Canada's Drug and
Health Technology Agency

CADTH Health Technology Review

Post–COVID-19 Condition Treatment and Management: Protocol for a Rapid Living Scoping Review

Protocol Registration

Open Science Framework: https://osf.io/u52k3

National Collaborating Centre for Methods and Tools:
https://www.nccmt.ca/covid-19/covid-19-evidence-reviews/540

Cite As: *Post–COVID-19 Condition Treatment and Management: Protocol for a Rapid Living Scoping Review*. Ottawa: CADTH; 2022 October. (CADTH Health Technology Review).

ISSN: 1927-0127 (online)

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Table of Contents

List of Tables

Abbreviations

PHAC	Public Health Agency of Canada
SARS-CoV-19	severe acute respiratory syndrome coronavirus-19

Introduction and Rationale

COVID-19 is an infectious disease caused by the severe acute respiratory syndrome coronavirus-19 (SARS-CoV-19).[1] COVID-19 was first identified in late 2019 and was initially characterized by WHO as a relatively short-term, acute disease.[1] Since its emergence in 2019, the COVID-19 pandemic has been spreading quickly. The number of cumulative confirmed cases globally was 572 million as of July 26, 2022.[2] As of August 20, 2022, there were 4,158,491 COVID-19 cases cumulatively in Canada;[3] however, Public Health Ontario has suggested that the number of cases collected by governments likely underestimates the actual numbers.[4] The COVID-19 pandemic has been evolving rapidly and its long-term consequences continue to be under investigation.[5]

Approximately 80% of COVID-19 cases are mild or even asymptomatic.[6] Mild cases typically resolve 2 weeks after symptom onset, and severe cases could take 3 to 6 weeks to resolve.[6] Post–COVID-19 condition, commonly referred to as long COVID (among many other terms being used), is a relatively new condition recognized by the Public Health Agency of Canada (PHAC) and WHO.[7,8] On October 6, 2021, WHO published a case definition of post–COVID-19 condition, developed by a Delphi consensus process that included patients, clinicians, researchers, and others, representing all WHO regions.[9] The definition indicates that post–COVID-19 condition is characterized by new or persistent symptoms, usually 3 months from the initial infection, lasting for at least 2 months, which cannot be explained by another cause.[9] The UK Office for National Statistics estimated the prevalence of post–COVID-19 condition was 4.0% and 9.2% at least 12 weeks after initial infection among doubly-vaccinated adults infected with Omicron BA.1 and Delta variants, respectively.[10] However, considerable variations in prevalence have been observed between hospitalized and non-hospitalized patients and across different regions.[11] Common symptoms include weakness, general malaise, fatigue, concentration impairment, and breathlessness.[12] A patient-led movement was launched in 2020 to raise awareness about post–COVID-19 condition.[13]

In May 2022, CADTH published a scoping review that mapped the available evidence up to February 2022 and gaps regarding post–COVID-19 condition across the following concepts: risk factors and prevention, classification, diagnostic tests, treatment and management, and health system issues (e.g., increased health care services use and policy impact).[14] A relatively small proportion (n = 74; 11.6%) of the published reports evaluated the treatment or management of post–COVID-19 condition.[14] Most of the evidence-based guidelines did not provide recommendations specific to post–COVID-19 condition according to the WHO definition (i.e., patients with symptoms at least 3 months after initial infection).[14] However, there were 67 registrations or protocols of clinical trials that aimed to investigate interventions for the treatment of post–COVID-19 condition.[14] In another article, at least 26 clinical trials that evaluated the interventions of post–COVID-19 condition were identified.[15] An update was planned to respond to stakeholder requests and to understand the direction of treatment and management of post–COVID-19 condition.[14] However, the characteristics of post–COVID-19 condition have been addressed by systematic reviews and large surveys.[12,16-19] There are ongoing and living systematic reviews on the prevention and diagnosis of post–COVID-19

condition by PHAC,[20,21] and Cochrane Rehabilitation is conducting a living review on COVID-19 rehabilitation.[22] A number of scoping reviews on treatment of post–COVID-19 condition have been published.[23-25] However, the CADTH review published in May 2022 used a broader scope, and both the CADTH review[14] and a review by Ceban et al.[24] identified new and emerging interventions to treat or manage post–COVID-19 condition. The rapidly changing evidence base warrants continuous efforts to characterize the literature and identify research gaps. To avoid duplication of efforts, the scope of this review focuses on the treatment and management of post–COVID-19 condition, excluding rehabilitation (covered in the aforementioned Cochrane living review).[22]

The purpose of the report is to provide an updated mapping of the current evidence landscape related specifically to treatment and management of post–COVID-19 condition, and to identify research gaps. In clinical practice, management can refer to a broad spectrum that includes specific treatments and interventions.[26] The final deliverable of this project will be an updated scoping review report. 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. The findings will also contribute to the condition-level review's online platform that will include an evidence map. A condition-level review is an assessment that incorporates all aspects of a condition, from prevention and detection to treatment and management.

Objective

The purpose of this rapid living scoping review is to provide an up-to-date map of the latest evidence (including primary studies, evidence syntheses, and guidelines) available in peer-reviewed journals and grey literature, and to identify research gaps regarding the treatment and management of post–COVID-19 condition in any population and setting to better assess additional research requirements and support health care decision-making needs in Canada.

Research Questions

The rapid living scoping review will address the following research questions using published methods.[27,28] Details on the specific populations, concepts, and contexts of interest are included in Table 1.

1. What is the current evidence landscape on the treatment and management of post–COVID-19 condition for people of any age in any setting?
2. What are the knowledge gaps on the treatment and management of post–COVID-19 condition for people of any age in any setting?

Methods

Protocol Development

The protocol for this rapid living scoping review was adapted from the protocol of the previously published CADTH scoping review.[14] Modifications were made to match available resources for this report and to avoid duplication in the research for post–COVID-19 condition (refer to Appendix 2, Table 3 for changes and reasons to change). Due to time and resource constraints, and considering that the topic area is continually evolving, we adapted our previous methodology to enable the review to be performed rapidly (i.e., fewer databases searched, single reviewer for screening and data charting). We chose to focus on final reports of studies with results (rather than protocols, registrations, and pre-prints) because we plan to move the scoping review into living mode to keep pace with developments in the evidence base. The scope of this update is restricted to 1 of the concepts studied in the previous CADTH scoping review: treatment and management (aside from rehabilitation). Treatment and management include all interventions that aim to treat post–COVID-19 condition. We have excluded rehabilitation from this review because it is the subject of a living review by Cochrane.[22] A definition of "rehabilitation" was not reported in the Cochrane review and the corresponding authors could not be reached. We have defined rehabilitation to include interventions designed to improve physical functioning and minimize disability.[29] The interventions searched by the Cochrane living review were rehabilitation, respiratory rehabilitation, exercise, physical therapy modalities, physical therapy, functional recovery, and occupational therapy.[22] This review will not include these interventions. This protocol was written a priori based on well-established methods,[28] using appropriate reporting guidelines (i.e., the Preferred Reporting Items for Systematic reviews and Meta-Analyses for Protocols [PRISMA-P],[30] with adaptations for scoping reviews). The protocol and final scoping review report will be externally reviewed by content experts, and targeted feedback on the draft scoping review report will be sought from knowledge users, including key stakeholders that may include clinicians and policy-makers, and patient representatives. We will register the review topic at the National Collaborating Centre for Methods and Tools (NCCMT) to increase awareness and avoid duplication, and post the protocol on the Open Science Framework (OSF). Any deviations from the protocol will be disclosed in the final report and posted alongside the protocol in OSF.[31]

Study Design

We will conduct a rapid living scoping review of primary studies and other relevant research, including systematic reviews, overviews of reviews, rapid reviews, and evidence-based guidelines.

Selection and Eligibility Criteria

The review's eligibility criteria, including the specific populations, concepts, and contexts (PCC) of interest can be found in Table 1. The inclusion criteria were informed by CADTH

Horizon Scanning[32] and adapted from CADTH's published scoping review on post–COVID-19 condition,[14] with a focus on treatment and management. We plan to include full reports with results of primary studies, evidence syntheses, economic evaluations, and evidence-based guidelines that provide results related to any treatment or management option used for post–COVID-19 condition among people of all ages in any setting.

