



Canada's Drug and
Health Technology Agency

CADTH Health Technology Review

**Post-COVID-19
Condition Treatment
and Management
Rapid Scoping Review:
October 2023 Update**

Key Messages

- This report presents an overview of a scoping review that maps out the current evidence landscape on post-COVID-19 condition and identifies evidence gaps. This is the last update to a report published in December 2022.
- There are many studies on the management of post-COVID-19 condition. This review included 256 records evaluating pharmacological interventions, non-pharmacological interventions (excluding rehabilitation), and care models:
 - 5 Canadian guidelines, 6 international guidelines, 56 intervention studies, 153 observational studies, 3 qualitative studies, 8 rapid reviews, and 25 systematic reviews.
 - There are living guidelines and systematic reviews on the management of post-COVID-19 condition that may aid clinical decision-making in different settings.
- In this final update, since the December 2022 report, most of the research we found focused on pulmonary, otorhinolaryngological, and generalized post-COVID-19 condition using pharmacological or non-pharmacological interventions. There are fewer studies on care models or the management of renal conditions.
- We identified 1 more Canadian guideline and 3 more international guidelines. The Canadian guideline includes recommendations for COVID-19 and post-COVID-19 condition in primary care settings.
- The evidence gap is narrowing with 3 or more primary studies reporting pharmacological or non-pharmacological interventions for most indications (e.g., fatigue, olfactory dysfunction, tachycardia, cough, and cognitive dysfunction). However, we did not identify additional primary studies for care models since December 2022.

What Is the Issue?

- Post-COVID-19 (coronavirus disease 2019) condition includes symptoms or syndromes that patients have at least 3 months after the initial COVID-19 infection.²
- Statistics Canada estimated that 1.4 million people living in Canada who were 18 years and older experienced post-COVID-19 condition in October 2022.²
- The symptoms commonly reported include fatigue, cough, shortness of breath, and brain fog.²
- The rapidly changing evidence base warrants continuous efforts to characterize the literature and identify research gaps.

What Did CADTH Do?

- We conducted a scoping review, a type of evidence synthesis that helps us understand the body of evidence about a certain topic. It can be used to look at key concepts related to that topic and assess how much research there is for each concept.
- We adopted the WHO's definition of post-COVID-19 condition and specified the criteria for eligible publications in the baseline review³ and a previous update.¹ Any pharmacological or non-pharmacological interventions and care models in any contexts were eligible for this review.
- This report supplements other ongoing work that characterizes the literature, including living systematic reviews on the prevention and diagnosis of post-COVID-19 condition,^{4,5} and on COVID-19 rehabilitation.⁶ To avoid duplication of efforts, the scope of this review focused on the treatment and management of post-COVID-19 condition.
- We identified published literature, limited to English and French, from January 1, 2019 to July 17, 2023. Further details on the literature strategy can be found in the supplemental document.⁷
- CADTH staff read each study, and extracted data on:
 - study characteristics (e.g., country where the study was conducted, date of publication)
 - how the study was done (e.g., study design), information about the study patients (e.g., number of participants, age, sex, vaccination status), concept (i.e., type of treatment, classification of indication, and comparators), and context (e.g., rural, urban, site of treatment during post-COVID-19 condition).

Why Did We Do This?

A clear overview of the current evidence landscape is necessary to understand emerging issues that have not been well studied and the topics that may be neglected in recent studies.

Based on jurisdictional feedback received from CADTH customers in September of 2021, it was noted that there was a need for an evidence hub on the post-COVID-19 condition.

What Did We Find?

Study Characteristics

We found 256 publications.

- 5 Canadian guidelines (2%)
- 6 international guidelines (2%)
- 8 rapid reviews (3%)
- 25 systematic reviews (10%)
- 56 intervention studies (22%)
- 153 observational studies (60%)
- And 3 qualitative studies (1 %)

The majority of the identified primary studies were case reports or series (43.8%).



