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Clinical Classification and Interventions for Post–COVID-19 Condition: A Scoping Review

Protocol Registration

Open Science Framework Registration: https://www.osf.io/xmusb

National Collaborating Centre for Methods and Tools: https://www.nccmt.ca/covid-19/covid-19-evidence-reviews/492

Scoping Review

CADTH

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Abbreviations

HTA	health technology assessment
ICD	International Classification of Diseases
ICU	intensive care unit
IQR	interquartile range
NICE	National Institute for Health and Care Excellence
PRISMA-ScR	Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SD	standard deviation

Table 1: Protocol Amendments

Section	Amendment	Page in protocol	Rationale
Literature Search Strategy	Searches were not supplemented by reviewing bibliographies of key papers or through contacts with experts.	11	Due to resource and time constraints, this was not feasible.
Literature Search Strategy	References of included studies were not searched and no content experts were contacted.	11	Due to resource and time constraints, this was not feasible.
Selection and Eligibility Criteria	More details on eligibility criteria for guidelines were added. Eligibility was expanded to include Canadian guidelines regardless of the definition used for post–COVID-19 condition.	11	The criteria used to include guidelines were added for improved clarity. Canadian guidelines were included regardless of definition, as they were believed to be contextually important.
Selection and Eligibility Criteria	Additional details added regarding eligibility of studies with broad follow-up time that includes some participants followed up for < 12 weeks.	11	Due to these studies likely providing data of interest, they were included, and the eligibility criteria were specified.
Selection and Eligibility Criteria	Preprints were only considered for inclusion if they were systematic reviews; preprints of other study designs were excluded.	12	Due to resource and time constraints, it was not feasible to include preprints of primary studies.
Charting	Age, median, interquartile range, range, eligible age, and categories, as reported by the references, were additionally extracted.	13	An extraction of only mean and standard deviation age data was originally planned, but after the realization that not all publications reported this, it was decided that median, interquartile range, range, eligible age, and categories, as reported by the references, would also be extracted.
Charting	Variables related to the PROGRESS-Plus framework (i.e., place of residence, race/ethnicity/culture/language, occupation, religion, education, socioeconomic status, social capital, and other characteristics that may be associated with disadvantage) were not extracted.	13	Partway through charting, it was determined that these were infeasible to extract due to resource and time constraints; thus, they were removed.
Charting	Study authors were not contacted.	13	Due to resource and time constraints, no attempts were made to contact study authors for missing or unclear information.

Key Messages

- Most of the identified published research focused on characteristics or outcomes of having post–COVID-19 condition (e.g., symptoms, quality of life) or predictors for developing post–COVID-19 condition. There were fewer studies related to preventing post–COVID-19 condition or treatments. Ongoing studies, according to published protocols, will investigate interventions to prevent or treat this condition.
- Notable evidence gaps included post–COVID-19 condition as it relates to people living in rural or remote areas, children and adolescents, and vaccination status. There were few economic studies, qualitative studies, and studies assessing health systems issues.
- Most identified guidelines regarding the diagnosis, treatment, and management of post–COVID-19 condition, including all Canadian guidelines, provided limited guidance specific to patients meeting the WHO definition. These guidelines will need continual updates as new evidence emerges.

Abstract

Background

According to WHO, post‐COVID-19 condition is characterized by new or persisting symptoms 12 or more weeks following an initial COVID-19 infection. People with post–COVID-19 condition have been reported to experience a range of heterogenous symptoms, including fatigue, shortness of breath, muscle aches, and cognitive and mental health challenges. With the vast numbers of COVID-19 cases worldwide and estimates from the literature suggesting a substantial proportion of these individuals may develop long-term complications, there is much interest in developing a clearer understanding of this condition.

The objective of this scoping review is to characterize the current evidence landscape on post–COVID-19 condition and to identify evidence gaps. Clinical classification (e.g., symptom classification, severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] variant quantification, and reporting of pathophysiological markers), risk factors related to developing post–COVID-19 condition, diagnostic tests, interventions to prevent or manage symptoms (e.g., drugs, rehabilitation), and evidence related to health systems for people of all ages in any context were of interest.

Methods

A scoping review of primary studies and other relevant research, including systematic reviews, guidelines, and economic evaluations was undertaken. Studies and protocols or clinical trial registrations needed to be published (commercially or as grey literature); preprints were included for systematic reviews only. Studies that followed up with participants for at least 12 weeks or 3 months after COVID-19 diagnosis or symptom onset and assessed the clinical classification, predictive variables, preventive measures, diagnostic approaches, and treatments, in any setting, were eligible for inclusion. Included references were categorized by the following concepts: risk factors and prevention, classification, diagnostic tests, treatment or management, and health system issues (e.g., increased health care services use and policy impact). Country, age, sex (proportion of male participants), and rural or remote residence

were also charted to identify characteristics that stratify health opportunities and outcomes related to health equity and equity considerations.

Results

Between January 1, 2019, and December 20, 2021, 637 published articles, 247 protocols, and 8 preprints of systematic reviews were identified and included. The majority of studies came from only a few countries, particularly the US (n = 180), Italy (n = 96), and the UK (n = 81). Some countries had a moderate number of studies (36 to 66), including China, Canada, and several European countries (the Netherlands, Spain, France, and Germany). Relatively few studies (30 or fewer) were found that included participants from Africa, South America, Australia, New Zealand, and Asia. We identified 10 or more systematic reviews related to characteristics or outcomes (e.g., symptoms, quality of life) of post–COVID-19 condition, as well as risk factors. Areas with fewer systematic reviews but 50 or more primary studies included pathophysiological markers assessed at fewer than 12 weeks, as well as diagnostic tests at 12 weeks or later. Fewer than 50 primary studies for preventive or treatment interventions were identified, but a large number of protocols indicate research is in progress for these topics. Finally, several areas with few protocols and fewer than 50 primary studies were identified, including economic evaluations, qualitative studies, studies related to health system issues, and guidelines specific to 12 weeks or longer (differences between variants of SARS-CoV-2, subtypes of post–COVID-19 condition, people under 18 years old, people living in rural or remote areas, and people who have received the COVID-19 vaccine).

Conclusions

A substantial amount of research has been conducted and published on post–COVID-19 condition as of December 2021. The majority of the identified evidence has looked at symptoms, risk factors, and different diagnostic tests to assess individuals with post–COVID-19 condition. As of December 2021, there appears to be limited evidence regarding preventive interventions and interventions to treat or manage post–COVID-19 condition, but published protocols indicate research in this area is ongoing. Some areas where few published studies and protocols were found include in pediatric populations, in people living in rural or remote areas, and the impact of different variants of SARS-CoV-2.

Introduction and Rationale

COVID-19 was first identified in late 2019 and has since had an enormous impact on countries around the world. As of March 1, 2022, WHO has reported more than 433 million confirmed cases and more than 5.9 million deaths globally.[1] While COVID-19 was initially considered a short-term acute disease, it has since become clear that some people do not fully recover for several weeks or months after the acute phase, or experience a recurrence of symptoms.[2] Initially referred to as *long COVID* by patient advocates, several other names have also been suggested and used, including *chronic COVID condition* and *post-acute sequelae of COVID-19*.[2,3] In addition to various terms being used, there has also been a lack of consensus definition for post–covid-19 condition: some have defined it as symptoms occurring 4 weeks after infection, diagnosis, or symptom onset, while others have suggested 12 weeks or 3 months.[4]

At the time of writing this report (March 2022), the Government of Canada defines post–COVID-19 condition as symptoms experienced for "weeks or months after initial recovery" and differentiates between short-term (4 to 12 weeks) and long-term (12 or more weeks) symptoms.[5] This Canadian definition was published in September 2021. In December 2020, the National Institute for Health and Care Excellence (NICE) in the UK released its first iteration of a rapid guideline for managing the long-term effects of COVID-19, and suggested using *acute COVID-19* for the first 4 weeks of illness, *ongoing symptomatic COVID-19* for symptoms occurring between weeks 4 and 12, and *post–COVID-19 syndrome* for symptoms occurring after 12 weeks that cannot be explained by an alternative diagnosis.[6] These terms are still used in their updated guideline from November 2021. WHO released its clinical case definition of *post–COVID-19 condition* in October 2021, and also defined it as symptoms occurring at least 3 months after COVID-19 infection.[7] Both NICE and WHO stated that symptoms can have persisted since the acute phase, or can be new symptoms that were not present during the acute phase but developed afterwards (e.g., a person's post–COVID-19 condition symptoms include a rash even if they did not have a rash during the acute phase).[6,7] This also includes people who were asymptomatic during the acute phase. The WHO and NICE definitions also state that symptoms may fluctuate or relapse.[6,7]

To be consistent with the WHO definition, this report uses the term *post–COVID-19 condition* and defines it as symptoms or sequelae occurring at least 12 weeks or 3 months after COVID-19 infection, diagnosis, or symptom onset.[6,7] We have chosen the WHO definition over the Canadian definition because the WHO definition is newer, and was built on existing empirical evidence that used robust methodology to identify the domains and variables to be included.[7] Development of the definition engaged patients, clinicians, researchers, and other stakeholders from all WHO regions (n = 265) in a two-round Delphi consensus (defined as at least 70% agreement) building exercise, which was followed by a mixed iterative survey.[7] We recognize that some patient advocates may prefer other terms as the term *post–COVID-19 condition* may be interpreted as patients have recovered or imply that there is no active disease process.[8] Throughout this review, *post–COVID-19* may be interpreted as occurring after the acute COVID-19 and ongoing symptomatic COVID-19 phases.

With the vast numbers of COVID-19 cases worldwide and estimates from preprint systematic reviews suggesting that approximately 43% to 53% of people infected by COVID-19 may develop post–COVID-19 condition,[9,10] there is much interest in developing a clearer understanding of this condition. We identified 3 previous scoping reviews on COVID-19 sequelae, or long COVID[11-13]; however, none focused specifically on follow-up after at least 3 months or 12 weeks, perhaps because WHO's definition of post–COVID-19 condition is relatively new. Thus, it is unclear where evidence exists about post–COVID-19 condition as defined as sequelae after 12 weeks, from its characteristics and symptoms, what tests are being used to assess symptoms and potential causes, which interventions have been assessed, and what guidelines are available. The rapidly evolving pandemic and rapid accumulation of new research poses challenges for policy-makers and researchers as to resource allocation and task prioritization.[14] As a precursor to meaningful evidence synthesis activities (e.g., systematic reviews), we believed it important to address the aforementioned lack of clarity about the depth and breadth of rapidly emerging evidence on post–covid-19 condition. As a result, a scoping review was believed to be the most relevant methodology to characterize the evidence landscape. In addition, this would address the need to understand what evidence is available on a broader range of topics compared to previous scoping reviews, including symptoms, risk factors, pathophysiology, preventive interventions, diagnostic methods, treatment and management, and issues related to health systems.

The goal of this review was to characterize the existing evidence and to identify gaps in the evidence base and determine areas where further research is needed to help support Canadian health care decision-making needs. The findings of this scoping review, specifically the identified knowledge gaps and uncertainties, will be used to inform a larger CADTH condition-level review on post–COVID-19 condition and serve as a foundation for future rapid evidence queries. The findings will also contribute to the condition-level review's online platform that will aim to share information, provide evidence to inform decision-making, increase awareness of ongoing initiatives, reduce duplication of effort, and support connection and collaboration. A condition-level review is an assessment of the evidence that incorporates all aspects of a condition, from prevention and detection to treatment and management.

Objective

The objective of this scoping review is to characterize the current evidence landscape on post–COVID-19 condition and to identify evidence gaps. We aim to use the findings to identify areas where it may be feasible and informative to perform future systematic reviews, which will contribute to CADTH's larger condition-level review. Clinical classification (classifying post–COVID-19 condition at least 12 weeks or 3 months after initial infection by symptoms, pathophysiological markers, variants of SARS-CoV-2, subtypes, or other approaches); risk factors related to developing post–COVID-19 condition; diagnostic tests; interventions to prevent, treat, or manage symptoms (e.g., drugs, rehabilitation); and topics related to health systems (e.g., increased health care services use, policy impact) for people of all ages in any context were of interest.

Research Questions

The scoping review addressed the following research questions:

1. What is the current evidence landscape on the clinical classification, preventive measures, prognostic factors, diagnostic tests, and treatment for post–COVID-19 condition for people of any age in any setting?
2. What are the knowledge gaps on the clinical classification, preventive measures, prognostic factors, diagnostic tests, and treatment for post–COVID-19 condition for people of any age in any setting?

Methods

Protocol Development

To inform the preparation of the protocol for this scoping review, a CADTH Horizon Scanning report of the existing literature, including health technology assessments (HTAs) and systematic reviews was conducted.[15] The protocol was written a priori based on well-

established methods,[16] and was externally reviewed by a content expert and methodologist. The review topic was registered at the National Collaborating Centre for Methods and Tools and posted the protocol on the Open Science Framework.

Study Design

The research questions were addressed by conducting a scoping review of primary studies and other relevant research, including systematic reviews, scoping reviews, rapid reviews, preprints, and grey literature. The methodology of the scoping review was informed by the methods outlined in the *JBI Manual for Evidence Synthesis*[17] and reporting adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR), with relevant adaptations based on PRISMA 2020 statement.[18] The final report was externally reviewed by a content expert and methodologist.[19]

Literature Search Strategy

The literature search was performed by an information specialist using a peer-reviewed search strategy according to the Peer Review of Electronic Search Strategies (PRESS) checklist.[20] The complete search strategy is presented in Appendix 1 (refer to Table 9 for a guide to Ovid syntax and Table 10 for a guide to EBSCO syntax).

Published literature was identified by searching the following bibliographic databases: MEDLINE All (1946–), Embase (1974), APA PsycInfo (1806–), and the Cochrane Central Register of Controlled Trials (CENTRAL), via the Ovid platform; and CINAHL (Cumulative Index to Nursing and Allied Health Literature) via EBSCO. All Ovid searches were run simultaneously as a multi-file search. Duplicates were removed using Ovid deduplication for multi-file searches, followed by manual deduplication in Endnote. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concept was post–COVID-19 condition and synonyms. Parts of the strategy were adapted from CADTH's COVID-19 search string.[21] Detailed search strategies are provided in Appendix 1.

Retrieval was limited to documents published from January 1, 2019, onwards, and in the English or French language. As COVID-19 was first identified in late 2019, we expected that all relevant papers would have been published in or after 2019. Where possible, retrieval was limited to the human population. No filters were applied to limit the retrieval by study type. Comments, newspaper articles, editorials, and letters were excluded.

The following clinical trial registries were searched: the US National Institutes of Health's ClinicalTrials.gov, WHO's International Clinical Trials Registry Platform search portal, Health Canada's Clinical Trials Database, and the European Union Clinical Trials Register. Preprints (preliminary reports that have not been peer reviewed) were searched through the Europe PMC database.

Grey literature (literature that is not commercially published) was identified by searching sources listed in relevant sections of the Grey Matters: A Practical Tool For Searching Health-Related Grey Literature resource,[22] and the CADTH COVID-19 Grey Literature Resources,[23] which includes the websites of regulatory agencies, HTA agencies, clinical guideline repositories, systematic review repositories, patient-related groups, and professional associations. Refer to Appendix 1 for more information on the grey literature search strategy.

The initial search was completed on October 15, 2021. Regular alerts updated the database literature searches, grey literature, preprints, and clinical trial registries searches until December 20, 2021. Studies meeting the selection criteria and identified in the alerts were incorporated into the final report.

Selection and Eligibility Criteria

The study eligibility criteria for the research questions can be found in Table 2. Studies of people of all ages that investigated the clinical classification (classifying post–COVID-19 condition at least 12 weeks or 3 months after initial infection by symptoms, pathophysiological markers, variants of SARS-CoV-2, subtypes, or other approaches), prevention, diagnostic tests, or treatment of post–COVID-19 condition in any setting were included. Studies that followed up with patients at least 12 weeks (equivalent to 3 months or 84 days) after initial infection or diagnosis or symptom onset were eligible for inclusion. Studies were included even if not all eligible participants developed post–COVID-19 condition; for example, this could include studies aimed at identifying incidence or risk factors for developing post–COVID-19 condition. This also includes studies that measured immunological markers or other biomarkers after 12 weeks, as these may provide insight into methods of identifying post-COVID-19 sequelae or potential causes of sequelae (e.g., assessments of inflammatory markers after 12 weeks in people experiencing persistent symptoms, compared to people who had COVID-19 but did not experience persistent symptoms or to people who did not have COVID-19 at all). For studies where follow-up time varied between participants, with some followed up for less than 12 weeks, the following criteria were used:

- If the study provided the median and interquartile range (IQR) for follow-up time, if the lower quartile was at least 12 weeks, it was included.
- If the study provided the mean and standard deviation (SD) follow-up time, if the mean was at least 12 weeks, it was included.

Primary studies of any design, systematic reviews (i.e., quantitative, qualitative, or mixed-methods reviews that include a research question; a list of the sources searched and a reproducible search strategy; clear inclusion and exclusion criteria; a description of methods for study selection; information about how the data were synthesized),[24] scoping reviews, economic analyses, and ethical analyses were eligible. Systematic reviews that included primary studies meeting our criteria and primary studies that did not (i.e., some studies assessed at 12 weeks or later while some assessed within 12 weeks) were included. These could be commercially published or available as grey literature, and could be available as a full-text article, conference abstract, presentation, or thesis. Evidence-based guidelines and clinical practice guidelines related to post-acute COVID-19 care were included if they provided at least 1 recommendation for patients at 12 weeks or later after initial infection or diagnosis related to diagnosis or treatment. Though none of the available Canadian guidelines used this definition, they were included as they were believed to be contextually important. Though informal literature reviews and consensus statements can sometimes include relevant data, we deemed it infeasible to sift through a large volume of editorials, letters, and commentaries; therefore these were excluded.