Table 1: Selection Criteria

Criteria	Description
Population	People of all ages with post–COVID-19 condition, defined as any symptoms experienced 12 weeks or more after initial infection, diagnosis, or symptom onset that cannot be explained by another cause.
Concept	Any health care options related to treatment and/or management of post–COVID-19 conditions, including but not limited to: • pharmacological interventions (e.g., drugs, biologics) • non-pharmacological interventions (e.g., supplements, traditional Chinese medicine, medical devices, acupuncture, and surgery) • care models (e.g., pathways, trajectories, frameworks, or structured clinics). Exclude: rehabilitation.[a]
Context	Any contextual setting (e.g., provided in person or virtually).
Study design(s)	Full reports of: • quantitative and qualitative primary studies of any design • evidence syntheses (i.e., systematic reviews[b], rapid reviews[c], overviews of reviews[d]) • economic evaluations • evidence-based guidelines (Canadian evidence-based guidelines will be included regardless of the definition used for post–COVID-19 condition). Exclusions: • protocols and registrations • scoping reviews • consensus statements • editorials, letters, and commentaries • review articles that are not conducted systematically • ethical analyses • studies of any design available as pre-prints, conference abstracts, presentations, or thesis documents.
Time frame	2019 to present (sources searched between 2019 and February 2022,[14] rescreened as needed, and merged with those searched in this update).

[a] Rehabilitation includes interventions designed to improve physical functioning and minimize disability.[25] Although the Cochrane Rehabilitation team did not publish a definition of rehabilitation,[22] publications were identified by searching bibliographic databases using keywords and subject headings for rehabilitation, respiratory rehabilitation, exercise, physical therapy modalities, physical therapy, functional recovery, and occupational therapy.[33] These interventions are considered rehabilitation interventions and will not be eligible in this report.

[b] 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; information about how the data were synthesized. Though appraisal of the quality of the included studies is often recommended for systematic reviews,[34] we did not consider this to be required for the purpose of the present scoping review.

[c] Systematic reviews using abbreviated methods.

[d] The same criteria as systematic reviews, except the unit of analysis is systematic reviews rather than primary studies.

Literature Search Methods

The literature search will be performed by an information specialist using a peer-reviewed search strategy according to the PRESS (Peer Review of Electronic Search Strategies) checklist.[35] The complete search strategy is presented in Appendix 1.

Published literature will be identified by searching the following bibliographic databases: MEDLINE All (1946–), Embase (1974–) via the Ovid platform, and the Cochrane Database of Systematic Reviews. All Ovid searches will be run simultaneously as a multi-file search. Duplicates will be removed using Ovid deduplication for multi-file searches, followed by manual deduplication in Endnote. The literature search strategy used in this report is a modification of the strategy developed for the original CADTH post–COVID-19 condition scoping review.[14] The search strategy will be comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concept will be post–COVID-19 condition or synonyms, plus a new concept for treatment and management. Parts of the strategy will be adapted from CADTH's COVID-19 search string.[36] Detailed search strategies are provided in Appendix 1.

The initial search was limited to English or French-language documents published between January 1, 2019, and December 21, 2021, with search updates until February 4, 2022. For the current report, database searches will be rerun in summer 2022 to capture any articles published or made available on post–COVID-19 treatment or management since the initial search date. Where possible, retrieval will be limited to the human population. No filters will be applied to limit the retrieval by study type. For this update, conference abstracts and pre-prints will be excluded, as well as comments, newspaper articles, editorials, and letters.

Grey literature (literature that is not commercially published) will be identified by searching sources listed in relevant sections of the *Grey Matters: A Practical Tool For Searching Health-Related Grey Literature* checklist[37] and *CADTH COVID-19 Grey Literature Resources*,[38] which includes the websites of regulatory agencies, HTA agencies, clinical guideline repositories, systematic review repositories, patient-related groups, and professional associations. Google will be used to search for additional internet-based materials. These searches will be supplemented by reviewing bibliographies of key papers and through contact with experts (via email), as appropriate. Refer to Appendix 1 for more information on the grey literature search strategy.

The database literature searches will be updated every 3 months to support the living mode of the review. To ensure feasibility, the grey literature searches will be updated every 6 months. Both a final database and grey literature search alert will be conducted for the final update.

Study Selection

The systematic review management software DistillerSR (Evidence Partners, Ottawa, Canada) will be used to facilitate study selection. Pilot testing will be conducted for a

random sample of 50 references identified in the literature search to ensure a thorough understanding of the eligibility criteria; adaptations will be made if needed. One reviewer will then screen titles and abstracts of all citations retrieved from the literature search (i.e., academic database and grey literature searches). Full texts of records that are judged to be potentially relevant by the reviewer will be retrieved based on the pre-determined selection outlined in Table 1. One reviewer will examine all full-text articles for inclusion in the review. If the reviewer is uncertain about whether to include certain articles, the reviewer will discuss these articles with the team, who will come to consensus on inclusion or exclusion. The core review team includes 3 authors, a reviewer, a research information specialist, and a methodologist, who authored a previous CADTH scoping review report on post–COVID-19 condition.[14] Other team members contributing to this project have expertise in knowledge mobilization, project oversight, and topic scope. The team will meet regularly (e.g., weekly) to discuss review processes, data extraction, and interim findings. Due to time and resource constraints, the reviewer will not contact article authors in the event of unclear or conflicting information in the literature. Instead, a team decision about inclusion or exclusion will be made based on the available information. The reasons for exclusion of articles at the full-text level will be documented.

Sources included in the previous CADTH review[14] that are relevant to treatment and management will be included in the current scoping review. These will be rescreened by a single reviewer to exclude those that focus solely on rehabilitation. Sources identified via search alerts meeting the selection criteria of the review will be incorporated into the synthesis if they are identified before the end of the open call for feedback, which will take place during the final update.

Charting (Data Extraction)

Charting will be performed by one reviewer, who authored the previously published CADTH scoping review.[14] Before charting begins, the 2 members of the review team will test the data extraction form on a random sample of 5 included studies and meet to review discrepancies. The form will be edited and further pilot exercises will be run if needed, until the single reviewer is ready to proceed with the full data charting. In the event of unclear or conflicting information, the reviewer will consult the team. Relevant information will be charted, including the following:

- study characteristics (e.g., first author's name, publication year, country or countries where the study was conducted) and methodology (e.g., study design, methods to confirm COVID-19 infection)
- population (e.g., number of participants, age, sex and/or gender, race, vaccination status)
- concept (any concepts related to treatment and management of post–COVID-19 condition, including pharmaceutical and non-pharmaceutical treatments given at least 3 months after initial infection; no limits on the comparators)
- context in which the treatment is being offered (any contextual settings including but not limited to clinical, community, care home, and rural settings reported by source authors).

Data will be charted for all relevant concepts and contexts for this study at any duration of follow-up. Specific population characteristics (including race, ethnicity, culture, and language; occupation; sex and/or gender; education; socioeconomic status; and other characteristics that may be associated with inequities) will be charted to identify characteristics that stratify health opportunities and outcomes related to health equity and equity considerations.[39] We will use customized charting forms for guidelines, systematic reviews, or overviews of reviews. The characteristics of the included guidelines and systematic reviews will be summarized in separate tables.[14] Characteristics will be extracted directly as reported by the authors of the guidelines and systematic reviews. We will not retrieve their included primary studies for further information. When applicable, population characteristics will be described using available data, such as ranges of median ages and sample sizes reported in primary studies.

Given the findings of our previous scoping review,[14] we anticipate there will be a large volume of case reports and case series in the literature that include small numbers of patients. To ensure the feasibility of data charting with a small review team, we will not perform full data charting, and instead only collect and report the types of treatment or management for case reports and case series (fewer than 10 participants).

Attempts will not be made to contact the corresponding authors of these studies to obtain missing information or to clarify conflicting information, due to time and resource constraints. Data charting will be an iterative process, whereby additional items may be added as the research team learns about the research base and recognizes new items of importance. The full list of data that will be charted can be found in Appendix 3.

Critical Appraisal

The focus of this review is the available evidence and gaps in evidence related to the treatment and management of post–COVID-19 condition. The risk of bias in the sources will not be assessed.

