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CADTH Horizon Scan

An Overview of Post–COVID-19 Condition (Long COVID)

CADTH

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Key Messages

- Long-term symptoms after developing COVID-19, known as post–COVID-19 condition or colloquially as long COVID, is a new condition estimated to affect millions of people worldwide. While standard diagnostic criteria have not yet been developed, current estimates suggest that 21% to 23% of people suspected of having had COVID-19 may have symptoms 4 weeks after their COVID-19 infections and 14% may have symptoms 12 weeks post-infection. Among people with self-reported post–COVID-19, an estimated 40% may continue to experience symptoms for at least a year.
- To provide health care providers and people with post–COVID-19 condition advice regarding diagnosis and treatment, guidelines have been published by the National Institute for Health and Care Excellence (NICE) and by the Centers for Disease Control and Prevention (CDC). The CDC guidelines were published more recently and refer to newer data on post–COVID-19 condition.
- Post-COVID symptoms can affect multiple organ systems and symptoms may vary by patient characteristics such as age and sex, as well as change over time. Some people may develop more severe symptoms or have increased risk of developing other illnesses. As there are currently no known unique symptoms and no tests available to diagnose post–COVID-19 syndrome, guidelines from NICE and the CDC recommend diagnosing based on symptoms, suspected previous COVID-19 infection, and ruling out other potential causes of symptoms.
- Current treatment recommendations focus on multidisciplinary care and personalized treatment to address the potential range of symptoms unique to each patient. Different methods of delivering treatment have been suggested and implemented around the world, including specialized post–COVID-19 clinics and integrating treatment into primary care.
- Post–COVID-19 condition can result in a reduced ability to work or attend school, and reduced independence, which can impact quality of life. These effects may have a disproportionate impact on disadvantaged groups, which will have important implications for health equity.
- Limited evidence on the clinical effectiveness and cost-effectiveness of therapies for post–COVID-19 condition was identified. However, many trials have been registered and are in progress to address this knowledge gap.

Purpose

The purpose of this Horizon Scan is to present health care stakeholders in Canada with an overview of information related to long-term symptoms after a COVID-19 infection — often referred to as long COVID or post–COVID-19 condition. The Horizon Scan also aims to include ongoing or emerging research regarding this topic and how to treat, manage, or rehabilitate the symptoms of post–COVID-19. This report is not a systematic review and does not involve a critical appraisal or include a detailed summary of study findings. It is not intended to provide recommendations.

The content of this report was considered up to date as of September 9, 2021 and only citations retrieved before September 8, 2021 were considered for inclusion. Care has been taken to ensure that the information is accurate, but it should be noted that international scientific evidence about COVID-19 is changing and growing rapidly.

Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE and Embase through Ovid, the Cochrane Database of Systematic Reviews, the international HTA database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concept was post-acute (sequelae of) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) — or long COVID — and synonyms. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English-language documents published between January 1, 2019 and June 4, 2021.

Regular alerts updated the database literature searches until the publication of the final report.

One author screened the literature search results and reviewed the full text of all potentially relevant studies. Studies were considered for inclusion if the population was people with long-term symptoms after a confirmed or suspected COVID-19 infection. Preprint publications, conference abstracts, and grey literature were included when they provided additional information to that available in the published studies.

Peer Review

A draft version of this bulletin was reviewed by 1 clinical expert.

Background

The coronavirus disease 2019 (COVID-19) has spread rapidly around the globe since it was first identified in late 2019.[1] Caused by the SARS-CoV-2 virus, it was initially characterized by WHO as a relatively short-term, acute disease. In March 2020, WHO stated that, on average, mild cases would recover 2 weeks after symptom onset, while severe cases would recover 3 to 6 weeks after symptom onset.[2] The focus was on severe cases, with mild cases expected to make a quick and full recovery.[3]

However, some people were not experiencing the expected full recovery within that time frame and began to share their experiences on social media as early as March of 2020.[3] Online support groups were established and editorials were published by people experiencing these long-term symptoms. Dubbing themselves "long-haulers" experiencing "long COVID," the term "long COVID" moved from social media to print media and was formally acknowledged in name as an issue by WHO during the summer of 2020.[3] Since then, research related to this new condition is aiming to understand the long-term effects of long COVID, its prevalence and risk factors, and to determine the most effective models of treatment.

The evidence base about post–COVID-19 condition, also known as long COVID, is emerging. Its long-term effects on people and health systems are uncertain, but based on the latest estimates, hundreds of thousands of people in Canada and millions of people around the world may be affected. As the evidence base continues to evolve, the purpose of this bulletin is to provide health care decision-makers in Canada an awareness about:

- what is known about post–COVID-19 condition
- what the major emerging research questions being explored are
- what the important implications could be for health systems to consider.

What is Post–COVID-19 Condition?