The review was limited to studies published in English and French due to resource and time constraints. One deviation from the original protocol is that we included preprints of systematic reviews only, rather than preprints for all study designs. This decision was made for feasibility reasons, given the large volume of eligible studies.

Study Selection

The systematic review management software DistillerSR (Evidence Partners, Ottawa, Canada) was used to facilitate study selection. Pilot testing was conducted for the first 50 references identified in the literature search to ensure the eligibility criteria were interpreted similarly by the reviewers. Thereafter, 2 reviewers independently screened titles and abstracts of all citations retrieved from the literature search, following a liberal-accelerated approach.[25,26] That is, titles and abstracts marked as *include* by a single reviewer moved to full-text appraisal, while only those marked as *exclude* were screened by a second reviewer to confirm or reject the exclusion. A liberal-accelerated approach was also used for the full-text screening of articles included after the title and abstract screening. This may have led to the inclusion of irrelevant studies at this stage; however, all included articles were read by a second reviewer during the data validation phase, at which time disagreements about the relevance of any included study were discussed between reviewers until consensus was reached about their inclusion or exclusion from the review. The reasons for exclusion of articles at the full-text level were documented.

Protocols that were implemented with results published and included in this scoping review were considered duplicate and excluded.

Table 2: Selection Criteria for Clinical Research Questions

Category	Selection criteria
Population	People of all ages with post–COVID-19 condition (i.e., defined as any symptoms experienced 12 weeks or more after initial infection, diagnosis, or symptom onset)
Concept	Clinical classification, preventive measures, diagnostic approaches, treatments, for post–COVID-19 condition
Context	Any context or setting
Study designs	Comparative and noncomparative study designs, economic evaluations, protocols, and clinical guidelines, including: • systematic reviews[a] and preprints of systematic reviews • scoping reviews • quantitative or qualitative primary studies of any design • studies of any design available as a conference abstract, presentation, or thesis • economic evaluations • ethical analysis • guidelines. Exclusions: • consensus statements • editorials, letters, and commentaries, including editorials and letters with data • literature reviews.
Time frame	2019 to present
Language of publication	English or French

[a]These may be quantitative, qualitative, or mixed methods, and must include a research question, a list of the sources searched and a reproducible search strategy, clear inclusion and exclusion criteria, a description of methods for study selection, and information about how the data were synthesized. Though appraisal of the quality of the included studies is often recommended for systematic reviews, this was not considered a requirement for the purpose of the present scoping review.[24]

Charting (Data Extraction)

A charting form was developed in DistillerSR (Evidence Partners, Ottawa, Canada) and adapted for Microsoft Excel (version 2112, Microsoft, Washington, US). Charting was performed by 1 reviewer in either DistillerSR or Microsoft Excel; DistillerSR was used for most of the literature search results, while Microsoft Excel was used for the results from clinical trial registries, preprint searches, Philosopher's Index, and grey literature, and independently checked for accuracy and completeness by a second reviewer. Before charting began, the reviewers independently tested the charting form on a sample of 10 included studies to ensure a mutual understanding and that the form adequately captured the desired information. Following piloting, the reviewers met to review discrepancies. Disagreements were resolved through discussion until consensus was reached. Relevant information was charted, including the following:

- study characteristics (e.g., first author's name, publication year, country where the study was conducted) and methodology (e.g., study design and objectives)
- population (e.g., number of participants, age, sex and/or gender, methods to confirm COVID-19 infection, severity of acute illness, vaccination status)
- concept (i.e., risk factors and prevention, classification, diagnostic tests, treatment or management, health systems issues; subcategories were collected within each)
- context (i.e., country, setting [urban, rural, remote], site of treatment during acute illness, site of treatment during follow-up).

The full list of items extracted are available in Table 11 in Appendix 2. For reviews, data presented in the review was extracted; the included primary studies were not checked, nor were extract data from them. Data were charted for all relevant concepts and contexts for this study at any duration of follow-up. If studies included a noninfected control group, population characteristics were extracted only for participants who had COVID-19, not for noninfected controls.

Charting was an iterative process, whereby additional items were added as the research team learned about the research base and recognized new items of importance. Added items were the publication date (adding the month and day), whether a study specified it was focused on patient(s) with persistent infection, and additional age data. For age data, we originally planned to extract only mean and SD, but upon realizing not all publications reported this, we decided to also extract median, IQR, range, eligible age, and categories, as reported by the studies. We also intended to extract PROGRESS-Plus framework data (i.e., place of residence, race/ethnicity/culture/language, occupation, religion, education, socioeconomic status, social capital, personal characteristics associated with discrimination, features of relationships, and time-dependent relationships) to identify characteristics that stratify health opportunities and outcomes related to health equity and equity consideration[27]; however, given the volume and complexity of the literature, it was not feasible to extract and validate all of these characteristics; thus, not all of the characteristics were present in this report's results. The same charting form was used for all study designs. In addition, guideline development methods were extracted, including databases searched, literature search methods, and funding sources. We also extracted the recommendations specific to post–COVID-19 condition.

If data were missing for any variables being extracted, they was considered as missing and not estimated or imputed. No studies were excluded due to missing data. Due to resource and time constraints, no attempts were made to contact study authors for missing or unclear

information. No risk of bias assessment was conducted, as the goal of the scoping review was not to comment on the quality of the evidence. The overlap between systematic reviews was not investigated, nor was the overlap between primary studies and systematic reviews. Due to the broad topic area and limited resources, details of the interventions, comparators, and outcomes in the included studies were not validated at this stage and not reported.

Descriptive Synthesis

We presented the study characteristics and findings within summary tables, visual displays, and in the main text. The number of studies identified were summarized by publication type (published commercially or as grey literature, protocols or registered clinical trials, preprints of systematic reviews) and country or countries of participants. We presented the number of studies by month of publication. We also summarized data on participants' age, including reported mean and median ages, whether the studies included children or adolescents (younger than 18 years old), adults (18 to 64), and/or older adults (65 or older), participants' severity of acute illness (defined as asymptomatic, symptomatic but not hospitalized, hospitalized, and intensive care unit [ICU]), and how COVID-19 was diagnosed (e.g., laboratory test, self-report). Median values and their IQRs were reported when applicable. The number of studies for each of the 5 main concepts, as well as their subcategories, were also summarized in tables, including the number and proportion by publication type, participant age categories included (younger than 18 years, 18 to 64, and 65 or older), and participants' acute illness severity.

Results

Quantity of Research Available

A total of 3,535 unique citations were identified in the electronic literature search. Following screening of titles and abstracts, 1,998 citations were excluded, and 1,537 potentially relevant reports were retrieved for full-text review. An additional 180 potentially relevant publications were retrieved for full-text review from the grey literature search. Of these 1,717 potentially relevant articles, 825 were excluded and 892 reports of studies were included in this scoping review (refer to the list of included studies published on the Scoping Review webpage). The study selection process is outlined in Appendix 2 using a PRISMA flow chart (Figure 4). A PRISMA-ScR checklist is included in Appendix 4 (Table 2). As there were a large number of excluded studies, it did not seem informative to present the full list. We have therefore listed a sample of the included and excluded citations for each main exclusion reason, based on their order in the literature searches, in Appendix 3.

Study Characteristics

Of the 892 included studies, 637 were published commercially or as grey literature (71.4%), 247 were protocols (including clinical trial registries; 27.7%), and 8 were preprints of systematic reviews (0.9%). The published sources included 584 primary studies (91.7%), 40 systematic reviews (including scoping reviews; 6.3%), 12 guidelines (1.9%), 1 economic evaluation (0.2%), 1 qualitative primary study (0.2%), and 2 mixed-methods primary studies (0.4%). There were no ethical analyses located. Among the protocols, 239 were for primary studies (96.8%) and 8 were for systematic reviews (3.2%).

Eligible studies, including protocols and preprints, were published between January 10, 2020, and January 31, 2022 (including publications that were available online and indexed by December 20, 2021, but were officially published later). On average, there was 1 included study that became available daily (median = 2; IQR = 1 to 3). The highest number of included studies that became available in 1 day was 22 on May 14, 2021. The number of studies published over time is presented in Figure 1.

The number of sources (of any design) by country of the included participants (in countries with at least 10 included studies) is presented in Figure 2. A large proportion of studies included participants from only a few countries, particularly the US (n = 180), Italy (n = 96), and the UK (n = 81). There was lesser representation (36 to 66 studies) of participants from China, Canada, and certain European countries (primarily the Netherlands, Spain, France, and Germany). Relatively few studies (30 or fewer) included participants from areas such as Africa, South America, Australia, New Zealand, and Asia.

Additionally, lists of scoping reviews and systematic reviews are in Appendix 3 (Table 16 and Table 17, respectively).

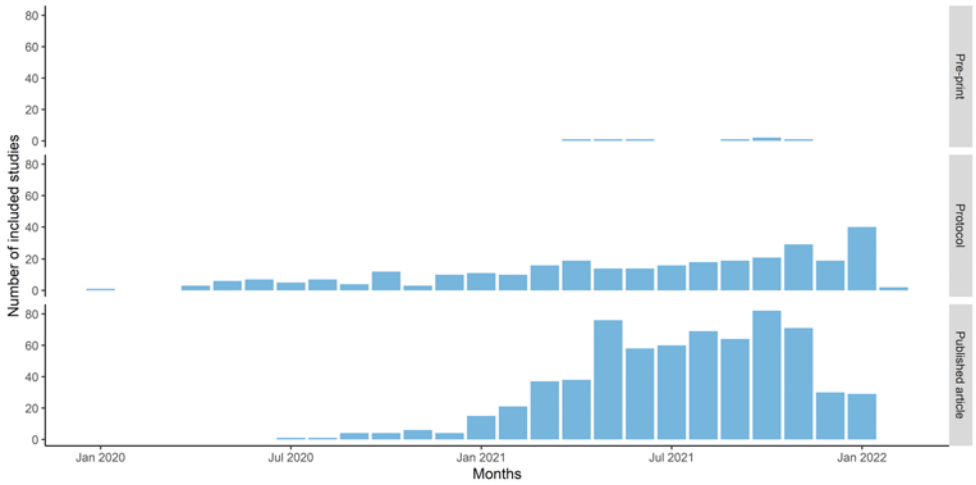
Patient Characteristics

Demographic Characteristics

Most studies, including protocols with estimated sample sizes and systematic reviews reporting sample sizes in primary studies (n = 833; 93.4%), reported the numbers of included participants with post–COVID-19 condition. Sample sizes in guidelines were not applicable. The median sample size was 103 (range = 1 to 886,228).

The mean or median ages were reported in 503 (56.4%) studies among all sources (range = 8.5 months to 89 years). Based on reported age data in published articles and the eligible age ranges in protocols or guidelines, we determined whether studies included or planned to

Figure 1: Number of Included Studies by Month of Publication



Note: Based on literature available by December 20, 2021. The first date online was extracted where available, but this was not always available, in which case the publication date was used. Some studies may have been available by December 20, 2021, but were not officially published until after; thus, some of the studies in the figure are presented as published in January.

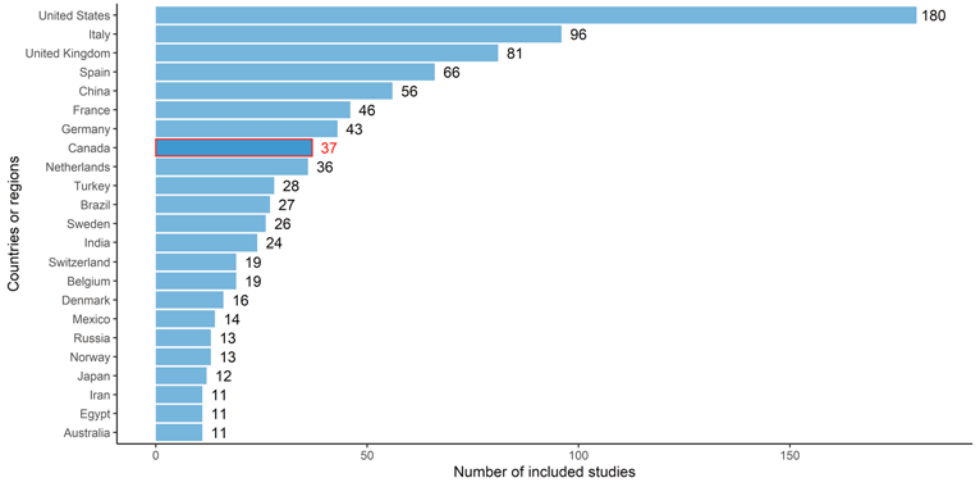
include children and adolescents (defined as younger than 18 years), adults (defined as 18 to 64 years), and/or older adults (defined as 65 years or older). We found that 85 (9.5%) sources included participants younger than 18 years, 720 (80.7%) included only adults between 18 and 64 years, and 473 (53.0%) included older adults who were older than 65 years. Thus, there is a notable gap in studies related to children and adolescents. The sex and/or gender distribution of the population was reported in 547 (61.3%) studies, and within these a median of 50% (IQR = 36.4% to 63.7%) of the population was male.

Data related to ethnicity and socioeconomic factors (e.g., income, education) were not widely reported in the included studies (115 [12.9%] and 54 [6.1%], respectively), which are important factors to consider when considering the potential for health inequities. Participants' comorbidities as defined by the study authors were reported in 297 (33.3%) studies (refer to Figure 5 in Appendix 3 for the frequencies of comorbidities reported).

Few sources reported that they included individuals in rural and/or remote areas: only 11 (1.2%) and 3 (0.3%) stated they included individuals in rural and remote settings, respectively. It is possible that people living in rural or remote areas could be captured by some studies, such as those using telephone or online surveys, or online-based interventions (e.g., telerehabilitation). However, most studies did not include this information or provide subgroup analyses specific to people in rural or remote populations.

There was limited evidence identified on the role of COVID-19 vaccines. Vaccination status was not often reported in the included studies, even after COVID-19 vaccines became available in many parts of the world. Only 35 (3.9%) included references that reported data related to vaccination status, with 21 (2.4%) studies stating that participants were not vaccinated and 14 (1.6%) studies reporting that they included some participants who had received at least 1 dose of a COVID-19 vaccine. Five (0.6%) protocols have been published that plan to compare people who have been vaccinated to people who are not at risk of developing post–COVID-19 condition.

Figure 2: Number of Included Studies by Country of Participants With More Than 10 Included Studies



Acute Infection

The severity of acute infection (defined as asymptomatic, symptomatic but not hospitalized, hospitalized, or in ICU) was identified, though 207 (23.2%) did not report this information. Of the 685 studies where it was reported, 57 (8.3%) included participants who had been asymptomatic, 295 (43.1%) included participants who had been symptomatic but not hospitalized, 514 (75.0%) included participants who had been hospitalized, and 302 included participants (44.1%) who had been treated in the ICU. Thus, a large proportion of identified studies included people who had been hospitalized and/or treated in the ICU during the acute phase; there were comparatively fewer studies that included people who were asymptomatic in the acute phase. The frequencies of the severity of acute infection are available in Figure 6 in Appendix 3.

There were multiple methods for diagnosing or identifying COVID-19 infection used by 866 (97.1% of included sources) identified sources. Overall, there were 473 (54.6%) studies that used polymerase chain reaction tests, 122 (13.8%) that used antibody or antigen tests, 105 (11.9%) that used other or unspecified lab tests, 84 (9.5%) that used other tests (e.g., chest CT), 57 (6.5%) that confirmed using unspecified tests at the hospital or in the ICU, 53 (6.0%) that diagnosed by clinician, 11 (1.2%) that used the International Classification of Diseases (ICD) code for COVID-19, 2 (0.2%) that used the ICD code for long COVID or post–COVID-19 condition, and 9 (1.0%) that used self-report. The frequencies of these methods can be found in Figure 7 in Appendix 3.

Concepts

Main Concepts

Included studies were categorized as belonging to at least 1 main concept: risk factors and prevention, classification (e.g., classifying post–COVID-19 condition by symptoms, SARS-CoV-2 variant quantification, and reporting of pathophysiological markers), diagnostic tests, treatment or management, and health system issues (e.g., usage of health care services and pharmaceutical drugs). All concepts had additional subcategories except health system issues.

Across the 5 main categories, the most common for published studies, protocols, and preprints of systematic reviews was classification, followed by risk factors and prevention. Diagnostic tests had a high number of published studies but relatively few protocols, while treatment and management had few published studies but several protocols. We identified few sources related to few health systems issues across all publication types. The number of included sources by concept and publication status is presented in Figure 3, and a more detailed breakdown of the number of sources by various characteristics (e.g., study design, age groups) is presented in Table 3.

Classification

Studies related to classification were included in at least 1 of 5 subcategories, including:

- studies that assessed characteristics or outcomes of post–COVID-19 condition (e.g., symptoms or quality of life)
- pathophysiological markers that were assessed within 12 weeks (e.g., inflammation markers or lung function tests)
- different variants of SARS-CoV-2 (e.g., if studies specified the variant being assessed)

- subtypes of post–COVID-19 condition (e.g., studies that attempted to categorize patients with post–COVID-19 condition into different groups, based on symptoms, trajectory, and/or other factors)
- other (studies that may have assessed other characteristics, such as genome sequences or follow-up studies of interventions designed for acute infection).