Data Analysis and Synthesis

Descriptive Synthesis

Descriptive mapping will be performed, including the presentation of study characteristics within summary tables, visual displays, and in the main text. For example, we will tabulate the treatment and management strategies against population characteristics, diagnoses, and study design. Findings will be summarized across studies (by research questions), including treatment and management of post–COVID-19 condition. Study characteristics will be presented in tables as suggested by the JBI manual.[28] When possible, we will present the case series separately from other study designs to avoid overemphasizing these studies that include few participants. Specifically, other tables will be developed to present the answers to the research questions. The treatment and management strategies may be grouped in categories, such as clinical manifestations by the organ systems the interventions aim to treat.[40,41] In July 2021, INESSS published a post–COVID-19 condition management support tool

intended for front-line clinicians.[42] The tool's development included a systematic review of accepted clinical practice guidelines at the time it was drafted, and relied on the knowledge, experience, and contribution of stakeholders across Québec.[42] This scoping review will chart data using the same categorization.

The results will also be presented in diagrams, such as bar charts or other visual displays, to demonstrate the distributions of the publications across different topics, disciplines, countries, and other categories. The visualization may help to identify potential gaps in research related to the treatment of post–COVID-19 condition. We acknowledge that not all gaps may be easily identified, because our understanding of post–COVID-19 condition is continuing to evolve. However, we may be able to identify populations, symptoms, or treatments that have been evaluated in few studies or only in case studies. The gaps may also be identified through the examination of the distributions of studies in patient characteristics, levels of care, and other characteristics. Findings related to evidence gaps will also be shared with the CADTH condition-level review stakeholder panel who will help with the categorization of evidence. The stakeholder panel will include representation from cross-jurisdictional decision-makers, clinicians actively working in the area of post–COVID-19 condition, and patient representatives.

Future Updates

The COVID-19 pandemic remains an ongoing issue and new SARS-CoV-2 variants are spreading quickly in Canada.[43] With more new cases of infection, the burden of post–COVID-19 condition is expected to grow.[44] The rapid changes in the pandemic and the increasing number of therapeutic interventions tested in clinical trials make it important to continue monitoring new and emerging strategies to manage and treat post–COVID-19 condition. Considering the need to keep pace with the evolving evidence base, we plan to initially update this report every 3 months. The team will meet and decide whether there is a need to continue to perform regular updates or to change the PCC criteria to exclude certain study designs, and may modify the frequency of the updates or choose to take the review out of living mode. This decision will be based on the volume of accumulating literature or the significance of the findings in primary studies at each update; for example, if few studies are identified in previous updates, it may be reasonable to extend the time lag between updates without the scoping review becoming substantially out of date. We may choose to transition out of living mode when the accumulation of new information becomes slow enough that continual updates do not seem informative, or if there is a shift in priorities to other topics. At this time, we will publish a final version of the report. To accomplish the updates, we will continue using the same review methods until specified otherwise. The reasons to transition out of living mode, or deviations from the methods in this protocol, will be listed with explanations in the latest version of the report. In each update, the literature search results will be screened at once. The number of newly identified sources will be reported with a PRISMA diagram. We will synthesize the data extracted in previous reports and the update to draw conclusions. We will determine and report whether there are any changes in the conclusions, compared to previous reports. Moreover, post–

COVID-19 condition is an issue that attracts public attention. The results will help the public understand existing evidence and research gaps about the treatment and management of post–COVID-19 condition. We plan to use interactive visual tools to display the distributions of the literature by study design, type of treatment and management, target population, and other factors.

Knowledge Mobilization

In addition to the scoping review report, additional knowledge mobilization activities to disseminate the findings of this scoping review and the larger condition-level review will be conducted, and could include relevant educational outreach and related activities. Outreach for this project and the condition-level review will be done by CADTH's Knowledge Mobilization and Implementation Support team to meet the needs of key stakeholders, such as jurisdictional bodies, health care providers, and other users of health evidence.

Opportunities for Stakeholder Feedback

All stakeholders will be given the opportunity to provide feedback on the scoping review report and updates as they are published on CADTH's website by contacting requests@CADTH.ca. An open call for feedback will take place during the final update. Unpublished data identified as part of the feedback process may only be included if the source of data is in the public domain.

Patient Engagement

Prior to completion of the scoping review, we will identify 3 adults (aged 18 years or older) who are currently living with post–COVID-19 condition through contact with support groups, clinical experts involved in the project, CADTH Liaison Officers, and other CADTH networks across Canada. These people with lived experience will be invited to attend a meeting to discuss the scoping review. At the meeting, CADTH staff will present the findings of the scoping review, and a Patient Engagement Officer will facilitate a discussion about interventions or treatments, areas of controversy, uncertainty, or priorities from their perspectives. The patients will have the chance to ask questions, and provide context and considerations about the findings. These views and comments will be incorporated into the scoping review.

Their contribution will be acknowledged in the report, and their involvement will be reported using the Guidance for Reporting Involvement of Patients and the Public 2 (GRIPP2) Framework.[45] CADTH will continue to inform these patients as work in the area continues, and will notify them when the review is published and updated. Other opportunities to give feedback or get involved will be shared with the patients. Upon completion of the final report, the same participants that were engaged previously will be invited to provide feedback on the clarity of writing and comment on the relevance of the

findings to Canadian patients and families. At this point they will also be asked if they feel their contributions to the project are reflected in the final report. CADTH will share the key results of the full assessment and describe how engagement activities were used.

Limitations

This scoping review is expected to have some limitations related to the rapid approach; however, the abbreviated methodology was necessary due to time and resource constraints, and the rapid evolution of the topic area. We will search a reduced number of databases (those believed to be most relevant to the topic area) compared to CADTH's previous scoping review.[14] We have shifted our focus to full reports with results and guidelines, and plan to exclude protocols and study registrations. We applied this limit with the knowledge that the living approach means that new evidence will be incorporated at regular intervals. Only 1 reviewer will screen and chart the literature and it is therefore possible that eligible publications will be missed or that errors in data extraction will be overlooked; we will mitigate this possibility by running a pilot round.

Protocol Amendments

If amendments are required at any time during the study, reasons for changes and their timing in the review process will be recorded in a study file and subsequently reported within the final study report.

Updates to the online registration will be made accordingly (i.e., OSF).[31]

References

1. World Health Organization. Report of the WHO-China Joint Mission on coronavirus disease 2019 (COVID-19). Geneva (Switzerland): WHO; 2020: https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf. Accessed 2021 Jul 21.
2. Cumulative confirmed COVID-19 cases. Oxford (UK): Our World in Data; 2022: https://ourworldindata.org/grapher/cumulative-covid-cases-region. Accessed 2022 Jul 26.
3. Government of Canada. COVID-19 epidemiology update. Ottawa (ON): Government of Canada; 2022: https://health-infobase.canada.ca/covid-19/?stat=num&measure=deaths_total&map=pt#a2. Accessed 2022 Aug 22.
4. COVID-19 in Ontario: Focus on August 21, 2022 to August 27, 2022 (Week 34). Weekly epidemiological summary. Toronto: Public Health Ontario; 2022: https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-weekly-epi-summary-report.pdf?sc_lang=en. Accessed 2022 Sep 1.
5. Bull-Otterson L, Baca S, Saydah S, et al. Post–COVID conditions among adult COVID-19 survivors aged 18–64 and≥ 65 years—United States, March 2020–November 2021. *Morb Mortal Weekly Rep.* 2022;71(21):713.
6. World Health Organization. Coronavirus (COVID-19) update no. 20. Geneva (Switzerland): WHO; 2020: https://www.who.int/docs/default-source/coronaviruse/risk-comms-updates/update-20-epi-win-covid-19.pdf?sfvrsn=5e0b2d74_2. Accessed 2021 Jul 21.
7. Public Health Agency of Canada. Statement from the Chief Public Health Officer of Canada on July 7, 2021. Ottawa (ON): Government of Canada; 2021: https://www.canada.ca/en/public-health/news/2021/07/statement-from-the-chief-public-health-officer-of-canada-on-july-7-2021.html. Accessed 2021 Sep 1.
8. Rajan S, Khunti K, Alwan N, et al. In the wake of the pandemic: preparing for Long COVID. *(European Observatory Policy Brief 39)*. Copenhagen (Denmark): European Observatory on Health Systems and Policies; WHO; 2021: https://www.euro.who.int/en/about-us/partners/observatory-old/publications/policy-briefs-and-summaries/in-the-wake-of-the-pandemic-preparing-for-long-covid-2021. Accessed 2021 Sep 1.
9. World Health Organization. A clinical case definition of post COVID-19 condition by a Delphi consensus. Geneva (Switzerland): World Health Organization; 2021: https://apps.who.int/iris/rest/bitstreams/1376291/retrieve. Accessed 2021 Oct 20.
10. Self-reported long COVID after infection with the Omicron variant in the UK: 18 July 2022. London (UK): Office for National Statistics; 2022: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/selfreportedlongcovidafterinfectionwiththeomicronvariant/18july2022. Accessed 2022 Sep 1.
11. Chen C, Haupert SR, Zimmermann L, Shi X, Fritsche LG, Mukherjee B. Global prevalence of post COVID-19 condition or Long COVID: a meta-analysis and systematic review. *J Infect Dis.* 2022;16:16.
12. Michelen M, Manoharan L, Elkheir N, et al. Characterising long COVID: a living systematic review. *BMJ Glob Health.* 2021;6(9):e005427.
13. Alwan NA. The road to addressing Long Covid. *Science.* 2021;373(6554):491-493.
14. Chao Y-S, Vu T, McGill SC, Gates M. Clinical classification and interventions for post–COVID-19 condition: a scoping review. *Can J Health Technol.* 2022;2(5).
15. Ledford H. Long-COVID treatments: why the world is still waiting. *Nature.* 2022;608(7922):258-260.
16. Ziauddeen N, Gurdasani D, O'Hara ME, et al. Characteristics and impact of Long Covid: findings from an online survey. *PLoS One.* 2022;17(3):e0264331.
17. Danesh V, Boehm LM, Eaton TL, et al. Characteristics of post-ICU and post-COVID recovery clinics in 29 U.S. health systems. *Crit Care Explor.* 2022;4(3):e0658.