To accompany this review, CADTH has developed an [interactive dashboard](#) that summarizes key findings from the scoping review. The online map allows users to filter by category and directly access the included publications

Information About the Study Patients

Of the 13 reports (5%) included patients from Canada. Most studies came from the US (66 reports), followed by Italy (25), the UK (21), India (14), Germany (12), Spain (11), and Japan (10). Of the reports, 9 or fewer included patients from France, Australia, 12 other European countries, 7 African countries, 15 other Asian countries, and South America.

The number of people participating in each primary study varied widely. The median sample size was 10 people. Studies ranged from 1 patient to 945,676 patients. Of the included reports, 240 reported the age of patients or target populations. Most of these reports (213 or 83 %) were about adults 18 years to 64 years old.

Fewer reports looked at children or adolescents (28 or 11%), or adults aged 65 years and older (70 or 27%). Of the included 212 primary studies, 204 reported on the sex of the patients. While the proportion of female to male patients varied in each study, a median of 38.8% (interquartile range = 9.59% to 83.3%) of the population was male.

Appendix 1 shows the selection of included reports.

What Did We Find?

What Is the Current State of the Evidence at the Time of CADTH's Scoping Review?

Systematic evidence syntheses have been published for pharmacological and non-pharmacological interventions and care models.

Certain post-COVID-19 conditions were reviewed or reported more often than others, such as pulmonary and otorhinolaryngological conditions. A living systematic review by Cochrane Canada and others assessed and summarized the guidelines for COVID-19 care, including post-COVID-19 care.⁸

Table 1

Evidence by Treatment Type and Classification of Indication

Summary (amount of evidence)	Non-pharmacological interventions	Pharmacological interventions	Care models
—	There were more evidence syntheses for pulmonary, mental health, otorhinolaryngological, and generalized post-COVID-19 condition and few primary studies for hematological, dermatological, and renal post-COVID-19 condition.	There were more evidence syntheses for pulmonary, otorhinolaryngological, and generalized post-COVID-19 condition and few primary studies for renal post-COVID-19 condition.	There were more evidence syntheses for generalized post-COVID-19 condition and few primary studies for most types of post-COVID-19 condition, except for pulmonary post-COVID-19 condition.
At least 1 systematic or rapid review	Pulmonary; Mental health and behavioural; Post-COVID-19 condition (generalized); Otorhinolaryngological.	Pulmonary; Post-COVID-19 condition (generalized); otorhinolaryngological	Post-COVID-19 condition (generalized); others (including eye, dentistry)
More than 8 primary studies	Fatigue; neurological; pulmonary; mental health and behavioural; otorhinolaryngological; Post-COVID-19 condition (generalized); rheumatological.	Neurological; pulmonary; cardiovascular; Post-COVID-19 condition (generalized); fatigue; otorhinolaryngological; rheumatological; others (including autoimmune, oncology)	None identified
8 to 3 primary studies	Cardiovascular; gastrointestinal; others (including autoimmune, oncology).	Gastrointestinal; mental health and behavioural; dermatological; hematological	Pulmonary
Fewer than 3 primary studies	Hematological; dermatological; Renal	Renal	Cardiovascular; fatigue; Post-COVID-19 condition (generalized); mental health and behavioural; dermatological; gastrointestinal; hematological; neurological; otorhinolaryngological; rheumatological; renal; others (including autoimmune, oncology)

What Did We Find?

What Are the Current Evidence Gaps?

- Certain populations, including children, those being asymptomatic during initial infection, and those vaccinated against COVID-19 before infection were reported less often.
- Reports of all contexts were eligible. However, there were limited numbers of sources reporting on long-term (6 months or longer) follow-up (n = 10, 4.0%), community-based interventions (n = 16, 6.3%), interventions for nursing home residents (n = 0), and virtual care (n = 0).
- In terms of study design, we found only 3 qualitative studies and no economic evaluations.
- When compared to the symptoms that people with post-COVID-19 condition often reported,⁹ we noticed that the symptoms that were frequently reported are not the conditions that were commonly studied in the included studies.