Research on classifying post–COVID-19 condition is developing and at the time of this report consensus on the terminology had yet to be reached. "Acute COVID-19" is typically used to refer to the acute infection phase, defined as the period up to 4 weeks after being infected.[4] After 4 weeks, new or ongoing symptoms were initially referred to on social media as "long COVID" by people with these long-term symptoms.[3] WHO uses the term "post COVID-19 condition" but notes that multiple names have been used, including long COVID, chronic COVID syndrome, late sequelae of COVID-19, post-acute sequelae SARS-CoV-2 infection (PASC), and long haul COVID, among others.[5] Different groups may use slightly different definitions for any of these terms.[4] WHO is convening a multidisciplinary panel consisting of patients and patient advocates, clinicians, researchers, and other stakeholders to develop a clinical case definition of post–COVID-19 condition.[5,6]

This report will also use "post–COVID-19 condition" to refer to symptoms beyond the acute infection phase (i.e., 4 weeks after being infected), while recognizing that some patient advocates may dislike the term post–COVID-19, as it may be interpreted as having no active disease process or suggest that they have recovered.[7] In this context, post–COVID-19 can be considered a short form of post-acute infection phase of COVID-19.

Classifying Post–COVID-19 Condition

By Time

A common method of describing the stages of post–COVID-19 condition has been by the amount of time a person has had symptoms or the time elapsed since contracting the SARS-CoV-2 infection. The National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network, and the Royal College of General Practitioners use the following terms to characterize different stages of post–COVID-19 condition:[4,8]

- ongoing symptomatic COVID-19: symptoms from 4 to 12 weeks after being infected
- post–COVID-19 syndrome: symptoms beyond 12 weeks, or continuing 3 months after infection.

However, these terms are not universally agreed upon; as previously mentioned, WHO uses "post COVID-19 condition" to refer to symptoms after 4 weeks. As another example, a research group from Spain proposed the following groupings:

- potentially infection-related symptoms (weeks 4 to 5)
- acute post–COVID-19 symptoms (weeks 5 to 12)
- long post–COVID-19 symptoms (weeks 12 to 24)
- persistent post–COVID-19 symptoms (beyond 24 weeks).[9]

Generally, clinical groups are proposing that post–COVID-19 refers to new or persisting symptoms occurring after 4 to 5 weeks of the infection and lasting up to 12 weeks or longer.

By Subtypes or Syndromes

Post–COVID-19 symptoms can vary widely across multiple organ systems, which may indicate that it consists of multiple subtypes or syndromes. It may include:[7,10]

- **Post-viral chronic fatigue syndrome** (or myalgic encephalomyelitis/chronic fatigue syndrome [ME/CFS]). ME/CFS can occur after a viral infection and features some symptoms similar to post–COVID-19 condition (e.g., fatigue).[11]
- **Post-intensive care syndrome (PICS)**, also sometimes referred to as post–critical-illness syndrome. PICS is caused by medical treatment in the intensive care unit (ICU).[12] Its symptoms may include chronically impaired pulmonary function, neuromuscular weakness, and long-term psychological impacts.[8]
- **Post-traumatic stress disorder (PTSD).** Acute illness and intense treatment can be deeply stressful experiences that may lead to increased risk of developing PTSD. Approximately 9% of people hospitalized for COVID-19, or 23% of those with post–COVID-19 condition, may develop PTSD symptoms.[13,14]
- **Exacerbation of a pre-existing health condition or disability**. For example, a case-controlled study reported that 7 months after hospital discharge for COVID-19, 53% of people who had pre-existing musculoskeletal pain reported that their pain had worsened.[15]
- **A unique post-acute COVID syndrome**.[7,10]

Other proposed methods of classifying people with post–COVID-19 condition are based on when the symptoms appear (i.e., persistent symptoms after acute infection or new symptoms that appear after the acute phase), by pathogenesis (e.g., residual damage from acute infection versus persistent immune activation), or by multiple factors.[16-19]

Distinguishing between subtypes may help to provide targeted treatment options. For example, people experiencing symptoms related to prolonged mechanical ventilation in the ICU will likely require different treatment courses from people who developed symptoms caused by organ damage. However, limited published research on characterizing the different subtypes or potential syndromes with specific diagnostic criteria was identified. The ongoing initiative of WHO to develop clinical case definitions based on international consensus will help to standardize the different characterizations and identify specific subtypes that would be important for making treatment decisions.[5]

Symptoms

Symptoms of post–COVID-19 condition can vary widely due to COVID-19's ability to impact multiple organs, with some studies assessing over 200 possible post–COVID-19 symptoms with a broad range of reported prevalence estimates.[4,20-22] People seeking care for post–COVID-19 condition may present with any combination of:

- generalized symptoms (e.g., fatigue, fever, pain)
- respiratory symptoms (e.g., breathlessness, cough)
- cardiovascular symptoms (e.g., chest tightness or pain, palpitations)
- neurologic symptoms (e.g., cognitive impairment [also sometimes referred to as "brain fog" or not being able to think clearly], headache, sleep disturbance, dizziness, delirium [in older patients])
- gastrointestinal symptoms (e.g., abdominal pain, nausea, diarrhea, anorexia, and reduced appetite [in older patients])

- musculoskeletal symptoms (e.g., joint and muscle pain)
- psychological or psychiatric symptoms (e.g., depression, anxiety)
- ear, nose, and throat symptoms (e.g., tinnitus, earache, sore throat, dizziness, loss of taste and/or smell)
- dermatological symptoms (e.g., skin rashes, hair loss).