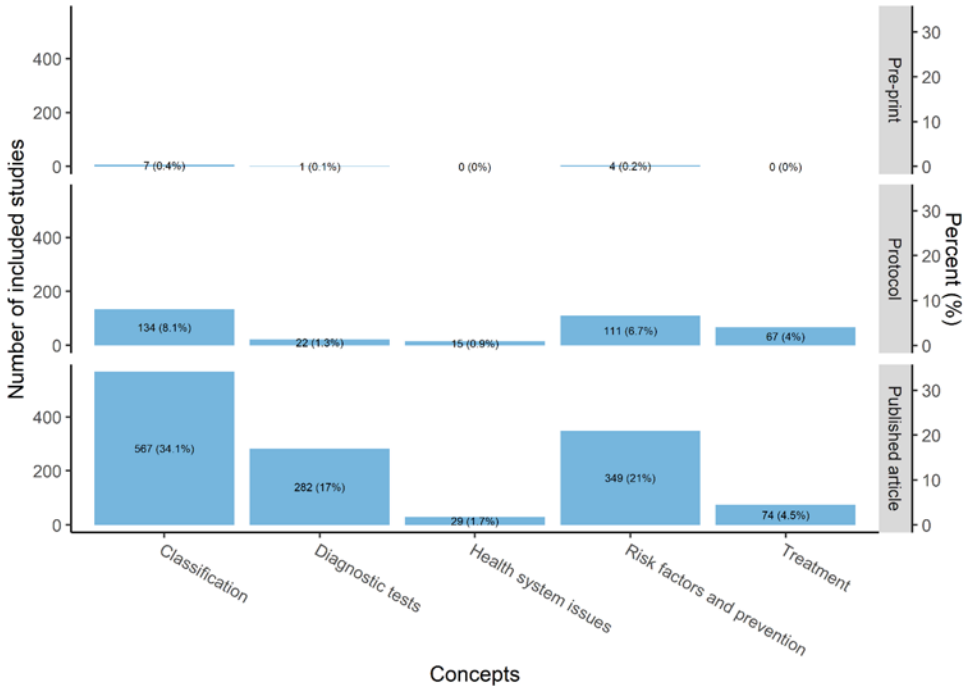
Overall, the largest subcategory represented under classification was characteristics for both published studies and protocols, followed by pathophysiological markers. In comparison, there were very few published studies related to different variants of the SARS-CoV-2 virus and subtypes of post–COVID-19 condition, and no protocols for either. A more detailed breakdown of the number of sources by various characteristics and publication status (published or protocols) is presented in Table 4.

Risk Factors and Prevention

Sources were considered as related to prevention if the intervention was provided within 12 weeks, including during the acute phase (e.g., a drug was provided during the acute phase or immediately after discharge, and the study assessed participants' symptoms at 12 weeks or later). Studies under risk factors and prevention were included in at least 1 of the following subcategories:

- risk factors (i.e., assessed any risk factors and their association with developing post–COVID-19 condition, such as age, sex, and comorbidities)
- preventive drug interventions

Figure 3: Number of Studies Included Within Each Concept, by Publication Status



Note: Included references could be included under more than 1 main concept category.

Table 3: Characteristics of Included Studies by Concept and Publication Status

Characteristic	Treatment, n (%)		Risk factors and prevention, n (%)		Classification, n (%)		Diagnostic tests, n (%)		Health system issues, n (%)	
	Published (n = 74)	Protocol (n = 67)	Published (n = 349)	Protocol (n = 111)	Published (n = 567)	Protocol (n = 134)	Published (n = 282)	Protocol (n = 22)	Published (n = 29)	Protocol (n = 15)
Report type										
Primary study	60 (81.1)	65 (95.6)	315 (90.3)	109 (94)	521 (92.4)	135 (97.1)	261 (93.2)	21 (95.5)	25 (89.3)	15 (100)
Systematic review	4 (5.4)	3 (4.4)	27 (7.7)	7 (6)	39 (6.9)	4 (2.9)	10 (3.6)	1 (4.5)	1 (3.6)	0
Scoping review	2 (2.7)	0	3 (0.9)	0	3 (0.5)	0	1 (0.4)	0	0	0
Guideline	11 (14.9)	0	7 (2)	0	6 (1.1)	0	11 (3.9)	0	2 (7.1)	0
Economic evaluation	0	0	1 (0.3)	0	1 (0.2)	0	0	0	1 (3.6)	0
Study design[a]										
Interventional	14 (18.9)	64 (94.1)	11 (3.2)	69 (59.5)	10 (1.8)	15 (10.8)	7 (2.5)	8 (36.4)	0	0
Observational	52 (70.3)	4 (5.9)	332 (95.1)	48 (41.4)	549 (97.3)	124 (89.2)	264 (94.3)	14 (63.6)	25 (89.3)	15 (100)
Age categories included										
< 18 included	4 (5.4)	1 (1.5)	33 (9.5)	13 (11.7)	54 (9.5)	21 (15.7)	20 (7.1)	3 (13.6)	3 (10.3)	3 (20)
18 to 64 included	50 (67.6)	61 (91)	277 (79.4)	103 (92.8)	445 (78.5)	128 (95.5)	215 (76.2)	19 (86.4)	20 (69)	15 (100)
≥ 65 included	18 (24.3)	51 (76.1)	170 (48.7)	96 (86.5)	238 (42)	111 (82.8)	102 (36.2)	20 (90.9)	15 (51.7)	15 (100)
Not reported	12 (16.2)	3 (4.5)	29 (8.3)	3 (2.7)	43 (7.6)	4 (3)	29 (10.3)	1 (4.5)	4 (13.8)	0
Severity of acute illness										
Asymptomatic	4 (5.4)	1 (1.5)	27 (7.7)	6 (5.2)	39 (6.9)	10 (7.2)	20 (7.1)	2 (9.1)	2 (7.1)	1 (6.7)
Symptomatic, not hospitalized	25 (33.8)	12 (17.6)	138 (39.5)	28 (24.1)	216 (38.3)	35 (25.2)	96 (34.3)	6 (27.3)	16 (57.1)	7 (46.7)
Hospitalized	29 (39.2)	16 (23.5)	268 (76.8)	54 (46.6)	366 (64.9)	71 (51.1)	183 (65.4)	11 (50)	23 (82.1)	8 (53.3)
ICU	16 (21.6)	12 (17.6)	154 (44.1)	36 (31)	210 (37.2)	48 (34.5)	94 (33.6)	7 (31.8)	13 (46.4)	8 (53.3)

Characteristic	Treatment, n (%)		Risk factors and prevention, n (%)		Classification, n (%)		Diagnostic tests, n (%)		Health system issues, n (%)	
	Published (n = 74)	Protocol (n = 67)	Published (n = 349)	Protocol (n = 111)	Published (n = 567)	Protocol (n = 134)	Published (n = 282)	Protocol (n = 22)	Published (n = 29)	Protocol (n = 15)
Not reported	20 (27)	41 (60.3)	38 (10.9)	40 (34.5)	92 (16.3)	57 (41)	41 (14.6)	6 (27.3)	3 (10.7)	3 (20)

ICU = intensive care unit; n (%) = number of references (proportions relative to all references in the same categories).

Note: Included studies could be included under more than 1 main concept category and/or study design and may have included multiple age groups and/or severity of acute illness categories.

[a]Systematic reviews and primary studies were classified as interventional and/or observational. Other publication types (e.g., guidelines) were not classified as either; thus, these numbers may not add up to 100%.

Table 4: Characteristics of Included Studies Reporting on Classification, by Publication Status

Characteristic	Post–Covid-19 Characteristics, n (%)		Pathophysiological markers, n (%)		Different variants of SARS-CoV-2, n (%)		Subtypes, n (%)		Other,[a] n (%)	
	Published (n = 542)	Protocol (n = 130)	Published (n = 96)	Protocol (n = 43)	Published (n = 2)	Protocol (n = 0)	Published (n = 7)	Protocol (n = 0)	Published (n = 2)	Protocol (n = 4)
Study design										
Primary study	498 (91.9)	126 (96.9)	92 (95.8)	43 (100)	2 (100)	0	7 (100)	0	2 (100)	4 (100)
Systematic review	39 (7.2)	4 (3.1)	4 (4.2)	0	0	0	0	0	0	0
Scoping review	3 (0.6)	0	1 (1)	0	0	0	0	0	0	0
Guideline	7 (1.3)	0	1 (1)	0	0	0	0	0	0	0
Economic evaluation	1 (0.2)	0	0	0	0	0	0	0	0	0
Interventional or observational[b]										
Interventional	10 (1.8)	14 (10.8)	1 (1)	3 (7)	0	0	1 (14.3)	0	0	0
Observational	526 (97)	116 (89.2)	95 (99)	40 (93)	2 (100)	0	6 (85.7)	0	2 (100)	4 (100)
Age groups										
< 18 included	52 (9.5)	19 (15.2)	8 (8.3)	5 (11.6)	0	0	0	0	0	3 (75)
18 to 64 included	427 (78.3)	119 (95.2)	74 (77.1)	42 (97.7)	2 (100)	0	6 (85.7)	0	1 (50)	4 (100)
≥ 65 included	229 (42)	105 (84)	40 (41.7)	36 (83.7)	0	0	4 (57.1)	0	2 (100)	3 (75)
Not reported	41 (7.5)	4 (3.2)	10 (10.4)	0	0	0	0	0	0	0
Severity of acute illness										
Asymptomatic	35 (6.5)	9 (6.9)	11 (11.5)	2 (4.7)	0	0	0	0	0	0
Symptomatic, not hospitalized	211 (38.9)	31 (23.8)	34 (35.4)	8 (18.6)	1 (50)	0	2 (28.6)	0	0	3 (75)
Hospitalized	352 (64.9)	66 (50.8)	64 (66.7)	17 (39.5)	1 (50)	0	6 (85.7)	0	1 (50)	4 (100)
ICU	202 (37.3)	45 (34.6)	35 (36.5)	8 (18.6)	0	0	4 (57.1)	0	1 (50)	3 (75)

Characteristic	Post–Covid-19 Characteristics, n (%)		Pathophysiological markers, n (%)		Different variants of SARS-CoV-2, n (%)		Subtypes, n (%)		Other,[a] n (%)	
	Published (n = 542)	Protocol (n = 130)	Published (n = 96)	Protocol (n = 43)	Published (n = 2)	Protocol (n = 0)	Published (n = 7)	Protocol (n = 0)	Published (n = 2)	Protocol (n = 4)
Not reported	88 (16.2)	53 (40.8)	16 (16.7)	25 (58.1)	0	0	1 (14.3)	0	0	0

ICU = intensive care unit; n (%) = number of references (proportions relative to all references in the same categories); SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Included references could be included under more than 1 main concept category and/or study design and may have included multiple age groups and/or severity of acute illness categories.

[a]Studies that may have assessed other characteristics (e.g., genome sequences, follow-up studies of interventions designed for acute infection).

[b]Systematic reviews and primary studies were classified as interventional and/or observational. Other publication types (e.g., guidelines) were not classified as either; thus, these numbers may not add up to 100%.

- preventive rehabilitation interventions (e.g., rehabilitation during hospital stay or immediately after discharge within 12 weeks of initial infection, may reduce the risk of developing post–COVID-19 condition)
- other preventive interventions (e.g., supplements, Chinese medicine, medical devices, or surgery).

Most (n = 311; 89.1%) of the published articles in this category assessed risk factors, especially published studies. There were comparatively fewer published studies related to preventive interventions (drug: n = 34; 9.7%; rehabilitation: n = 20; 5.7%), but we identified several protocols (41 and 26 for drug and rehabilitation, respectively, or 36.9% and 24.3% of protocols in this category), indicating that these areas are currently under study and more work will be published over time. A more detailed breakdown of the number of sources by publication status (published and protocol) and various characteristics is presented in Table 5. We also identified 4 preprints of systematic reviews, all related to risk factors.

Diagnostic Tests

Studies were considered relevant to diagnostic tests if they conducted any kind of laboratory test, imaging test, or other kind of health assessment test (e.g., pulmonary function test) at or after 12 weeks. Thus, we categorized all sources based on whether they conducted a laboratory test, imaging test, and/or other unspecified test. Overall, there were similar numbers of published studies and protocols for imaging and laboratory tests (165 and 146 published studies, respectively, or 58.5% and 51.8% of published studies within this category; and 12 protocols for both categories, or 54.5% within this category). A more detailed breakdown of the number of sources by publication status (published or protocol) and various characteristics is presented in Table 6.

Type of Treatment or Management

Any intervention provided at or after 12 weeks or 3 months was considered a treatment intervention. Treatment interventions could fall into 1 or more subcategories:

- drug (any pharmaceutical intervention)
- rehabilitation (i.e., any kind of exercise rehabilitation, provided in a medical setting or at home [e.g., telehealth])
- care models (i.e., pathways, trajectories, frameworks, or structured clinics)[28]
- other (e.g., supplements, Chinese medicine, medical devices, virtual reality exercise, and surgery).

References that assessed, or protocols that planned to assess, vaccines as a potential treatment for post–COVID-19 condition were considered both drug and other interventions. We identified relatively few published studies related to treatment or management interventions, but several protocols indicate that research in these areas is ongoing. However, we identified comparatively fewer published studies and protocols related to care models. A more detailed breakdown of the number of sources by publication status and various characteristics is presented in Table 7.

Guidelines

Among the included studies described and summarized in the previous sections, there were 12 guidelines identified. Guidelines were eligible for inclusion if they provided at least

1 recommendation specific to patients experiencing symptoms 12 or more weeks after diagnosis or symptom onset.

In Canada, guidelines from Alberta, British Columbia, Ontario, and Quebec were identified; the methods and relevant recommendations (i.e., recommendations specific to 12 weeks or later) are summarized in Table 12 and Table 13 in Appendix 2, respectively. All included guidelines define post–COVID as 4 or more weeks post-infection or diagnosis but provide limited

Table 5: Characteristics of Included Studies Reporting on Risk Factors and Prevention, by Publication Status

Characteristic	Drug prevention, n (%)		Preventive rehabilitation, n (%)		Risk factors, n (%)		Other, n (%)	
	Published (n = 34)	Protocol (n = 41)	Published (n = 20)	Protocol (n = 27)	Published (n = 311)	Protocol (n = 37)	Published (n = 9)	Protocol (n = 17)
Study design								
Primary study	33 (97.1)	39 (95.1)	15 (75)	24 (88.9)	279 (89.7)	33 (89.2)	7 (77.8)	17 (100)
Systematic review	0	2 (4.9)	1 (5)	3 (11.1)	27 (8.7)	4 (10.8)	0	0
Scoping review	0	0	0	0	3 (1)	0	0	0
Guideline	0	0	4 (20)	0	5 (1.6)	0	1 (11.1)	0
Economic evaluation	1 (2.9)	0	0	0	1 (0.3)	0	1 (11.1)	0
Interventional or observational[a]								
Interventional	2 (5.9)	35 (85.4)	7 (35)	26 (96.3)	3 (1)	4 (10.8)	0	12 (70.6)
Observational	31 (91.2)	7 (17.1)	9 (45)	2 (7.4)	304 (97.7)	34 (91.9)	7 (77.8)	5 (29.4)
Age groups								
< 18 included	1 (2.8)	2 (5)	0	2 (7.7)	33 (10.6)	7 (20.6)	1 (10)	2 (11.8)
18 to 64 included	29 (80.6)	38 (95)	15 (75)	22 (84.6)	244 (78.7)	31 (91.2)	8 (80)	16 (94.1)
≥ 65 included	14 (38.9)	34 (85)	5 (25)	22 (84.6)	157 (50.6)	27 (79.4)	3 (30)	15 (88.2)
Not reported	0	1 (2.5)	5 (25)	1 (3.8)	27 (8.7)	2 (5.9)	1 (10)	1 (5.9)
Severity of acute illness								
Asymptomatic	0	3 (7.3)	1 (5)	0	27 (8.7)	3 (8.1)	0	1 (5.9)
Symptomatic, not hospitalized	9 (26.5)	13 (31.7)	5 (25)	2 (7.4)	129 (41.5)	8 (21.6)	2 (22.2)	5 (29.4)
Hospitalized	20 (58.8)	18 (43.9)	14 (70)	12 (44.4)	249 (80.1)	21 (56.8)	3 (33.3)	7 (41.2)
ICU	14 (41.2)	9 (22)	11 (55)	12 (44.4)	133 (42.8)	12 (32.4)	3 (33.3)	7 (41.2)
Not reported	2 (5.9)	12 (29.3)	2 (10)	8 (29.6)	36 (11.6)	15 (40.5)	2 (22.2)	7 (41.2)

ICU = intensive care unit; n (%) = number of references (proportions relative to all references in the same categories).

Note: Included references could be included under more than 1 main concept category and/or study design and may have included multiple age groups and/or severity of acute illness categories. No qualitative or mixed-methods studies were identified.

[a]Systematic reviews and primary studies were classified as interventional and/or observational. Other publication types (e.g., guidelines) were not classified as either; thus, these numbers may not add up to 100%.

guidance for patients experiencing symptoms after 12 weeks. Recommendations specific to people experiencing symptoms at 12 weeks or later were referral to a specialty clinic (Alberta[29] and British Columbia[30]) and using a chest X-ray for those experiencing respiratory symptoms (Ontario[31] and Quebec).[32]

Eight guidelines were identified from countries other than Canada and are summarized in Table 14. Most guidelines from other countries also focus on the 4 or more weeks definition, with limited diagnosis guidance for patients at 12 or more weeks post-infection or diagnosis.