18. Garner O, Kumari Narendra D, Guntupalli K. Characteristics of survivors of Covid-19 seen at a post-acute Covid-19 syndrome clinic. *Chest.* 2021;160(4 Supplement):A1141-A1142.
19. Patel P, DeCuir J, Abrams J, Campbell AP, Godfred-Cato S, Belay ED. Clinical characteristics of multisystem inflammatory syndrome in adults: a systematic review. *JAMA Netw Open.* 2021;4(9):e2126456.
20. CANCOVID. Public Health Agency of Canada (PHAC) – Emerging Science Group (ESG) Evidence Reviews. CANCOVID; 2021: https://cancovid.ca/resources/phac-esg/. Accessed 2022 Jul 1.
21. Domingo FR, Waddell LA, Cheung AM, et al. Prevalence of long-term effects in individuals diagnosed with COVID-19: a living systematic review. *medRxiv.* 2021.
22. Ceravolo MG, De Sire A, Andrenelli E, Negrini F, Negrini S. Systematic rapid" living" review on rehabilitation needs due to COVID-19: update to March 31st, 2020. *Eur J Phys Rehabil Med.* 2020;56(3):347-353.
23. Cha C, Baek G. Symptoms and management of long COVID: a scoping review. *J Clin Nurs.* 2021;n/a(n/a).
24. Ceban F, Leber A, Jawad MY, et al. Registered clinical trials investigating treatment of long COVID: a scoping review and recommendations for research. *Infect Dis.* 2022:1-11.
25. Carson E, Hemenway AN. A scoping review of pharmacological management of postacute sequelae of severe acute respiratory syndrome coronavirus 2 infection in 2021. *Am J Ther.* 2022;29(3):e305-e321.
26. Ghany MG, Strader DB, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C: an update. *Hepatology (Baltimore, Md).* 2009;49(4):1335.
27. Peters MDJ, Marnie C, Tricco AC, et al. Updated methodological guidance for the conduct of scoping reviews. *JBI Evidence Synthesis.* 2020;18(10).
28. Aromataris E, Munn Z, editors. JBI Manual for Evidence Synthesis. Adelaide (Australia): JBI; 2020: https://doi.org/10.46658/JBIMES-20-01. Accessed 2021 Sep 1.
29. World Health Organization. Rehabilitation. Geneva (Switzerland): World Health Organization; 2021: https://www.who.int/news-room/fact-sheets/detail/rehabilitation. Accessed 2021 Jul 1.
30. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ.* 2015;349:g7647.
31. National Collaborating Centre for Methods and Tools. Repository of public health evidence syntheses. *(Synthesized evidence for COVID-19)* 2021; https://www.nccmt.ca/covid-19/covid-19-evidence-reviews. Accessed 2021 Nov 5.
32. Vu T, McGill SC. CADTH horizon scan: an overview of post-COVID-19 condition (Long Covid). *Can J Health Technol.* 2021 Sep;1(9). https://www.cadth.ca/overview-post-covid-19-condition-long-covid. Accessed 2021 Sep 28.
33. Ceravolo MG, Sire Ad, Andrenelli E, Negrini F, Negrini S. Supplementary digital material 1. *Eur J Phys Rehabil Med.* 2020;56(3).
34. Krnic Martinic M, Pieper D, Glatt A, Puljak L. Definition of a systematic review used in overviews of systematic reviews, meta-epidemiological studies and textbooks. *BMC Med Res Methodol.* 2019;19(1):203.
35. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 guideline statement. *J Clin Epidemiol.* 2016;75:40-46.
36. CADTH COVID-19 search strings. Ottawa (ON): CADTH; 2019: https://covid.cadth.ca/literature-searching-tools/cadth-covid-19-search-strings/. Accessed 2021 Sep 28.
37. Grey matters: a practical tool for searching health-related grey literature. Ottawa (ON): CADTH; 2019: https://www.cadth.ca/grey-matters. Accessed 2022 Sep 21.
38. CADTH COVID-19 grey literature resources: a curated list of evidence-based sources for health professionals, librarians, and researchers. Ottawa (ON): CADTH; 2021: https://covid.cadth.ca/literature-searching-tools/cadth-covid-19-grey-literature-resources/. Accessed 2022 Sep 21.

39. O'Neill J, Tabish H, Welch V, et al. Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health. *J Clin Epidemiol.* 2014;67(1):56-64.

40. Yan Z, Yang M, Lai C-L. Long COVID-19 syndrome: a comprehensive review of its effect on various organ systems and recommendation on rehabilitation plans. *Biomedicines.* 2021;9(8):966.

41. Crook H, Raza S, Nowell J, Young M, Edison P. Long covid—mechanisms, risk factors, and management. *BMJ.* 2021;374:n1648.

42. Management support tool - post-COVID-19 conditions. Montreal (QC): Institut National d'Excellence En Santé et Services Sociaux (INESSS); 2022: https://www.inesss.qc.ca/fileadmin/doc/INESSS/COVID-19/2022_Outil_Covid_Affections_postCov19_AN-VF_01.pdf. Accessed 2022 Sep 11.

43. Government of Canada. COVID-19 daily epidemiology update. 2022; https://health-infobase.canada.ca/covid-19/epidemiological-summary-covid-19-cases.html. Accessed 2022 Sep 21.

44. Rubin R. As their numbers grow, COVID-19 "Long Haulers" stump experts. *JAMA.* 2020;324(14):1381-1383.

45. Staniszewska S, Brett J, Simera I, et al. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. *BMJ.* 2017;358:j3453.

46. O'Blenis P. One simple way to speed up your screening process. Ottawa (ON): Evidence Partners, DistillerSR; 2017: https://blog.evidencepartners.com/one-simple-way-to-speed-up-your-screening-process. Accessed 2021 Jul 1.

47. Khangura S, Konnyu K, Cushman R, Grimshaw J, Moher D. Evidence summaries: the evolution of a rapid review approach. *Sys Rev.* 2012;1(1):10.

Appendix 1: Literature Search Strategy

Note that this appendix has not been copy-edited.

For the original literature search strategy, please see the appendices of the original scoping review: Chao Y-S et al. Clinical Classification and Interventions for Post–COVID-19 Condition: A Scoping Review. *Canadian Journal of Health Technologies*. 2022;2(5).[14]

Overview

Interface: Ovid

Databases:

- MEDLINE All (1946-present) via Ovid
- Embase (1974-present) via Ovid
- **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 update: July 21, 2022

Alerts: Alerts every 3 months until project completion.

