old) Mean age: Ward patients, 70.5 years (20-93) ICU patients, 58.5 years (34-84) Female Ward (48.5%) ICU (40.6%)	Hospitalized with COVID-19	Between 29 and 71 days post-discharge (mean 48 days and SD 10.3 days).	Fatigue Breathlessness PTSD symptoms related to illness Neuropsychological symptoms Thoughts of self-harm New or worsened concentration problem New or worsened short-term memory problem Swallow problem Laryngeal sensitivity Voice change Communication difficulty SLT referral criteria Concern about weight/nutrition Appetite problem Dietetics referral criteria met New bowel control problem New bladder control problem Quality of life Worsened mobility Worsened self-care Worsened usual activities

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					Worsened pain/discomfort Worsened anxiety/depression Perceived health Decrease
Han, 2021 Six-Month Follow-up Chest CT findings after Severe COVID-19 Pneumonia; 7841877 CSR - Reports results	China, Prospective Cohort Study, December 25, 2019 and February 20, 2020	114 patients mean age, 54 years ± 12 30.0 % female	Severe COVID-19 patients who were discharged from the hospital	6-month follow-up	fibrotic-like changes or abnormalities residual ground glass opacity or interstitial thickening ground glass opacities consolidation reticulation Pleural effusion Emphysema Thickening of the adjacent pleura Interlobar pleural traction Honeycombing Pulmonary atelectasis Bronchiectasis dry cough expectoration slight dyspnea on exertion abnormal pulmonary diffusion
Havervall, 2021 Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers	Sweden, Prospective Cohort Study, April 2020-May 2020	1395 patients Seropositive: Median (IQR) 43 (33-52) years; seronegative: 47 (36-56) years 86 % female	Mild symptoms	8 months after positive antibody test	Any persistent symptom Anosmia Fatigue Ageusia Dyspnea Sleeping disorder Headache Palpitations Concentration impairment Muscle/ joint pain

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					memory impairment moderately or markedly disrupted work life moderate or marked disruption in any Sheehan Diasbility Scale Category and at least 1 moderate or severe symptom lasting at least 8 months
Horn, 2021 Is COVID-19 Associated With Posttraumatic Stress Disorder?	France, Prospective Cohort Study, March-May 2020	180 adults (≥18 years) Median age was 53 years (± 16) 56.1% female	n/a	7 weeks after onset of COVID-19 symptoms	Post-traumatic stress disorder
Huang, 2021 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study	China, Ambi-Directional Cohort Study, January- May 2020	1733 individuals median age of 57·0 (IQR 47·0–65·0) years 48% female	Hospitalized with COVID-19	At 6 months after acute infection, Time from symptom onset to follow-up, days 186·0 (175·0–199·0)	Reported 1 symptom at follow-up Fatigue or muscle weakness Sleep difficulties Hair loss Smell disorder Palpitations Joint pain Decreased appetite Taste disorder Dizziness Diarrhoea or vomiting Chest pain Sore throat or difficult to swallow Skin rash Myalgia Headache

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					Low grade fever Dyspnoea Mobility: problems with walking around Personal care: problems with washing or dressing problems with usual activity Pain or discomfort Anxiety or depression distance walked in 6 minutes
Jacobs, 2020 Persistence of symptoms and quality of life at 35 days after hospitalization for COVID-19 infection	US, Prospective Cohort Study, March–April 2020	183 adults 57yrs (48–68) median age 38.5% female	Hospitalized with COVID-19	35 ± 5 days after hospital discharge	Fatigue Shortness of breath Cough Lack of taste Muscular pain Diarrhea Lack of smell Phlegm Headache Joint pain Confusion Eye irritation Fever Ulcer General health - poor, fair Quality of life - poor, fair Physical health - poor, fair Mental health - poor, fair Social relationships - poor, fair Social active role - poor, fair Physical activity - not at all, a little

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					Emotional - always, often fatigue Dressing - some/much difficulty Walking - some/much difficulty Stairs - some/much difficulty Meal preparation - some/much difficulty Wash dishes - some/much difficulty Sweep - some/much difficulty Make bed - some/much difficulty Lift - some/much difficulty Lift and carry - some/much difficulty Walk fast - some/much difficulty
Jacobson, 2021 Patients with uncomplicated COVID-19 have long-term persistent symptoms and functional impairment similar to patients with severe COVID-19: a cautionary tale during a global pandemic	United States of America, Prospective Cohort Study, Aug, 2020-Nov-2020	118 patients 43.3 (14.4) 46.6 % female	Confirmed COVID-19 infection	Median of 119.3 days after initial COVID-19 diagnosis	Fatigue Dyspnea Loss of taste/smell Myalgias Memory problems Chest pain Hair loss Cough Headache Congestion/Rhinorrhea Nausea/Vomiting/Diarrhea Palpitations Sore throat Fever/Chills

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					Any Symptom Missed work due to health Any work impairment due to health Any activity impairment due to health
Khasawneh, 2020 The correlation between BMI and COVID-19 outcomes	Jordan, Retrospective Cohort Study, July - August 2020	210 individuals 34.7-years old, SD ± 18 years 37% female	n/a	>4 weeks post COVID-19 infection	Duration of symptoms
Klein, 2021 Onset, duration and unresolved symptoms, including smell and taste changes, in mild COVID-19 infection: a cohort study in Israeli patients	Israel, Prospective Cohort Study, March 2020 -April 2020	103 patients 35 ± 12 38.0 % female	Mild symptoms	Over a 6-month period	Any unresolved symptom Fatigue Smell changes breathing difficulty Taste changes Memory disorder Muscle aches Headache Musculoskeletal pain Hair loss Anxiety and depression Abdominal pain Concentration disorders Diarrhea Dizziness Ear pain Eye disorders Hearing disorder Low physical performance Mouth sores Nose blockage

