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

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Abstract

Background: Patients have described symptoms persisting or recurring for weeks after acute COVID-19 illness referred to as post COVID-19 conditions. The objective of this living systematic review is to document the prevalence of post COVID-19 conditions 4-12 weeks (short-term) and >12 weeks (long-term) after COVID-19 diagnosis.

Methods: We conducted a systematic review of primary peer-reviewed published literature reporting on the prevalence of the symptoms, sequelae and difficulties conducting usual activities ≥4 weeks after COVID-19 diagnosis. 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 research published until January 15, 2021 in Embase, Medline, PsychInfo, and Cochrane Central. Two independent reviewers screened references; one reviewer extracted data and assessed risk of bias and certainty in the evidence while another verified them. Prevalence data from laboratory-confirmed individuals were meta-analyzed, where appropriate, using a random effects model and synthesized separately in the short- and long-term periods after COVID-19 diagnosis; data from clinically-diagnosed populations were synthesized narratively.

Results: Of the 2807 unique citations, 36 observational studies met our inclusion criteria. Over 100 post COVID-19 conditions were reported in laboratory-confirmed individuals. Eighty-three percent (95%CI: 65-93%; *low certainty*) and 56% (95%CI: 34-75%; *very low certainty*) reported persistence or presence of one or more symptoms in the short- and long-term, respectively. The most prevalent symptoms in both periods included: fatigue, general pain or discomfort, sleep disturbances, shortness of breath and anxiety or depression (point estimates ranging from 22-51%; *low* to *very low certainty*).

Interpretation: Our data indicate that a substantial proportion of individuals reported a variety of symptoms ≥4 weeks after COVID-19 diagnosis. Due to low certainty in the evidence, further research is needed to determine the true burden of post COVID-19 conditions.

Introduction

The coronavirus disease 2019 (COVID-19) caused by infection with severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) has resulted in over 3 million deaths worldwide as of May 2021 (1). In Canada, COVID-19 has accounted for over 1.3 million cases and twenty-five thousand deaths as of May 2021 (2). The typical duration of acute COVID-19 illness is two to six weeks; however, some patients have described debilitating symptoms persisting or recurring for weeks or months after acute illness (3). In this review, we used the term "post COVID-19 conditions" to describe persistent symptoms; however, these are also referred to as long COVID, post-COVID conditions, chronic COVID syndrome and post-acute sequelae of SARS-CoV-2 infection (PASC) (4-7). Definitions of 'long-term' also vary from ≥4 to ≥12 weeks after COVID-19 diagnosis (8-10). Affected patients are commonly referred to as "COVID-19 long-haulers" (11-13).

It's been estimated that over one million people in each of the United States (14) and United Kingdom (15) suffer from post COVID-19 conditions. The burden of these conditions will likewise be great in Canada and will have serious ramifications on health care utilization and workforce productivity. A good understanding of the prevalence of these conditions, its effects on COVID-19 survivors, and its resolution over time is important to address this issue. Other reviews (8,16-18) are older, lack a systematic approach or have not accounted for the evidence quality. Therefore, the objective of this living systematic review is to document the prevalence of post COVID-19 conditions (4-12 and >12 weeks), including the frequency of symptoms, sequelae and difficulties individuals living with post COVID-19 conditions have conducting usual activities, according to a globally accepted standard of systematic review methodology.

Methods

We adhered to Cochrane methodology and the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) guidelines for this systematic review (19,20). The review team was multidisciplinary and included methodologists and subject matter experts currently treating patients with post COVID-19 conditions. We determined the review question and methodology *a priori* (protocol registered in PROSPERO: CRD42021231476) (21). This is the first publication of this living review that will be periodically updated as critical additions to the literature are published. More detailed methods and any associated files are provided in Supplementary File 1 – Detailed methodology.

Search strategy

We conducted a formative search and identified a systematic review conducted by the National Institute for Health and Care Excellence (NICE) (10) that could be adapted and updated. We adapted the NICE search strategy (which included a search of relevant literature published between January 1st to October 21st, 2020) and used it to search for new research published between October 22, 2020 to January 15, 2021 in the following databases: Embase, Medline, PsycINFO, and Cochrane Central. All studies included in the NICE review and any French articles they excluded were eligible for inclusion. We conducted a complementary search for grey literature in January 2021 and any relevant literature that was eligible for inclusion.

Study selection and data collection process

We included primary studies published since January 1st, 2020 in English or French, which included 50 or more participants with laboratory confirmed SARS-CoV-2 infection (termed "laboratory-confirmed") or with COVID-19 clinically-diagnosed by a health professional (termed "clinically-diagnosed"), and reported the prevalence of long-term symptoms or sequelae 4 weeks or more from COVID-19 diagnosis. We excluded pre-print and non-peer reviewed articles and primary studies that recruited participants specifically because they reported long-term effects 4 or more weeks after COVID-19 diagnosis.

A priori, we developed title and abstract and full text screening forms and two data extraction forms that were piloted by all reviewers. Two reviewers screened citations and full texts independently. One reviewer extracted data which were verified by a second reviewer. Reviewers resolved conflicts through consensus or consultation with a third reviewer. We defined several terms as follows: (a) time since COVID-19 diagnosis was used synonymously as time since symptom onset, positive laboratory result or diagnosis by a health professional and (b) outcomes measured between 4 and 12 weeks and more than 12 weeks since COVID-19 diagnosis were defined as short-term and long-term, respectively.