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: articles published or added to the databases from January 30, 2022 – present.
- Humans
- Languages: English or French

Table 2: 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

Syntax	Description
.ot	Original title
.ab	Abstract
.hw	Heading word; usually includes subject headings and controlled vocabulary
.kf	Author keyword heading word (MEDLINE, Embase)
.nm	Name of substance, including CAS and other registry numbers and chemical names (MEDLINE)
.ox	Organism supplementary concept word for emerging virus and other organism terms (MEDLINE)
.rx	Rare disease supplementary concept for emerging rare disease terms (MEDLINE)
.px	Protocol supplementary concept (MEDLINE)
freq=#	requires that the term(s) occur # number of times or more within the field(s) searched
.pt	Publication type
.ez	Medline Entrez date (YYYYMMDD with * for any truncation)
.da	Medline entry date (YYYYMMDD with * for any truncation)
.dt	Medline creation date (YYYYMMDD with * for any truncation)
Limit to dc	Embase date created. Format as: dc=YYYYMMDD-YYYYMMDD
medall	Ovid database code: MEDLINE All, 1946 to present, updated daily
oemezd	Ovid database code; Embase, 1974 to present, updated daily

Ovid Multi-Database Strategy — MEDLINE, Embase, Cochrane Central, and PsycInfo

MEDLINE post–COVID-19 treatment or management terms by themselves

1. ((post covid* or post coronavirus* or long covid* or long coronavirus*) adj2 (treatment* or management)).ab.

MEDLINE main post–COVID-19 terms

2. (long COVID* or long coronavirus* or longCOVID* or longcoronavirus*).ti,ab,kf.
3. (sequela* adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or SARSCOV2)).ti,ab,kf.
4. ((post or chronic or long term or longterm) adj3 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or SARSCOV2) adj4 (condition* or sequela* or syndrome* or subsyndrome* or clinical syndrome* or disorder* or symptom* or outcome* or clinical outcome* or function* or followup or follow-up or subtyp* or sub-typ* or phenotyp* or complication* or survivor*)).ti,ab,kf.
5. ((post acute or postacute or late complication*) adj3 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or SARSCOV2)).ti,ab,kf.
6. PASC.ti,kf.
7. (post-COVID* adj fatigue).ti,ab,kf.
8. or/2-7

MEDLINE COVID-19 set

9. COVID-19/ or SARS-CoV-2/

10. (COVID* or coronavirus* or corona virus* 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.
11. 9 or 10

MEDLINE additional post–COVID-19 terms and subtypes, to combine with COVID set

12. (((post acute or postacute or sub-acute or subacute or chronic or long or longterm or late) adj sequela*) or PASC).ti,ab,kf.
13. (long haul* or longhaul*).ti,ab,kf.
14. ((persist* or long* or residual or prolonged) adj8 ((olfactory or chemosensor*) adj (disorder* or dysfunction*))).ti,ab,kf.
15. (post* or chronic* or long or longterm or sequela*).ti,ab,kf.
16. (PFS or (pulmonary adj3 fibro*) or (lung adj3 fibro*) or fatigue syndrome? or myalgic encephalomyelitis or ME-CFS or ME?CFS or (postural adj3 tachycardia*) or POTS or MIS-C or MIS-A or PIMS or PIMSTS or PIMS-TS).ti,ab,kf.
17. ((multisystem* or multi-system*) adj3 (inflamm* or hyperinflamm*)).ti,ab,kf.
18. 15 and (16 or 17)
19. or/12-14,18
20. 11 and 19

MEDLINE treatment or management set

21. Therapeutics/
22. (dh or dt or pd or su).fs. [diet therapy, drug therapy, pharmacology superheading, surgery]
23. (treatment* or therap* or management or managing or drug? or medication? or pharmacolog* or pharmaceutic* or non-drug? or nonpharmacolog* or non-pharmacolog* or biologic or biologics or diet* or supplement* or vitamin* or treat or treated or treating or placebo* or off-label*).ti,kf.
24. (treatment* or therap* or management or managing or drug? or medication? or pharmacolog* or pharmaceutic* or non-drug? or nonpharmacolog* or non-pharmacolog* or biologic or biologics or diet* or supplement* or vitamin* or treat or treated or treating or placebo* or off-label*).ab. /freq=3
25. ((care or treatment or healthcare) adj2 (model* or path* or plan*)).ti,ab,kf.
26. ((interdisciplin* or inter-disciplin* or cross-disciplin* or multidiscipline* or multi-disciplin* or inter-disciplin*) adj3 (team* or clinic? or centre? or center? or model* or program*)).ti,ab,kf.
27. (recovery adj2 (team* or clinic? or centre? or center? or model* or program*)).ti,ab,kf.
28. (care adj2 (coordinat* or co-ordinat*)).ti,ab,kf.
29. (patient-centred care or patient-centered care or case manag*).ti,ab,kf.
30. exp Drug Therapy/ or exp Biological Therapy/ or exp "Nebulizers and Vaporizers"/
31. (infusion* or inhaler* or nasal spray* or nebulize*).ti,ab,kf.
32. vaccin*.ti,kf.
33. vaccin*.ab. /freq=3
34. (anticoagulants or (anticoagulant* adj2 (therap* or oral* or intravenous* or IV)) or apixaban* or clopidogrel* or heparin*).ti,ab,kf.

35. (aceclofenac* or antibiotic* or antidepressant* or antihistamine* or ((antiviral* or anti-viral*) adj2 (agent* or oral*)) or atenolol* or atorvastatin*).ti,ab,kf.
36. (bamlanivimab* or beta blocker* or casirivimab* or cilgavimab* or convalescent plasma* or corticosteroid* or dexamethasone* or enol-oxaloacetate* or enoxaparin* or etanercept* or Evusheld* or fludrocortisone* or hydroxychloroquine* or intravenous immunoglobulin* or immune-modulator* or immunomodulator* or imdevimab* or meglucocorticoid* or glucocorticosteroid* or indomethacin* or ivermectin*).ti,ab,kf.
37. (levocetirizine* or megestrol* or methylnicotinamide* or methylprednisolone* or monoclonal antibod* or montelukast* or N115 or N-115 or Nacetylcysteine* or sodium pyruvate* or naltrexone* or nicotinamide* or nintedanib* or nirmatrelvir* or Paxlovid* or perflubron* or pirfenidone* or prednisolone* propranolol* or remdesivir* or ritonavir* or rituximab*).ti,ab,kf.
38. (S1226 or S-1226 or selective serotonin reuptake inhibitor* or SSRI* or sildenafil* or sotrovimab* or steroid* or sulodexide* or tiazotic acid* or tixagevimab* or thiotriazolin* or vasodilator* or vasopressin* or vortioxetine* or vinpocetine*).ti,ab,kf.
39. (cellular therap* or cell-based therap* or stem cell* or actovegin* or amniotic epithelial cell* or hAEC? or Ampion* or Cerebrolysin* or COVI-MSC* or cSVF or Leronlimab* or MON002 or RSLV-132 or Ruconest*).ti,ab,kf.
40. exp Dietary Supplements/ or exp Nutrition Therapy/ or Medical Marijuana/ or exp Cannabinoids/
41. (dietician? or nutritionist?).ti,ab,kf.
42. (sublingual or oral drops).ti,ab,kf.
43. (antioxidant* or anti-oxidant* or Bioarginina C or L-arginine or CBD or cannabis or Myoquinon or coenzyme Q10 or Niagen or nicotinamide riboside or probiotic* or pro-biotic* or prebiotic* or pre-biotic* or lactobacill* or inulin* or bacteriotherap*).ti,ab,kf.
44. exp Surgical Procedures, Operative/ or Blood Component Removal/ or exp Compression Bandages/ or exp Electric Stimulation Therapy/ or exp Organ Transplantation/ or Neuromuscular Blocking Agents/ or exp Radiofrequency Therapy/
45. (device? or procedure? or technique?).ti,kf.
46. (surgery or surgeries or surgical* or operation).ti,ab,kf.
47. (apheresis or blood washing or blood component removal or plasmapheresis).ti,ab,kf.
48. ((compression or pressure) adj3 (bandage* or garment* or clothing* or socks or stocking? or hose)).ti,ab,kf.
49. ((lung? or organ?) adj2 transplantation).ti,ab,kf.
50. ((electrical or bioelectric or nerve or transcranial or trans-cranial) adj3 (stimulator or stimulation*)).ti,ab,kf.
51. ((monopolar or intervention*) adj3 (radiofrequenc* or radio frequenc*)).ti,ab,kf.
52. (neurophysiological facilitation or neuromodulation or Parasym? or Dolphin* or tDCS or INDIBA).ti,ab,kf.
53. (nerve block* or neuromuscular block* or ganglion block).ti,ab,kf.
54. (hyperbaric oxygen therap* or HBOT or supplemental oxygen or hydrogen therap* or (hydrogen adj3 inhalation) or molecular hydrogen).ti,ab,kf.
55. exp Phototherapy/ or exp Psychiatric Somatic Therapies/ or exp Psychotherapy/ or exp Therapy, Computer-Assisted/ or exp Virtual Reality/
56. (cognitive restructuring or ICBT or CBT or mind-body or meditation* or mentalPlus or hypnotherapy* or hypnosis or phototherapy or psychotherap* or progressive muscle relaxation or breathing retraining or pranayama* or olfactory training).ti,ab,kf.
57. ((cognitive or singing or breathing or breath or breathe or choral or choir or opera or ENO) adj2 (class or classes or instruction* or intervention* or training or program*)).ti,ab,kf.