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					Palpitations Paresthesia Throat ache Vomiting
Konstantinidis, 2020 Short-Term Follow-Up of Self-Isolated COVID-19 Patients with Smell and Taste Dysfunction in Greece: Two Phenotypes of Recovery	Greece, Prospective Cohort Study, March- May 2020	79 individuals mean age of 30.7 ± 5.3 years 46.7% female	Individuals with mild-to-moderate disease who were instructed to quarantine at home	4 weeks after COID-19 diagnosis	Persistent chemosensory deficits
Landi, 2021 Predictive Factors for a New Positive Nasopharyngeal Swab Among Patients Recovered From COVID-19	Italy, Retrospective Cohort, April 2020 - May 2020	131 adults 55.8 ± 14.8 years 39% female	Hospitalized with COVID-19	Days from COVID-19 onset 55.8± 10.8	Cough Fatigue Diarrhea Headache Smell disorders Dysgeusia Red eyes joint pain Short of breath Loss of appetite Sore throat Rhinitis Fever No clinical improvement
Lascarrou, 2021 Identifying Clinical Phenotypes in Moderate to Severe Acute Respiratory Distress Syndrome Related to COVID-19: The COVADIS Study	Multiple Prospective Cohort Study, between March 10, 2020 and April 15, 2020	416 patients 63 (55-71) 22.8 % female	Moderate to severe symptoms	28 ventilatory free days	Breathing with assistance

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
Liang, 2020 Three-month Follow-up Study of Survivors of Coronavirus Disease 2019 after Discharge	China, Prospective Cohort Study	76 adult (≥ 18 years old) median age was 41.3 ± 13.8 years (age range 24-76 years) 72% females	Hospitalized with COVID-19	follow-up at 3-months after hospital discharge	Return to work Impaired pulmonary function Abnormal Lung HRCT
Logue, 2021 Sequelae in Adults at 6 Months After COVID-19 Infection	United States of America, Prospective Cohort Study, between August and November 2020	177 patients 48.0 (15.2) 57.1 % female	Any	6 months after COVID-19 infection	Number of persistent symptoms Fatigue Loss of smell or taste Brain fog Quality of Life (HRQoL) Activity of daily living (ADL)
Mafort, 2021 One-month outcomes of patients with SARS-CoV-2 infection and their relationships with lung ultrasound signs	Brazil, Retrospective Cohort Study, prior to April 2020	447 patients 40 (34–50) years 68.2 % female	Need for hospitalization, ICU and death.	1 month after LUS screening	general fatigue dyspnoea cough fever
Mandal, 2020 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19	UK Cross-Sectional Study	384 patients Mean age of 59.9±16.1 years 38% female	Hospitalized with COVID-19	Median of 54 (IQR 47–59) days following hospital discharge	breathlessness Cough fatigue depression anosmia one or more of the following persistent symptoms (breathlessness, cough, fatigue & poor sleep quality)

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
Mazza, 2021 Persistent psychopathology and neurocognitive impairment in COVID-19 survivors: Effect of inflammatory biomarkers at three-month follow-up	Italy, Prospective Cohort Study, April 6-June 9, 2020	226 patients 58.52 ± 12.79 34.0 % female	COVID-19 pneumonia survivors after admission to the ED	Three months (90.1 ± 13.4 days) after hospital discharge	Depression PTSD Anxiety Obsessive compulsive Insomnia Verbal memory Verbal fluency Working Memory Attention and Information Processing Psychomotor coordination Executive Functions Symptoms in at least one psychopathological dimension At least one current major psychiatric disorder Major depressive disorder Anxiety Disorders Insomnia Other major psychiatric disorder
Moradian, 2020 Delayed Symptoms in Patients Recovered from COVID-19	Iran, Cross-Sectional February to April, 2020	200 patients 55.58±13.52 20 % female	Hospitalized due to COVID-19	6 weeks after discharge	Fever Dyspnea Cough myalgia activity intolerance fatigue weakness weight loss dizziness headache shivering

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					otalgia sore throat sputum sneezing rainfall odor disorder taste disorder nausea vomiting diarrhea anorexia dyspepsia anxiety one or more symptoms
Moreno-Perez, 2021 Post-acute COVID-19 syndrome. Incidence and risk factors: A Mediterranean cohort study	Spain, Prospective Cohort Study, February 2020 to April 2020	277 patients Median age 62.0 years (53.0–72.0) 47.3 % female	Mild to severe symptoms	77 days (IQR 72–85) after disease onset	Post-acute COVID-19 syndrome (PCS) not recovered relevant neurological symptoms Fatigue Anosmia-dysgeusia Myalgias-arthralgias Dyspnea Cough Any headache Mnesic complaints Diarrhoea Skin features Visual loss Fever
Niklassen, 2021 COVID-19: Recovery from Chemosensory Dysfunction.	Multiple Prospective Cohort Study,	111 patients	Any	3 days of diagnosis and 28	Anosmia Hyposmia

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
A Multicentre study on Smell and Taste	April 2020- October 2020	age of 44.5 years (standard deviation 15.0) ranging from 18 to 77 years 47.0 % female		to 169 days after infection	combined olfactory and gustatory dysfunction Gustatory dysfunction
Otte, 2020 Olfactory dysfunction in patients after recovering from COVID-19	Germany, Prospective Cohort Study	91 adults mean age was 43.01 years (±12.69) 49.5% female	Mild course of COVID-19 disease (non-hospitalized)	An average of 57.94 (±1.40) days since onset of symptoms	Self-reported olfactory and tasting impairment Hyposmia Anosmia
Petersen 2020 Long COVID in the Faroe Islands - a longitudinal study among non-hospitalized patients	Faroe Islands, Prospective Cohort Study, April- August 2020	180 individuals mean (SD, range) age was 39.9 years (19.4, 0-93), 54.4% female	n/a	number of days (mean (SD, range)) from onset of symptoms to last follow-up was 125 (17, 45-153) days	Loss of smell Loss of taste Fatigue Headache Had symptoms at last follow-up Had 1-2, 3-5, 6-8, 9-12 or 13+ symptoms at last follow-up Fever Headache Chills Myalgia Dry cough Rhinorrhea Anorexia Sore throat Arthralgia Dyspnea Diarrhea