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 4 or more weeks after a COVID-19 diagnosis, with key symptoms or sequelae of interest identified as the following: fatigue shortness of breath, neurocognitive impairment, pain (in the joints, chest or muscles), organ damage, dizziness, tachycardia, chest tightness or heaviness, olfactory and taste 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 only.

Evidence synthesis

Our primary synthesis focused on outcomes in individuals who had laboratory-confirmed COVID-19 to minimize likelihood of capturing long-term sequelae from unrelated conditions. We synthesized short- and long-term outcomes separately, and where multiple outcomes were available within a study, we used results from the longest follow-up time point. We conducted meta-analyses for outcomes with two or more studies using a random effects model, where appropriate. We determined, *a priori,* potential sub-group analyses if data were available, and we considered these for some key outcomes to explore reasons for high heterogeneity across studies. We performed the analyses using R statistical software version 4.0.4 (22), with package metafor version 2.4-0 (23) and package meta version 4.18-0 (24). We presented pooled results in forest plots with 95% confidence intervals. We conducted additional narrative syntheses for the outcomes in the clinically-diagnosed population but we did not explore heterogeneity across 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 (25) to assess risk of bias for each study (questions 1, 2 and 9) and for each outcome reported by the study (questions 6, 7 and 8). We omitted questions 3-5 to avoid duplication with the criteria used to assess the certainty of the evidence. We divided the questions into three domains (participants,

outcome measures and statistics) and rated studies as having low risk of bias if sufficient criteria were met for all three domains. We assessed certainty in the body of evidence for select outcomes (i.e. key symptoms or sequelae or those found to be most prevalent) using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (26). We adapted the GRADE framework for assessment of incidence estimates in the context of prognostic studies to assess prevalence estimates (27). After piloting the tools, one reviewer assessed and graded the evidence which was verified by a second reviewer. Reviewers resolved conflicts through consensus or consultation with a third reviewer.

Results

Study Selection

We found 2807 unique citations and 390 met criteria for full-text screening (Figure 1). Thirty-six studies met our inclusion criteria; 28 included prevalence data for individuals with laboratory-confirmed COVID-19 (28-55) and 8 included prevalence data for individuals who were clinically-diagnosed with COVID-19 (56-63).

Prevalence in individuals who had laboratory-confirmed COVID-19

Study Characteristics

Study characteristics from 28 studies on laboratory-confirmed COVID-19 cases are shown in Table 1. All studies were observational (cohort or cross-sectional) and included between 58 and 1733 individuals, with the majority of studies having less than 200 participants (21/28). The majority were conducted in Europe (16/28), with the remaining in Asia (6/28), North America (3/28 of which 1 was in Canada) and others (3/28). More than half of the studies only recruited adult participants (17/28), 10/28 did not restrict recruitment by age, and 1/28 studies focused on a pediatric sample. Forty-three percent of studies (12/28) only recruited participants who were hospitalized or admitted to the intensive care unit (ICU) due to COVID-19. Seventy-nine percent (22/28) of studies measured short-term outcomes (i.e., between 4-12 weeks from COVID-19 diagnosis) and 21% (6/28) measured outcomes beyond 12 weeks (5/6 measured outcomes up to 6 months).

Risk of Bias and certainty in the evidence

Of the 28 studies, we assessed 19 to be at moderate risk of bias and nine to be at high risk of bias [supplementary tables – RoB assessments]. We found that 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) in the body of evidence for 63 key outcomes; there was moderate certainty in 5% (3/63), low certainty in 40% (25/63) and very low certainty in 55% (35/63) of these key outcomes. (Table 2, Supplementary tables – GRADE certainty in the evidence)

Prevalence of symptoms, sequelae and difficulties conducting usual activities

Over 100 symptoms, sequelae or difficulties conducting usual activities were reported (Table 2).

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

Approximately 4 in 5 individuals (83%, 95% CI: 65-93%, *low certainty*) reported the persistence or presence of one or more symptoms in the short-term. The most prevalent symptoms in the short-term were fatigue (51%, 95% CI: 39-64%, *low certainty*), general pain or discomfort (40%, 95% CI: 24-58%, *low certainty*), shortness of breath (38%, 95% CI: 27-51%, *very low certainty*), sleep disturbances (36%, 95% CI: 10-74%, *low certainty*), anxiety (29%, 95% CI: 16-48%, *very low certainty*) and cough (28%, 95% CI: 22-35%, *low certainty*). Fifty-two percent of individuals (95% CI: 35-68%, *low certainty*) reported feeling ill or not back to full health in the short-term.

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

Approximately 3 in 5 individuals (56%, 95% CI: 34-75%, *very low certainty*) reported persistence or presence of one or more symptoms in the long-term. The most prevalent symptoms were fatigue (47%, 95% CI: 27-68%, *very low certainty*), general pain or discomfort (27%, 95% CI: 25-29%, *low certainty*) and sleep disturbances (26%, 95% CI: 24-29%, *low certainty*). The following symptoms had similar prevalence of 22%-23% (*low to very low certainty*): anxiety or depression, depression or post-traumatic stress disorder (PTSD), shortness of breath and hair fall/loss. The most prevalent complication from acute COVID-19 was unresolved impaired pulmonary function (42%, 95%CI: 25-29%, *very low certainty*).