Table 6: Characteristics of Included Studies Reporting on Diagnostic Tests for Post–COVID-19 Condition, by Publication Status

Characteristic	Imaging tests, n (%)		Laboratory tests, n (%)		Other kind of health assessment test (e.g., pulmonary function test), n (%)	
	Published (n = 165)	Protocol (n = 12)	Published (n = 146)	Protocol (n = 12)	Published (n = 85)	Protocol (n = 11)
Study design						
Primary study	152 (92.1)	12 (100)	138 (94.5)	12 (100)	73 (85.9)	10 (90.9)
Systematic review	7 (4.2)	0	4 (2.7)	0	4 (4.7)	1 (9.1)
Scoping review	1 (0.6)	0	0	0	0	0
Guideline	6 (3.6)	0	5 (3.4)	0	8 (9.4)	0
Economic evaluation	0	0	0	0	0	0
Interventional or observational[a]						
Interventional	2 (1.2)	1 (8.3)	5 (3.4)	4 (33.3)	3 (3.5)	5 (45.5)
Observational	158 (95.8)	11 (91.7)	137 (93.8)	8 (66.7)	74 (87.1)	6 (54.5)
Age groups						
< 18 included	11 (6.6)	1 (8.3)	15 (10.2)	2 (16.7)	5 (6)	1 (9.1)
18 to 64 included	129 (77.7)	9 (75)	107 (72.8)	11 (91.7)	63 (75)	9 (81.8)
≥ 65 included	51 (30.7)	10 (83.3)	55 (37.4)	11 (91.7)	32 (38.1)	10 (90.9)
Not reported	14 (8.4)	1 (8.3)	15 (10.2)	0	12 (14.3)	1 (9.1)
Severity of acute illness						
Asymptomatic	4 (2.4)	2 (16.7)	16 (11)	1 (8.3)	5 (5.9)	2 (18.2)
Symptomatic, not hospitalized	48 (29.1)	3 (25)	61 (41.8)	4 (33.3)	25 (29.4)	2 (18.2)
Hospitalized	106 (64.2)	7 (58.3)	98 (67.1)	6 (50)	59 (69.4)	6 (54.5)
ICU	60 (36.4)	5 (41.7)	43 (29.5)	5 (41.7)	35 (41.2)	3 (27.3)
Not reported	17 (10.3)	3 (25)	21 (14.4)	4 (33.3)	14 (16.5)	3 (27.3)

ICU = intensive care unit; n (%) = number of references (proportions relative to all references in the same categories).

Note: Included references could be included under more than 1 main concept category and/or study design and may have included multiple age groups and/or severity of acute illness categories.

[a]Systematic reviews and primary studies were classified as interventional and/or observational. Other publication types (e.g., guidelines) were not classified as either; thus, these numbers may not add up to 100%.

Four guidelines were identified that provided guidance for diagnosis as well as management for patients at 12 weeks or later.[6,33-35] A summary of these guidelines' methods and relevant recommendations are available in Table 14 and Table 15 in Appendix 2, respectively.

Evidence Gap Mapping

A summary of areas where sources were and were not identified is presented in Table 8. Thus far, much of the published literature on post–COVID-19 condition has focused on symptoms, outcomes, and risk factors, with some studies assessing for long periods of

Table 7: Characteristics of Included Studies Reporting on Treatment or Management, by Publication Status

Characteristic	Rehabilitation, n (%)		Drug, n (%)		Care model, n (%)		Other, n (%)	
	Published (n = 27)	Protocol (n = 42)	Published (n = 35)	Protocol (n = 19)	Published (n = 7)	Protocol (n = 3)	Published (n = 24)	Protocol (n = 16)
Study design								
Primary study	15 (55.6)	40 (95.2)	33 (94.3)	17 (89.5)	2 (28.6)	2 (66.7)	20 (83.3)	16 (100)
Systematic review	4 (14.8)	2 (4.8)	2 (5.7)	2 (10.5)	2 (28.6)	1 (33.3)	0	0
Scoping review	2 (7.7)	0	1 (2.9)	0	1 (16.7)	0	0	0
Guideline	9 (33.3)	0	1 (2.9)	0	4 (57.1)	0	4 (16.7)	0
Economic evaluation	0	0	0	0	0	0	0	0
Interventional or observational[a]								
Interventional	8 (29.6)	40 (95.2)	3 (8.6)	18 (94.7)	1 (14.3)	1 (33.3)	4 (16.7)	16 (100)
Observational	12 (44.4)	2 (4.8)	33 (94.3)	1 (5.3)	3 (42.9)	2 (66.7)	16 (66.7)	0
Age groups								
< 18 included	3 (11.5)	1 (2.4)	3 (8.6)	0	1 (16.7)	0	1 (4)	0
18 to 64 included	14 (53.8)	38 (90.5)	26 (74.3)	17 (89.5)	1 (16.7)	2 (66.7)	15 (60)	13 (86.7)
≥ 65 included	7 (26.9)	34 (81)	7 (20)	11 (57.9)	2 (33.3)	2 (66.7)	6 (24)	11 (73.3)
Not reported	9 (34.6)	2 (4.8)	1 (2.9)	2 (10.5)	3 (50)	1 (33.3)	5 (20)	1 (6.7)
Severity of acute illness								
Asymptomatic	2 (7.4)	0	3 (8.6)	1 (5.3)	1 (14.3)	0	0	0
Symptomatic, not hospitalized	12 (44.4)	8 (19)	13 (37.1)	3 (15.8)	3 (42.9)	0	7 (29.2)	4 (25)
Hospitalized	11 (40.7)	7 (16.7)	17 (48.6)	8 (42.1)	3 (42.9)	1 (33.3)	5 (20.8)	6 (37.5)
ICU	9 (33.3)	10 (23.8)	5 (14.3)	0	2 (28.6)	0	4 (16.7)	3 (18.8)
Not reported	11 (40.7)	26 (61.9)	5 (14.3)	11 (57.9)	4 (57.1)	2 (66.7)	8 (33.3)	7 (43.8)

ICU = intensive care unit; n (%) = number of references (proportions relative to all references in the same categories).

Note: Included references could be included under more than 1 main concept category and/or study design and may have included multiple age groups and/or severity of acute illness categories.

[a]Systematic reviews and primary studies were classified as interventional and/or observational. Other publication types (e.g., guidelines) were not classified as either; thus, these numbers may not add up to 100%.

time; for example, a year after infection or hospital discharge.[36-38] More than 450 studies have also assessed factors associated with a higher risk of experiencing post–COVID symptoms, and used different diagnostic tests (e.g., using biomarkers or imaging tests). We noted few systematic reviews on diagnostic tests for post–COVID-19 symptoms despite the high number of primary studies, which may be a potential area for future systematic reviews. We identified fewer than 90 published sources on treatment and management, but noted an increasing number of clinical trial registrations, indicating ongoing work to determine the effectiveness of different treatments, including pharmaceutical drugs, COVID-19 vaccines used after infection, and rehabilitation.

Table 8: Summary of Evidence

State of evidence map	Concepts and populations
Areas where evidence was identified: several published primary studies (≥ 50) and SRs (≥ 10)	• Characteristics or symptoms of post–COVID-19 condition • Risk factors for developing post–COVID-19 condition
Areas where there were several (≥ 50) primary studies but few SRs (< 10)	• Pathophysiological markers assessed at < 12 weeks • Imaging and laboratory diagnostic tests used when assessing at ≥ 12 weeks
Areas expecting to see evidence soon (< 50 published primary studies and/or < 10 SRs, several trial protocols, and a few SR protocols)	• Preventive interventions, including those provided during the acute phase or < 12 weeks after symptom onset or diagnosis (e.g., drug, rehabilitation) • Treatment or management interventions provided ≥ 12 weeks after symptom onset or diagnosis (drug, rehabilitation, other [e.g., supplements])
Areas with gaps in evidence (< 50 published primary studies and < 50 protocols)	Study types: • Economic evaluations • Qualitative studies • Ethical analyses • Health systems issues • Guidelines using the WHO definition of post–COVID-19 condition[a] Concepts: • Differences between variants of SARS-CoV-2 virus related to post–COVID-19 condition • Subtypes of post–COVID-19 condition based on symptoms, trajectory, and/or other factors Participant demographics: • Children and adolescents (< 18 years) (except regarding characteristics or symptoms) • People living in rural and remote areas[b] • People who were asymptomatic during the acute phase (except regarding characteristics/symptoms and risk factors)[c] • People who have received the COVID-19 vaccine

SR = systematic reviews.

[a]In total 12 guidelines were identified, but most provided limited recommendations specific to patients at 12 or more weeks and instead focused on 4 or more weeks. It is unclear if these recommendations can be applied to patients after 12 or more weeks.

[b]This is based on limited studies that explicitly reported they included rural and remote or conducted a subanalysis of rural and remote. Certain study designs may include rural and remote populations (e.g., online surveys), but unless they stated that they recruited participants from rural and remote locations, they were not counted.

[c]The proportion of trial protocols where severity of acute illness was not reported was relatively high for preventive and treatment and management, so it is possible that some of these trials will include participants who were asymptomatic and may have conducted subanalyses by acute illness severity. However, we identified relatively few published studies focused on this group, compared to participants who had been hospitalized.

Discussion

There were some notable evidence gaps and areas with large numbers of studies. There were limited evaluations on the economic impact of post–COVID-19 condition or the cost-effectiveness of interventions. There were also few guidelines providing recommendations for individuals living with post–COVID-19 condition according to the WHO definition (12 or more weeks after initial infection). Many of the identified guidelines provide guidance for people who still have symptoms at 4 or more weeks, and it is unclear whether these recommendations will be revised for people who are experiencing symptoms at 12 or more weeks. Early estimates suggest a lower prevalence of persistent symptoms at 12 weeks compared to 4 to 5 weeks,[10,39] which may indicate that some people who have symptoms at 4 weeks will recover by 12 weeks. Currently, it is unclear if they represent a different clinical phenotype than people who have symptoms at 12 or more weeks. If this is the case, different guidance may be required at 12 or more weeks than 4 to 12 weeks. We also identified few published sources and protocols that assessed the impact of different variants of SARS-CoV-2 and different subtypes of post–COVID-19 condition (i.e., whether post–COVID-19 condition may encapsulate multiple different syndromes[40,41]; such as, based on different symptom trajectories).[42] For example, people who had been treated in the ICU may be experiencing post-intensive care syndrome,[43] which is characterized as "the worsening of the physical, mental or cognitive patient's status after a critical illness" (p. 2),[43] and may be a separate clinical phenotype from people who had milder acute illness but are also experiencing persistent symptoms.[44-46]

We identified few published studies and protocols for certain population groups. Relatively few studies and protocols included or plan to include children, and there may be important differences between adults and children (e.g., while many studies report shortness of breath as a common post–COVID-19 symptom, the NICE guidelines suggest that it is less common in children and older adults[6]). In addition, while numerous protocols for management and treatment were identified, many are not including participants under 18 years old. Thus, even if these trials indicate treatments to be effective in adults, it is not known if they can be used to treat children or adolescents with similar effects. We also did not identify many studies that included people who had been asymptomatic during the acute illness phase or focused on people living in rural and/or remote areas. This may be due in part to lack of COVID-19 testing, particularly earlier in the pandemic when access may have been restricted or otherwise difficult to access for people who were asymptomatic. It is possible the clinical phenotype of post–COVID-19 condition may differ between people who had milder acute illness (i.e., were not hospitalized) and people who had more severe acute illness and were hospitalized. Thus, the lack of published evidence and lack of planned protocols focused on people who had milder acute illness, particularly people who had been asymptomatic, is an important evidence gap. There was also a gap in studies that reported specifically on participants living in rural and/or remote areas. Many studies were conducted by major hospitals that are generally located in urban areas. While some study designs may include people living in rural and remote areas, such as surveys conducted by telephone or online,[47] few studies included data on participants' location (e.g., how many participants were living in rural or remote areas), making it unclear whether living in a rural or remote area may be associated with the severity of initial infection or influence outcomes. For example, individuals living far from a major hospital may not have received the same level of care for acute infection or may not have had access to certain treatment and management options for post–COVID-19 condition, such as a specialized clinic in the city. While telehealth-based rehabilitation has been evaluated in several primary studies,[48,49] whether participants' location may hinder

accessibility and thus long-term outcomes requires further research. The lack of literature on rural and remote populations should also be considered to ensure equitable access to high-quality post–COVID care.

In Canada and many other countries, the COVID-19 vaccination coverage has reached more than 80% of adults.[50] However, we did not identify many published studies that assess the impact of the COVID-19 vaccination on the development of post–COVID-19 condition. Nor many studies that reported if their participants had received the COVID-19 vaccine: thus, it is still unclear whether receiving a COVID-19 vaccine before or after developing post–COVID-19 condition will impact symptoms. We did identify some registered trials that aim to assess the impact of vaccination on post–COVID-19 condition.[51-53] There are also limited studies assessing post–COVID-19 condition in breakthrough infections (i.e., for individuals who had been vaccinated, then become infected with COVID-19). This may be an important consideration with the spread of the Omicron variant, which has become dominant in Canada and many other countries, as vaccines are less effective at preventing infection from this variant, and breakthrough infections have become increasingly common.[54] There was also a lack of information regarding the SARS-CoV-2 variant being assessed in studies.[55,56] Determining whether different variants have different long-term effects may also be important to plan for diagnosis, treatment, or management. Finally, future guidelines or updates to existing guidelines may be needed to ensure clear and consistent recommendations for post–COVID-19 condition that incorporate the findings of emerging evidence, so that health care providers can provide adequate care.

In contrast, we identified areas with large numbers of sources. There were more systematic reviews addressing the characteristics and outcomes of post–COVID-19 condition and risk factors than other concepts. There were many recently published primary studies reporting on pathophysiological markers and diagnostic tests. These issues may be suitable for evidence synthesis or meta-analysis to provide summaries on the pandemic. While there are new SARS-CoV-2 variants emerging and new strategies are created for the long-term consequences, continued efforts in exploring these concepts in the short-term are expected.

Identified previous scoping reviews on post–COVID-19 condition were published before WHO's release of a clinical definition for post–COVID-19 condition, and did not use the definition of 12 weeks (or 3 months) after diagnosis or symptom onset.[11-13] Thus, this report has a broader scope and differs from previous scoping reviews as it focuses on studies that assessed participants at least after 12 weeks, aligning with the current NICE and WHO definitions of post–COVID-19 condition.[6,7] We have also added to the evidence that pertains to a broader range of topics than previous scoping reviews, such as mapping evidence related to preventive interventions and health systems issues. Finally, we have also characterized the volume of literature by various demographic variables, allowing for a better sense of where evidence is lacking and for which groups.

Limitations

This review was limited to studies available in English or French; as this limitation was applied at the level of the search, it is not clear how many studies may have been excluded for this reason, and findings could differ slightly had other languages been included. Due to the wide breadth of topics covered and time constraints, we chose to exclude literature reviews, correspondence, editorials, and preprints of primary studies, and did not search reference lists of included studies nor contact experts to supplement the search; as a result, there is a possibility that some relevant studies were missed, but it is unlikely that this would

have a large impact on the overall high-level findings. While ethical analyses were eligible for inclusion, it is possible and likely that some were missed given the specialized expertise required to identify such analyses and that these reports might be presented as narrative reviews, commentaries, or editorials, which were not eligible for this review. We also chose specific follow-up time definitions based on the reported mean with SD or median with IQR, but these are imperfect measures and had other threshold been used, there may have been differences in which studies were included and excluded. Some included sources may not have intended to assess post–COVID-19 condition; for example, a study assessed rehabilitation post-discharge to treat post-intensive care syndrome, but followed participants for at least 12 weeks after symptom onset or diagnosis. As there was no differentiation made between post-intensive care syndrome and post–COVID-19 condition, this review could include both. The overlap between systematic reviews was not investigated and certain primary studies are likely to be included in multiple systematic reviews. Resource and time constraints also prevented us from abstracting several measures, such as the definition of post–COVID-19 condition used in individual studies, details of specific interventions, and outcomes collected by the studies. Although the PROGRESS-Plus variables were charted, the text data were complex and it became infeasible to extract, validate, and organize them all in a meaningful way; thus, the data are not presented. Finally, stakeholder input on the scoping review was limited to peer review and select clinical experts. Persons with post–COVID-19 condition are an integral part of the stakeholder panel, a group of cross-jurisdictional decision-makers, clinicians, researchers, and patient representatives who are providing support for the overall direction for the larger condition-level review, but they did not provide direct input for this scoping review.

Future Updates

With the emergence of published sources of this topic monthly, an update to this scoping review will be conducted and certain aspects will transition to a living mode. A living review is one that is continually updated, incorporating relevant new evidence as it becomes available.[57] Details of the exact scope of future updates are still to be determined, and future iterations will be shaped based on input from knowledge users and the patient community. This future work will provide a deeper understanding of the evidence base for post–COVID-19 condition. Additional knowledge mobilization activities to disseminate the findings of this scoping review and the larger condition-level review will also be conducted, and could include relevant educational outreach and related activities. Outreach of this project and the condition-level review will be made by CADTH's Knowledge Mobilization and Implementation Support team to meet the needs of key stakeholders, such as patients, jurisdictional bodies, health care providers, and other users of health evidence.

Conclusions

In conclusion, as of December 2021, there has been a great deal of research conducted and published on post–COVID-19 condition. Much of the evidence identified has looked at symptoms, risk factors, and different diagnostic tests to assess individuals with post–COVID-19 condition, particularly adults and people who had been hospitalized or treated in the ICU. There is currently relatively limited research available on preventive interventions and interventions to treat or manage post–COVID-19 condition, but published protocols indicate research in this area is ongoing. Some areas where few published evidence and

protocols were found include pediatric populations, people living in rural and remote areas, and the impact of different variants of SARS-CoV-2. In addition, there was a notable lack of evidence on PROGRESS-Plus variables, including few studies from low- and middle-income countries, and studies that reported factors related to disadvantage and equity (e.g., participants' socioeconomic status, occupation, education, race, ethnicity, culture, language, and place of residence). More research in these areas may help to close some of the current evidence gaps.

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Appendix 1: Literature Search Methods

Note that this appendix has not been copy-edited.

Overview

Interface: Ovid and EBSCOhost

Databases:

- MEDLINE All (1946-present) via Ovid
- Embase (1974-present) via Ovid
- APA PsycInfo (1806-present) via Ovid
- Cochrane Central Register of Controlled Trials via Ovid
- CINAHL (Cumulative Index to Nursing and Allied Health Literature) via EBSCO

Note: Subject headings and search fields have been customized for each database. Duplicates were removed using Ovid deduplication for multi-file searches, followed by manual deduplication in Endnote.

Date of search: October 15, 2021

Alerts: Monthly search updates until December 20, 2021.