Table 2

Summary of Evidence Gaps by Characteristics, Study Design, and Prevalent Symptoms

Population and study characteristics	Specific areas with notable gaps
Population characteristics	<ul style="list-style-type: none"> • People younger than 18 years of age • Those who were asymptomatic during initial infection
Study design	<ul style="list-style-type: none"> • Qualitative research • Economic evaluation
Contexts	<ul style="list-style-type: none"> • Long-term (6 months or longer) follow-up • Community-based interventions • Interventions for residents of nursing homes • Virtual care
Mismatch between prevalent symptoms and those often reported in primary studies	
<p>Symptoms most often reported by people with post-COVID-19 condition⁹ (prevalence in %):</p> <ul style="list-style-type: none"> • fatigue (> 30%) • sleep disorder, anxiety, depression, and shortness of breath (15% to 30%) • new hypertension, sweating, memory deficits, and others (5% to 15%). 	<p>Conditions among people with post-COVID-19 condition in 212 primary studies:</p> <ul style="list-style-type: none"> • pulmonary (n = 43, 20.3%) • fatigue (n = 40, 18.9%) • neurological (n = 39, 18.4%) • mental health and behavioural (n = 35, 16.5%) • cardiovascular (n = 35, 16.5%) • otorhinolaryngological (n = 35, 16.5%) • generalized post-COVID-19 condition (n = 35, 16.5%).

What Did We Learn?

- We found 256 eligible reports that met our inclusion criteria, 52 of which were available after the 2023 April search.
- We identified evidence gaps by summarizing the number of sources by classification of indication and type of treatment. With more evidence, we identified 23 rapid or systematic reviews and more than 8 primary studies reporting pharmacological or non-pharmacological interventions to manage pulmonary and otorhinolaryngological post-COVID-19 condition.
- The evidence gap is narrowing in terms of the numbers of primary studies. Compared to the 2022 December update,¹ there are more indications (e.g., fatigue, olfactory dysfunction, tachycardia, cough, and cognitive dysfunction) reported in 3 to 8 primary studies and fewer classifications reported in fewer than 3 primary studies using pharmacological or non-pharmacological interventions. However, we did not find additional primary studies evaluating care models since the update in December 2022.
- The number of evidence-based guidelines increased from 7 in the December 2022 update to 11 in this update.
- We included 5 Canadian guidelines and 6 international guidelines. The latest Canadian guideline authored by the Centre for Effective Practice (CEP) and others provides recommendations for the management of both COVID-19 infection and post-COVID-19 condition in primary care settings.¹⁰
- Among the 3 international guidelines identified in the latest literature search, a living guideline by the World Health Organization published in January 2023 focuses on rehabilitation for post-COVID-19 condition and has recommendations related to care referral, care coordination, and drug use.¹¹ We identified 2 Australian guidelines authored by the New South Wales Agency for Clinical Innovation in this update.^{12,13} One of the Australian guidelines provides recommendations for post-COVID-19 care models.¹³ The other recommends approaches to assess and manage various post-COVID-19 conditions.¹²
- There is an international collaboration project led by Cochrane Canada, “COVID19 Recommendations,” that facilitates decision-making in COVID-19 care through systematically reviewing and appraising recommendations in published guidelines.⁸ As part of this project, CADTH collaborated with Cochrane Canada to provide features for users to search for recommendations relevant to their contexts, including management for [post-COVID-19 condition](#).⁸ CADTH also features the guidelines and recommendations in its site.¹⁴
- There will be more evidence-based resources specifically for the management of post-COVID-19 condition. Cochrane Canada and the McMaster GRADE Centre are systematically reviewing the evidence to develop Canadian guidelines on post-COVID-19 condition.^{15,16}

What Else Do We Need to Consider?

- Scoping reviews are a strategy to identify evidence gaps. Unlike systematic reviews, this scoping review did not critically appraise the literature or summarize the study findings. The risk of bias in the included reports is unknown.
- The findings of the included sources may be applicable to certain patients in similar settings. For example, many of the included reports are case reports or case series, in which clinicians may report rare cases, for which the management strategy may not be applicable to other patients.
- As the evidence gaps are narrowing, the lack of primary studies for certain classifications of indication may be due to lower incidence of these conditions, rather than insufficient research on them. It is unclear whether the remaining evidence gaps require further research.
- We have identified living guidelines,^{11,17} living systematic reviews,¹⁸⁻²⁰ and living scoping activities²¹ that aim to provide up-to-date recommendations and summaries for clinical decision-making. Despite the evidence gaps, there are resources that provide up-to-date overviews of the management of post-COVID-19 condition in different settings.