58. (virtual reality or virtual environment? or virtual technolog* or ((computer* or digital or online or smartphone or virtual or web or webbased) adj3 (game? or gaming or app)) or gamification).ti,ab,kf.
59. exp Alternative Medicine/ or exp Biological Products/ or exp Complementary therapies/ or Osteopathic Medicine/
60. (complementary medicine? or alternative medicine? or traditional medicine?).ti,ab,kf.
61. (acupuncture or acupressure or auriculotherap* or acupoint? or chiropract* or osteopath* or reflexology*).ti,ab,kf.
62. (biofeedback or bio-feedback or sensory feedback).ti,ab,kf.
63. (Ayurved* or Agastya Haritaki or Ashwagandha or CIM-Meg19 or Pippali).ti,ab,kf.
64. (homoeopath* or naturopath*).ti,ab,kf.
65. (ozone or autohemotherapy*).ti,ab,kf.
66. or/21-65

MEDLINE results before limits: post–COVID-19 combined with treatment or management

67. (8 or 20) and 66
68. 1 or 67
69. 68 use medall

Embase post–COVID-19 treatment or management terms by themselves

70. long COVID/dm, dt, th [Disease Management, Drug Therapy, Therapy]
71. ((post covid* or post coronavirus* or long covid* or long coronavirus*) adj2 (treatment* or management)).ab.
72. 70 or 71

Embase main post–COVID-19 terms

73. Long covid/
74. (long COVID* or long coronavirus* or longCOVID* or longcoronavirus*).ti,ab,kf.
75. (sequela* adj5 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or SARSCOV2)).ti,ab,kf.
76. ((post or chronic or long term or longterm) adj3 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or SARSCOV2) adj4 (condition* or sequela* or syndrome* or subsyndrome* or clinical syndrome* or disorder* or symptom* or outcome* or clinical outcome* or function* or followup or follow-up or subtyp* or sub-typ* or phenotyp* or complication* or survivor*)).ti,ab,kf.
77. ((postCOVID* or postcoronavirus* or postcorona virus* or postSARS-COV-2 or postSARS-COV2 or postSARSCOV-2 or postSARSCOV2) adj4 (condition* or sequela* or syndrome* or disorder* or symptom* or outcome* or clinical outcome* or function* or followup or follow-up or subtyp* or sub-typ* or phenotyp* or complication* or survivor*)).ti,ab,kf.
78. ((post acute or postacute or late complication*) adj3 (COVID* or coronavirus* or corona virus* or SARS-COV-2 or SARS-COV2 or SARSCOV-2 or SARSCOV2)).ti,ab,kf.
79. PASC.ti,kf.
80. (post-COVID* adj fatigue).ti,ab,kf.
81. or/73-80

Embase COVID-19 set

82. exp Coronavirus disease 2019/
83. exp Severe acute respiratory syndrome coronavirus 2/
84. (COVID* or coronavirus* or corona virus* 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.
85. or/82-84

Embase additional post–COVID-19 terms and subtypes, to combine with COVID-19 set

86. (((post acute or postacute or sub-acute or subacute or chronic or long or longterm or late) adj sequela*) or PASC).ti,ab,kf.
87. (long haul* or longhaul*).ti,ab,kf.
88. ((persist* or long* or residual or prolonged) adj8 ((olfactory or chemosensor*) adj (disorder* or dysfunction*))).ti,ab,kf.
89. (post* or chronic* or long or longterm or sequela*).ti,ab,kf.
90. (PFS or (pulmonary adj3 fibro*) or (lung adj3 fibro*) or fatigue syndrome? or myalgic encephalomyelitis or ME-CFS or ME?CFS or (postural adj3 tachycardia*) or POTS or MIS-C or MIS-A or PIMS or PIMSTS or PIMS-TS).ti,ab,kf.
91. ((multisystem* or multi-system*) adj3 (inflamm* or hyperinflamm*)).ti,ab,kf.
92. 89 and (90 or 91)
93. or/86-88,92
94. 85 and 93

Embase treatment or management set

95. therapy/
96. (pr or su or th).fs. [Embase pharmaceutics, surgery, therapy]
97. (treatment* or therap* or management or managing or drug? or medication? or pharmacolog* or pharmaceutic* or non-drug? or nonpharmacolog* or non-pharmacolog* or biologic or biologics or diet* or supplement* or vitamin* or treat or treated or treating or placebo* or off-label*).ti,kf.
98. (treatment* or therap* or management or managing or drug? or medication? or pharmacolog* or pharmaceutic* or non-drug? or nonpharmacolog* or non-pharmacolog* or biologic or biologics or diet* or supplement* or vitamin* or treat or treated or treating or placebo* or off-label*).ab. /freq=3
99. ((care or treatment or healthcare) adj2 (model* or path* or plan*)).ti,ab,kf.
100. ((interdisciplin* or inter-disciplin* or cross-disciplin* or multidiscipline* or multi-disciplin* or inter-disciplin*) adj3 (team* or clinic? or centre? or center? or model* or program*)).ti,ab,kf.
101. (recovery adj2 (team* or clinic? or centre? or center? or model* or program*)).ti,ab,kf.
102. (care adj2 (coordinat* or co-ordinat*)).ti,ab,kf.
103. (patient-centred care or patient-centered care or case manag*).ti,ab,kf.
104. exp *biological therapy/ or exp *drug therapy/ or exp *biological product/ or exp inhaler/ or exp nebulizer/
105. (infusion* or inhaler* or nasal spray* or nebulize*).ti,ab,kf.
106. vaccin*.ti,kf.
107. vaccin*.ab. /freq=3

108. (anticoagulants or (anticoagulant* adj2 (therap* or oral* or intravenous* or IV)) or apixaban* or clopidogrel* or heparin*).ti,ab,kf.

109. (aceclofenac* or antibiotic* or antidepressant* or antihistamine* or ((antiviral* or anti-viral*) adj2 (agent* or oral*)) or atenolol* or atorvastatin*).ti,ab,kf.

110. (bamlanivimab* or beta blocker* or casirivimab* or cilgavimab* or convalescent plasma* or corticosteroid* or dexamethasone* or enol-oxaloacetate* or enoxaparin* or etanercept* or Evusheld* or fludrocortisone* or hydroxychloroquine* or intravenous immunoglobulin* or immune-modulator* or immunomodulator* or imdevimab* or meglucocorticoid* or glucocorticosteroid* or indomethacin* or ivermectin*).ti,ab,kf.

111. (levocetirizine* or megestrol* or methylnicotinamide* or methylprednisolone* or monoclonal antibod* or montelukast* or N115 or N-115 or Nacetylcysteine* or sodium pyruvate* or naltrexone* or nicotinamide* or nintedanib* or nirmatrelvir* or Paxlovid* or perflubron* or pirfenidone* or prednisolone* propranolol* or remdesivir* or ritonavir* or rituximab*).ti,ab,kf.