Evidence from a preprint systematic review[23] suggests that 83% of people with confirmed COVID-19 may experience 1 or more symptoms after 4 to 12 weeks of their infections. These symptoms may include body and muscle aches, dyspnea (i.e., shortness of breath) or breathing difficulties, and weakness or fatigue, which have been reported by multiple studies.[21,23-29] After 12 weeks, the systematic review reported that 56% of people may experience 1 or more symptoms, with fatigue being 1 of the most common symptoms and experienced by nearly half of people (47%).[23] Other new or persisting symptoms after 12 weeks include breathing difficulties or shortness of breath, post-exertional malaise (worsening of symptoms after physical or mental activity), cognitive dysfunction, reduced exercise capacity, and loss of taste and/or smell.[22,30-34] The preprint systematic review noted that there is relatively little research examining the prevalence of symptoms after 12 weeks and that many studies have limited sample sizes (fewer than 200 people) and are often without comparison groups, increasing the risk of bias.[23] Without comparatives, studies are limited in attributing the reported symptoms specifically to post–COVID-19, as other pre-existing health conditions and factors may also be contributing to symptom occurrence. There may be differences by age, sex, and other factors, and symptoms may change over time, all of which warrants more in-depth and longer-term research.[21,22,30,32,35]

While comparative studies are emerging, a large cohort study of adults (more than 73,000 with confirmed COVID-19) from the US found that people who had confirmed COVID-19 but were not hospitalized were more likely to develop a variety of other health conditions in the 6 months after their initial diagnosis compared to adults (matched based on age, sex, ethnicity, and other factors) who did not have a COVID-19 diagnosis and were also not hospitalized.[20] The study also found that people who had acquired COVID-19 were significantly more likely to be diagnosed with neurologic, respiratory, mental health, cardiovascular, and other health conditions over the follow-up period.[20] Evidence from 3 additional non-randomized studies comparing people who were hospitalized with COVID-19 to matched control (people who were hospitalized without COVID-19) also suggest that people who acquire COVID-19 may be more likely to develop other diseases in the long-term (defined variably), including respiratory, cardiovascular, and neurologic diseases, among other conditions and disorders.[36-38]

Researchers are also investigating the similarities between post–COVID-19 condition and the long-term health consequences of previous coronaviruses, particularly the SARS outbreak in 2003 and Middle East respiratory syndrome.[39] One systematic review found that 6 months after hospital discharge, people who had SARS or Middle East respiratory syndrome had similar symptoms as post–COVID-19 condition including lung abnormalities, reduced exercise capacity, and psychological impairment.[40] An estimated 40% of people who had SARS had chronic fatigue 3.5 years after being diagnosed.[40] It is possible that a similar trend could be found for post–COVID-19 condition.

Overall, the emerging evidence about the type of symptoms and long-term health effects of post–COVID-19 condition suggests that many people can experience a heterogenous range of symptoms after their initial COVID-19 infection. The diversity, length, and severity of symptoms reported vary considerably in different studies and more research is needed to

characterize the factors that may be associated with symptoms.[23] The emerging comparative studies examining the health effects of people who acquire COVID-19 to those who do not suggest that there could be a rise in other health conditions. However, longer-term research understanding the mechanisms of how COVID-19 may exacerbate or contribute to other conditions is needed.

Pediatric Population

The effects of post–COVID-19 condition on children are more uncertain, with fewer studies compared to adults. Many studies of post–COVID-19 condition follow up with people who were hospitalized, but, as children are more likely to have mild symptoms or be asymptomatic, they are less likely to be hospitalized.[41] Children may also have been less likely to be tested for COVID-19 when testing recommendations were focused on symptomatic acute illness. Detecting post–COVID-19 in children can be complicated by differences in common post–COVID-19 symptoms between children and adults, by the fact that children may have more difficulty explaining specific symptoms (e.g., brain fog), by a lack of diagnostic criteria, and because of the variations of post–COVID-19 symptoms in children.[42]

Like adults, post–COVID-19 symptoms in children can range widely: the most frequently reported symptoms include pain, breathing difficulties, fatigue, cough, and headache.[43-45] Other symptoms include insomnia, rash, and neuropsychiatric symptoms such as concentration difficulties.[43-46] A preprint survey study of children with symptoms lasting for more than 4 weeks reported that symptoms lasted, on average, for months and that 94% of study participants reported experiencing at least 4 symptoms.[46]

Post–COVID-19 condition in children may include multiple subtypes or syndromes. Based on an analysis of 570 pediatric patients, the CDC suggested that there may be 3 subtypes: multisystem inflammatory syndrome in children (MIS-C), atypical Kawasaki disease, and pediatric post–COVID-19 condition.[47] MIS-C is a post-viral hyperinflammatory condition that affects multiple organ systems. Its symptoms typically occur 2 to 6 weeks after exposure to COVID-19 and can include persistent fever, gastrointestinal symptoms, cardiovascular symptoms, abdominal pain, and rash.[47,48] It has been compared to Kawasaki disease because of similarities in clinical presentation but differs on the average age and biomarker test results (e.g., neutrophil counts), which suggests that it could be a different disease.[47]

Diagnosis

Currently, post–COVID-19 condition is primarily diagnosed based on 2 factors: having been infected with COVID-19 in the past and presenting with post–COVID-19 symptoms. The Mayo Clinic released its definition and diagnostic criteria for post–COVID-19 condition, which includes several criteria to help health care providers determine probable or possible cases.[49]