Investigations into potential reasons for heterogeneity

Based on our sub-group analyses for fatigue and shortness of breath, stratifying 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. such that patients with more severe COVID-19 were more likely to require hospitalized care), appeared to explain some of the heterogeneity (Figure 2). However, we still observed moderate to high heterogeneity within some of the sub-groups, particularly among hospitalized populations. Differences in how outcomes were measured (i.e. self-reported versus validated tests) and the thresholds used by each study to indicate an adverse outcome (e.g. binary versus a multi-point scale) may also 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 also have contributed to differences in prevalence estimates across studies; however, there were insufficient data to conduct subgroup analyses at each separate time point. Despite methodological and clinical variability, I^2 was low to moderate in 44% of the pooled outcomes. [supplementary figures – all forest plots]

Prevalence in populations who had clinically-diagnosed COVID-19

The characteristics of the eight included studies with prevalence data for individuals who had clinically-diagnosed COVID-19 are presented in supplementary tables (Table S1). All but one study (7/8) recruited participants who were hospitalized for COVID-19 and half were conducted in Europe (4/8). One of eight studies reported on short-term outcomes only, 2/8 reported on both short- and long-term outcomes and 5/8 reported on long-term outcomes only. Five of eight studies were assessed to be at moderate risk of bias while 3/8 were at high risk of bias. [supplementary tables – RoB assessments]

Sixty-four outcomes were reported in the clinically diagnosed population. (supplementary Table S4)

Interpretation

In this systematic review, most laboratory-confirmed COVID-19 patients continued to experience one or more symptoms in the short- (83%) and long-term (56%) after diagnosis. Although the most commonly reported symptoms included fatigue, general pain or discomfort, sleep disturbances, shortness of breath and mental health symptoms such as anxiety and depression, many other mild to severe and debilitating symptoms were experienced by a large proportion of convalescent COVID-19 cases. Consequently, roughly 30% and 10% of individuals were unable to return to work in the short- and long-term following COVID-19 diagnosis, respectively. However, due to low certainty in the evidence, true clarity around the burden of post COVID-19 conditions will require further work to untangle the sequelae caused directly by COVID-19 infection from those arising from related factors such as extensive hospital care due to severe illness. The prevalence and complex nature of these conditions 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 conditions.

Several systematic reviews (64,65) and rapid reviews (16,17) evaluating the long-term effects of COVID-19 similarly reported fatigue, shortness of breath, sleeping disorders, anxiety and smell and taste abnormalities as the most frequently reported symptoms. The prevalence estimates for the various symptoms and sequelae reported in these reviews differed slightly from ours; these discrepancies may in part be explained by methodological differences. To minimize heterogeneity in the outcomes, and to minimize bias in capturing symptoms that may be due to other causes, we chose to synthesize prevalence data separately for laboratory-confirmed and clinically-diagnosed populations. We consulted with clinical experts to determine which outcomes could be grouped together and/or statistically combined through meta-analyses, and where appropriate, we pooled outcomes to provide an indication of the precision of the estimate across studies. Finally, we critically assessed each study for risk of bias and we provided certainty in the evidence for select outcomes in our review using the GRADE approach which will provide clinicians and policy-makers with a sense of how much value can be placed on the results of this review considering the limitations of the data available.

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 (10). To minimize the potential for missing relevant studies, we used a peer-reviewed search strategy, supplemented with grey-literature searches, and ensured two reviewers agreed prior to excluding any studies. Another limitation is the inclusion of only English and French articles that may have introduced a language bias, however only 17 potentially relevant articles were excluded on the basis of language. 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 evidence gaps or limited data for many outcomes in this systematic review. The majority of studies in this review included adults or individuals who were hospitalized or treated for moderate-to-severe COVID-19; therefore, the prevalence of long-term effects in children, 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. We found few studies reporting on long-term effects beyond 12 weeks post-infection. Many of the studies included in our review had small sample sizes (<200 participants) or were at risk of bias due to the selection of participants and outcome measures used. Given the lack of contemporaneous control groups, it was not possible to determine whether symptoms were due 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).

This research area is rapidly evolving with new evidence, thus it is expected that future research will reduce the heterogeneity in the results and further refine the understanding of post COVID-19 conditions. Research investigating evidence gaps, including the prevalence of long-term effects in subsets of the population (i.e. children, indigenous and other racialized populations, those with underlying conditions), in those who presented with mild symptoms or asymptomatic infections in the acute phase, and symptoms and sequelae beyond 6 months post-infection, are needed to determine how post COVID-19 conditions differ across populations and how they can change or resolve over time. Confidence in the review findings would be improved by studies designed to minimize bias in participant selection and that use validated measures and tools to assess symptoms and sequelae. We aim to update our findings regularly as new evidence arises, including an update in the fall of 2021.

Health policy Implications

Understanding the burden and characteristics of post COVID-19 conditions is a good starting point for 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 public health organizations who are in the process of planning for and developing supportive measures for patients with post COVID-19 conditions. Such efforts include establishing case definitions for surveillance and data collection networks or systems, 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 (66).

Conclusion

A substantial proportion of individuals reported a variety of symptoms and sequelae 4 weeks or more after COVID-19 diagnosis. These physical and mental health symptoms have led to difficulties in conducting usual activities and result in diminished quality of life among COVID-19 survivors. This review provides a snap shot of symptoms presenting in COVID-19 survivors in the months after diagnosis. The data indicate that many are experiencing post COVID-19 conditions, 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 conditions is rapidly being produced and work is on-going to develop definitions which will lead to better and more refined estimates and understanding of the burden of post COVID-19 conditions, the social and economic impacts and resources needed to support a large number of survivors.