Search filters applied: No filters were applied to limit the retrieval by study type. Comments, newspaper articles, editorials, and letters were removed.

Limits:

- Publication date limit: 2019-present
- Humans
- Languages: English or French

Table 9: Ovid Syntax Guide

Syntax	Description
/	At the end of a phrase, searches the phrase as a subject heading
MeSH	Medical Subject Heading
.fs	Floating subheading
exp	Explode a subject heading
*	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
#	Truncation symbol for one character
?	Truncation symbol for one or no characters only
adj#	Requires terms to be adjacent to each other within # number of words (in any order)
.ti	Title
.ot	Original title

Syntax	Description
.ab	Abstract
.hw	Heading word; usually includes subject headings and controlled vocabulary
.kf	Author keyword heading word (MEDLINE, Embase)
.id	Author keyword (PsycInfo)
.dq	Candidate term word (Embase)
.pt	Publication type
.yr	Publication year
medall	Ovid database code: MEDLINE All, 1946 to present, updated daily
oemezd	Ovid database code; Embase, 1974 to present, updated daily
cctr	Ovid database code; Cochrane Central Register of Controlled Trials
psyh	Ovid database code; APA PsycInfo for the years 2019 and 2020-present.

Ovid Multi-Database Strategy – Medline, Embase, Cochrane Central, and PsycInfo

1. (long COVID* or long coronavirus*).ti,ab,kf.
2. ((chronic or post) adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj2 (sequela* or syndrome* or disorder* or condition* or symptom*)).ti,ab,kf.
3. ((post acute or postacute or post viral or postviral or post virus* or postvirus* or long duration or long last or long lasting or longstanding or long standing) adj3 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
4. (late sequela* adj2 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
5. ((long term or longterm) adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
6. PASC.ti,kf.
7. ((postcovid* or post covid* or postcoronavirus* or post coronavirus* or post SARS-COV-2 or postSARS-COV-2 or post SARS-COV2 or postSARS-COV2 or post SARSCOV-2 or post SARSCOV-2) adj3 (sequela* or syndrome* or disorder* or illness* or condition* or symptom* or prognos* or followup* or follow up*)).ti,ab,kf.
8. (post-covid* adj5 (care or aftercare*) adj5 (center* or centre or clinic*)).ti,ab,kf.
9. or/1-8 [Medline CCTR set 1 Main Long Covid Terms]
10. (((post acute or postacute or sub-acute or subacute or chronic) adj sequela*) or PASC).ti,ab,kf.
11. (long haul* or longhaul*).ti,ab,kf.
12. ((post-intensive care or postintensive care or post-ICU) adj syndrome*).ti,ab,kf.
13. ((persist* or long* or residual or prolonged) adj8 ((olfactory or chemosensor*) adj (disorder* or dysfunction*))).ti,ab,kf.
14. or/10-13 [Medline CCTR set 2 Post Acute Subtype terms to AND with COVID]
15. COVID-19/ or exp COVID-19 Testing/ or COVID-19 Vaccines/ or SARS-CoV-2/
16. (coronavirus/ or betacoronavirus/ or coronavirus infections/) and (disease outbreaks/ or epidemics/ or pandemics/)

17. (nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARS-COV2 or SARSCOV2 or SARS coronavirus 2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kf,nm,ot,ox,rx,px.
18. ((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kf,ot.
19. (longCOVID* or postCOVID* or postcoronavirus* or postSARS*).ti,ab,kf,ot.
20. ((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kf,ot.
21. ((Wuhan or Hubei) adj5 pneumonia).ti,ab,kf,ot.
22. or/15-21 [Medline CCTR set 3 CADTH Covid-19 filter]
23. (recovery adj2 (clinic or clinics or centre or center or centres or centers or program*)).ti,ab,kf.
24. (post* adj3 rehabilitation adj2 (clinic or clinics or centre or center or centres or centers or program*)).ti,ab,kf.
25. or/23-24 [Medline CCTR set 4 Post Covid Recovery Clinics]
26. (post adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj3 infection* adj8 (chronic* or persist* or residual or prolonged or non-recover* or nonrecover* or recover* or rehabilitat* or month or months or year or years or sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*)).ti,ab,kf.
27. ((chronic or post) adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj3 (rehabilitat* or recover* or fatigue or function*)).ti,ab,kf.
28. ((chronic* or persist* or residual or prolonged or non-recover* or nonrecover*) adj2 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
29. ((chronic* or persist* or residual or prolonged or non-recover* or nonrecover*) adj2 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj5 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*)).ti,ab,kf.
30. ((long-term or longterm) adj (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
31. ((post acute or postacute or post viral or postviral or post virus* or postvirus* or long duration or long last or long lasting or longstanding or long standing or late-onset or (illness adj2 duration)) adj3 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
32. ((survivor* or survived or discharg* or postdischarg* or post infect* or postinfect*) adj3 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
33. ((survivor* or survived or discharg* or postdischarg* or post infect* or postinfect*) adj3 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj5 (sequela* or syndrome* or

disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*)).ti,ab,kf.

34. or/26-33 [Medline CCTR set 5 Top Up set]
35. 14 and 22
36. 22 and 25
37. 9 or 34 or 35 or 36
38. 37 use medall
39. 37 use cctr
40. (long COVID* or long coronavirus*).ti,ab,kf.
41. ((chronic or post) adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj2 (sequela* or syndrome* or disorder* or condition* or symptom*)).ti,ab,kf.
42. ((post acute or postacute or post viral or postviral or post virus* or postvirus* or long duration or long last or long lasting or longstanding or long standing) adj3 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
43. (late sequela* adj2 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
44. ((long term or longterm) adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
45. PASC.ti,kf.
46. ((postcovid* or post covid* or postcoronavirus* or post coronavirus* or post SARS-COV-2 or postSARS-COV-2 or post SARS-COV2 or postSARS-COV2 or post SARSCOV-2 or post SARSCOV-2) adj3 (sequela* or syndrome* or disorder* or illness* or condition* or symptom* or prognos* or followup* or follow up*)).ti,ab,kf.
47. (post-covid* adj5 (care or aftercare*) adj5 (center* or centre or clinic*)).ti,ab,kf.
48. or/40-47 [Embase set 1 Main Long Covid terms]
49. (((post acute or postacute or sub-acute or subacute or chronic) adj sequela*) or PASC).ti,ab,kf.
50. (long haul* or longhaul*).ti,ab,kf.
51. ((post-intensive care or postintensive care or post-ICU) adj syndrome*).ti,ab,kf.
52. ((persist* or long* or residual or prolonged) adj8 ((olfactory or chemosensor*) adj (disorder* or dysfunction*))).ti,ab,kf.
53. or/49-52 [Embase set 2 Post Acute Subtype terms to AND with COVID]
54. sars-related coronavirus/
55. (coronavirinae/ or betacoronavirus/ or coronavirus infection/) and (epidemic/ or pandemic/)
56. (nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARS-COV2 or SARSCOV2 or SARS coronavirus 2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,kf,hw,ot.
57. ((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kf,hw,ot.
58. (longCOVID* or postCOVID* or postcoronavirus* or postSARS*).ti,ab,kf,hw,ot.

59. ((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kf,ot.
60. ((Wuhan or Hubei) adj5 pneumonia).ti,ab,kf,ot.
61. or/54-60 [Embase set 3 CADTH Covid Filter]
62. (recovery adj2 (clinic or clinics or centre or center or centres or centers or program*)).ti,ab,kf.
63. (post* adj3 rehabilitation adj2 (clinic or clinics or centre or center or centres or centers or program*)).ti,ab,kf.
64. or/62-63 [Embase set 4 Post Covid Recovery Clinics to AND with Covid set 3]
65. (post adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj3 infection* adj8 (chronic* or persist* or residual or prolonged or non-recover* or nonrecover* or recover* or rehabilitat* or month or months or year or years or sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*)).ti,ab,kf.
66. ((chronic or post) adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj3 (rehabilitat* or recover* or fatigue or function*)).ti,ab,kf.
67. ((chronic* or persist* or residual or prolonged or non-recover* or nonrecover*) adj2 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
68. ((chronic* or persist* or residual or prolonged or non-recover* or nonrecover*) adj2 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj5 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*)).ti,ab,kf.
69. ((long-term or longterm) adj (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
70. ((post acute or postacute or post viral or postviral or post virus* or postvirus* or long duration or long last or long lasting or longstanding or long standing or late-onset or (illness adj2 duration)) adj3 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
71. ((survivor* or survived or discharg* or postdischarg* or post infect* or postinfect*) adj3 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,kf.
72. ((survivor* or survived or discharg* or postdischarg* or post infect* or postinfect*) adj3 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj5 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*)).ti,ab,kf.
73. or/65-72 [Embase set 5 Top Up set]
74. 53 and 61
75. 61 and 64
76. 48 or 73 or 74 or 75

77. 76 use oemezd
78. (long COVID* or long coronavirus*).ti,ab,id.
79. ((chronic or post) adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj2 (sequela* or syndrome* or disorder* or condition* or symptom*)).ti,ab,id.
80. ((post acute or postacute or post viral or postviral or post virus* or postvirus* or long duration or long last or long lasting or longstanding or long standing) adj3 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,id.
81. (late sequela* adj2 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,id.
82. ((long term or longterm) adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,id.
83. PASC.ti,id.
84. ((postcovid* or post covid* or postcoronavirus* or post coronavirus* or post SARS-COV-2 or postSARS-COV-2 or post SARS-COV2 or postSARS-COV2 or post SARSCOV-2 or post SARSCOV-2) adj3 (sequela* or syndrome* or disorder* or illness* or condition* or symptom* or prognos* or followup* or follow up*)).ti,ab,id.
85. (post-covid* adj5 (care or aftercare*) adj5 (center* or centre or clinic*)).ti,ab,id.
86. or/78-85 [PsycInfo set 1 Main Long Covid terms]
87. (((post acute or postacute or sub-acute or subacute or chronic) adj sequela*) or PASC).ti,ab,id.
88. (long haul* or longhaul*).ti,ab,id.
89. ((post-intensive care or postintensive care or post-ICU) adj syndrome*).ti,ab,id.
90. ((persist* or long* or residual or prolonged) adj8 ((olfactory or chemosensor*) adj (disorder* or dysfunction*))).ti,ab,id.
91. or/87-90 [PsycInfo set 2 Post Acute Subtype terms to AND with COVID]
92. COVID-19/ or exp COVID-19 Testing/ or COVID-19 Vaccines/ or SARS-CoV-2/
93. (coronavirus/ or betacoronavirus/ or coronavirus infections/) and (disease outbreaks/ or epidemics/ or pandemics/)
94. (nCoV* or 2019nCoV or 19nCoV or COVID19* or COVID or SARS-COV-2 or SARSCOV-2 or SARS-COV2 or SARSCOV2 or SARS coronavirus 2 or Severe Acute Respiratory Syndrome Coronavirus 2 or Severe Acute Respiratory Syndrome Corona Virus 2).ti,ab,id,ot.
95. ((new or novel or "19" or "2019" or Wuhan or Hubei or China or Chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,id.
96. (longCOVID* or postCOVID* or postcoronavirus* or postSARS*).ti,ab,id.
97. ((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,id.
98. ((Wuhan or Hubei) adj5 pneumonia).ti,ab,id.
99. or/92-98 [PsycInfo set 3 CADTH Covid Filter]
100. (recovery adj2 (clinic or clinics or centre or center or centres or centers or program*)).ti,ab,id.
101. (post* adj3 rehabilitation adj2 (clinic or clinics or centre or center or centres or centers or program*)).ti,ab,id.
102. or/100-101 [PsycInfo set 4 Post Covid Recovery Clinics to AND with Covid]
103. (post adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or

19nCoV or SARSCOV2) adj3 infection* adj8 (chronic* or persist* or residual or prolonged or non-recover* or nonrecover* or recover* or rehabilitat* or month or months or year or years or sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*)).ti,ab,id.

104. ((chronic or post) adj (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj3 (rehabilitat* or recover* or fatigue or function*)).ti,ab,id.
105. ((chronic* or persist* or residual or prolonged or non-recover* or nonrecover*) adj2 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,id.
106. ((chronic* or persist* or residual or prolonged or non-recover* or nonrecover*) adj2 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj5 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*)).ti,ab,id.
107. ((long-term or longterm) adj (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,id.
108. ((post acute or postacute or post viral or postviral or post virus* or postvirus* or long duration or long last or long lasting or longstanding or long standing or late-onset or (illness adj2 duration)) adj3 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,id.
109. ((survivor* or survived or discharg* or postdischarg* or post infect* or postinfect*) adj3 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*) adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2)).ti,ab,id.
110. ((survivor* or survived or discharg* or postdischarg* or post infect* or postinfect*) adj3 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or nCoV* or 2019nCoV or 19nCoV or SARSCOV2) adj5 (sequela* or syndrome* or disorder* or condition* or symptom* or consequence* or outcome* or clinical outcome* or aftercare* or after-care* or issue* or complication* or following or follow-up or followup or function*)).ti,ab,id.
111. or/103-110 [PsycInfo set 5 Top Up set]
112. 91 and 99
113. 99 and 102
114. 86 or 111 or 112 or 113
115. 114 use psyh
116. exp animals/
117. exp animal experimentation/ or exp animal experiment/
118. exp models animal/
119. nonhuman/
120. exp vertebrate/ or exp vertebrates/

121. animal.po.
122. or/116-121
123. exp humans/
124. exp human experimentation/ or exp human experiment/
125. human.po.
126. or/123-125
127. 122 not 126
128. (comment or newspaper article or editorial or letter or note).pt.
129. 38 not 127
130. 129 not 128
131. limit 130 to (english or french)
132. limit 131 to yr="2019 -Current" [Medline results with limits]
133. 39 not 127
134. 133 not 128
135. limit 134 to yr="2019 -Current" [CCTR with limits, no language limit available]
136. 77 not 127
137. 136 not 128
138. limit 137 to (english or french)
139. limit 138 to yr="2019 -Current" [Embase with limits]
140. 115 not 127
141. 140 not 128
142. limit 141 to (english or french)
143. limit 142 to yr="2019 -Current" [PsycInfo with limits]
144. 132 or 135 or 139 or 143 [All database results with limits, combined]
145. remove duplicates from 144.

Table 10: EBSCO Syntax Guide

Syntax	Description
TI	Title
AB	Abstract
MH	Medical Subject Heading
PT	Publication type
*	A truncation symbol (wildcard) to retrieve plurals or varying endings
N#	Near operator: requires terms to be adjacent to each other within # number of words, in any order
W#	Within operator: requires terms to be adjacent to each other within # number of words, in the order entered

EBSCO Strategy – Cumulative Index to Nursing and Allied Health Literature (CINAHL)

The CINAHL search was translated from the Ovid Medline search with the assistance of the Polygot Search Translator.[58]

S1. ((TI "long COVID*" OR AB "long COVID*") OR (TI "long coronavirus*" OR AB "long coronavirus*"))

S2. (((TI chronic OR AB chronic) OR (TI post OR AB post)) W1 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)) N2 ((TI sequela* OR AB sequela*) OR (TI syndrome* OR AB syndrome*) OR (TI disorder* OR AB disorder*) OR (TI condition* OR AB condition*) OR (TI symptom* OR AB symptom*)))

S3. (((TI "post acute" OR AB "post acute") OR (TI postacute OR AB postacute) OR (TI "post viral" OR AB "post viral") OR (TI postviral OR AB postviral) OR (TI "post virus*" OR AB "post virus*") OR (TI postvirus* OR AB postvirus*) OR (TI "long duration" OR AB "long duration") OR (TI "long last" OR AB "long last") OR (TI "long lasting" OR AB "long lasting") OR (TI longstanding OR AB longstanding) OR (TI "long standing" OR AB "long standing")) N3 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)))

S4. ((TI "late sequela*" OR AB "late sequela*") N2 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)))

S5. (((TI "long term" OR AB "long term") OR (TI longterm OR AB longterm)) W1 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)))

S6. TI PASC

S7. (((TI postcovid* OR AB postcovid*) OR (TI "post covid*" OR AB "post covid*") OR (TI postcoronavirus* OR AB postcoronavirus*) OR (TI "post coronavirus*" OR AB "post coronavirus*") OR (TI "post SARS-COV-2" OR AB "post SARS-COV-2") OR (TI postSARS-COV-2 OR AB postSARS-COV-2) OR (TI "post SARS-COV2" OR AB "post SARS-COV2") OR (TI postSARS-COV2 OR AB postSARS-COV2) OR (TI "post SARSCOV-2" OR AB "post SARSCOV-2") OR (TI "post SARSCOV-2" OR AB "post SARSCOV-2")) N3 ((TI sequela* OR AB sequela*) OR (TI syndrome* OR AB syndrome*) OR (TI disorder* OR AB disorder*) OR (TI illness* OR AB illness*) OR (TI condition* OR AB condition*) OR (TI symptom* OR AB symptom*) OR (TI prognos* OR AB prognos*) OR (TI followup* OR AB followup*) OR (TI "follow up*" OR AB "follow up*")))

S8. ((TI post-covid* OR AB post-covid*) N5 ((TI care OR AB care) OR (TI aftercare* OR AB aftercare*)) N5 ((TI center* OR AB center*) OR (TI centre OR AB centre) OR (TI clinic* OR AB clinic*)))

S9. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8

S10. ((((TI "post acute" OR AB "post acute") OR (TI postacute OR AB postacute) OR (TI sub-acute OR AB sub-acute) OR (TI subacute OR AB subacute) OR (TI chronic OR AB chronic)) W1 (TI sequela* OR AB sequela*)) OR (TI PASC OR AB PASC))

S11. ((TI "long haul*" OR AB "long haul*") OR (TI longhaul* OR AB longhaul*))