Guidelines from NICE and the Mayo Clinic, as well as a UK-based clinical practice guideline, state that a positive COVID-19 test (polymerase chain reaction, antibody, or antigen) or hospitalization due to COVID-19 should not be necessary to diagnose post–COVID-19 condition. Suspected previous COVID-19 illness (e.g., having symptoms closely linked to a COVID-19 infection) is an adequate reason to suspect post–COVID-19 condition as a cause for any new or ongoing symptoms beyond 4 weeks.[4,49,50] This flexibility is important because some people may have contracted COVID-19 but did not need to be hospitalized, did not get tested (e.g., certain areas had recommended people only get tested if they were symptomatic, or community testing may not have been available or accessible), or may have received a false-negative test result. People in Canada with post–COVID-19 condition have reported

frustrations over not being able to access post–COVID-19 clinics because they did not have a positive test result despite their health care provider diagnosing them with post–COVID-19 condition after ruling out other likely causes.[51]

The Mayo Clinic's criteria recommends looking for symptoms affecting at least 2 of 6 major organ symptoms (general, cardiac, respiratory, gastrointestinal, musculoskeletal, and neurologic), as well as for a decrease in functional status.[49] NICE recommends that health care providers consider any ongoing or new symptoms after acute COVID-19 as potentially being caused by post–COVID-19 condition, but also that people with suspected post–COVID-19 condition undergo tests to determine if their symptoms are being caused by another condition.[4] This will help prevent misdiagnosis by attributing symptoms to post–COVID-19 condition when these same symptoms may have another cause, and allow for targeted treatment where possible.

NICE also recommends that health care providers use a screening questionnaire during the consultation to develop a clearer understanding of each person's symptoms.[4] Specific populations (e.g., children and older adults) may not show the most common symptoms of post–COVID-19 condition, which should be taken into account during diagnosis.[4] WHO have also developed a post–COVID-19 case report form to help collect standardized clinical data from people suspected of having post–COVID-19 condition.[52]

In the absence of diagnostic tests, providing health care professionals with training and education about recognizing post–COVID-19 condition will be important. In surveys, people have reported being misdiagnosed by having their symptoms attributed to anxiety or being dismissed by health care professionals.[53,54] This may be because of a lack of awareness of how to diagnose post–COVID-19 condition. Developing clear diagnosis criteria may help reduce misdiagnosis and improve access to care.

Prevalence

Estimates of the prevalence of post–COVID-19 condition vary widely across studies. One systematic review noted that estimates ranged from 5% to 80%,[55] which may be due to various factors:

- study methodology (e.g., choosing to limit to people who had a positive COVID-19 test or were hospitalized for COVID-19, health administrative data versus survey data)
- a lack of a consistent definition for post–COVID-19 condition (e.g., timing [e.g., 4 weeks or 3 months; timing after infection versus after hospital discharge], what conditions and symptoms are considered to be caused by post–COVID-19 condition)
- local factors (e.g., COVID testing availability for different areas at different times).

Prevalence in People With Positive COVID-19 Tests and/or People Hospitalized for COVID-19

Many studies focus on people with laboratory-confirmed COVID-19 and/or people who had been hospitalized for COVID-19. Two systematic reviews[23,29] (including 1 that has not yet been peer-reviewed[23]) estimated that 63% to 84% of people with confirmed COVID-19 had symptoms 4 weeks after either diagnosis or hospitalization and 46% to 56% experienced symptoms after 12 weeks. Three cohort studies[32,34,56] reported that 33% to 39% of people may experience symptoms after 6 to 9 months. Two cohort studies[57,58] reported that 28% to 49% of people who had been hospitalized for COVID-19 experienced symptoms after 12 months.

Although estimates range widely, it appears that the prevalence decreases with time (i.e., fewer people report symptoms at 6 to 9 months compared to at 3 months), which may indicate that some people with post–COVID-19 condition will recover gradually over time. Studies of people who had been hospitalized during the acute phase tend to show a higher prevalence of post–COVID-19 condition compared to people who had milder acute illness and who did not require hospitalization.[7,21]

Prevalence When Including Suspected COVID-19

A major limitation recognized by researchers and health care stakeholders is that there are people who may not have had access to COVID-19 testing. As emerging evidence indicates that people who were initially asymptomatic or had mild acute illness can develop post–COVID-19 condition,[21] understanding the prevalence among this subset of people is needed to better characterize the prevalence of people who have or could develop post–COVID-19 condition. Studies that include suspected cases, together with confirmed COVID-19 cases, estimate that 21% to 23% of people who had COVID-19 develop ongoing or new symptoms after 4 weeks or 30 days[21,59] and approximately 14% experience symptoms after 12 weeks.[59] Limited studies about longer-term (beyond 12 weeks) prevalence rates among this subset of people was identified. However, based on household surveys, the Office for National Statistics from the UK has estimated that among people who experience self-reported post–COVID-19 symptoms, 40% may continue to experience symptoms for at least 1 year.[60]

Prevalence in Canada

A rapid systematic review published in June 2021 estimated that 150,000 Canadians have post–COVID-19 condition, although it is unclear if this is limited to confirmed COVID-19.[61] A survey of 1,048 people in Canada with suspected or confirmed post–COVID-19 condition conducted by the COVID Long-Haulers Support Group Canada found that 80% of respondents had symptoms for more than 3 months and almost 50% had symptoms had symptoms for more than 11 months.[51]

Prevalence in Children

In cohort studies limited to children with a positive COVID-19 test, a survey study found that 4% of children aged 5 to 17 had symptoms beyond 4 weeks and 2% had symptoms beyond 8 weeks,[45] while another cohort study found that 13% of participants aged 15 or younger had symptoms after 6 months.[30] An Italian survey that included children without a confirmed COVID-19 test reported that 43% of children had symptoms for more than 60 days after infection.[43]

The prevalence of MIS-C, a subtype of post–COVID-19 condition that may occur in some children, appears to be relatively low. One cohort study assessed 99 children (95 with a positive COVID-19 test) and estimated prevalence at around 2 cases per 100,000 children,[62] but the prevalence may be higher among children who had been hospitalized.[48] A survey study from Italy reported that about 2% of children who had COVID-19 developed MIS-C.[43] The variability in prevalence estimates between different studies may be due to low testing rates among children.