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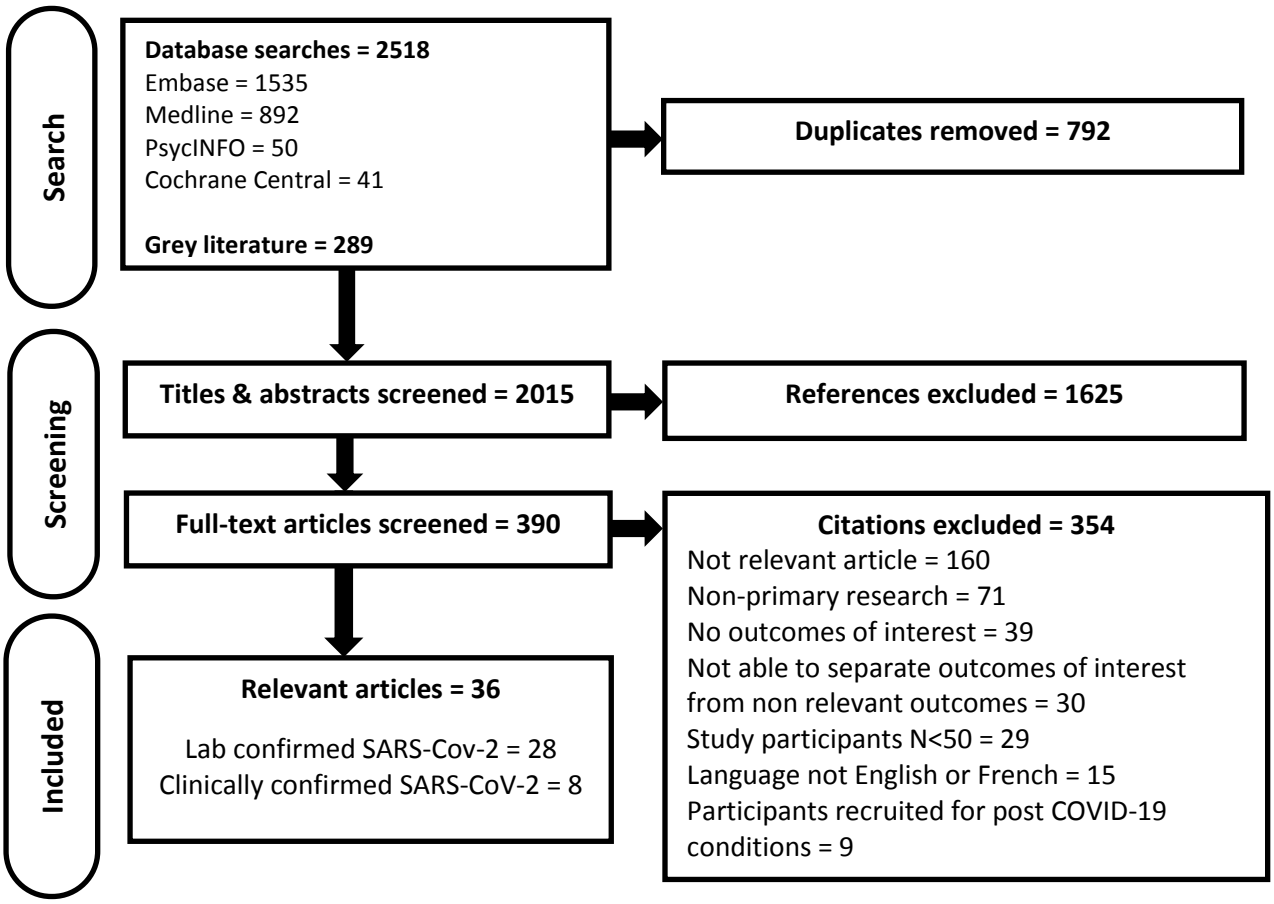
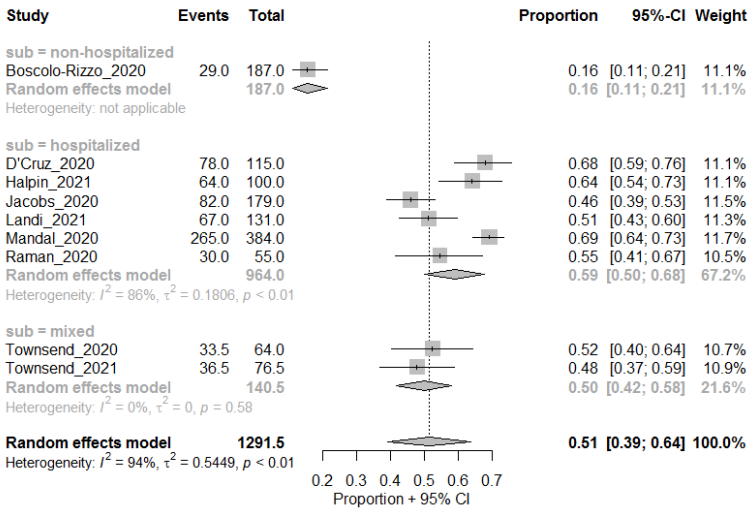