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
					Cough with expectoration Nausea Chest tightness Rashes
Printza, 2021 Smell and taste loss recovery time in covid-19 patients and disease severity	Greece, Cross-Sectional Study, March 2020-April, 2020	150 patients Mean age of 51.6 ± 16.8 (ranging from 18 to 89 years) 38.0 % female	Mild/moderate/severe, and critical (ICU-treated) symptoms	2 months	non-recovery of sense of smell non-recovery of sense of taste
Qu, 2021 Health related quality of life of COVID-19 patients after discharge: A multicenter follow up study	China, Cross-Sectional Study, February 2020-March, 2020	540 patients 47.50 years (IQR: 37.00–57.00) 50.0 % female	Mild to severe symptoms; hospitalized	3 months after discharge	One or more uncomfortable symptoms Number of physical symptoms HRQoL - physical component summary (PCS) HRQoL - mental component summary (MCS) Fatigue Cough Sputum Dyspnoea Diarrhoea Shortness of breath Joint pain Dysbasia Palpitations Other symptoms
Raman, 2020 Medium-term effects of SARS-CoV-2 infection on	UK, Prospective Cohort Study,	58 individuals 55.4yrs (13-2)	Hospitalized individuals with moderate to	2-3 months from disease-onset	breathlessness Fatigue

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
multiple vital organs, exercise capacity, cognition, quality of life and mental health, post hospital discharge	March-May 2020	41.4% female	severe COVID-19 infection		desaturation at the end of a 6-minute walk test cognitive function - abnormal anxiety depression
Riestra-Ayora, 2021 Long-term follow-up of olfactory and gustatory dysfunction in COVID-19: 6 months case-control study of health workers	Spain, Case-Control March 15, 2020-October 15, 2020	320 patients Control & Case-group 46.5 (20–64) 41.62 (18–65) 80.0 % female	Any	6 months	olfactory symptoms
Rusetsky 2021 Smell Status in Children Infected with SARS-CoV-2	Russia Cross-Sectional Study, April-May 2020	79 children 12.9yrs ± 3.4 (range: 6-17 years) 53.2% female	Hospitalized with COVID-19	60 days after hospital discharge	hyposmia
Shah, 2020 A prospective study of 12-week respiratory outcomes in COVID-19-related hospitalisations	Canada, Prospective Cohort Study, March-May 2020	60 adults Median age was 67 years (IQR 54–74) 32% female	Hospitalized with COVID-19	12 weeks following symptom onset (permitted range 8–12 weeks)	Dyspnoea 6MWT - abnormal Cough
Song, 2021 Self-reported Taste and Smell Disorders in Patients with COVID-19: Distinct Features in China	China, Retrospective Cohort Study, January 2020-March, 2020	117 patients 61 years (IQR, 48–68) 50.8 % female	Laboratory-confirmed cases - severe and non-severe symptoms at the time of admission	30 days after discharge from hospital	Loss of smell Loss of taste

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
Stavem, 2020 Persistent symptoms 1.5–6 months after COVID-19 in non-hospitalised subjects: a population-based cohort study	Norway, Cross-Sectional Study until 1 June 2020	451 adults (≥18 years) 49.8 years (15.2) 56% female	non-hospitalised COVID- 19 patients	median 117 days (range 41–193) after symptom onset	Fever Loss/disturbance of taste Headache Dry cough Loss/disturbance of smell Myalgia Chills Dyspnoea Sore throat Arthralgia Runny nose Diarrhoea Abdominal pain Productive cough Vomiting/nausea Wheeze Confusion/changed consciousness Skin rash Vision disturbance/blurring ear pain seizures/cramps Conjunctivitis Any symptom
Stavem, 2021 Prevalence and risk factors for post-traumatic stress in hospitalized and non-hospitalized COVID-19 patients	Norway, Cross-Sectional Study, June, 2020	458 patients Mean age (range): 49.6 (17.7 to 87.9) 56.0 % female	Non-hospitalized	Median of 117.5 days (range = 41–200) after first symptom ofCOVID-19	Fatigue

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
Sykes, 2021 Post-COVID-19 Symptom Burden: What is Long-COVID and How Should We Manage It?	United Kingdom, Prospective Cohort Study, prior to November 2020	134 patients 59.6 (14.0) 34.3 % female	Any	Median of 113 days (range = 46–167) post-discharge	At least one residual symptom Dyspnoea Myalgia Anxiety Extreme fatigue Low mood Memory impairment Sleep disturbances Cough Attention deficit Pleuritic chest pain Sore throat Fever Anosmia Cognitive impairment Taste deficiency Rash Symptom clusters
Townsend, 2020 Persistent fatigue following SARS-CoV-2 infection is common and independent of severity of initial infection	Ireland, Cross-Sectional Study, March – May 2020	128 individuals mean age: 49.5 ± 15 years 54% female	COVID-19 severity (need for inpatient admission, supplemental oxygen or critical care) and fatigue following COVID-19	Median (IQR) was 71 days (68-85) to 73 days (56-88)	Fatigue Not feeling back to full health Not returning to work
Townsend, 2021 Persistent Poor Health Post-COVID-19 Is Not Associated with Respiratory Complications or Initial Disease Severity	Ireland, Cross-Sectional Study, March – May 2020	153 individuals (Admitted, non-ICU N = 55) Age - 56.4 years (15.5) 47.3% female	n/a	Median 78 days (IQR 66-108) after diagnosis	Significant oxygen desaturation during 6MWT Perceived lack of full health Fatigue

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
		(Admitted, ICU N = 19) Age - 54.5 years (11.6) 26.3% female (Non-admitted, N = 79) Age - 40.2 years (11.4) 72.2% female			
Townsend, 2021-2 Prolonged elevation of D-dimer levels in convalescent COVID-19 patients is independent of the acute phase response	Ireland, Prospective Cohort Study, May 2020-September, 2020	150 patients Mean 47.3 (SD 15.4) 56.7 % female	Any	Median 80.5 (range 44–155) days after initial diagnosis	Fatigue Breathlessness
Trunfio, 2021 Diagnostic SARS-CoV-2 Cycle Threshold Value Predicts Disease Severity, Survival, and Six-Month Sequelae in COVID-19 Symptomatic Patients; 7917896 CSR - Reports results	Italy, Cross-Sectional Study, March 2020	200 patients Median age was 56 years (43–69) 42.0 % female	Hospital admission, worst oxygen support required, and survival	(194 (181–198) days after COVID-19 onset	any sequelae dyspnea olfactory/gustatory dysfunction chronic cough others