Risk Factors

Understanding potential risk factors that may be associated with developing post–COVID-19 condition may help characterize the cause or causes of the condition, support the development and implementation of preventive interventions, and tailor treatment and

management plans. However, a variation in how studies are defining the condition, a heterogenous and complex range of symptoms, and other factors have made it challenging to clearly determine specific risk factors. Retrospective and cross-sectional studies suggest that some potential risk factors for developing post–COVID-19 condition may include:

- **severity of acute illness.** People who were hospitalized may have a higher risk of developing or having a more severe post–COVID-19 condition compared to people who had milder symptoms.[7,20,21,23,55,63] Other studies have found no association.[64-67] Acute illness severity may be associated with specific post–COVID-19 symptoms or with PICS.[68]
- **female sex and older age.** Females[26,39,55,69] and older people (defined variably)[26,55,67] may be associated with higher risk of developing post–COVID-19 condition, although others have also found no correlation.[31,67,70,71] Specific symptoms may vary by age and sex, and may change over time.[21,22,30,32,33,35,72] Symptoms may peak for people between ages 40 and 60.[18,37]
- **comorbidities.** Asthma, autoimmune disease, and obesity have been associated with greater risk.[26,73,74] A survey cohort study[75] and a preprint cohort study[76] reported that anxiety, depression, and neurologic disabilities may also be risk factors. However, another cohort study reported no association between comorbidities and the presence of post–COVID-19 condition.[31]
- **specific symptoms during the acute phase.** People who experience certain symptoms during the acute phase such as fatigue, shortness of breath, headache, voice hoarseness, and muscle aches and pains may be more likely to develop post–COVID-19.[18,26,65,77]
- **number of symptoms during the acute phase.** Experiencing a higher number of different symptoms during the acute phase may be associated with developing post–COVID-19.[26,78,79]

Other factors that have been investigated but show mixed findings include:

- **ethnicity.** Evidence on the association between ethnicity and the risk of developing post–COVID-19 condition has been mixed,[25,37,80-82] potentially due to high heterogeneity across studies.[83] This could be because of people from ethnic minority groups having less access to testing[84] or being underrepresented in survey studies.[51]
- **socioeconomic factors.** Some studies indicate an association between socioeconomic factors (e.g., low income) and post–COVID-19 symptoms after 1 month but not beyond 2 months.[63,82] Data from the UK indicate that self-reported post–COVID-19 condition is highest among people from areas with higher deprivation (deprivation calculated by a composite score of neighbourhood level income, education, and health deprivation and disability).[60] These mixed findings may also be because of differences in access to testing or underrepresentation in surveys or the heterogeneity of post–COVID-19 symptoms.[63,82]

Among children, a case series has reported that siblings and parents of children with post–COVID-19 condition may also report long-term symptoms, which could suggest genetic and/or environmental factors impacting the likelihood of developing post–COVID-19 condition.[85] One study using health administrative data reported that children who were symptomatic during the acute phase were more likely to develop post–COVID-19 symptoms compared to children who were asymptomatic.[86] The risk of developing MIS-C may be higher in children who are Black or Latino, male, and aged 6 to12 years, as well as children who had been hospitalized.[48,87] Overall, research assessing risk factors associated with developing post–COVID-19 condition in adults and children is developing and emerging findings should be interpreted with caution until rigorous studies have been completed.

Prevention

Cochrane Rehabilitation has published a living systematic review, REH-COVER or Rehabilitation – COVID-19 Evidence-based Response, assessing rehabilitation for people with COVID-19.[88] Two cohort studies of early rehabilitation clinics treating people after the acute COVID-19 phase reported improvements in pulmonary symptoms and physical performance (e.g., 6-minute walking distance) when comparing participants before and after completing rehabilitation.[89,90] These studies were short-term interventions (8 weeks) for people who had been hospitalized. It is unclear how rehabilitation may affect people who had not been hospitalized, particularly people who present with ME/CFS-like symptoms such as post-exertional malaise (i.e., the worsening of symptoms after even minor physical, mental, or emotional exertion, also known as post-exertional symptom exacerbation) or exercise intolerance (i.e., reduced ability to exercise).