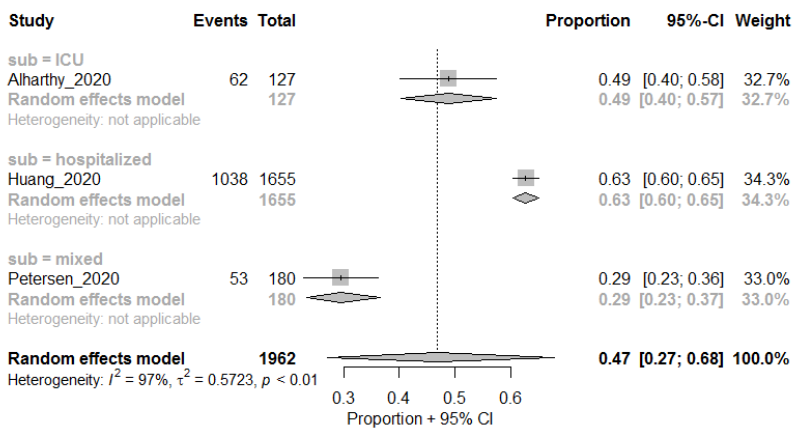
Figure 1: PRISMA flow diagram of articles through the systematic review process

(a) Fatigue

4-12 WEEKS



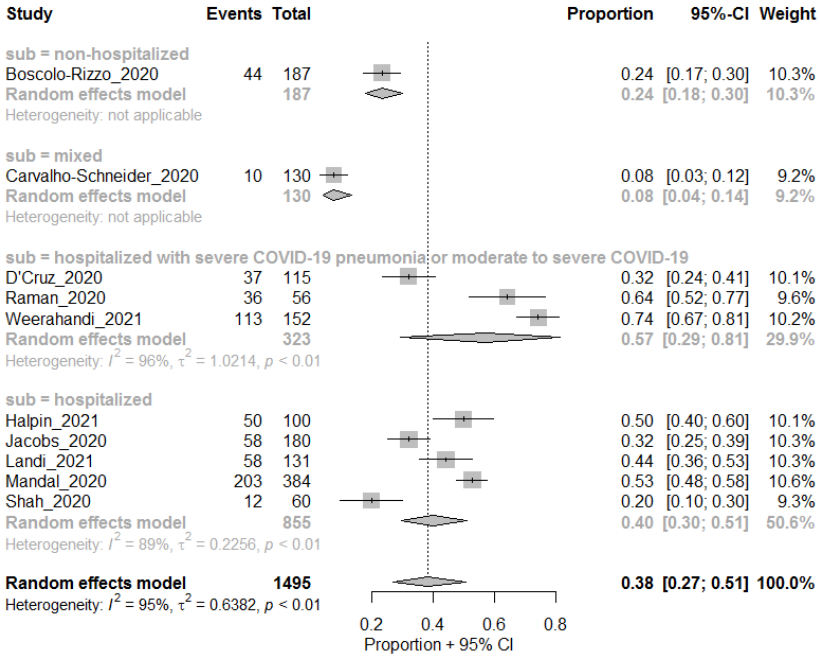
>12 WEEKS



(b) Shortness of breath

4-12 WEEKS

>12 WEEKS



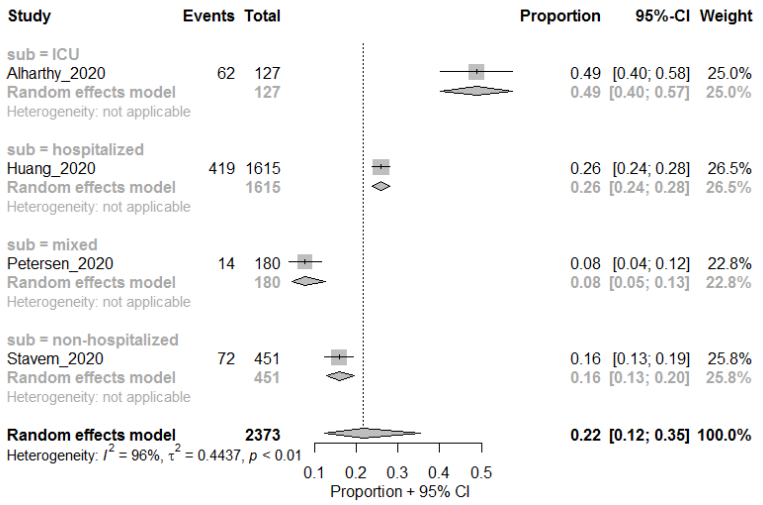


Figure 2. Prevalence (proportion of study sample) of (a) fatigue and (b) shortness of breath, at 4-12 weeks and >12 weeks after COVID-19 diagnosis and by level of care received at the acute stage of COVID-19 infection. Note that level of care may be considered a proxy for severity of COVID-19 (i.e.,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

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
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
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
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
Halpin, 2020	UK,	100 adults (≥18 years old)	Hospitalized with COVID-19	Between	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
Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross‐sectional evaluation	Cross-Sectional Study, May-June 2020	Mean age: Ward patients, 70.5 years (20‐93) ICU patients, 58.5 years (34‐84) Female Ward (48.5%) ICU (40.6%)		29 and 71 days post-discharge (mean 48 days and SD 10.3 days).	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 Worsened pain/discomfort Worsened anxiety/depression Perceived health Decrease
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

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
					Sore throat or difficult to swallow Skin rash Myalgia Headache 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 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