112. (S1226 or S-1226 or selective serotonin reuptake inhibitor* or SSRI* or sildenafil* or sotrovimab* or steroid* or sulodexide* or tiazotic acid* or tixagevimab* or thiotriazolin* or vasodilator* or vasopressin* or vortioxetine* or vinpocetine*).ti,ab,kf.

113. (cellular therap* or cell-based therap* or stem cell* or actovegin* or amniotic epithelial cell* or hAEC? or Ampion* or Cerebrolysin* or COVI-MSC* or cSVF or Leronlimab* or MON002 or RSLV-132 or Ruconest*).ti,ab,kf.

114. exp dietary supplement/ or exp supplementation/ or exp cannabinoid/ or exp probiotic agent/

115. (dietician? or nutritionist?).ti,ab,kf.

116. (sublingual or oral drops).ti,ab,kf.

117. (antioxidant* or anti-oxidant* or Bioarginina C or L-arginine or CBD or cannabis or Myoquinon or coenzyme Q10 or Niagen or nicotinamide riboside or probiotic* or pro-biotic* or prebiotic* or pre-biotic* or lactobacill* or inulin* or bacteriotherap*).ti,ab,kf.

118. medical procedures/ or exp device therapy/ or exp surgery/ or exp compression bandage/ or exp electrotherapy/ or exp neuromuscular blocking agent/ or exp radiofrequency therapy/ or exp phototherapy/ or exp extracorporeal therapy/

119. (device? or procedure? or technique?).ti,kf.

120. (surgery or surgeries or surgical* or operation).ti,ab,kf.

121. (apheresis or blood washing or blood component removal or plasmapheresis).ti,ab,kf.

122. ((compression or pressure) adj3 (bandage* or garment* or clothing* or socks or stocking? or hose)).ti,ab,kf.

123. ((lung? or organ?) adj2 transplantation).ti,ab,kf.

124. ((electrical or bioelectric or nerve or transcranial or trans-cranial) adj3 (stimulator or stimulation*)).ti,ab,kf.

125. ((monopolar or intervention*) adj3 (radiofrequenc* or radio frequenc*)).ti,ab,kf.

126. (neurophysiological facilitation or neuromodulation or Parasym? or Dolphin* or tDCS or INDIBA).ti,ab,kf.

127. (nerve block* or neuromuscular block* or ganglion block).ti,ab,kf.

128. (hyperbaric oxygen therap* or HBOT or supplemental oxygen or hydrogen therap* or (hydrogen adj3 inhalation) or molecular hydrogen).ti,ab,kf.

129. exp mental health care/ or exp psychiatric treatment/ or virtual reality/ or exp computer assisted therapy/ or exp experimental therapy/

130. (cognitive restructuring or ICBT or CBT or mind-body or meditation* or mentalPlus or hypnotherapy* or hypnosis or phototherapy or psychotherap* or progressive muscle relaxation or breathing retraining or pranayama* or olfactory training).ti,ab,kf.

131. ((cognitive or singing or breathing or breath or breathe or choral or choir or opera or ENO) adj2 (class or classes or instruction* or intervention* or training or program*)).ti,ab,kf.
132. (virtual reality or virtual environment? or virtual technolog* or ((computer* or digital or online or smartphone or virtual or web or webbased) adj3 (game? or gaming or app)) or gamification).ti,ab,kf.
133. exp alternative medicine/ or chiropractic/ or exp osteopathic medicine/ or exp acupuncture/ or homeopathy/
134. (complementary medicine? or alternative medicine? or traditional medicine?).ti,ab,kf.
135. (acupuncture or acupressure or auriculotherap* or acupoint? or chiropract* or osteopath* or reflexology*).ti,ab,kf.
136. (biofeedback or bio-feedback or sensory feedback).ti,ab,kf.
137. (Ayurved* or Agastya Haritaki or Ashwagandha or CIM-Meg19 or Pippali).ti,ab,kf.
138. (homoeopath* or naturopath*).ti,ab,kf.
139. (ozone or autohemotherapy*).ti,ab,kf.
140. or/95-139

Embase results before limits: post–COVID-19 combined with treatment or management

141. (81 or 94) and 140
142. 72 or 141
143. 142 use oemezd

MEDLINE and Embase results combined before limits

144. 69 or 143

Human filter

145. exp animals/
146. exp animal experimentation/ or exp animal experiment/
147. exp models animal/
148. nonhuman/
149. exp vertebrate/ or exp vertebrates/
150. or/145-149
151. exp humans/
152. exp human experimentation/ or exp human experiment/
153. or/151-152
154. 150 not 153
155. 144 not 154

Limits for publication types, language, and date

156. (comment or newspaper article or editorial or letter or note).pt.
157. 155 not 156
158. 157 not (conference abstract or conference review or preprint).pt.

159. limit 158 to (english or french)

160. 159 use medall

161. 160 and (2022013* or 202202* or 202203* or 202204* or 202205* or 202206* or 202207*).dt,ez,da. [Create Date, Entrez date, Entry date]

162. 159 use oemezd

163. limit 162 to dc=20220130-20220720 [Embase date created]

Final Results, deduplicated in Ovid

164. 161 or 163

165. remove duplicates from 164

Grey Literature

Search dates: Summer 2022.

Keywords: post-COVID-19, long COVID, post acute sequelae of COVID, chronic COVID condition, and synonyms; along with treatments (drug, device, or other non-drug) or care models. Publications solely on rehabilitation or exercise were excluded.

Limits: Publication years: 2019-present. 2019-present. As this grey literature search is an update of the original grey literature searches for the first scoping review, particular attention was paid to new publications since 2022.

Updates: Search updates will be conducted every 6 months, with an additional update before the final update.

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:

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

Appendix 2: Changes in the Review Methods From Baseline Review[14]

Note that this appendix has not been copy-edited.

Table 3: Changes in the Review Methods From Initial Review[14]

Criteria	Baseline review[14]	First update	Reasons for changes
Search period	Jan 1, 2019 – Feb 4, 2022	Jan 30, 2022 – present	A continuation of the living review. Overlap in the search periods to avoid missing any relevant sources.
Selection criteria: Concept	Clinical classification, preventive measures, diagnostic approaches, treatments, for post–COVID-19 condition	Any health care options related to treatment and/or management (aside from rehabilitation)	There are ongoing reviews on classification, prevention, diagnosis, and rehabilitation of post–COVID-19 condition
Selection criteria: Study design	• Primary studies of any design • Evidence syntheses (i.e., systematic reviews, rapid reviews, overviews of reviews), and pre-prints of systematic reviews • Scoping reviews • Economic evaluations • Evidence-based guidelines and Canadian guidelines regardless of the definition used for post–COVID-19 condition • Studies of any design available as a pre-print, conference abstract, presentation, or thesis • Protocols and study registrations **Exclusions:** • Consensus statements • Editorials, letters, and commentaries, including editorials and letters with data • Reviews not conducted systematically • Ethical analyses	Full reports with results of: • primary studies of any design • Evidence syntheses (i.e., systematic reviews, rapid reviews, overviews of reviews) • Economic evaluations Evidence-based guidelines and Canadian guidelines regardless of the definition used for post–COVID-19 condition **Exclusions:** • Protocols and registrations • Scoping reviews • Consensus statements • Editorials, letters, and commentaries • Reviews not conducted systematically • Ethical analyses • Studies of any design available as a pre-print, conference abstract, presentation, or thesis document	We excluded protocols, study registrations, conference presentations, abstracts, theses, and pre-prints of systematic reviews. We instead focused on only peer-reviewed full reports to report on interventions that had been tested. It became apparent following the first iteration of the scoping review, that inclusion of other scoping reviews was not relevant. We instead used these as background information.
Study selection	Liberal-accelerated approach[46,47]	1 reviewer screened the sources following a pilot round	Due to time and resource constraints.
Charting (data extraction)	1 reviewer extracted information from the sources and the other verified the data extracted	1 reviewer extracted information from the sources following a pilot round	Due to time and resource constraints.

Criteria	Baseline review[14]	First update	Reasons for changes
Charting (data extraction)	The review protocol aimed to use the PROGRESS-Plus framework (place of residence, race/ethnicity/culture/ language, occupation, gender/sex, religion, social capital, socioeconomic position, age, disability, sexual orientation, other vulnerable groups).[39]	This review used selected items of the PROGRESS-Plus framework,[39] including socioeconomic status, race/ethnicity, and sex and/or gender, in the charting form.	The results in the previous report[14] indicated that few eligible sources reported on certain PROGRESS-Plus items, such as social capital and sexual orientation.