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
Tudoran, 2021 Alterations of left ventricular function persisting during post-acute COVID-19 in subjects without previously diagnosed cardiovascular pathology; 8004210 CSR - Reports results	Romania, Cross-Sectional Study, February 2020-July, 2020	125 patients Median age 47 (40–51.5) 50.4 % female	Hospitalized for mild/moderate SARS-CoV-2 with pneumonia	6–10 weeks after discharge	Symptoms (most frequently fatigue, dyspnea, and palpitations)
Vaira 2020 Smell and taste recovery in coronavirus disease 2019 patients: a 60-day objective and prospective study	Italy, Prospective Cohort Study	138 adults (≥18 years) 51.2 years (8.8) with IQR 46.7–58.0 50.7% female	n/a	30-60 days after onset of symptoms	olfactory dysfunction taste disorder Combined chemosensitive dysfunction Isolated smell impairments Isolated taste disorders Persistent chemosensitive disorders
Walle-Hansen, 2021 Health-related quality of life, functional decline, and long-term mortality in older patients following hospitalisation due to COVID-19	Norway, Prospective Cohort Study, March 1- July 1, 2020	106 patients 74.3 (range 60–96) years 43.0 % female	Individuals admitted to hospital with COVID-19	6 months	Worse health-related quality of life Decline in mobility Decline in ability to perform daily activities More pain or discomfort Increased anxiety Decline in self-care ability Major change in mobility Major change in usual activities Negative change in cognitive function

First author, publication year, study title & link	Country, study design, study recruitment dates	Study Population (# with lab-confirmed COVID- 19; mean or median age or range; % female)	COVID-19 disease severity inclusion criteria	Time of outcome follow-up	Main symptoms/sequelae measured at follow-up
Wang, 2020 Impact of Covid-19 in pregnancy on mother's psychological status and infant's neurobehavioral development: a longitudinal cohort study in China	China, Prospective Cohort Study, May-July 2020	72 pregnant females 31 years (28, 34) 100% female	n/a	35 (± 5 days) after delivery/abortion	Post-traumatic stress disorder Postpartum depression Suffering from post-traumatic stress disorder or depression
Weerahandi, 2021 Post-Discharge Health Status and Symptoms in Patients with Severe COVID-19	US, Prospective Cohort Study	161 adults (≥18 years) 62 years (IQR], 50–677) 37% female	Hospitalized with severe COVID-19	median of 55 days (range 38–95) after hospital admission	Dyspnea Requiring oxygen
Zhang, 2021 Thin-section computed tomography findings and longitudinal variations of the residual pulmonary sequelae after discharge in patients with COVID-19: a short-term follow-up study	China, Cross-Sectional January 11- July 5, 2020	310 patients 51 (31.8, 61.0) 50.3 % female	(Severe and non-severe COVID-19)	1-4 weeks; 5-8 weeks; 9-12 weeks; >12 weeks	cumulative values of incomplete absorption cumulative values of non-absorption of fibrosis-like findings Incomplete absorption of lesions Density Fibrosis like findings Irregular interface of the pleural surfaces Irregular interface of the bronchovascular surfaces Irregular interface of the mediastinal surfaces

Table 2. Prevalence of various symptoms, sequelae and difficulties conducting usual activities post-COVID-19 infection in laboratory-confirmed individuals

Symptoms, sequelae and difficulties conducting usual activities	**Short-term (4-12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)	**Long-term (>12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)
One or more symptoms		
Persistence or presence of one or more symptoms at follow-up	61% [44%, 76%] (9 studies)(1-9) ■ *low certainty*	53% [41%, 65%] (14 studies)(3,4,10-21) ■ *low certainty*
Cluster of symptoms:		
Neurological (headache, memory disorders/cognitive deterioration)	12% [8%, 16%] (1 study)(2) ■	No studies
Myalgia, fatigue	No studies	31% [23%, 38%] (1 study)(14) ■
Low mood, anxiety, sleep disturbance	No studies	16% [10%, 22%] (1 study)(14) ■
Symptoms lasting >4 weeks	4% [1%, 6%] (1 study)(22) ■	No studies
Number of symptoms:		
1-2	39% [22%, 56%] (1 study)(4) ■	27% [21%, 35%] (4 studies)(4,13,15,16) ■
≥2	No studies	50% [41%, 59%] (1 study)(17) ■
≥3	26% [10%, 41%] (1 study)(4) ■	23% [17%, 31%] (5 studies)(4,13,15-17) ■
≥5	No studies	9% [7%, 12%] (1 study)(13) ■
>5	8% [4%, 12%] (1 study)(8) ■	6% [3%, 10%] (1 study)(15) ■
Fatigue		
All	41% [30%, 52%] (16 studies)(3,4,10,11,13-18,23,24) ■ *low certainty*	25% [19%, 34%] (12 studies)(3,4,10,11,13-18,21,23) ■ *low certainty*
By level of care received during the acute phase:		
Non-hospitalized	16% [11%, 21%] (1 study)(24) ■ *low certainty*	46% [42%, 51%] (1 study)(21) ■ *low certainty*
Both (hospitalized & non-hospitalized)	34% [21%, 50%] (8 studies)(2-4,25-29) ■ *low certainty*	17% [9%, 27%] (6 studies)(3,4,15-18) ■ *low certainty*
Hospitalized	53% [38%, 67%] (7 studies)(5,6,8,30-33) ■ *low certainty*	31% [25%, 39%] (3 studies)(13,14,23) ■ *low certainty*
Admitted to ICU	No studies	39% [23%, 59%] (2 studies)(10,11) ■ *very low certainty*
Fatigue or muscle weakness	No studies	63% [60%, 65%] (1 study)(12) ■
Weakness	16% [13%, 21%] (2 studies)(8,9) ■	No studies
Respiratory		
Shortness of breath:		
All	34% [25%, 45%] (17 studies)(1-3,5,6,8,25-27,30-37) ■ *low certainty*	18% [13%, 24%] (16 studies)(2,3,10-15,17-21,23,38,39) ■ *low certainty*