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
					Sweep - some/much difficulty Make bed - some/much difficulty Lift - some/much difficulty Lift and carry - some/much difficulty Walk fast - some/much difficulty
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
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
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
Mandal, 2020 'Long-COVID': a cross-sectional study of persisting	UK Cross-Sectional Study	384 patients Mean age of 59.9±16.1 years	Hospitalized with COVID-19	Median of 54 (IQR 47–59) days following hospital discharge	breathlessness Cough 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
symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19		38% female			depression anosmia one or more of the following persistent symptoms (breathlessness, cough, fatigue & poor sleep quality)
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 Cough with expectoration Nausea Chest tightness Rashes
Raman, 2020 Medium-term effects of SARS-CoV-2 infection on multiple vital organs, exercise capacity, cognition, quality of life and mental	UK, Prospective Cohort Study, March-May 2020	58 individuals 55.4yrs (13-2) 41.4% female	Hospitalized individuals with moderate to severe COVID-19 infection	2-3 months from disease-onset	breathlessness Fatigue desaturation at the end of a 6-minute walk test cognitive function - abnormal anxiety depression

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
health, post hospital discharge					
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
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
Townsend, 2020 Persistent fatigue following SARS-CoV-2 infection is	Ireland, Cross-Sectional Study,	128 individuals mean age: 49.5 ± 15 years	COVID-19 severity (need for inpatient admission, supplemental	Median (IQR) was 71 days (68-85) to 73 days (56-88)	Fatigue Not feeling back to full health Not returning to work

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
common and independent of severity of initial infection	March – May 2020	54% female	oxygen or critical care) and fatigue following COVID-19		
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 (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	n/a	Median 78 days (IQR 66-108) after diagnosis	Significant oxygen desaturation during 6MWT Perceived lack of full health Fatigue
Vaira 2020Smell 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
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

