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CADTH Scoping Summary

A Condition-Level Review on Post–COVID-19 Condition (Long COVID)

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CADTH

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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.

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Purpose of This Document

This document describes the preliminary scoping and rationale for a condition-level review on the topic of post–COVID-19 condition, also known as long COVID. A condition-level review is an assessment of the evidence on a range of health technologies and emerging issues on all aspects of a condition, including prevention, identification, treatment, and management. As part of the scoping process, CADTH is consulting with jurisdictions across Canada, together with experts and stakeholders who are leading different research initiatives, clinical programs, and health systems planning related to post–COVID-19.

This scoping summary is not based on the findings of a systematic search but rather provides an overview about the evidence and emerging research questions that can help frame the development of a condition-level review. It also outlines published or preprint evidence resources that provide additional context about the condition and a preliminary assessment about potential evidence gaps that could be relevant for health systems in Canada.

Background

What Is Post–COVID-19 or Long COVID?

As health authorities in Canada and across the world continue efforts to help control the spread of severe acute respiratory syndrome coronavirus 2 (SARS CoV-2), there is growing concern that a subset of people with COVID-19 may not adequately recover from initial phases of the infection and could experience long-term effects for weeks and months. Post–COVID-19 condition, commonly referred to as long COVID (among many other terms being used), is a new condition recognized by the Public Health Agency of Canada (PHAC) and the World Health Organization (WHO). The condition affects some people following the acute phase of COVID-19 and could potentially affect hundreds of thousands of people in Canada and millions of people worldwide.[1,2] A patient-led movement was launched in 2020 to raise awareness about post–COVID-19 condition and those affected with it continue to advocate for its recognition, as it is not given similar attention as acute COVID-19.[3]

The National Institute for Health and Care Excellence (NICE) and the Centers for Disease Control and Prevention (CDC) define post–COVID-19 condition as a diverse illness or possibly a set of multiple illnesses, whereby people experience new or persisting symptoms for several weeks or months after being initially infected with SARS CoV-2. The differentiation between acute phases of COVID-19 and post–COVID-19 condition varies with each organization and has been defined as occurring either 4 weeks[4] or 12 weeks[5] after the initial infection. However, a positive COVID-19 molecular test is not necessary for a potential diagnosis of post–COVID-19 condition, as testing may not be available to all people at the time of initial infection.[5] Post–COVID-19 condition may affect different organ systems including pulmonary, cardiovascular, neurological, and musculoskeletal systems, among others.[5,6] Symptoms also vary widely, but the most frequently reported symptoms are fatigue, body aches, respiratory difficulties such as shortness of breath, and cognitive and mental health challenges.[7,8] The condition may have severe effects on people's well-bring and quality of life, and the relatively high number of people who could be affected will have important implications for health systems.[3,6]

Prevalence

Owing to a lack of standardized diagnostic criteria, varied study designs, and inclusion criteria (e.g., some studies consider people hospitalized with COVID-19, whereas others include anyone suspected of having had COVID-19), there is substantial variability in prevalence estimates. Two systematic reviews report that between 63%[9] and 83%[7] of people with a confirmed diagnosis of COVID-19 may experience new or persisting symptoms after 4 weeks of their initial diagnosis. These systematic reviews also report that 56%[7] and 46%[9] of people continue to experience symptoms after 12 weeks and 90 days, respectively. One study reports that after 6 months, 26%[10] of people may continue to experience symptoms. A COVID-19 infection survey in the UK showed that 13.7% of people with a positive COVID-19 test self-reported experiencing symptoms for 12 weeks or longer.[11] Based on the lower prevalence estimates, with more than 1.4 million[12] people in Canada testing positive for the infection, potentially more than 140,000 to 190,000 people may have or develop post–COVID-19 condition in the future.

Risk Factors

People of all ages, from all demographic backgrounds, and with pre-existing health conditions can be affected by post–COVID-19.[3,6] However, evidence from cohort studies suggest that people who experience more symptoms during the acute phase of the infection and people with certain comorbidities (such as hypertension or obesity) may be more likely to develop the condition.[13,14] One systematic review has reported that age, sex, and hospitalization may be associated with a higher risk of developing persistent symptoms following the acute phase of COVID-19.[15] Although there is relatively less research examining the experiences of children, they can also develop post–COVID-19; some may even develop specific pediatric subtypes that may resemble other inflammatory diseases.[16,17] The long-term effects of COVID-19, whether the effect is a new condition or an exacerbation of existing health issues, may increase the risk of developing other health conditions. Emerging evidence from 1 cohort study reported that people who contracted the virus but were not hospitalized were more likely to develop pulmonary, neurological, metabolic, and cardiovascular conditions in the 6 months following the infection compared to similar people within the same health care database who did not get infected.[18] These emerging findings suggest that post–COVID-19 may affect a wide range of people and, given the diagnostic uncertainty and varied symptoms, this could increase the demand on many different health services. Further research is needed to analyze individual risk factors for developing post–COVID-19 condition and understand if and how the condition may be associated with other health concerns.

Published Evidence Reviews

Preliminary scoping of the published literature has identified a wide range of published studies, preprint papers, and grey literature reports about post–COVID-19. These reports help better understand various aspects of post–COVID-19 condition and to frame questions that could be included in the condition-level review. Following, we describe highlights (i.e., not a comprehensive list of literature identified to date) of some of the published evidence reviews that could be relevant for health care decision-makers in Canada to help frame the emerging evidence needs. Some questions that have emerged from these published reviews or have been developed based on our scoping work to date are shown in Table 1.