Symptoms, sequelae and difficulties conducting usual activities	**Short-term (4-12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)	**Long-term (>12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)
By level of care received during the acute phase:		
Non-hospitalized	24% [18%, 30%] (1 study)(34) ■ *very low certainty*	16% [13%, 20%] (1 study)(21) ■ *very low certainty*
Both (hospitalized & non-hospitalized)	21% [11%, 36%] (7 studies study)(1-3,8,25-27) ■ *low certainty*	10% [6%, 16%] (7 studies)(2,3,15,17-20) ■ *low certainty*
Hospitalized	44% [34%, 54%] (6 studies)(6,30-32,36,37) ■ *low certainty*	14% [8%, 26%] (3 studies)(12,13,38) ■ *low certainty*
Hospitalized (with moderate to severe COVID-19 or severe COVID-19 pneumonia)	60% [35%, 80%] (3 studies)(5,33,35) ■ *low certainty*	34% [14%, 62%] (3 studies)(14,23,39) ■ *low certainty*
Admitted to ICU	No studies	48% [41%, 55%] (2 studies)(10,11) ■ *low certainty*
Other respiratory symptoms/sequelae:		
Cough		
Any kind	21% [15%, 27%] (12 studies)(2,4-6,8,9,26,27,31,32,34,36) ■	7% [4%, 12%] (12 studies)(2,4,11,13-15,17,20,21,23,38,39) ■
Dry cough	21% [9%, 40%] (2 studies)(9,34) ■	8% [5%, 12%] (5 studies)(11,15,21,23,39) ■
Productive cough	No studies	8% [3%, 18%] (3 studies)(11,15,21) ■
Rhinitis or runny nose	10% [5%, 19%] (4 studies)(4,8,26,32) ■	7% [4%, 11%] (4 studies)(4,15,17,21) ■
Sore throat	8% [4%, 15%] (4 studies)(8,26,32,34) ■	3% [1%, 7%] (6 studies)(14,15,17,18,21,38) ■
Voice change	20% [12%, 28%] (1 study)(30) ■	No studies
Laryngeal sensitivity	17% [10%, 24%] (1 study)(30) ■	No studies
Phlegm	12% [7%, 21%] (3 studies)(8,26,31) ■	10% [8%, 12%] (2 studies)(13,39) ■
Blocked nose	14% [10%, 18%] (2 studies)(34,40) ■	1% [0%, 3%] (1 study)(18) ■
Requiring supplemental oxygen: - after discharge - at exercise	 14% [8%, 19%] (1 study)(35) ■ No studies	 8% [1%, 15%] (1 study)(11) ■ 3% [0%, 6%] (1 study)(23) ■
Still needing mechanical ventilation at 28 days post-ICU admission	58% [54%, 63%] (1 study)(41) ■	No studies
Wheezing	7% [12%, 23%] (1 study)(26) ■	3.% [2%, 5%] (2 studies)(11,21) ■
Sinonasal pain	3% [1%, 6%] (1 study)(34) ■	No studies
Sneezing	0.5% [0%, 3%] (1 study)(8) ■	No studies
Flu-like symptoms		
Flu-like symptoms	22% [14%, 29%] (1 study)(1) ■	No studies
Headaches	9% [6%, 14%] (8 studies)(2-4,8,26,31,32,34) ■	4% [2%, 7%] (9 studies)(2-4,12,15,17,18,21,38) ■

Symptoms, sequelae and difficulties conducting usual activities	**Short-term (4-12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)	**Long-term (>12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)
Fever	1% [0%, 3%] (7 studies)(1,2,8,27,31,32,34) ■	1% [0%, 5%] (6 studies)(11,12,14,15,21,38) ■
Fever/chills	No studies	1% [0%, 3%] (1 study)(17) ■
Chills	0.5% [0%, 1%] (1 study)(8) ■	2% [0%, 13%] (2 studies)(15,21) ■
Olfactory and Gustatory		
Smell or taste dysfunction	19% [12%, 28%] (8 studies)(1,2,26,34,42-45) ■ *low certainty*	13% [8%, 23%] (3 studies)(16,17,20) ■ *low certainty*
Smell dysfunction		
Any	13% [7%, 23%] (16 studies)(3,4,6,8,31,32,40,42,44-51) ■ *low certainty*	13% [9%, 19%] (10 studies)(3,4,12,14,15,18,21,38,45,48) ■ *low certainty*
Hyposmia	23% [8%, 49%] (3 studies)(42,45,50) ■ *low certainty*	18% [5%, 31%] (1 study)(45) ■ *very low certainty*
Anosmia	7% [3%, 14%] (4 studies)(3,6,42,45) ■ *low certainty*	7% [5%, 11%] (4 studies)(3,14,38,45) ■ *low certainty*
Taste dysfunction		
Any	7% [4%, 14%] (11 studies)(3,4,8,31,32,40,44-46,49,51) ■ *low certainty*	7% [5%, 10%] (8 studies)(3,4,12,14,15,18,21,38) ■ *low certainty*
Ageusia	8% [5%, 11%] (1 study)(3) ■ *low certainty*	4% [3%, 6%] (2 studies)(3,38) ■ *low certainty*
Dysgeusia	11% [6%, 17%] (1 study)(32) ■ *very low certainty*	No studies
Dysgeusia lasting >2 months	1% [0%, 2%] (1 study)(52) ■	No studies
Neurocognitive		
Cognitive impairment	29% [19%, 41%] (4 studies) (5,33,37,53) ■ *low certainty*	20% [5%, 54%] (4 studies)(14,16,54,55) ■ *very low certainty*
Concentration problems	11% [4%, 26%] (4 studies) (3,4,30,56) ■ *low certainty*	5% [1%, 19%] (4 studies)(3,4,14,18) ■ *low certainty*
Memory problem	11% [6%, 20%] (4 studies)(2,3,30,56) ■ *very low certainty*	12% [5%, 23%] (6 studies)(2,3,14,17,18,55) ■ *very low certainty*
Cluster of symptoms:		
Memory impairment, attention deficit, cognitive impairment	No studies	14% [8%, 20%] (1 study)(14) ■
Attention and Information Processing (poor performance)	No studies	33% [25%, 41%] (1 study)(55) ■
Confusion	9% [5%, 13%] (1 study)(31) ■ *very low certainty*	2% [1%, 4%] (1 study)(21) ■ *very low certainty*
Dizziness	3% [2%, 5%] (2 studies)(8,34) ■ *moderate*	3% [1%, 16%] (2 studies)(12,18) ■ *low certainty*