Pilot studies have assessed the efficacy of certain supplements;[91,92] however, due to limited evidence from larger studies, NICE currently does not recommend the use of over-the-counter supplements and vitamins for treating new or ongoing COVID-19 symptoms.[4]

Treatment and Management

Published guidelines from NICE, the CDC, and other research groups provide several options for treatment courses based on existing evidence that are primarily focused on symptoms management.[4,87,93-97] The CDC guidelines were published more recently than the NICE guidelines (June 2021 compared to December 2020) and draw on more recent data. The CDC guidelines also acknowledge that post–COVID-19 syndrome likely includes multiple syndromes and provides guidance based on research from other post-viral illnesses.[97] A rapid systematic review focused on care models for post–COVID-19 condition identified several studies from the US, UK, Spain, and Italy, with multiple common focuses across different models including:[61]

- **principles:** multidisciplinary teams, integrated care, self-management, coordination of care, and evidence-based care
- **medical specialists:** pulmonary, cardiovascular, psychiatry and psychology, physiotherapy, occupational therapy, social work, neurology, primary care, nutrition, speech and language therapy
- **components:** standardized symptom assessment, referral system, follow-up system, virtual care, home-based care.

Self-Management

NICE and a multidisciplinary clinical panel from the UK recommend that people suspected of having post–COVID-19 condition be provided with education and support for self-management strategies.[4,98] Self-management strategies may include providing up-to-date information about the condition, helping to set realistic goals, and providing information on available supports like online support networks.[4] Certain symptoms may be self-managed, such as breathing exercises for shortness of breath.[97] Online resources providing self-management advice, including the NHS's Your Covid Recovery, Post COVID-19 HUB by the Asthma UK and British Lung Foundation, and Long COVID Support created by a patient

advocacy group have also been established.[99-101] A program in Leeds, England introduced a fatigue management course delivered online that supports people with post–COVID-19 symptoms on how to manage their fatigue.[94]

Exercise

Evidence about exercise rehabilitation for people with post–COVID-19 is mixed and requires further assessment. Exercise may help reduce fatigue, a common post–COVID-19 symptom,[35] and may be helpful for people who had been bedridden (e.g., people who had been treated in the hospital or ICU) or people who had been hospitalized.[88]

However, there is limited research on the impact of exercise for people who had not been hospitalized and there are also concerns that exercise may be harmful to some people with post–COVID-19 condition who may present with post-exertional malaise or exercise intolerance.[102,103] Because of concerns surrounding post-exertional malaise, as well as cardiac or pulmonary symptoms that may be exacerbated from vigorous exercise, post–COVID-19 condition guidelines from World Physiotherapy and the CDC recommend a cautious and conservative approach to exercise based on existing recommendations for ME/CFS.[97,102]

World Physiotherapy's guidelines for post–COVID-19 condition and the CDC's guidelines for ME/CFS recommend pacing, also known as activity management, which is an intervention that focuses on balancing rest with activity, and staying within personal limits to avoid overexertion and worsening symptoms.[102,103] World Physiotherapy's report suggests that before recommending exercise, people with post–COVID-19 condition should be screened for post-exertional symptom exacerbation.[102] It also recommends against exercise rehabilitation for those with cardiac impairments, exertional oxygen desaturation (i.e., low oxygen levels during exertion), or autonomic nervous system dysfunction.[102] As post–COVID-19 condition may include multiple syndromes, exercise may be useful for treating certain syndromes but not others. Further research will be needed to determine who is most likely to benefit.

Vaccination

For people who have not been vaccinated and develop post–COVID-19 condition, receiving a COVID-19 vaccine after the acute infection phase may help to reduce their post–COVID-19 symptoms. In a survey study by the LongCOVIDSOS group, of the respondents who received at least their first dose, 57% reported an overall improvement in symptoms, 25% saw no change, and 19% saw their symptoms worsen.[104] The study reported variation in which symptoms and how many symptoms improved. A preprint survey study reported that in a group of people with post–COVID-19 condition who had received at least 1 dose, 23% saw an increase in symptom resolution compared to 15% in matched unvaccinated individuals.[105]

As some post–COVID-19 symptoms resolve with time, more studies are needed to determine if vaccinations, including receiving both doses, reduce post–COVID-19 symptoms and, if so, how this effect occurs. This topic is an active area of research. A non-randomized preprint study assessed the immune response of people who previously had COVID-19 (although it did not specifically include people who had post–COVID-19 symptoms) before and after vaccination and found immune system changes that could explain post-vaccination symptom improvement.[106] At least 1 study is in progress that is conducting immunological follow-up and surveys of people previously infected with COVID-19 to better understand the impact of vaccination on post–COVID-19 symptoms.[107]

Research is also ongoing to determine if vaccines affect the risk of developing post–COVID-19 condition for people who have breakthrough infections (i.e., developed COVID-19 after being vaccinated). One survey study has found that people who are fully vaccinated have lower odds of having symptoms 28 days after a breakthrough infection compared to people who are not vaccinated.[108] Preliminary work suggests some people with breakthrough infections could have post–COVID-19 symptoms for at least 6 weeks.[109-111]

Models of Care

Research to understand features of different models of care associated with supporting people with post–COVID-19 is ongoing. Key features that have been recommended — based on evidence from 2 systematic reviews and published position statements of different health care providers — are multidisciplinary care and personalized care.[4,20,61,112,113] The range of symptoms and potential impact on multiple organ systems for post–COVID-19 condition means that people will likely benefit from receiving a range of services from various specialists coordinating and selecting appropriate care based on each person's unique set of symptoms. Researchers and guidelines suggest that diagnostic tests, rehabilitation, and management plans should be personalized.[4,50,98,112,114] Selected tests can be used to rule out other conditions and assess potential causes (e.g., chest X-ray for respiratory symptoms) to provide targeted treatment or referrals, where possible.[50,71,115] The use of technologies such as virtual visits may also help to easily access multiple specialists, especially for people experiencing fatigue who may find it difficult to make multiple clinic visits.