Appendix 3: Data Extraction Form

Note that this appendix has not been copy-edited.

Objectives

Include: People of all ages with post–COVID-19 condition, defined as any symptoms experienced 12 weeks or more after initial infection, diagnosis, or symptom onset that cannot be explained by another cause

Any health care options related to treatment and/or for post–COVID-19 conditions including but not limited to:

- pharmacological interventions (e.g., drugs, biologics)
- non-pharmacological interventions (e.g., supplements, traditional Chinese medicine, medical devices, and surgery)
- care models (e.g., pathways, trajectories, frameworks, or structured clinics)

Exclude: Rehabilitation

Questions

1. **After full-text screening — include/exclude?**
    - Include
    - Exclude
    - Unsure
2. **Reasons of exclusion**
    - Acute infection (<3 months post infection)
    - Intervention: Rehabilitation
    - Intervention: Physical therapy modalities
    - Intervention: Exercise
    - Intervention: Respiratory rehabilitation Intervention: Physical therapy
    - *Note: reasons of exclusion can be added when encountered*

Category: Report

3. **First author's name (surname)**
4. **Year**
5. **Date: First online date (type as dd/mm/yyyy)**
6. **Date of publication (type as dd/mm/yyyy). NOTE: Skip if "first online date" is answered**
7. **Study design**
    - Primary study – interventional (i.e., RCT, nRCT)
    - Primary study – observational (i.e., any observational design, including case studies and case series)
    - Primary study – qualitative
    - Primary study – mixed methods

- Systematic review
- Rapid review
- Overview of reviews
- Economic evaluation
- Guideline – Canadian
- Guideline – other country

8. **Case report/series**
    - Yes, case reports/series
    - No

Category: Population

Note: unless otherwise stated, extract only for COVID+ group. If a study is all COVID+ patients but has different groups (e.g., one group has long COVID but the other does not), extract for whole sample

9. **Country of the first author**
10. **Countries of "participants"**
    - Note: If multiple, list all and separate by ";" If countries not reported, type "NR". If multiple or international or other, type "International".
11. **Total study N (including control group, where applicable. Leave blank if there is no COVID-negative control group):**
12. **Number of eligible participants (post–COVID-19 condition+):**
13. **Age category/categories**
    - Children/pediatric (0 to < 18)
    - Adults (18 and over)
    - Elder adults (65 and over)
    - Not reported - ONLY select "Not reported" for studies where no age data are available, numerical or categorical
14. **Sex and/or gender (% male only, report with % [e.g., 55%]). If not reported, please input NR.**
15. **Ethnicity data (check eligible options if >65% reported)**
    - Not reported White Black Asian Hispanic Indigenous Mixed Others Add % in the text boxes (e.g., "77%") when the options were checked
16. **Selected items from the PROGRESS-plus framework (check eligible options if >65% reported)**
    - Not reported
    - Low-income status
    - Unemployment status
    - Health care worker
    - Rural/remote area
    - Immigrants
    - Note: Add % in the text boxes (e.g., "77%") when the options were checked

17. **Comorbidities data (check eligible options if >65% reported)**
    - Not reported
    - Hypertension
    - Diabetes
    - CV or heart disease
    - Kidney disease
    - COPD
    - Cancer
    - Asthma
    - HIV/AIDS
    - Mental illnesses
    - Other
18. **Were the majority of COVID-19 cases diagnosed using a laboratory test (e.g., PCR, antigen/antibody)?**
    - Yes, at least 80% of COVID-19 cases were diagnosed using a laboratory test. (This also applies if the methods indicates "lab-confirmed" without specifying the type of test, and if different types of lab tests were done, e.g., patients were diagnosed using PCR or antibody tests.))
    - No, at least 80% of COVID-19 cases were not diagnosed using a laboratory test (e.g., self-reported based on symptoms or diagnosed by a clinician/at the hospital, and methods do not indicate a laboratory test was done).
    - Mixed: a mixture of confirmed (by lab test) and unconfirmed (e.g., self-report, clinician-diagnosed without lab test); e.g., if 60% are lab-confirmed at 40% are self-report.
    - Not reported/Unclear
19. **Method of confirmation/diagnosis of COVID**
    - PCR test
    - Antibody/antigen test
    - Lab test
    - Confirmed at hospital/ICU
    - Self-report Diagnosed by clinician
    - Not reported
    - Medical records, including database research
    - Other
20. **Method of confirmation/diagnosis of post–COVID-19 condition**
    - Confirmed at hospital/ICU
    - Self-report
    - Diagnosed by clinician
    - Not reported

- Medical records, including database research
- Other

21. **Severity of acute illness**
    - Asymptomatic
    - Symptomatic, not hospitalized
    - Hospitalized
    - ICU
    - Not reported
22. **Acute infection severity defined by WHO**
    - Yes
    - No
23. **Have participants received the COVID-19 vaccines?**
    - Yes: all participants have been fully vaccinated (1 or 2 doses depending on the vaccines).
    - Partly: participants have received at least one dose of the 2-dose vaccines
    - Mixed: some participants have received and others have not.
    - No: participants have not been vaccinated.
    - Not reported Other

Category: Concept

24. **Type of treatment/management**
    - Pharmacological interventions (e.g., drugs, biologics)
    - Vaccine
    - Non-pharmacological interventions (e.g., supplements, traditional Chinese medicine, medical devices, and surgery)
    - Care models (e.g., pathways, trajectories, frameworks, or structured clinics)
    - Other
    - Note: Add details, i.e., drug names or surgery methods, in the text boxes.
25. **Treatment details**
    - Drugs
    - Biologics
    - Supplements
    - Traditional Chinese medicine
    - Medical devices
    - Surgery/procedure
    - Care models

26. **Indication/diagnosis**
    - Text box
27. **Classification of clinical manifestations**
    - Cardiovascular
    - Dermatologic
    - Hematologic
    - Mental and behavioural
    - Neurological
    - Otorhinolaryngological
    - Pulmonary
    - Renal
    - Rheumatologic
    - Others
28. **Tests to assist in management of post–COVID-19 condition, at least 3 months post infection**
    - Basic tests (e.g., blood count, liver function, thyroid function, diabetes, and existing comorbidities)
    - Specialized tests (e.g., coagulation disorder, myocardial injury, NT-pro-BNP, viral infection, rheumatology)
    - Investigations (e.g., respiratory, or cardiac imaging)
29. **How many months after initial infection the treatment began?**
    - 1 month
    - 2 months
    - 3 months
    - 4 months
    - 5 months
    - 6 months
    - 7 to 12 months
    - 13 months or later
30. **Single treatment or multi-component?**
    - Single
    - Multiple
31. **Comparator(s) used (e.g., no treatment, before-after, no comparator)?**
    - No comparator
    - Drugs
    - Non-drug interventions

- Healthy controls
- Matched controls (not healthy)
- Placebo
- Standard care

32. **How many months after initial infection the comparator began?**
    - 1 month
    - 2 months
    - 3 months
    - 4 months
    - 5 months
    - 6 months
    - 7 to 12 months
    - 13 months or later
33. **Single or multi-component comparator**
    - Single
    - Multiple
34. **Outcomes assessed:**
    - Not reported
    - Mortality
    - Quality of life
    - Symptoms/signs
    - Diagnoses/syndromes
    - Biomarkers
    - Harms
    - Note: add details in the text boxes. Additional outcomes can be added when encountered
35. **Follow-up time (months)**
    - 0 - cross-sectional
    - 1 month
    - 2 months
    - 3 months
    - 4 months
    - 5 months
    - 6 months

- 7 to 12 months
- 13 months or longer
- Note: Check multiple options when patients were not followed up uniformly

36. **Are the timepoints clear?**
    - Yes, all timepoints are clear
    - No, something is unclear (add details: beginning of follow-up, intervention timing, when follow-up ends, etc.)

Category: Context

37. **Setting of the treatment/management**
    - Not reported
    - Virtual care
    - Acute care hospital
    - Intensive care unit
    - Community
    - Nursing home
38. **Trial registration**
    - Add any trial identifiers or trials names for the purpose of identifying duplicate publications. Separate them with; if multiple.
39. **Validated by**
    - Text box