Symptoms, sequelae and difficulties conducting usual activities	**Short-term (4-12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)	**Long-term (>12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)
Dysbasia	No studies	4% [2%, 6%] (1 study)(13) ■
Psychomotor coordination (poor performance)	No studies	57% [48%, 66%] (1 study)(55) ■
Executive Functions (poor performance)	No studies	50% [41%, 59%] (1 study)(55) ■
Communication difficulty	6% [1%, 11%] (1 study)(30) ■	No studies
Verbal fluency (poor performance)	No studies	32% [24%, 40%] (1 study)(55) ■
Verbal memory (poor performance)	No studies	10% [4%, 16%] (1 study)(55) ■
Neuromuscular		
Muscle or joint pain	9% [4%, 23%] (3 studies)(2,3,34) ■ *very low certainty*	0.6% [0%, 1%] (1 study)(3) ■ *low certainty*
Muscle pain	18% [10%, 32%] (4 studies)(4,8,26,31) ■ *very low certainty*	9% [4%, 22%] (8 studies)(4,12,14,15,17,18,21,38) ■ *very low certainty*
Joint pain	18% [14%, 24%] (4 studies)(1,4,31,32) ■ *low certainty*	10% [6%, 16%] (6 studies)(4,12,13,15,21,38) ■ *low certainty*
Musculoskeletal pain	No studies	4% [0%, 8%] (1 study)(18) ■
Paresthesia	No studies	1% [0%, 3%] (1 study)(18) ■
Swallow problem Sore throat or difficulties with swallowing	8% [3%, 13%] (1 study)(30) ■ No studies	No studies 4% [3%, 5%] (1 study)(12) ■
Referral to a Speech and Language Therapist	23% [15%, 31%](30) (1 study) ■	No studies
Cardiovascular		
Palpitations	8% [3%, 19%] (3 studies)(1,3,37) ■ *very low certainty*	5% [3%, 11%] (6 studies)(3,4,12,13,17,18) ■ *moderate certainty*
Chest pain	14% [7%, 25%] (5 studies)(1,4,26,34,37) ■ *very low certainty*	6% [2%, 13%] (5 studies)(4,12,14,17,38) ■ *low certainty*
Chest tightness	16% [5%, 34%] (1 study)(4) ■ *very low certainty*	5% [3%, 8%] (3 studies)(4,15,23) ■ *moderate certainty*
Digestive		
Digestive disorders	12% [6%, 17%] (1 study)(1) ■	No studies
Appetite problem	10% [7%, 13%] (3 studies)(30,32,34) ■	8% [7%, 10%] (1 study)(12) ■
Diarrhea	5% [3%, 8%] (6 studies)(2,8,26,31,32,34) ■	2% [1%, 5%] (6 studies)(4,13,15,18,21,38) ■
Abdominal pain	4% [1%, 6%] (1 study)(34) ■	3% [1%, 5%] (3 studies)(11,18,21) ■
Weight loss	9% [6%, 13%] (3 studies)(1,4,8) ■	8% [3%, 14%] (1 study)(4) ■
New bladder control problem	10% [4%, 16%] (1 study)(30) ■	No studies
New bowel control problem	3% [0%, 6%] (1 study)(30) ■	No studies

Symptoms, sequelae and difficulties conducting usual activities	**Short-term (4-12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)	**Long-term (>12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)
Nausea	1% [1%, 3%] (2 studies)(8,34) ■	4% [1%, 8%] (1 study)(15) ■
Vomiting	1% [0%, 2%] (2 studies)(8,34) ■	1% [0%, 3%] (1 study)(18) ■
Cluster of symptoms:		
Diarrhea or vomiting	No studies	5% [4%, 6%] (1 study)(12) ■
Vomiting/nausea	No studies	2% [1%, 4%] (1 study)(21) ■
Nausea/Vomiting/Diarrhea	No studies	7% [2%, 11%] (1 study)(17) ■
Stomach/abdominal pain	3% [0%, 9%] (1 study)(4) ■	1% [0%, 3%] (1 study)(4) ■
Indigestion	1% [0%, 2%] (1 study)(8) ■	No studies
Constipation	No studies	6% [2%, 10%] (1 study)(4) ■
Ulcer	1% [0%, 3%] (1 study)(31) ■	No studies
Nutritional concerns:		
Necessitating a dietetics referral	16% [9%, 23%] (1 study)(30) ■	No studies
Concern about weight/nutrition	12% [6%, 18%] (1 study)(30) ■	No studies
Organ damage		
No studies		
Eye-related		
Eye irritations	21% [3%, 68%] (2 studies)(31,57) ■	No studies
Red eyes	8% [2%, 33%] (2 studies)(32,57) ■	No studies
Conjunctivitis	4% [1%, 7%] (1 study)(26) ■	2% [1%, 4%] (1 study)(21) ■
Vision disturbance/blurring	No studies	4% [2%, 6%] (1 study)(21) ■
Visual loss	5% [3%, 8%] (1 study)(2) ■	No studies
Dry eye disease:		
From objective tests	62% [51%, 74%] (1 study)(57) ■	No studies
From subjective tests	47% [35%, 59%] (1 study)(57) ■	No studies
Eye disorders	No studies	1% [0%, 3%] (1 study)(18) ■
Mental Health		
At least one mental health symptom (depression/anxiety/PTSD/obsessive compulsive)	No studies	36% [30%, 42%] (1 study)(55) ■
At least one current major psychiatric disorder (DSM-5 criteria for diagnosis)	No studies	24% [19%, 30%] (1 study)(55) ■
Anxiety	19% [10%, 32%] (4 studies)(5,8,33,37) ■ *low certainty*	32% [22%, 43%] (4 studies)(11,14,54,55) ■ *very low certainty*
Major anxiety disorder (DSM-5 criteria for diagnosis)	No studies	9% [5%, 13%] (1 study)(55) ■
Depression	23% [14%, 34%] (5 studies)(5,6,33,37,53) ■ *low certainty*	17% [13%, 22%] (3 studies)(11,55,58) ■ *low certainty*
Major depressive disorder (DSM-5 criteria for diagnosis)	No studies	9% [5%, 13%] (1 study)(55) ■