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	83% [65%, 93%] (3 studies)(32,34,44) ■ *low certainty*	56% [34%, 75%] (4 studies)(29,38,46,50) ■ *very low certainty*
Symptoms lasting >4 weeks	4% [1%, 6%] (1 study)(40) ■	No studies
Number of symptoms: 1-2 3-5 6-8 9-12 ≥13	No studies	 33% [26%, 40%] (1 study)(6) ■ 14% [9%, 19%] (1 study)(46) ■ 5% [2%, 8%] (1 study)(46) ■ 1% [0%, 3%] (1 study)(46) ■ 0% [0%, 0%] (1 study)(46) ■
Fatigue		
All	51% [39%, 64%] (9 studies)(30,34,36,39,42,44,47,51,52) ■ *low certainty*	47% [27%, 68%] (3 studies)(29,38,46) ■ *very low certainty*
By level of care received during the acute phase: Non-hospitalized Both (hospitalized & non-hospitalized) Hospitalized Admitted to ICU	 16% [11%, 21%] (1 study)(30) ■ *low certainty* 50% [42%, 58%] (2 studies)(51,52) ■ *low certainty* 59% [50%, 68%] (6 studies)(34,36,39,42,44,47) ■ *very low certainty* No studies	 No studies 29% [23%, 37%] (1 study)(46) ■ *very low certainty* 63% [60%, 65%] (1 study)(38) ■ *very low certainty* 49% [40%, 57%] (1 study)(29) ■ *very low certainty*
Respiratory		
Shortness of breath:		
All	38% [27%, 51%] (10 studies)(30,32,34,36,39,42,44,47,49,55) ■ *very low certainty*	22% [12%, 35%] (4 studies)(29,38,46,50) ■ *very low certainty*
By level of care received during the acute phase: Non-hospitalized Both (hospitalized & non-hospitalized) Hospitalized Hospitalized (with moderate to severe COVID-19 or severe COVID-19 pneumonia)	 24% [18%, 30%] (1 study)(30) ■ *very low certainty* 8% [4%, 14%] (1 study)(32) ■ *very low certainty* 40% [30%, 51%] (5 studies)(36,39,42,44,49) ■ *low certainty* 57% [29%, 81%] (3 studies)(34,47,55) ■ *very low certainty*	 16% [13%, 20%] (1 study)(50) ■ *very low certainty* 8% [5%, 13%] (1 study)(46) ■ *very low certainty* 26% [24%, 28%] (1 study)(38) ■ *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*)
Admitted to ICU	No studies	49% [40%, 57%] (1 study)(29) ■ *very low certainty*
Other respiratory symptoms/sequelae:		
Cough		
Any kind	28% [22%, 35%] (6 studies)(30,34,39,42,44,49) ■ *low certainty*	No studies
Dry cough	No studies	6% [4%, 8%] (2 studies)(46,50)■
Productive cough	No studies	5% [3%, 7%] (2 studies)(46,50,50) ■
Rhinitis or runny nose	14% [8%, 21%] (1 study)(42) ■	6% [3%, 13%] (2 studies)(46,50) ■
Sore throat	7% [5%, 10%] (2 studies)(30,42) ■	4% [2%, 8%] (2 studies)(46,50) ■
Voice change	20% [12%, 28%] (1 study)(36) ■	No studies
Laryngeal sensitivity	17% [10%, 24%] (1 study)(36) ■	No studies
Phlegm	15% [10%, 21%] (1 study)(39) ■	No studies
Blocked nose	15% [10%, 20%] (1 study)(30) ■	No studies
Requiring oxygen	14% [8%, 19%] (1 study)(55) ■	No studies
Wheezing	No studies	3.% [2%, 5%] (1 study)(50) ■
Flu-like symptoms		
Flu-like symptoms	22% [14%, 29%] (1 study)(32) ■	No studies
Headaches	12% [10%, 15%] (3 studies)(30,39,42) ■	4% [2%, 10%] (3 studies)(38,46,50) ■
Fever	1% [0%, 5%] (4 studies)(30,32,39,42) ■	0% [0%, 1%] (3 studies)(38,46,50) ■
Chills	No studies	2% [0%, 13%] (2 studies)(46,50) ■
Olfactory and Gustatory		
Smell or taste dysfunction	22% [12%, 36%] (5 studies)(30,32,41,45,53)(1,9,18-20) ■ *very low certainty*	No studies
Smell dysfunction		
Any	13% [3%, 38%] (5 studies)(31,33,39,42,53) ■ *very low certainty*	14% [9%, 22%] (3 studies)(38,46,50) ■ *very low certainty*
Hyposmia	8% [0%, 91%] (2 studies)(45,48) ■ *very low certainty*	No studies
Anosmia	4% [1%, 24%] (2 studies)(44,45) ■ *moderate certainty*	No studies
Taste dysfunction		
Any	7% [5%, 11%] (3 studies)(31,39,53) ■ *low certainty*	10% [7%, 15%] (3 studies)(38,46,50) ■ *very 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*)
Dysgeusia	11% [6.0%, 17%] (1 study)(42) ■ *very low certainty*	No studies
Neurocognitive		
Cognitive impairment	24% [18%, 31%] (2 studies)(34,47) ■ *low certainty*	No studies
Concentration problems	25% [22%, 28%] (2 studies)(28,36) ■ *moderate certainty*	No studies
Memory problem	19% [17%, 22%] (2 studies)(28,36) ■ *moderate certainty*	No studies
Confusion	9% [5%, 13%] (1 study)(39) ■ *very low certainty*	2% [1%, 4%] (1 study)(50) ■ *very low certainty*
Dizziness	3% [0%, 5%] (1 study)(30) ■ *low certainty*	6% [5%, 7%] (1 study)(38) ■ *low certainty*
Communication difficulty	6% [1%, 11%] (1 study)(36) ■	No studies
Neuromuscular		
Muscle or joint pain	16% [11%, 21%] (1 study)(30) ■ *very low certainty*	No studies
Muscle pain	22% [16%, 28%] (1 study)(39) ■ *very low certainty*	5% [2%, 12%] (3 studies)(38,46,50) ■ *low certainty*
Joint pain	19% [14%, 25%] (3 studies)(32,39,42) ■ *very low certainty*	9% [8%, 11%] (3 studies)(38,46,50) ■ *low certainty*
Swallow problem Sore throat or difficulties with swallowing	8% [3%, 13%] (1 study)(36) ■ No studies	No studies 4% [3%, 5%] (1 study)(38) ■
Referral to a Speech and Language Therapist	23% [15%, 31%] (1 study)(36) ■	No studies
Cardiovascular		
Palpitations	11% [5%, 16%] (1 study)(32) ■ *very low certainty*	9% [8%, 11%] (1 study)(38) ■ *low certainty*
Chest pain	9% [4%, 19%] (2 studies)(30,32) ■ *low certainty*	5% [4%, 6%] (1 study)(38) ■ *low certainty*
Chest tightness	No studies	6% [3%, 10%] (1 study)(46) ■ *very low certainty*
Digestive		
Digestive disorders	12% [6%, 17%] (1 study)(32) ■	No studies
Appetite problem	10% [7%, 13%] (3 studies)(30,36,42) ■	8% [7%, 10%] (1 study)(38) ■
Diarrhea	5% [3%, 7%] (3 studies)(30,39,42) ■	2% [1%, 4%] (2 studies)(46,50) ■
Diarrhea or vomiting	No studies	5% [4%, 6%] (1 study)(38) ■
Abdominal pain	4% [1%, 6%] (1 study)(30) ■	3% [2%, 5%] (1 study)(50) ■
Weight loss (≥5%)	12% [6%, 17%] (1 study)(32) ■	No studies
New bladder control problem	10% [4%, 16%] (1 study)(36) ■	No studies