S12. (((TI "post-intensive care" OR AB "post-intensive care") OR (TI "postintensive care" OR AB "postintensive care") OR (TI post-ICU OR AB post-ICU)) W1 (TI syndrome* OR AB syndrome*))

S13. (((TI persist* OR AB persist*) OR (TI long* OR AB long*) OR (TI residual OR AB residual) OR (TI prolonged OR AB prolonged)) N8 (((TI olfactory OR AB olfactory) OR (TI chemosensor* OR AB chemosensor*)) W1 ((TI disorder* OR AB disorder*) OR (TI dysfunction* OR AB dysfunction*))))

S14. S10 OR S11 OR S12 OR S13

S15. (MH COVID-19) OR (MH "COVID-19 Testing"+) OR (MH "COVID-19 Vaccines") OR (MH SARS-CoV-2)

S16. ((MH coronavirus) OR (MH betacoronavirus) OR (MH "coronavirus infections")) AND ((MH "disease outbreaks") OR (MH epidemics) OR (MH pandemics))

S17. ((TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI COVID19* OR AB COVID19*) OR (TI COVID OR AB COVID) OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV2 OR AB SARSCOV2) OR (TI "SARS coronavirus 2" OR AB "SARS coronavirus 2") OR (TI "Severe Acute Respiratory Syndrome Coronavirus 2" OR AB "Severe Acute Respiratory Syndrome Coronavirus 2") OR (TI "Severe Acute Respiratory Syndrome Corona Virus 2" OR AB "Severe Acute Respiratory Syndrome Corona Virus 2"))

S18. (((TI new OR AB new) OR (TI novel OR AB novel) OR (TI 19 OR AB 19) OR (TI 2019 OR AB 2019) OR (TI Wuhan OR AB Wuhan) OR (TI Hubei OR AB Hubei) OR (TI China OR AB China) OR (TI Chinese OR AB Chinese)) N3 ((TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI betacoronavirus* OR AB betacoronavirus*) OR (TI CoV OR AB CoV) OR (TI HCoV OR AB HCoV)))

S19. ((TI longCOVID* OR AB longCOVID*) OR (TI postCOVID* OR AB postCOVID*) OR (TI postcoronavirus* OR AB postcoronavirus*) OR (TI postSARS* OR AB postSARS*))

S20. (((TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI betacoronavirus* OR AB betacoronavirus*)) N3 ((TI pandemic* OR AB pandemic*) OR (TI epidemic* OR AB epidemic*) OR (TI outbreak* OR AB outbreak*) OR (TI crisis OR AB crisis)))

S21. (((TI Wuhan OR AB Wuhan) OR (TI Hubei OR AB Hubei)) N5 (TI pneumonia OR AB pneumonia))

S22. S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21

S23. ((TI recovery OR AB recovery) N2 ((TI clinic OR AB clinic) OR (TI clinics OR AB clinics) OR (TI centre OR AB centre) OR (TI center OR AB center) OR (TI centres OR AB centres) OR (TI centers OR AB centers) OR (TI program* OR AB program*)))

S24. ((TI post* OR AB post*) N3 (TI rehabilitation OR AB rehabilitation) N2 ((TI clinic OR AB clinic) OR (TI clinics OR AB clinics) OR (TI centre OR AB centre) OR (TI center OR AB center) OR (TI centres OR AB centres) OR (TI centers OR AB centers) OR (TI program* OR AB program*)))

S25. S23 OR S24

S26. ((TI post OR AB post) W1 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)) N3 (TI infection* OR AB infection*) N8 ((TI chronic* OR AB chronic*) OR (TI persist* OR AB persist*) OR (TI residual OR AB residual) OR (TI prolonged OR AB prolonged) OR (TI non-recover* OR AB non-recover*) OR (TI nonrecover* OR AB nonrecover*) OR (TI recover* OR AB recover*) OR (TI rehabilitat* OR AB rehabilitat*) OR (TI month OR AB month) OR (TI months OR AB months) OR (TI year OR AB year) OR (TI years OR AB years) OR (TI sequela* OR AB sequela*) OR (TI syndrome* OR AB syndrome*) OR (TI disorder* OR AB disorder*) OR (TI condition* OR AB condition*) OR (TI symptom* OR AB symptom*) OR (TI consequence* OR AB consequence*) OR (TI outcome* OR AB outcome*) OR (TI "clinical outcome*" OR AB "clinical outcome*") OR (TI aftercare* OR AB aftercare*) OR (TI after-care* OR AB after-care*) OR (TI issue* OR AB issue*) OR (TI complication* OR

AB complication*) OR (TI following OR AB following) OR (TI follow-up OR AB follow-up) OR (TI followup OR AB followup) OR (TI function* OR AB function*)))

S27. (((TI chronic OR AB chronic) OR (TI post OR AB post)) W1 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)) N3 ((TI rehabilitat* OR AB rehabilitat*) OR (TI recover* OR AB recover*) OR (TI fatigue OR AB fatigue) OR (TI function* OR AB function*)))

S28. (((TI chronic* OR AB chronic*) OR (TI persist* OR AB persist*) OR (TI residual OR AB residual) OR (TI prolonged OR AB prolonged) OR (TI non-recover* OR AB non-recover*) OR (TI nonrecover* OR AB nonrecover*)) N2 ((TI sequela* OR AB sequela*) OR (TI syndrome* OR AB syndrome*) OR (TI disorder* OR AB disorder*) OR (TI condition* OR AB condition*) OR (TI symptom* OR AB symptom*) OR (TI consequence* OR AB consequence*) OR (TI outcome* OR AB outcome*) OR (TI "clinical outcome*" OR AB "clinical outcome*") OR (TI aftercare* OR AB aftercare*) OR (TI after-care* OR AB after-care*) OR (TI issue* OR AB issue*) OR (TI complication* OR AB complication*) OR (TI following OR AB following) OR (TI follow-up OR AB follow-up) OR (TI followup OR AB followup) OR (TI function* OR AB function*)) N5 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)))

S29. (((TI chronic* OR AB chronic*) OR (TI persist* OR AB persist*) OR (TI residual OR AB residual) OR (TI prolonged OR AB prolonged) OR (TI non-recover* OR AB non-recover*) OR (TI nonrecover* OR AB nonrecover*)) N2 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)) N5 ((TI sequela* OR AB sequela*) OR (TI syndrome* OR AB syndrome*) OR (TI disorder* OR AB disorder*) OR (TI condition* OR AB condition*) OR (TI symptom* OR AB symptom*) OR (TI consequence* OR AB consequence*) OR (TI outcome* OR AB outcome*) OR (TI "clinical outcome*" OR AB "clinical outcome*") OR (TI aftercare* OR AB aftercare*) OR (TI after-care* OR AB after-care*) OR (TI issue* OR AB issue*) OR (TI complication* OR AB complication*) OR (TI following OR AB following) OR (TI follow-up OR AB follow-up) OR (TI followup OR AB followup) OR (TI function* OR AB function*)))

S30. (((TI long-term OR AB long-term) OR (TI longterm OR AB longterm)) W1 ((TI sequela* OR AB sequela*) OR (TI syndrome* OR AB syndrome*) OR (TI disorder* OR AB disorder*) OR (TI condition* OR AB condition*) OR (TI symptom* OR AB symptom*) OR (TI consequence* OR AB consequence*) OR (TI outcome* OR AB outcome*) OR (TI "clinical outcome*" OR AB "clinical outcome*") OR (TI aftercare* OR AB aftercare*) OR (TI after-care* OR AB after-care*) OR (TI issue* OR AB issue*) OR (TI complication* OR AB complication*) OR (TI following OR AB following) OR (TI follow-up OR AB follow-up) OR (TI followup OR AB followup) OR (TI function* OR AB function*)) N5 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)))

S31. (((TI "post acute" OR AB "post acute") OR (TI postacute OR AB postacute) OR (TI "post viral" OR AB "post viral") OR (TI postviral OR AB postviral) OR (TI "post virus*" OR AB "post virus*") OR (TI postvirus* OR AB postvirus*) OR (TI "long duration" OR AB "long duration") OR (TI "long last" OR AB "long last") OR (TI "long lasting" OR AB "long lasting") OR (TI longstanding OR AB longstanding) OR (TI "long standing" OR AB "long standing") OR (TI late-onset OR AB late-onset) OR ((TI illness OR AB illness) N2 (TI duration OR AB duration))) N3 ((TI sequela* OR AB sequela*) OR (TI syndrome* OR AB syndrome*) OR (TI disorder* OR AB disorder*) OR (TI condition* OR AB condition*) OR (TI symptom* OR AB symptom*) OR (TI consequence* OR AB consequence*) OR (TI outcome* OR AB outcome*) OR (TI "clinical outcome*" OR AB "clinical outcome*") OR (TI aftercare* OR AB aftercare*) OR (TI after-care* OR AB after-care*) OR (TI issue* OR AB issue*) OR (TI complication* OR AB complication*) OR (TI following OR AB following) OR (TI follow-up OR AB follow-up) OR (TI followup OR AB followup) OR (TI function* OR AB function*)) N5 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)))

S32. (((TI survivor* OR AB survivor*) OR (TI survived OR AB survived) OR (TI discharg* OR AB discharg*) OR (TI postdischarg* OR AB postdischarg*) OR (TI "post infect*" OR AB "post infect*") OR (TI postinfect* OR AB postinfect*)) N3 ((TI sequela* OR AB sequela*) OR (TI syndrome* OR AB syndrome*) OR (TI disorder* OR AB disorder*) OR (TI condition* OR AB condition*) OR (TI symptom* OR AB symptom*) OR (TI consequence* OR AB consequence*) OR (TI outcome* OR AB outcome*) OR (TI "clinical outcome*" OR AB "clinical outcome*") OR (TI aftercare* OR AB aftercare*) OR (TI after-care* OR AB after-care*) OR (TI issue* OR AB issue*) OR (TI complication* OR AB complication*) OR (TI following OR AB following) OR (TI follow-up OR AB follow-up) OR (TI followup OR AB followup) OR (TI function* OR AB function*)) N5 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)))

S33. (((TI survivor* OR AB survivor*) OR (TI survived OR AB survived) OR (TI discharg* OR AB discharg*) OR (TI postdischarg* OR AB postdischarg*) OR (TI "post infect*" OR AB "post infect*") OR (TI postinfect* OR AB postinfect*)) N3 ((TI COVID* OR AB COVID*) OR (TI coronavirus* OR AB coronavirus*) OR (TI "corona virus*" OR AB "corona virus*") OR (TI SARS-COV-2 OR AB SARS-COV-2) OR (TI SARS-COV2 OR AB SARS-COV2) OR (TI SARSCOV-2 OR AB SARSCOV-2) OR (TI nCoV* OR AB nCoV*) OR (TI 2019nCoV OR AB 2019nCoV) OR (TI 19nCoV OR AB 19nCoV) OR (TI SARSCOV2 OR AB SARSCOV2)) N5 ((TI sequela* OR AB sequela*) OR (TI syndrome* OR AB syndrome*) OR (TI disorder* OR AB disorder*) OR (TI condition* OR AB condition*) OR (TI symptom* OR AB symptom*) OR (TI consequence* OR AB consequence*) OR (TI outcome* OR AB outcome*) OR (TI "clinical outcome*" OR AB "clinical outcome*") OR (TI aftercare* OR AB aftercare*) OR (TI after-care* OR AB after-care*) OR (TI issue* OR AB issue*) OR (TI complication* OR AB complication*) OR (TI following OR AB following) OR (TI follow-up OR AB follow-up) OR (TI followup OR AB followup) OR (TI function* OR AB function*)))

S34. S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33

S35. S14 AND S22

S36. S22 AND S25

S37. S9 OR S34 OR S35 OR S36

S38. (PT “commentary”) or (PT "editorial") or (PT "letter") or (PT "letter to the editor") or (PT "newspaper")

S39. S37 NOT S38

Search limits were: Published Date: 20190101-20221231; Exclude MEDLINE records; Language: English, French.

Clinical Trials Registries

Date of searches: October 25 to 26, 2021. Updated December 21, 2021.

ClinicalTrials.gov

Produced by the U.S. National Library of Medicine. Targeted search used to capture registered clinical trials.

Search terms – "post COVID" OR "postCOVID" OR "post COVID19" OR postCOVID19 OR "post coronavirus" OR "long COVID" OR "long COVID19" OR ("post acute" AND (COVID* OR coronavirus)) OR (sequelae AND (COVID* OR coronavirus))

WHO ICTRP

International Clinical Trials Registry Platform, produced by the World Health Organization. Targeted search used to capture registered clinical trials. Duplicates removed with ClinicalTrials.gov by NCT.

Search terms – "post COVID" OR "postCOVID" OR "post COVID19" OR postCOVID19 OR "post coronavirus" OR "long COVID" OR "long COVID19" OR ("post acute" AND (COVID* OR coronavirus)) OR (sequelae AND (COVID* OR coronavirus))

Health Canada’s Clinical Trials Database

Produced by Health Canada. Targeted search used to capture registered clinical trials.

Search terms – COVID, coronavirus; and reviewed results mentioning long, chronic, acute, or sequela

EU Clinical Trials Register

European Union Clinical Trials Register, produced by the European Union. Targeted search used to capture registered clinical trials.

Search terms – "post COVID" OR "postCOVID" OR "post COVID19" OR postCOVID19 OR "post coronavirus" OR "long COVID" OR "long COVID19" OR ("post acute" AND (COVID* OR coronavirus)) OR (sequelae AND (COVID* OR coronavirus))

Other Databases

Preprints were searched via EuropePMC.org, which includes preprints from MedRxiv, bioRxiv, PsyArXiv, SSRN, and F1000 Research, among others. Preprint searches were limited to systematic reviews, meta-analyses, technology assessments, rapid reviews, scoping reviews, and other evidence reports where possible. Any preprints found in the Ovid Medline or Embase search were retained as well. Search strategies are available upon request. Date of search: October 25, 2021. Updated Dec 20, 2021.

A supplemental search of the Philosopher's Index via Ovid was conducted, with headings and keywords translated from the Ovid Medline search. Search strategies are available upon request. Date of search: October 29, 2021. Regular alerts sent with the other Ovid database alerts until December 20, 2021.

Grey Literature

Grey literature includes government information and other reports that are not published commercially and that may be inaccessible via bibliographic databases.

Search dates: October 25-29, 2021. Update of key sites on December 17-20, 2021.

Keywords: long COVID, post acute sequelae of COVID, post-COVID condition, chronic COVID condition, and synonyms.

Limits: Publication years: 2019-present

Updated: Search updated prior to the completion of stakeholder feedback period.

Relevant websites from the following sections of the CADTH grey literature checklist Grey Matters: A Practical Tool for Searching Health-Related Grey Literature were searched:

- HTA Agencies
- Clinical Practice Guidelines
- Clinical Trials Registries
- Databases (free)
- Internet Search
- Plus, CADTH COVID-19 Grey Literature Resources

Appendix 2: Large Tables and Figures

Note that this appendix has not been copy-edited.

Figure 4: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flowchart of Selected Reports

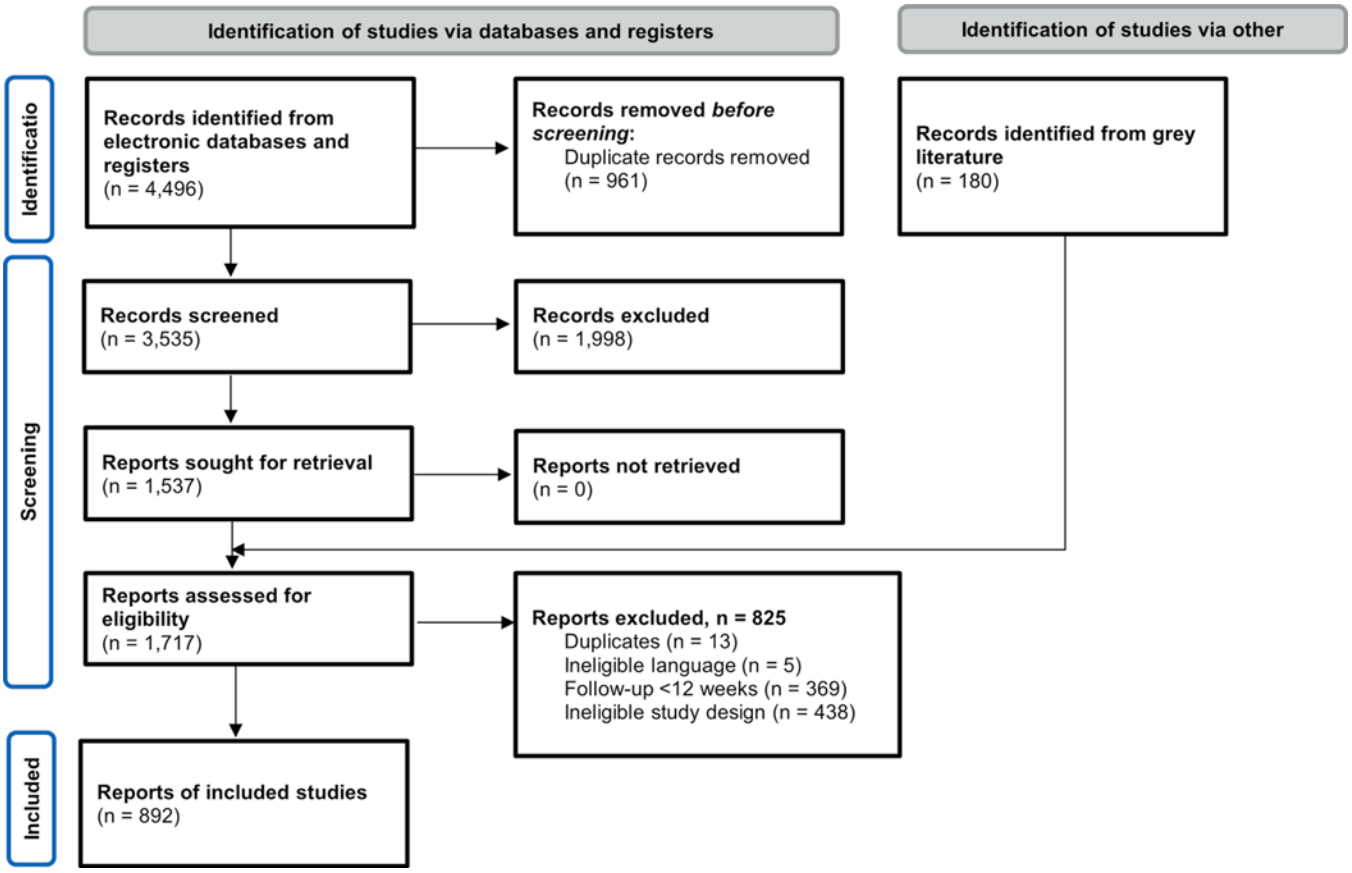


Table 11: Data Items

Category	Data items – Categorical (Options)	Data extracted – Open text
Report information	• Study design (systematic review [interventional, observational, or both], primary study [interventional, observational], guideline, economic evaluation, qualitative study, ethical analysis, mixed methods, conference abstract/presentation)[a] • Publication type (published study, preprint, protocol)	• First author name • Date of publication[b] • Study design – systematic review (other)[c]
Population	• Were the majority of COVID-19 cases diagnosed using a laboratory test, e.g., PCR, antibody/antigen? (yes, no, mixed, unclear)[c] • Methods of confirming COVID-19 (PCR, antibody/antigen, other lab test, ICD code, diagnosed by clinician, confirmed at hospital/ICU, self-report, other, not reported) [a] • Severity of acute illness (asymptomatic, symptomatic not hospitalized, hospitalized, ICU, not reported) [a] • Vaccination status (fully vaccinated, partly vaccinated/mixed, not vaccinated, not reported)	• Country (of participants; if not reported, the country of the first author was reported) • Number of study participants • Age (mean, SD, median, IQR, range, eligibility) • Sex (% male) • Comorbidities data