Symptoms, sequelae and difficulties conducting usual activities	**Short-term (4-12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)	**Long-term (>12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)
Anxiety or depression Anxiety and depression	22% [19%, 25%] (2 studies)(30,56) ■ *low certainty* No studies	23% [21%, 25%] (1 study)(12) ■ 2% [0%, 5%] (1 study)(18) ■
Postpartum depression	No studies	17% [8%, 27%] (1 study)(58) ■
Post-traumatic stress disorder	23% [14%, 35%] (5 studies)(5,30,37,53,59) ■ *low certainty*	18% [7%, 41%] (4 studies)(38,55,58,60) ■ *very low certainty*
Depression or post-traumatic stress disorder	No studies	22% [12%, 32%] (1 study)(58) ■ *very low certainty*
Obsessive compulsive	No studies	26% [18%, 34%] (1 study)(55) ■ *low certainty*
Feelings of distress due to symptoms (only a little/quite a lot/a great deal)	35% [19%, 52%] (1 study)(4) ■	42% [32%, 52%] (1 study)(4) ■
Overall mental health (poor/fair) Mental health - poor	17% [12%, 22%] (1 study)(31) ■ No studies	No studies 33% [27%, 37%] (1 study)(13) ■
Psychiatric morbidities	17% [7%, 27%] (1 study)(37) ■	No studies
Other mental health symptoms		
Low mood	No studies	40% [31%, 48%] (1 study)(14) ■
Panic attack	13% [11%, 16%] (1 study)(56) ■	No studies
Always/often emotional	14% [9%, 19%] (1 study)(31) ■	No studies
Thoughts of self-harm	2% [0%, 5%] (1 study)(30) ■	No studies
Anorexia	2% [0%, 4%] (1 study)(8) ■	No studies
Quality of life (QoL)		
Decreased or worsened QoL Worse health-related QoL	53% [43%, 63%] (1 study)(30) ■ No studies	30% [23%, 37%] (1 study)(16) ■ 54% [44%, 63%] (1 study)(54) ■
QoL (poor or fair)	23% [17%, 29%] (1 study)(31) ■	No studies
Social relationships (poor or fair)	60% [53%, 68%] (1 study)(31) ■	No studies
Social active role (poor or fair)	31% [25%, 38%] (1 study)(31) ■	No studies
Disrupted social life (moderately or markedly)	15% [11%, 19%] (1 study)(3) ■	No studies
Disrupted home life (moderately or markedly)	12% [9%, 16%] (1 study)(3) ■	No studies
Sleep-related		
Sleep disturbances or difficulties	18% [4%, 51%] (3 studies)(3,5,56) ■ *very low certainty*	15% [6%, 34%] (3 studies)(3,12,14) ■ *low certainty*
Insomnia Major insomnia disorder (DSM-5 criteria for diagnosis)	12% [5%, 25%] (2 studies)(4,56) ■ *low certainty* No studies	22% [17%, 28%] (2 studies)(4,55) ■ *moderate certainty* 3% [1%, 5%] (1 study)(55) ■
Hypersomnia	3% [0%, 9%] (1 study)(4) ■	3% [0%, 6%] (1 study)(4) ■
Nightmare	2% [1%, 3%] (1 study)(56) ■	No studies
Overall functioning		

Symptoms, sequelae and difficulties conducting usual activities	**Short-term (4-12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)	**Long-term (>12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)
General functional impairment (i.e. difficulties conducting usual activities)	35% [18%, 56%] (5 studies)(5,8,9,30,37) ■ *low certainty*	17% [5%, 44%] (6 studies)(3,12,16,17,38,54) ■ *very low certainty*
Still felt ill or not back to full health	41% [28%, 55%] (5 studies)(1,2,9,28,29) ■ *low certainty*	No studies
Decrease in perceived health	39% [29%, 49%] (1 study)(30) ■	No studies
General perception of health (poor/fair or poor)	10% [2%, 39%] (2 studies)(9,31) ■	No studies
Physical health (poor/fair or poor)	27% [21%, 34%] (1 study)(31) ■	15% [12%, 18%] (1 study)(13) ■
Decreased tolerance to exercise	No studies	21% [16%, 26%] (1 study)(38) ■
Physical activity (none/little) or inactive	14% [9%, 19%] (1 study)(31) ■	18% [14%, 22%] (1 study)(19) ■
Low physical performance	No studies	1% [0%, 3%] (1 study)(18) ■
Difficulties with the following activities related to mobility:		
Worsened or decline in mobility	37% [28%, 46%] (1 study)(30) ■	22% [14%, 30%] (1 study)(54) ■
Walking	15% [13%, 18%] (2 studies)(31,56) ■	7% [6%, 8%] (1 study)(12) ■
Walking fast	46% [37%, 54%] (1 study)(31) ■	No studies
Confined to bed (unable to walk)	2% [1%, 3%] (1 study)(56) ■	No studies
Climbing stairs	30% [23%, 37%] (1 study)(31) ■	No studies
Lifting	20% [14%, 27%] (1 study)(31) ■	No studies
Lifting and carrying	25% [19%, 32%] (1 study)(31) ■	No studies
Sweeping	12% [7%, 17%] (1 study)(31) ■	No studies
Making the bed	6% [2%, 10%] (1 study)(31) ■	No studies
Poor results in the 6-minute walk test:		
Unable to complete test	No studies	49% [40%, 58%] (1 study)(10) ■
Walked less than the normal range	No studies	23% [21%, 25%] (1 study)(12) ■
Desaturation or abnormal results at the end of the test	7% [4%, 13%] (2 studies)(33,36) ■	12% [0%, 88%] (2 studies)(11,61) ■
Desaturation during the test	3% [0%, 6%] (1 study)(28) ■	No studies
Difficulties with the following activities related to self-care:		
Worsened or decline in self-care	16% [9%, 23%] (1 study)(30) ■	17% [10%, 24%] (1 study)(54) ■
Washing or dressing oneself	10% [7%, 12%] (1 study)(56) ■	1% [0%, 1%] (1 study)(12) ■
Dressing oneself	3% [1%, 7%] (1 study)(31) ■	No studies
Meal preparation	6% [3%, 10%] (1 study)(31) ■	No studies
Washing dishes	4% [1%, 8%] (1 study)(31) ■	No studies
Employment-related:		
Not returned to work	31% [23%, 40%] (1 study)(28) ■ *very low certainty*	9% [3%, 16%] (1 study)(62) ■ *very low certainty*
Sick-leave	11% [5%, 16%] (1 study)(1) ■ *very low certainty*	No studies