As research on post–COVID-19 condition continues to develop, comprehensive and standardized symptom assessment (such as using WHO's case report form[52]) will help health care providers and researchers develop a clearer understanding of the effects of post–COVID-19 condition. Careful monitoring, follow-up, and open communication between health care providers, people with post–COVID-19 condition, and researchers has also been recommended to help determine what treatments work and for whom, to identify any adverse events so the treatment can be adjusted or withdrawn as needed, and to ensure cohesive and continuous care.[47,50,51,112,116]

Some models of care that have been suggested or implemented, and their characteristics, are summarized in Table 1. Emerging research questions are investigating what models are most clinically effective, most cost-effective (particularly in the Canadian context), and what the role of virtual care could be in support of people with post–COVID-19.

Ongoing Research

Research about post–COVID-19 condition is evolving at a rapid pace and different studies are ongoing in Canada and across the world to better understand the condition, its pathophysiology, effective treatments, and its impact on people's well-being. What follows is a description of some of the high-level research initiatives under way and the research questions being explored.

Cause(s) and Diagnosis of Post–COVID-19 Condition

It is possible that there are multiple mechanisms of post–COVID-19 condition based on the range of symptoms, including damage from intensive treatment (i.e., PICS), lingering viral antigens, inflammatory damage, alterations to the immune system or autonomic nervous system, or COVID-19–specific pathophysiological changes.[87,93] Researchers are assessing damage to organ systems and abnormal biomarker levels to better understand the biologic mechanisms underlying post–COVID-19 symptoms.[115,121-124] The pathophysiology in children with post–COVID-19 condition is also unknown and further studies on post–COVID-19

Table 1: Potential Models of Care for Post–COVID-19 Condition

Model	Description	Strengths	Limitations
Post–COVID-19 clinics	Specialized clinics featuring dedicated groups of health care providers, often multidisciplinary groups, to treat post–COVID-19 condition. These have been set up in multiple countries including Canada.[8,61,113,117,118] A pre-post study reported improved outcomes of people receiving rehabilitation at a post–COVID-19 clinic in Italy.[119]	• May be an efficient way to develop expertise on treating post–COVID-19, as providers see a higher number of people affected by the condition and can learn the effectiveness of different treatment strategies.[120] • Coordination and continuity of care between multiple care providers may be smoother in dedicated teams.	• Potential for long waiting lists.[61] • Difficulties training providers.[61] • Accessibility for those who live far from clinics. • Uncertainty about cost-effectiveness.[61]
Primary care–based model	PCPs carry out standardized assessments of symptoms, refer to and coordinate with specialists based on symptoms and needs, manage medications and comorbidities, and provide self-management support.[61]	• PCPs are already familiar with their rostered patients' health and preferences. • People affected by post–COVID-19 may feel more comfortable with their regular PCPs than going to a new clinic with unfamiliar care providers.	• PCPs may feel uncomfortable treating post–COVID-19 condition due to a lack of training or resources, especially for complex cases. • Coordination and continuity of care across multiple specialists may be complex, which could lead to fragmented care (e.g., contradictory advice).[53]
Hybrid model	A system that incorporates specialized clinics and primary care based on each person's needs. For example, in the tiered model used in Leeds, England[94]: • People with mild and typical symptoms are treated in primary care. • People who had been hospitalized and/or have moderately complex needs are treated by community therapy teams. • People with symptoms at 3+ months and/or have complex needs are treated by a specialized clinic.	• Could be more feasible and accessible than treating all cases of post–COVID-19 condition in specialized clinics. • Allows for people with complex needs to receive the intensive care that would be more difficult to receive in a primary care–based model.	• People with complex needs living far from specialized clinics may not be able to access needed care. • Model requires effective coordination of care across multiple providers.

PCP = primary care provider.

condition in children has been identified as a research priority by the international research community.[125]

A small pilot study from the UK has identified the presence of specific autoantibodies in people with post–COVID-19 condition that were not found in people who had not tested positive for COVID-19 or had recovered quickly and did not develop post–COVID-19 symptoms.[126] A blood test to diagnose post–COVID-19 condition may be developed based on these findings, allowing for a quicker diagnosis and therefore earlier access to appropriate treatment.

Suggested Treatments

As research is under way to understand the physiologic mechanisms that may be causing post–COVID-19 symptoms (e.g., organ damage), targeted treatments may follow. Several potential treatments for post–COVID-19 condition have been suggested by emerging clinical guidelines and/or are being explored in research trials. Treatments that are used for other illnesses or conditions with similar symptoms are being considered. These treatments may be more likely to be investigated and could be included as part of clinical guidelines should they demonstrate efficacy in research trials.[127] For example:

- treatments for ME/CFS or mast cell activation syndrome[79,128,129] (e.g., extracorporeal apheresis, which has been tested by 1 clinic on 3 people with post–COVID-19 condition with CFS-like symptoms and appeared to improve symptoms)[130]
- neuromuscular electrical stimulation for treating PICS[131]
- photobiomodulation therapy, which has been used to treat various neurologic and psychological disorders, and could be used to treat similar symptoms in people with post–COVID-19 condition[132]
- drugs that have been in development for other illnesses that have similar symptoms with post–COVID-19 condition; some are already under investigation as potential treatments for post–COVID-19 condition.[133,134]