Concept [a]	• Risk factors and prevention [a,e]
	  ◦ Risk factors associated with developing post–COVID condition
	  ◦ Preventive interventions – drug
	  ◦ Preventive interventions – rehabilitation
	  ◦ Preventive interventions – other (e.g., supplements, Chinese medicine, devices)
	• Classification (classifying post–COVID-19 condition at least 12 weeks or 3 months after initial infection by symptoms, pathophysiological markers, variants of the SARS-CoV-2 virus, subtypes, or other approaches) [a]
	  ◦ Characteristics (e.g., symptoms, quality of life)
	  ◦ Subtypes of post–COVID-19 condition
	  ◦ Pathophysiological markers assessed at <12 weeks
	  ◦ Different variants of SARS-CoV-2
	• Diagnostic tests [a]
	  ◦ Laboratory tests (e.g., blood chemistry) conducted at ≥12 weeks
	  ◦ Imaging tests (e.g., chest X-ray) conducted at ≥12 weeks
	  ◦ Other diagnostic tests
	• Treatment or management [a,e]
	  ◦ Drugs
	  ◦ Rehabilitation
	  ◦ Care model
	  ◦ Other treatments (e.g., supplements, Chinese medicine, devices)
	• Health systems issues (e.g., increased health care services use)[f]
		Intervention/Exposure

Context	• Setting (urban, rural, remote, not reported) [a] • Site of treatment during acute illness [a] • Site of follow-up [a]	NA

COVID-19 = coronavirus disease 2019; ICD = International Classification of Diseases; ICU = intensive care unit; IQR = interquartile range; NA = not applicable; PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SD = standard deviation.

[a]Indicates questions where multiple categories could be selected.

[b]Based on date available online where available; if unavailable, date of publication was used.

[c]"Systematic reviews – other" was used to identify scoping reviews.

[d]If at least 80% of participants must have had a COVID-19 laboratory test, defined as a PCR, antibody/antigen test, or other lab test (e.g., studies that simply stated "laboratory-confirmed"), it was considered as having a majority of laboratory-confirmed COVID-19 cases. Studies that had at least 80% of participants without a confirmed COVID-19 lab test (e.g., the methods stated patients had been diagnosed by a clinician or at the hospital, without any indication a lab test was done) were labelled as "no," while studies that had between 20% to 80% of laboratory-confirmed COVID-19 were labelled as "mixed," and the percentage of laboratory-confirmed participants was extracted if reported.

[e]Interventions were considered preventive if they occurred <12 weeks after diagnosis/discharge, including interventions provided during the acute illness phase. Interventions were considered as treatment/management if they occurred at least 12 weeks after diagnosis/discharge. If the methods were unclear regarding when the intervention occurred (e.g., if participants were eligible for the intervention if they were at least 6 weeks after diagnosis) the study was categorized as both prevention and intervention.

[f]Publications or protocols that assessed topics related to health ethics or equity, budget impact, and policy impact were relevant to health system issues. This included studies that assessed usage of health care services and pharmaceuticals (e.g., usage among people who had been infected with COVID-19 at least 12 weeks ago) as this was considered to potentially affect health care budget considerations.

Table 12: Methods Used by Canadian Guidelines for Post–COVID-19 Care

Method	Alberta[29]	British Columbia[30]	Ontario[31]	Quebec[32]
Funding/sponsorship	NR	NR	NR	NR
Did the guideline describe their methodology?	Yes	No	Yes	Yes
Method(s) used				
Systematic literature search (search strategy provided) [a]	No	NA	No	Yes
Literature search, unclear if systematic	Yes	NA	No	No
Expert feedback	No	NA	No	No
Stakeholder feedback/consultation	No	NA	No	No
Based on a specific guideline [b]	No	NA	Yes	No
Authors' clinical experience	No	NA	No	No
Literature searched				
CINAHL	No	NR	NR	No
Cochrane library	No	NR	NR	Yes
EMBASE	Yes	NR	NR	No
Guidelines databases	No	NR	NR	Yes
MEDLINE	Yes	NR	NR	No
PubMed	Yes	NR	NR	Yes
Other databases	No	NR	NR	Yes
Other (e.g., reference list searching)	No	NR	NR	No
End of literature search date	NR	NR	NR	June 2021
Publication date	July 2021	NR	December 2021	July 2021

COVID-19 = coronavirus disease 2019; NA = not applicable; NR = not reported.

[a]If the methods provided a detailed search strategy and/or specified their search was systematic.

[b]The guideline based their recommendations on what a previously published guideline recommends.

Table 13: Summary of Recommendations From Canadian Guidelines for Post–COVID-19 Care

Recommendation	Alberta[29]	British Columbia[30]	Ontario[31]	Quebec[32]
Population	Children, adults [a]	NR	Adults	Children, adults [a]
Diagnosis				
Health review/follow-up at 3 months or later	NR	NR	NR	NR
Laboratory/ imaging tests	NR	NR	NR	NR
Chest X-ray for respiratory symptoms	NR	NR	Yes	Yes
Management				
Rehabilitation	NR	NR	NR	NR
Referral to specialist(s)	Yes	NR	NR	NR
Referral to post–COVID-19 clinic	Yes	Yes	NR	NR

COVID-19 = coronavirus disease 2019; NR = not reported.

[a]Summarizes literature on children and adults, but unclear if guidance specific to 12+ weeks applies to children.

Table 14: Methods Used by International Guidelines for Post–COVID-19 Care

Method	Australia and New Zealand[33]	Australia[59]	Netherlands[60]	Spain[34]	Turkey[35]	United Kingdom[61]	United Kingdom[6]	USA[62]
Funding/sponsorship	NR	NR	None	None	None	NR	NR	NR
Did the guideline describe their methodology?	No	No	Yes	Yes	Yes	Yes	Yes	No
Method(s) used								
Systematic literature search [a]	NA	NA	No	Yes	No	Yes	Yes	NA
Literature search, unclear if systematic	NA	NA	No	NA	Yes	NA	NA	NA
Expert feedback	NA	NA	Yes	Yes	Yes	Yes	Yes	NA
Stakeholder feedback/ consultation	NA	NA	No	No	No	Yes	Yes	NA
Based on a specific methodological guideline [b]	NA	NA	Yes	No	No	No	No	NA
Authors' clinical experience	NA	NA	No	Yes	No	No	No	NA
Literature searched								
CINAHL	NR	NR	NR	NR	Yes	Yes	Yes	NR
Cochrane library	NR	NR	NR	NR	Yes	Yes	Yes	NR
Embase	NR	NR	NR	NR	NR	Yes	Yes	NR
Guidelines databases	NR	NR	NR	NR	NR	NR	NR	NR

Method	Australia and New Zealand[33]	Australia[59]	Netherlands[60]	Spain[34]	Turkey[35]	United Kingdom[61]	United Kingdom[6]	USA[62]
MEDLINE	NR	NR	NR	NR	NR	Yes	Yes	NR
PubMed	NR	NR	NR	Yes	Yes	NR	NR	NR
Other databases	NR	NR	NR	NR	Yes	Yes	Yes	NR
Other sources (e.g., reference checking)	NR	NR	NR	NR	NR	Yes	Yes	NR
End of literature search date	NR	NR	NR	January 13, 2021	NR	October 28, 2020	NR	NR
Publication date	September 2021	December 2021	November 2021	April 2021	April 2021	December 2020	November 2021	June 2021

COVID-19 = coronavirus disease 2019; NR = not reported; NA = not applicable.

[a]If the methods provided a detailed search strategy and/or specified their search was systematic.

[b]The guideline based their recommendations on what a previously published guideline recommends.

Table 15: Summary of Recommendations by International Guidelines for Post–COVID-19 Care

Recommendation	Australia and New Zealand[33]	Australia[59]	Netherlands[60]	Spain[34]	Turkey[35]	United Kingdom[61]	United Kingdom[6]	USA[62]
Population	Children, adults[a] treated for COVID-19 in the ICU	Children, adults[a]	Older adults	NR	Adults	Children, adults, older adults	Children, adults, older adults	Children, adults[a]
Diagnosis								
Health review/follow-up at 3+ months	Yes	NR	Yes	Yes	Yes	NR	Yes	NR
Laboratory tests	NR	NR	NR	NR	NR	NR	NR	Yes
Chest X-ray for respiratory symptoms	NR	Yes	NR	NR	NR	Yes	NR	NR
Management								
Rehabilitation	NR	NR	NR	NR	Yes	NR	NR	NR
Referral to specialist(s)	Yes	NR	NR	Yes	NR	NR	Yes	NR
Referral to post-COVID clinic	NR	NR	NR	NR	NR	NR	NR	NR

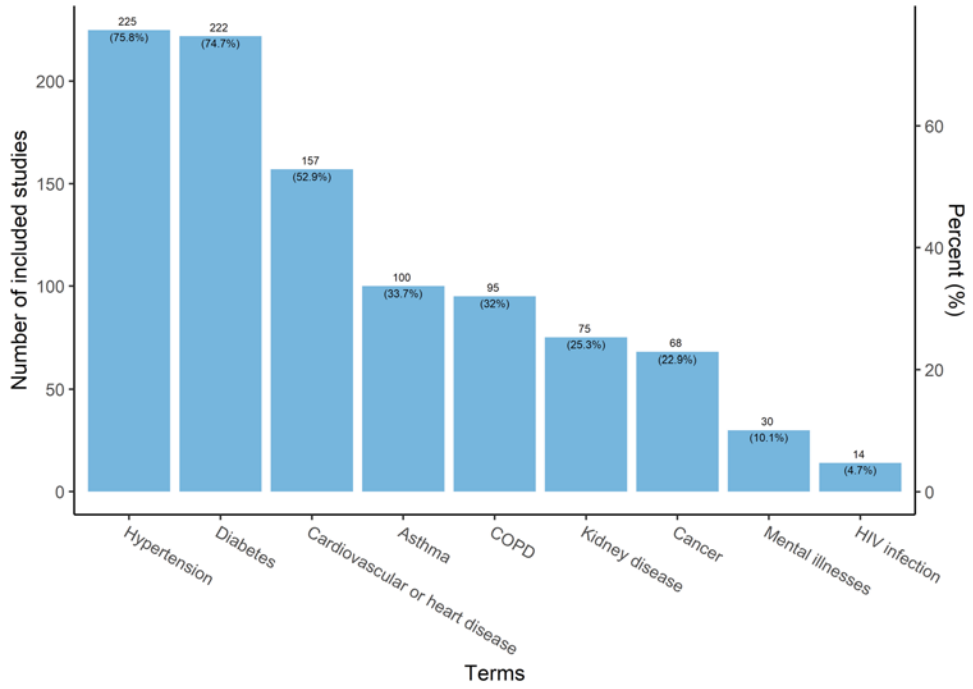
COVID-19 = coronavirus disease 2019; ICU = intensive care unit; NR = not reported.

[a]Summarizes literature on children and adults, but unclear if guidance specific to 12+ weeks applies to children.

Appendix 3: Additional Figures and Data

Note that this appendix has not been copy-edited.

Figure 5: Number of Included References by Terms Reported for Comorbidities



COPD = chronic obstructive pulmonary disease.

The comorbidities data were assessed in 297 (33.3%) references. The terms that were commonly investigated in 297 eligible references included hypertension (225, 75.8%), diabetes (222, 74.7%), cardiovascular or heart disease (157, 52.9%), asthma (100, 33.7%), COPD (95, 32%), kidney disease (75, 25.3%), cancer (68, 22.9%), mental health illnesses (30, 10.1%), and HIV infection or AIDS (14, 4.7%).

Table 16: Summary of 3 Included Scoping Reviews

First author's surname	Year published	Country[a]	Severity of acute illness				Main concepts				
			Asymptomatic	Symptomatic, not hospitalized	Hospitalized	ICU	Classification	Risk factors and prevention	Diagnostic tests	Treatment and management	Health system issues
Akbarialiabad[11]	2021	Iran	NR	NR	NR	NR	Yes	Yes	Yes	Yes	NR
Shanbehzadeh[12]	2021	Iran	NR	Yes	Yes	NR	Yes	Yes	NR	NR	NR
Cha[13]	2021	South Korea	NR	Yes	Yes	NR	Yes	Yes	NR	Yes	NR

ICU = intensive care unit; NR = not reported.

[a]CADTH reported the country/countries of included primary studies if it was provided in the review. If CADTH were unable to find this data, CADTH reported the country of the first author.

Table 17: Summary of Included Systematic Reviews

First author's surname	Year published	Country[a]	Severity of acute illness				Main concepts				
			Asymptomatic	Symptomatic, not hospitalized	Hospitalized	ICU	Classifi-cation	Risk factors and prevention	Diagnostic tests	Treatment and management	Health system issues
So[63]	2021	Japan	NR	NR	Yes	NR	NR	NR	Yes	NR	NR
Soriano-Moreno[64]	2021	NR	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR
Renaud-Charest[65]	2021	Canada, studies included from Italy, Austria, Spain, France, Netherlands, the US, Germany	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR
Anaya[66]	2021	Colombia	NR	Yes	Yes	Yes	Yes	NR	Yes	NR	NR
Fernandez-de-Las-Penas[67]	2021	Spain	NR	NR	NR	NR	Yes	Yes	NR	NR	NR
Van Kessel[68]	2021	Netherlands	NR	Yes	NR	NR	Yes	NR	NR	NR	NR
Malik[69]	2022	Europe, the UK, the US, Iran, and China	NR	NR	NR	NR	Yes	NR	NR	NR	NR
Groff[70]	2021	US	NR	NR	NR	NR	Yes	NR	NR	NR	NR
Sandler[71]	2021	Australia	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR
Long[72]	2021	China	NR	NR	NR	NR	Yes	Yes	NR	NR	NR

First author's surname	Year published	Country[a]	Severity of acute illness				Main concepts				
			Asymptomatic	Symptomatic, not hospitalized	Hospitalized	ICU	Classification	Risk factors and prevention	Diagnostic tests	Treatment and management	Health system issues
Sanchez-Ramirez[73]	2021	China (7), Canada (3), France (2), Norway (2), Italy (3), the US, (2), Switzerland (1), Austria (1), Iran (1), the Netherlands (1), and the UK	NR	Yes	Yes	Yes	Yes	NR	Yes	NR	NR
Iqbal[74]	2021	UK	NR	Yes	Yes	NR	Yes	Yes	NR	NR	NR
Salamanna[75]	2021	Italy	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR
Fernandez-de-Las-Penas[76]	2021	Spain	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR
Michelen[77]	2021	UK	NR	Yes	Yes	Yes	Yes	Yes	Yes	NR	NR
Ahmad[78]	2021	Saudi Arabia	NR	Yes	Yes	Yes	Yes	NR	NR	NR	NR
Schou[79]	2021	Asia, Europe, North America, and Oceania	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR
Martimbianco[80]	2021	Brazil	NR	NR	Yes	NR	Yes	Yes	NR	NR	NR
Sun[81]	2021	China	NR	NR	NR	NR	Yes	Yes	Yes	NR	NR
Ramadan[82]	2021	Italy	NR	Yes	Yes	NR	Yes	Yes	NR	NR	NR