Symptoms, sequelae and difficulties conducting usual activities	**Short-term (4-12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)	**Long-term (>12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)
Any work impairment due to health	No studies	39% [28%, 50%] (1 study)(17) ■ *low certainty*
Missed work due to health	No studies	12% [4%, 19%] (1 study)(17) ■ *very low certainty*
Disrupted work life (moderately or markedly)	8% [5%, 11%] (1 study)(3) ■	No studies
Complications from COVID-19⁺		
Interstitial lung disease	Not applicable	12% [6%, 17%] (1 study)(10) ■
Deep vein thrombosis	Not applicable	7% [3%, 12%] (1 study)(10) ■
Pulmonary hypertension	Not applicable	7% [3%, 12%] (1 study)(10) ■
Pulmonary embolism	Not applicable	3% [2%, 7%] (2 studies)(10,11) ■
Pleural effusion	Not applicable	0% [0%, 0%] (1 study)(39) ■
Emphysema	Not applicable	2% [0%, 4%] (1 study)(39) ■
Computed tomography findings:		
Abnormal findings	Not applicable	24% [3%, 78%] (2 studies)(61,62) ■
Incomplete absorption	Not applicable	61% [52%, 69%] (1 study)(63) ■
Ground glass opacities	Not applicable	49% [29%, 70%] (4 studies)(11,23,39,63) ■
Fibrosis-like findings	Not applicable	28% [20%, 37%] (3 studies)(23,39,63) ■
Bronchial dilation	Not applicable	11% [6%, 17%] (1 study)(63) ■
Parenchymal band	Not applicable	32% [24%, 40%] (1 study)(63) ■
Irregular interfaces	Not applicable	20% [13%, 28%] (1 study)(63) ■
Interlobular septal thickening	Not applicable	81% [70%, 91%] (1 study)(11) ■
Thickening of the adjacent pleura	Not applicable	32% [24%, 41%] (1 study)(39) ■
Bronchiectasis	Not applicable	47% [10%, 87%] (2 studies)(11,39) ■
Atelectasis	Not applicable	17% [8%, 34%] (2 studies)(11,39) ■
Nodules	Not applicable	28% [10%, 57%] (2 studies)(11,39) ■
Lesions:		
Reticular	Not applicable	49% [36%, 62%] (1 study)(11) ■
Fibrotic	Not applicable	4% [0%, 8%] (1 study)(11) ■
Lung parenchyma	Not applicable	38% [29%, 48%] (1 study)(23) ■
Interlobar pleural traction	Not applicable	17% [10%, 24%] (1 study)(39) ■
Honeycombing	Not applicable	3% [0%, 6%] (1 study)(39) ■
At least one lobe affected by ground glass or consolidative opacities	Not applicable	60% [47%, 72%] (1 study)(11) ■
Pulmonary function test findings:		
Impaired pulmonary function	Not applicable	42% [31%, 53%] (1 study)(62) ■
Less than expected or abnormal findings:		
Diffusing capacity (DLCO)	Not applicable	52% [38%, 65%] (5 studies)(11,23,38,39,61) ■
Total lung capacity (TLC)	Not applicable	37% [25%, 49%] (1 study)(11) ■
Forced vital capacity (FVC)	Not applicable	13% [5%, 29%] (2 studies)(23,61) ■

Symptoms, sequelae and difficulties conducting usual activities	**Short-term (4-12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)	**Long-term (>12 weeks after COVID-19 diagnosis)** (prevalence* in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment where applicable*)
Forced expiratory volume (FEV1) FVC/FEV1 Forced expiratory flow (FEF)	Not applicable Not applicable Not applicable	10% [4%, 24%] (2 studies)(23,61) ■ 0% [0%, 0%] (1 study)(61) ■ 4% [1%, 8%] (1 study)(23) ■
Other symptoms/sequelae		
General pain/discomfort	40% [24%, 58%] (2 studies)(5,56) ■ *low certainty*	28% [23%, 34%] (2 studies)(12,54) ■ *moderate certainty*
Worsened pain/discomfort	19% [11%, 27%] (1 study)(30) ■	No studies
Hair fall/loss	10% [8%, 12%] (2 studies)(26,56) ■	7% [3%, 19%] (4 studies)(4,12,17,18) ■
Skin-related	10% [8%, 13%] (3 studies)(1,2,26) ■	No studies
Sweating	17% [12%, 23%] (1 study)(26) ■	No studies
Rashes	3% [0%, 9%] (1 study)(4) ■	4% [2%, 7%] (5 studies)(4,12,14,15,21) ■
Change in menstruation	No studies	3% [0%, 8%] (1 study)(4) ■
Skin peeling	No studies	1% [0%, 2%] (1 study)(4) ■
Seizures/cramps	No studies	1% [0%, 2%] (1 study)(21) ■
Ear pain	0.5% [0%, 1%] (1 study)(8) ■	1% [0%, 2%] (2 studies)(18,21) ■
Hearing disorder	No studies	1% [0%, 3%] (1 study)(18) ■
Mouth sores	No studies	1% [0%, 3%] (1 study)(18) ■

Risk of Bias in the majority of studies reporting the outcome: ■ >50% were at low risk of bias; ■ >50% were at moderate risk of bias; ■ ≥50% were at high risk of bias

* Prevalence estimate and 95% confidence interval for the outcome; results of a random effects meta-analysis of proportions were provided where 2 or more studies were included.; [+] Prevalence data in the short-term for these outcomes were out of scope for this review.

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Table 3. Most prevalent symptoms post-COVID-19 infection in children

Symptoms, sequelae and difficulties conducting usual activities	**Prevalence (≥4 weeks after COVID-19 diagnosis)*** (prevalence in %, [95% CI], (number of studies), risk of bias across studies [low ■, moderate ■ or high ■], *GRADE assessment*)
Persistence or presence of one or more symptoms at follow-up	58% [50%, 67%] (1 study) ■ *low certainty*
Insomnia	19% [12%, 25%] (1 study) ■ *low certainty*
Nasal congestion or runny nose	12% [7%, 18%] (1 study) ■ *low certainty*
Fatigue	11% [5%, 16%] (1 study) ■ *low certainty*
Concentration difficulties	10% [5%, 15%] (1 study) ■ *low certainty*
Headache	10% [5%, 15%] (1 study) ■ *low certainty*
Muscle pain	10% [5%, 15%] (1 study) ■ *low certainty*
Weight loss	8% [3%, 12%] (1 study) ■ *low certainty*

* all findings were from a single study (Buonsenso 2021)