
■ Key Take-Away Messages for Decision-Makers

Subtypes of Post-COVID-19 Condition: A Summary of the Emerging Evidence

Post-COVID-19 condition, also known as long COVID, continues to be challenging to diagnose and treat due to its wide array of possible symptoms, symptom durations, and severities. As a result, **it may be helpful to further characterize post-COVID-19 condition into subtypes to better enable health care providers and health systems to tailor care for people living with long COVID.**

Emerging evidence indicates that there are different approaches being considered to identify possible subtypes. This report reveals that there may be subtypes based on the approach of grouping (or clustering) characteristics together, such as severity of symptoms, types and co-occurrence of symptoms, and symptoms affecting different organ systems. In this report, CADTH did not consider how factors like age, sex, and demographics could impact a person's manifestations and experiences of post-COVID-19 condition because of the complex and rapidly evolving research landscape in this area.

Presently, it is unclear whether there is an association between any of the proposed post-COVID-19 subtypes and different SARS-CoV-2 variants.

What Is Post-COVID-19 Condition?

CADTH has used WHO's definition of post-COVID-19, which is defined as persisting physical or psychological symptoms for more than 12 weeks or 3 months after the initial COVID-19 infection.

Why Did CADTH Look at the Evidence for Post-COVID-19 Condition Subtyping Methods?

Post-COVID-19 condition is a growing concern, estimated to have affected 14.8% of people after their initial infection or 1.4 million people in Canada as of October 2022; however, there is no standard way to identify or diagnose it. There are multiple reasons for this, including post-COVID-19 being a new health condition with varied clinical presentations, severities, and symptom durations. Collectively, this makes diagnosis complex and the resulting treatment and management uncertain. This has led to challenges for people living with long COVID, clinicians, and health care decision-makers.

By understanding the possible subtyping methods for post-COVID-19, Canada’s health systems may be better equipped to develop effective and tailored diagnostics and treatments to manage the diverse needs of people affected by this condition.

How Was the Literature Reviewed?

CADTH completed a narrative summary of the emerging literature on post-COVID-19 subtypes, focusing on classification methods based on symptoms and clinical presentation. An information specialist conducted a limited literature search from January 1, 2019, through April 20, 2022, with a supplementary search conducted up to September 16, 2022. CADTH did not quantify the strength of evidence of the literature found.

What Are the Possible Approaches to Subtyping Post-COVID-19 Condition?

CADTH found that symptom clustering was one approach to post-COVID-19 condition subtype classification. Reported clusters included symptom groupings based on severity, type and co-occurrence of symptoms, and organ system involvement.

Symptom clustering approach	Cluster examples
Severity	<ul style="list-style-type: none"> • Most severe functional activity impairment and highest number of symptoms • Moderate level of impairment on functional activities but with a high number of symptoms • Least functional impairment and number of symptoms
Type and co-occurrence	<ul style="list-style-type: none"> • Joint pain and muscle pain • Brain fog and poor memory • Fatigue and poor memory
Organ system involvement	<ul style="list-style-type: none"> • Neurological • Psychological/mental health • Respiratory • Musculoskeletal • Ear, nose, and throat • Dermatological • Gastrointestinal • Cardiovascular • Systemic • Non-specific

In addition, at least 5 studies examined possible neurological subtypes. For example, there may be 2 possible subtypes that primarily affect either the central nervous system or peripheral nervous system.

What Previously Established Conditions May Certain Subtypes of Post–COVID-19 Condition Present Similarly to?

In some cases, post–COVID-19 condition presents similarly to other previously established conditions, like pulmonary fibrosis, post–intensive care syndrome, and chronic fatigue syndrome. Some studies have proposed that the varied presentations of post–COVID-19 condition and its subtypes could be clinical manifestations of these other conditions. As a result, it may be possible that treatment and care approaches used for these previously established conditions may help inform effective treatment options and care for people with post–COVID-19 condition.

What Role Do the Different COVID-19 Variants Play in Post–COVID-19 Subtypes?

The evidence is rapidly evolving in this space. Some studies have reported differences in symptom presentation based on the variant of infection. However, other studies have not found similar associations. As such, the evidence remains uncertain.

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