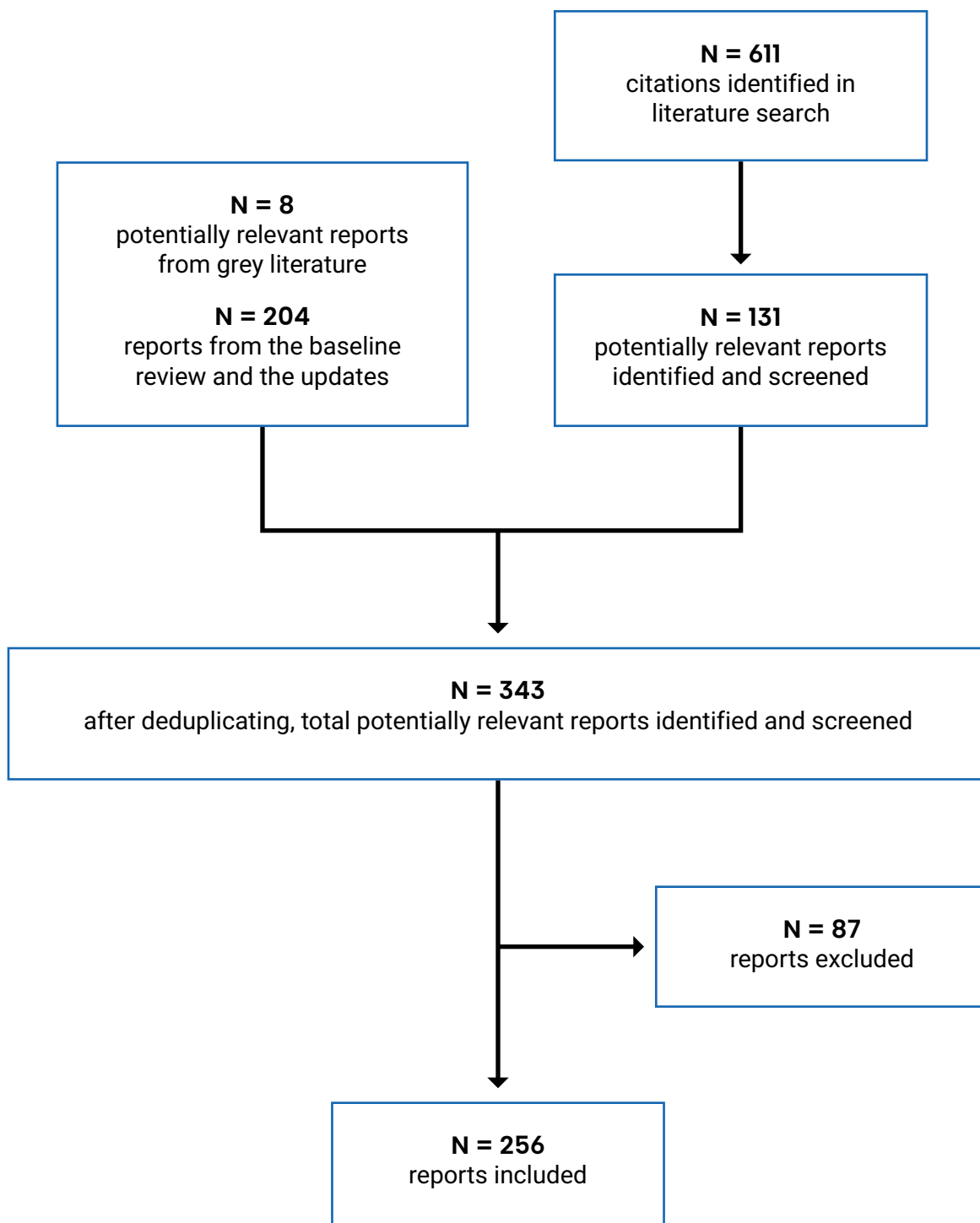
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Appendix 1: Data Tables

Figure 1
Flow Chart of Study Selection



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