Disease Classification

Several systematic reviews describe the different types, length, and prevalence of symptoms associated with post–COVID-19.[7-9] However, these reviews have noted that, given that the condition is not well-classified, there is a need for higher-quality methodological studies that use standardized case definitions and more studies measuring long-term outcomes (beyond 12 weeks).[7,8] The CANCOV study ongoing across 4 provinces in Canada will add to the evidence base about long-term outcomes (1 year after initial hospitalization) of people with COVID-19 and the impact on their caregivers. WHO is convening a multidisciplinary panel to develop a clinical or case definition of post–COVID-19; however, at the time of this report, there is no consensus available on its clinical classification.[19]

A scoping review reported that 120 peer-reviewed studies on post–COVID-19 were published by January 2021. Of these, 49.1% of the studies were focused on the signs and symptoms of the condition and 10.8% of the studies were focused on understanding the pathophysiology — the bodily processes associated with a disease — of the condition.[20] Emerging research and systematic reviews are aiming to better understand the condition's pathophysiology, risk factors, varied presentation in different people (including children), and possible preventive interventions.[3,21]

Clinical Guidance

Jointly with UK-based clinical networks, NICE published rapid guidelines for identifying, assessing, and managing the long-terms effects of COVID-19, including identifying and treating people with post–COVID-19.[5] These guidelines were developed for front-line health care professionals working in primary and community-level care. CDC produced a similar interim guidance for health care providers to support people with post–COVID-19 condition (may include multiple conditions).[22]

Within Canada, Alberta Health Services produced a rapid evidence report detailing guidance for health care professionals about the treatment and management of post–COVID-19 and its associated symptoms.[23] An additional report describes a rehabilitation response framework for the condition.[24] Institut national d'excellence en santé et services sociaux (INESSS) produced a management support tool for front-line health care professionals.[25] Emerging research examining the effectiveness of different preventive, rehabilitation, and treatment interventions will help inform clinical guidance. CADTH is also collaborating with PHAC and the Alberta Research Centre for Health Evidence (ARCHE) on a systematic review assessing risk factors and preventive interventions for post–COVID-19 condition.[26]

Review of Care Models

Ontario's Evidence Synthesis Network produced a briefing note describing the various program features, development, and governance structures of emerging long COVID clinics or specialized recovery clinics for people with post–COVID-19.[27] The report identified clinics operating in Canada, the US, the UK, and Italy, with different inclusion criteria, services, and funding structures.

A rapid systematic review by COVID-END and the Strategy for Patient-Oriented Research (SPOR) Evidence Alliance identified 12 studies describing different care models for treating

post–COVID-19 condition or long COVID such as specialized recovery clinics and care delivered through primary care.[28] Limited information about the effectiveness of care models was identified in the review but will be important for emerging research to explore as interventions begin to collect and report outcomes. In particular, the effectiveness of different models of care and their impact on health systems will be important to examine, as the condition may put increased demands on primary care.[2,6]

Table 1: Potential Research Questions That Could Be Included in the Condition-Level Review

Condition-level review area	Questions
Scoping	What is the research landscape about post–COVID-19 condition in terms of evidence gaps, concepts, context, and volume of research literature? *A scoping review is being conducted by CADTH.*
Prevention	What are risk factors for developing post–COVID-19 condition after a SARS CoV-2 infection? What is the clinical effectiveness of different interventions to prevent post–COVID-19 condition? What is the cost-effectiveness of different interventions to prevent post–COVID-19 condition?
Classification and diagnosis	What are the policy and clinical practice implications of post–COVID-19 in children? What are the diagnostic criteria for post–COVID-19 condition and its subtypes? What tools and strategies are being used in Canada and other similar countries to identify people who may have developed post–COVID-19?
Treatment and/or management	What is the clinical effectiveness of different pharmaceutical and rehabilitation therapies for treating post–COVID-19? What is the clinical effectiveness of vaccines to treat post–COVID-19? What is the evidence on different models of care being implemented in Canada and across the world? What are the policy, practice, and budget impact implications on health systems due to post–COVID-19 condition?

SARS = severe acute respiratory syndrome coronavirus 2.

Rationale for Condition-Level Review

CADTH's Implementation Support and Knowledge Mobilization team received early indications from various jurisdictions that addressing the needs of people and health systems for post–COVID-19 condition is a growing concern. Because post–COVID-19 condition or long COVID is not very well-understood, there is little consensus about different aspects of the condition and evidence is rapidly evolving. There are uncertainties about the number of people who have or could develop the condition in Canada, the risk factors for developing the condition, the effectiveness of interventions and health technologies that can support people in their recoveries, and the impact the condition may have on people and health systems.

As research continues to evolve, CADTH's condition-level review aims to inform health care decision-makers in Canada about the appropriate use of health technologies and interventions to support the prevention, clinical classification, diagnosis, treatment, and management of post–COVID-19 condition. Through this comprehensive lens on all aspects

of the condition, the review aims to support health systems to use the latest research to guide their planning and delivery of services. CADTH's Implementation Support and Knowledge Mobilization team is currently assessing and engaging with health care decision-makers across Canada to understand specific evidence needs, which, together with input from CADTH's Devices Advisory Committee, will guide final decisions of which evidence will be reviewed as part of the condition-level review. A systematic scoping review is also ongoing by CADTH to better understand evidence gaps.

Equipping health systems to address the needs of people with post–COVID-19 condition will require using the best available evidence. Amid the complexity and rapidly changing evidence base, the condition-level review will provide an accessible platform for health technology reviews, rapid response reports, evidence reviews, and recommendations — including those produced by other health technology assessment and evidence synthesis organizations — to inform jurisdictions across Canada.

If you have questions about the scoping of the condition-level review on post–COVID-19 or would like to be involved in helping shape its development, please reach out to a CADTH Liaison Officer in your jurisdiction.

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