New bowel control problem	3% [0%, 6%] (1 study)(36) ■	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% [0%, 3%] (1 study)(30) ■	4% [1%, 8%] (1 study)(46) ■
Vomiting	<1% [0%, 2%] (1 study)(30) ■	No studies
Vomiting/nausea	No studies	2% [1%, 4%] (1 study)(50) ■
Ulcer	1% [0%, 3%] (1 study)(39) ■	No studies
Nutritional concerns: Necessitating a dietetics referral Concern about weight/nutrition	 16% [9%, 23%] (1 study)(36) ■ 12% [6%, 18%] (1 study)(36) ■	 No studies No studies
Organ damage		
No studies		
Eye-related		
Eye irritations	21% [3%, 68%] (2 studies)(35,39) ■	
Red eyes	8% [2%, 33%] (2 studies)(35,42) ■	
Conjunctivitis		2% [1%, 4%] (1 study)(50) ■
Vision disturbance/blurring		4% [2%, 6%] (1 study)(50) ■
Dry eye disease: From objective tests From subjective tests	 62% [51%, 74%] (1 study)(35) ■ 47% [35%, 59%] (1 study)(35) ■	
Mental Health		
Anxiety	29% [16%, 48%] (2 studies)(34,47) ■ *very low certainty*	No studies
Depression	23% [11%, 40%] (3 studies)(34,44,47) ■ *very low certainty*	No studies
Anxiety or depression	22% [19%, 25%] (2 studies)(28,36) ■ *low certainty*	23% [21%, 25%] (1 study)(38) ■ *low certainty*
Postpartum depression	No studies	17% [8%, 27%] (1 study)(54) ■
Post-traumatic stress disorder	22% [14%, 34%] (3 studies)(34,36,37) ■	17% [8%, 27%] (1 study)(54) ■
Depression or post-traumatic stress disorder	No studies	22% [12%, 32%] (1 study)(54) ■ *very low certainty*
Overall mental health (poor/fair)	17% [12%, 22%] (1 study)(39) ■	No studies
Other mental health symptoms		
Panic attack	13% [11%, 16%] (1 study)(28) ■	No studies
Always/often emotional	14% [9%, 19%] (1 study)(39) ■	No studies
Thoughts of self-harm	2% [0%, 5%] (1 study)(36) ■	No studies
Quality of life (QoL)		
Decreased QoL	53% [43%, 63%] (1 study)(36) ■	No studies
QoL (poor or fair)	23% [17%, 29%] (1 study)(39) ■	No studies
Social relationships (poor or fair)	60% [53%, 68%] (1 study)(39) ■	No studies
Social active role (poor or fair)	31% [25%, 38%] (1 study)(39) ■	No studies
Sleep-related		
Sleep disturbances or difficulties	36% [10%, 74%] (2 studies)(28,34) ■ *low certainty*	26% [24%, 29%] (1 study)(38) ■ *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*)
Insomnia	9% [7%, 11%] (1 study)(28) ■ *low certainty*	No studies
Nightmare	2% [1%, 3%] (1 study)(28) ■ *low certainty*	No studies
Overall functioning		
Still felt ill or not back to full health	52% [35%, 68%] (3 studies)(32,51,52) ■ *low certainty*	No studies
Decrease in perceived health	39% [29%, 49%] (1 study)(36) ■	No studies
Worsened usual activities	44.0% [34%, 54%] (1 study)(36) ■	No studies
Problems with usual activity	No studies	2% [1%, 2%] (1 study)(38) ■
Disease-specific functional impairment	41% [32%, 50%] (1 study)(34) ■	No studies
General health (poor/fair)	20% [14%, 26%] (1 study)(39) ■	No studies
Physical health (poor/fair)	27% [21%, 34%] (1 study)(39) ■	No studies
Physical activity (none/little)	14% [9%, 19%] (1 study)(39) ■	No studies
Difficulties with the following activities related to mobility:		
Worsened mobility (in general)	37% [28%, 46%] (1 study)(36) ■	No studies
Walking	15% [13%, 18%] (2 studies)(28,39) ■	7% [6%, 8%] (1 study)(38) ■
Walking fast	46% [37%, 54%] (1 study)(39) ■	No studies
Confined to bed (unable to walk)	2% [1%, 3%] (1 study)(28) ■	No studies
Climbing stairs	30% [23%, 37%] (1 study)(39) ■	No studies
Lifting Lifting and carrying	20% [14%, 27%] (1 study)(39) ■ 25% [19%, 32%] (1 study)(39) ■	No studies No studies
Sweeping	12% [7%, 17%] (1 study)(39) ■	No studies
Making the bed	6% [2%, 10%] (1 study)(39) ■	No studies
Poor results in the 6-minute walk test: Unable to complete test Walked less than the normal range Desaturation or abnormal results at the end of the test Desaturation during the test	 No studies No studies 7% [4%, 13%] (2 studies)(47,49) ■ 3% [0%, 6%] (1 study)(52) ■	 49% [40%, 58%] (1 study)(29) ■ 23% [21%, 25%] (1 study)(38) ■ No studies No studies
Difficulties with the following activities related to self-care:		
Worsened self-care (in general)	16% [9%, 23%] (1 study)(36) ■	No studies
Washing or dressing oneself	10% [7%, 12%] (1 study)(28) ■	1% [0%, 1%] (1 study)(38) ■
Dressing oneself	3% [1%, 7%] (1 study)(39) ■	No studies
Meal preparation	6% [3%, 10%] (1 study)(39) ■	No studies
Washing dishes	4% [1%, 8%] (1 study)(39) ■	No studies
Employment-related:		
Not returned to work	31% [23%, 40%] (1 study)(51) ■ *very low certainty*	9% [3%, 16%] (1 study)(43) ■ *very low certainty*
Sick-leave	11% [5%, 16%] (1 study)(32) ■ *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*)
Complications from COVID-19⁺		
Impaired pulmonary function	Not applicable	42% [31%, 53%] (1 study)(43) ■ *very low certainty*
Interstitial lung disease	Not applicable	12% [6%, 17%] (1 study)(29) ■
Abnormal lung high-resolution computed tomography scan	Not applicable	8% [1%, 15%] (1 study)(43) ■
Deep vein thrombosis	Not applicable	7% [3%, 12%] (1 study)(29) ■
Pulmonary hypertension	Not applicable	7% [3%, 12%] (1 study)(29) ■
Pulmonary embolism	Not applicable	4% [1%, 7%] (1 study)(29) ■
Other symptoms/sequelae		
General pain/discomfort	40% [24%, 58%] (2 studies)(28,34) ■ *low certainty*	27% [25%, 29%] (1 study)(38) ■ *low certainty*
Worsened pain/discomfort	19% [11%, 27%] (1 study)(36) ■	No studies
Hair fall/loss	10% [8%, 12%] (1 study)(28) ■	22% [20%, 24%] (1 study)(38) ■ *low certainty*
Cutaneous signs	12% [6%, 17%] (1 study)(32) ■	No studies
Rashes	No studies	3% [2%, 3%] (3 studies)(38,46,50) ■
Seizures/cramps	No studies	1% [0%, 2%] (1 study)(50) ■
Ear pain	No studies	1% [0%, 2%] (1 study)(50) ■

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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