First author's surname	Year published	Country[a]	Severity of acute illness				Main concepts				
			Asymptomatic	Symptomatic, not hospitalized	Hospitalized	ICU	Classification	Risk factors and prevention	Diagnostic tests	Treatment and management	Health system issues
Cares-Marambio[83]	2021	Chile	NR	NR	Yes	Yes	Yes	NR	NR	NR	NR
Ludvigsson[84]	2021	Sweden	NR	Yes	NR	NR	Yes	NR	NR	NR	NR
Vanderlind[85]	2021	US	NR	NR	NR	NR	Yes	Yes	NR	NR	NR
Kim[86]	2021	Republic of Korea	NR	NR	NR	NR	NR	NR	NR	Yes	NR
Wong[87]	2021	US	NR	Yes	Yes	NR	NR	Yes	NR	NR	NR
Willi[88]	2021	Switzerland	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR
Wang[89]	2020	China	NR	NR	NR	Yes	NR	Yes	NR	NR	NR
Cabrera Martimbianco[80]	2021	Brazil	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR
Jennings[90]	2021	Ireland	NR	Yes	Yes	Yes	Yes	NR	Yes	NR	NR
Hoshijima[91]	2021	Japan	NR	NR	NR	NR	Yes	Yes	NR	NR	NR
Nna[92]	2021	Nigeria	NR	NR	NR	NR	Yes	Yes	NR	Yes	NR
Michelen[77]	2021	UK	NR	Yes	Yes	Yes	Yes	Yes	Yes	NR	NR
De-la-Rosa-Martinez[93]	2021	Mexico	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR
Domingo[10]	2021	Canada	NR	Yes	Yes	Yes	Yes	NR	NR	NR	NR
Michelen[94]	2021	UK	NR	NR	NR	NR	Yes	Yes	NR	NR	NR
Gyanpuri[95]	2020	India	NR	NR	NR	NR	NR	Yes	NR	Yes	NR
Zürcher[96]	2021	Switzerland	NR	Yes	Yes	NR	Yes	NR	NR	NR	NR
Malik[97]	2021	Pakistan	NR	Yes	Yes	NR	Yes	NR	NR	NR	NR
Yusuf[98]	2021	Indonesia	NR	NR	Yes	NR	Yes	Yes	NR	NR	NR

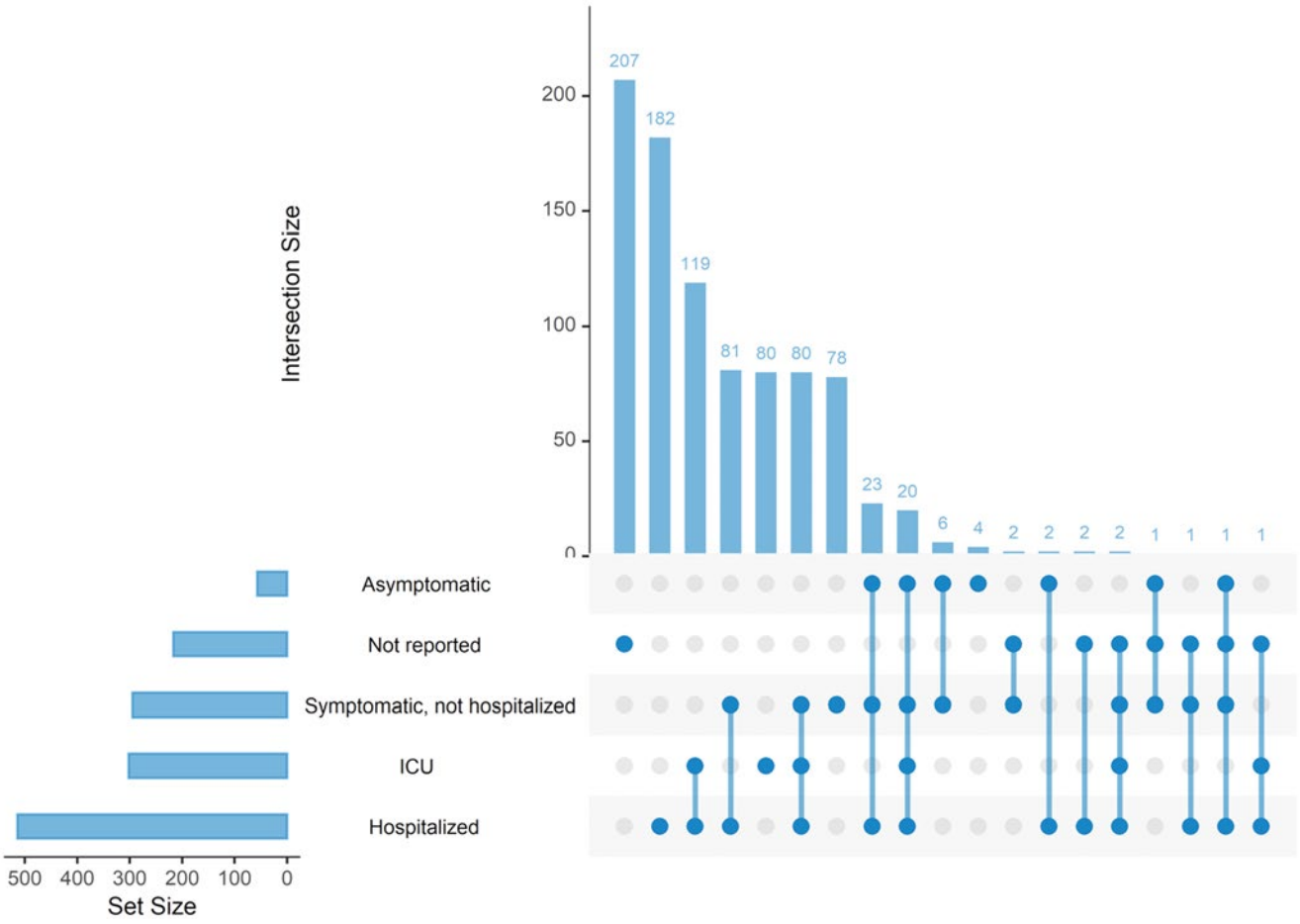
First author's surname	Year published	Country[a]	Severity of acute illness				Main concepts				
			Asymptomatic	Symptomatic, not hospitalized	Hospitalized	ICU	Classification	Risk factors and prevention	Diagnostic tests	Treatment and management	Health system issues
Fabbri[99]	2021	UK	NR	NR	Yes	NR	Yes	Yes	Yes	NR	NR
Fernandez-de-Las-Penas[100]	2021	Spain	NR	Yes	Yes	Yes	Yes	NR	NR	NR	NR
Rao[101]	2021	Denmark, Ireland, the UK, the US, Israel, Germany, Italy, Egypt, China, Saudi Arabia, the Netherlands	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR
d'Ettorre[102]	2021	Italy	NR	NR	NR	NR	Yes	Yes	Yes	NR	NR
Groff[70]	2021	US	NR	Yes	Yes	NR	Yes	Yes	NR	NR	NR
Chen[9]	2021	China, India, Bangladesh, Iran, Russia, Italy, Norway, France, Germany, the UK, Switzerland, Spain, the UK, the US, Brazil	NR	Yes	Yes	Yes	Yes	Yes	NR	NR	NR
Décary[103]	2021	Canada	NR	NR	NR	NR	NR	NR	NR	Yes	NR
Wu[104]	2021	China	NR	NR	NR	NR	Yes	Yes	NR	NR	NR

First author's surname	Year published	Country[a]	Severity of acute illness				Main concepts				
			Asymptomatic	Symptomatic, not hospitalized	Hospitalized	ICU	Classification	Risk factors and prevention	Diagnostic tests	Treatment and management	Health system issues
Nagarajan[105]	2021	India	NR	NR	Yes	Yes	Yes	Yes	NR	NR	NR
Patrucco[106]	2021	Italy	NR	NR	Yes	NR	Yes	Yes	NR	NR	NR
Behnood[45]	2021	Australia, Faroe Islands, Germany, Italy, Latvia, the Netherlands, Russia, Spain, Sweden, Switzerland, the UK, and the US	Yes	Yes	Yes	NR	Yes	Yes	NR	NR	NR
Razak[107]	2021	Canada	NR	NR	NR	NR	Yes	Yes	NR	NR	Yes
De la Rosa-Martinez[108]	2021	Mexico	NR	NR	NR	NR	Yes	Yes	NR	NR	NR
Pillay[109]	2021	Canada	NR	Yes	Yes	Yes	NR	Yes	NR	NR	NR
ECRI[110]	2021	US	NR	Yes	Yes	Yes	Yes	Yes	NR	Yes	NR
Castanares-Zapatero[111]	2021	Belgium	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

ICU = intensive care unit; NR = not reported.

[a]CADTH reported the country/countries of included primary studies if it was provided in the review. If CADTH were unable to find this data, CADTH reported the country of the first author.

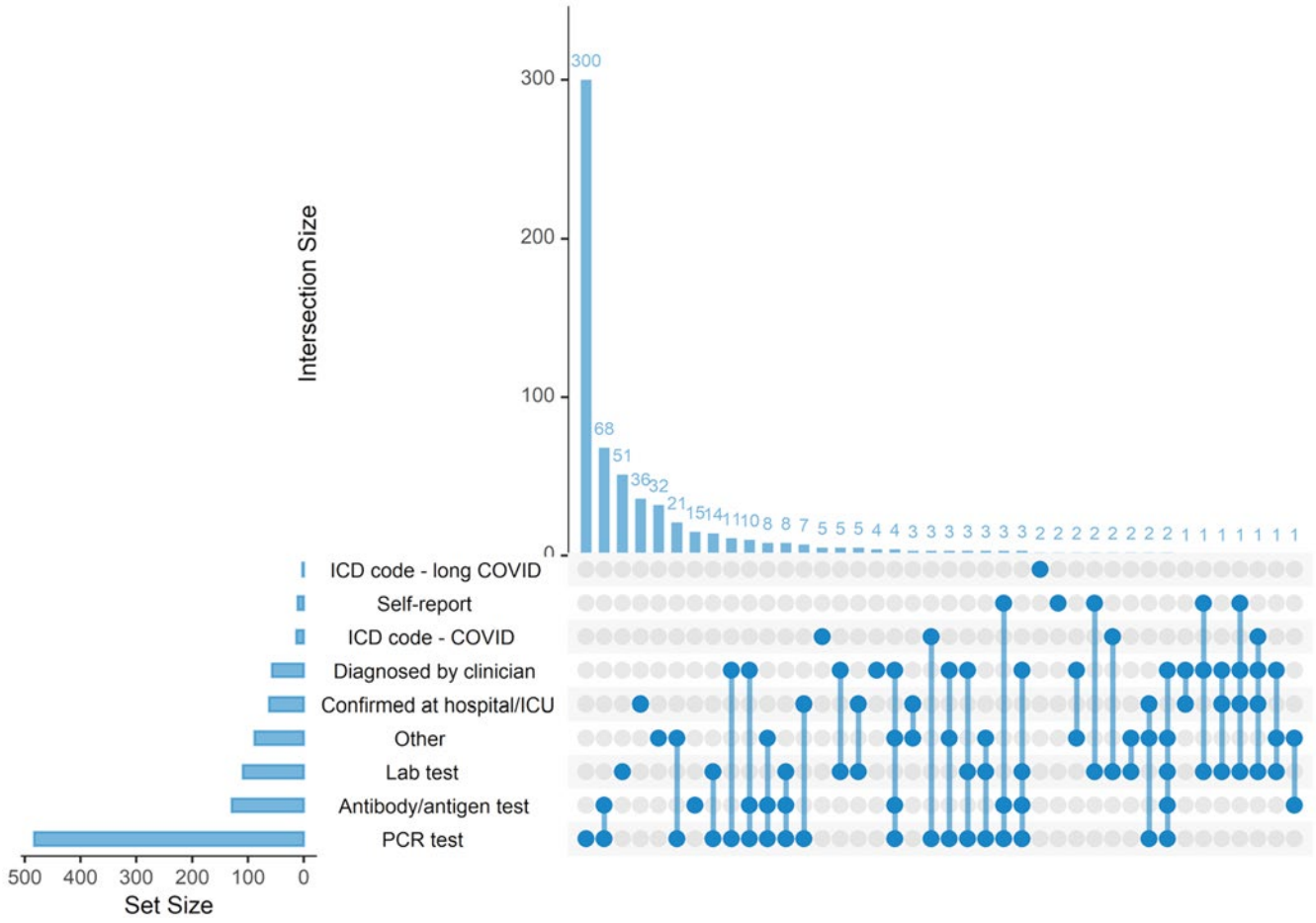
Figure 6: Severity of Initial COVID-19 Illness Reported in Included References



COVID-19 = coronavirus disease 2019; ICU = intensive care unit.

Note: An Upset plot is an alternative to a Venn diagram that is typically used when there are 4 or more categories. The horizontal bars represent the set sizes, or the total number of studies that are within each category. Categories are not mutually exclusive, so the sum of these sets exceeds the number of studies (e.g., a study that falls under both categories A and B would be counted in both). The vertical bars represent the intersection sizes, which are the number of studies for each unique combination of categories that was found. As these bars represent specific combinations, they are mutually exclusive groups (e.g., studies only under A, studies only under B, and studies under both A and B, are counted separately in their respective intersections). The number above the vertical bar states the number of studies in that specific combination. The dots represent which categories were included in the intersection/combination bars, with the dark blue dot representing it was included; a light grey dot indicates that category was not included.

Figure 7: Methods of Confirmation or Diagnosis of COVID-19 Reported in Eligible References



COVID = coronavirus disease; COVID-19 = coronavirus disease 2019; CT = computed tomography; ICD = International Classification of Diseases; ICU = intensive care unit; PCR = polymerase chain reaction.

Note: An Upset plot is an alternative to a Venn diagram that is typically used when there are 4 or more categories. The horizontal bars represent the set sizes, or the total number of studies that are within each category. Categories are not mutually exclusive, so the sum of these sets exceeds the number of studies (e.g., a study that falls under both categories A and B would be counted in both). The vertical bars represent the intersection sizes, which are the number of studies for each unique combination of categories that was found. As these bars represent specific combinations, they are mutually exclusive groups (e.g., studies only under A, studies only under B, and studies under both A and B, are counted separately in their respective intersections). The number above the vertical bar states the number of studies in that specific combination. The dots represent which categories were included in the intersection/combination bars, with the dark blue dot representing it was included; a light grey dot indicates that category was not included.

Sample List of Included Studies

1. Osteopathy and Physiotherapy Compared to Physiotherapy Alone on Fatigue and Functional Status in Long COVID. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT05012826. 2021.
2. Olfactory Training for Olfactory Dysfunction After Coronavirus Disease - 19 (COVID-19). ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04764981. 2021.
3. Olfactory Disfunction and Co-ultraPEALut. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04853836. 2021.
4. SOLIDARITY Finland Long *COVID-19. ClinicalTrials.gov.* Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04978259. 2021.
5. The Effect of Virtual Reality Exercises on Patients With Post-SARS-CoV-2 Syndrome. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04983394. 2021.
6. Pulmonary Rehabilitation *Post-COVID-19. ClinicalTrials.gov.* Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT05003271. 2021.

7. Phase 2 Study of RSLV-132 in Subjects With Long COVID. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04944121. 2021.
8. Impact of Colchicine To Improve long-COVID-19 or ARDS Outcomes. WHO International Clinical Trials Registry Platform (ICTRP) http://trialsearch.who.int/?TrialID=ACTRN12621000637842. 2021.
9. tDCS for Post COVID-19 Fatigue. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04876417. 2021.
10. Coenzyme Q10 as Treatment for Long Term COVID-19. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04960215. 2021.
11. Internet-based Multidisciplinary Rehabilitation for Longterm COVID-19 Syndrome. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04961333. 2021.
12. Cardiopulmonary Rehabilitation in COVID-19 Longhaulers. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04898205. 2021.
13. Statin TReatment for COVID-19 to Optimise NeuroloGical recovERy. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04904536. 2021.
14. Inspiratory Muscle Trainer and Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) COVID-19 Persistent Symptoms. https://clinicaltrials.gov/show/NCT04919031. 2021.
15. Chinese Medicine for Patients With LCOVID-19 Symptoms. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04924881. 2021.
16. Coenzym Q10 til behandling af senfolger efter COVID-19 (QVID studiet). WHO International Clinical Trials Registry Platform (ICTRP) http://trialsearch.who.int/?TrialID=EUCTR2020-005961-16-DK. 2020.
17. The Kidney BEAM Trial. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04872933. 2021.
18. COVID-19 Pneumonia: pulmonary Physiology, Health-related Quality of Life and Benefit of a Rehabilitation Program. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04881214. 2021.
19. Safety and Efficacy of Hyperbaric Oxygen Therapy for Long COVID Syndrome. ClinicalTrials.gov. Bethesda (MD): U.S. National Library of Medicine: https://clinicaltrials.gov/show/NCT04842448. 2021.
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Appendix 4: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) Checklist

Note that this appendix has not been copy-edited.

Table 18: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) Checklist

Section	Item	Prisma-Scr Checklist Item	Reported on Page #
Title			
Title	1	Identify the report as a scoping review.	1
Abstract			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives. Use the abstract reporting checklist (refer to Item 2 in PRISMA 2020).	7-8
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	9
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	10
Methods			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number. Report any protocol amendments (refer to item 24 in PRISMA 2020).	10
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	11-12
Information sources	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	10-11
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated. Include the full search strategies for all databases, registers, and websites (refer to item 7 in PRISMA 2020).	28-42

Section	Item	Prisma-Scr Checklist Item	Reported on Page #
Selection of sources of evidence	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review. Describe if automation tools were used for study selection (refer to item 8 in PRISMA 2020).	12
Data charting process	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators. If outcomes were included, describe how they were defined and which results were sought (refer to item 10 in PRISMA 2020).	13
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	44-45
Critical appraisal of individual sources of evidence	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	NA
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	13
Results			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram. Use the updated PRISMA 2020 flow diagram, which has optional boxes for review updates, as well as studies that were identified through means other than searching databases/ registers and cite any studies that appeared to meet the inclusion criteria but were excluded (refer to item 16 in PRISMA 2020)	13, 43
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	Not conduced
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (refer to item 12).	NA
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	NA
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	14-23
Discussion			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	23-24
Limitations	20	Discuss the limitations of the scoping review process.	24

Section	Item	Prisma-Scr Checklist Item	Reported on Page #
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	24-25
Funding			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review. Report conflicts of interest (refer to item 26 in PRISMA 2020) 1	Funding

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.