Other potential treatments are more exploratory and have been suggested by different research groups. These include polypharmacy (to treat post–COVID-19 condition's wide range of symptoms),[135] antibiotics,[136] corticosteroids (prednisolone),[137] personalized medicine by genetic testing,[136] and supplements (e.g., luteolin, vitamin C).[138,139]

Some suggested treatments specific for pediatric post–COVID-19 condition have included those:

- for brain fog symptoms, providing the same treatment a child with a concussion would receive[140]
- for MIS-C; currently, it is treated the same way as Kawasaki disease, although — as they may be separate conditions — it is unclear how effective that treatment is; anti-inflammatory agents may be a useful option.[47]

Ongoing Systematic Reviews and Trials

Several systematic reviews on post–COVID-19 condition have been registered or are being updated regularly as living reviews. The Cochrane group has a rapid living systematic review on COVID-19 rehabilitation that is updated monthly and includes an interactive living evidence page that maps the included extracted studies.[88] The PROSPERO international prospective

register of systematic reviews website also has a section dedicated to COVID-19 and, at the time of writing this report (September 9, 2021), has registered more than 100 systematic reviews related to post–COVID-19 condition.[141]

Multiple trials are also under way around the world regarding developing a clearer understanding of the symptoms and best management of post–COVID-19 condition. In the UK, the National Institute for Health Research approved £19.6 million in July of 2021 for studies assessing post–COVID-19 condition's causes, symptoms, diagnosis, treatment, and rehabilitation.[142] A few examples include:

- the EU-COGER study, which will assess the recovery from COVID-19 in a geriatric population[143]
- the longitudinal survey study from ISARIC — the International Severe Acute Respiratory and emerging Infection Consortium — to assess long-term outcomes[144]
- the national UK HEAL-COVID trial, which is under way to identify treatments that can lead to better long-term outcomes for people who had been hospitalized for acute COVID-19.[145]

The U.S. National Library of Medicine's clinical trials registry has a dedicated section for COVID-19–related studies.[146] Developing a national surveillance system has also been recommended by WHO and international classifications of diseases (or ICD) codes have been developed to track post–COVID-19 condition.[8] More research using health administrative data with these codes may emerge with time.

In Canada, several cohort studies have been registered that aim to better understand the recovery trajectories of adults with COVID-19 using imaging, blood tests, functional tests, and/or questionnaires to understand symptoms, as well as quality of life (e.g., daily activity limitations).[147-150] Two studies have also planned to establish a biobank to store biologic samples (e.g., DNA, saliva) for research.[147,150] Two studies plan to follow up after 1 year[149,150] and 1 study plans to follow up for 4 years.[148] A planned cohort study aims to assess the impact of lung ventilation and lung perfusion in adults who had COVID-19, which may help to better understand the specific injuries caused by intensive treatment and lead to the development of targeted treatments for people who received lung ventilation and/or perfusion.[151] Some of these studies will also stratify between mild and moderate/severe acute illness, which will develop a better understanding of the impact of acute infection severity on long-term outcomes.[148,150] The Canadian Institutes of Health Research (or CIHR) has a funding opportunity for its Emerging COVID-19 Research Gaps and Priorities competition, which includes including studies for post–COVID-19 condition, with some studies anticipated to begin by December 2021.[152]

Economic Impact

The economic impact and cost-effectiveness of post–COVID-19 treatment options and care models are not yet established, as they have only recently been launched. A rapid systematic review found 1 study that assessed the economic impact of post–COVID-19, which was focused on health care utilization outcomes and the proportion of people who were able to return to work.[61] The review also found 1 study that estimated the costs of implementing post–COVID-19 clinics in the UK. Further research on the health care costs of various specialists was recommended by the authors of the rapid systematic review.[61]

Considerations for Health Systems

Increase in Demand for Health Care Services

Although the prevalence estimates vary widely, between 14%[59] to 56%,[23,29] of people with COVID-19 experiencing new or persisting symptoms after 12 weeks, based on these estimates, as of August 2021 more than 100,000 people in Canada may have or could develop post–COVID-19 symptoms. Providing appropriate care to affected people, many of whom could also be health care professionals, could put additional pressures on health systems. A Canadian survey of 1,048 people with self-reported post–COVID-19 condition reported that 50% of respondents visited a health care provider 5 times over the past year and 30% of respondents visited more than 10 times.[51] As more people develop post–COVID-19 condition and/or become aware that their symptoms may be due to post–COVID-19 condition, additional resources may be needed to ensure that health care systems and providers are not overwhelmed.[95] A number of health care services could see increases in demand, including in:

- **primary care.** Many people will likely turn to their primary care providers first, regarding their suspected post–COVID-19 condition.
- **multidisciplinary rehabilitation services.** Post–COVID-19 condition can manifest with a variety of symptoms and will likely require various types of care from multiple specialists working in coordinated teams.
- **prescription drugs.** A US cohort study of health administrative data found that after 30 days, those who had COVID-19 had more billings for several drugs including pain medications, antidepressants, hypertensives, sedatives, and oral hypoglycemic drugs.[20]
- **mental health treatments and supports.** As post–COVID-19 symptoms may include depression, anxiety, and/or PTSD, the use of psychological supports and treatment have been recommended by a clinical group from Italy.[112]
- **medical imaging procedures and blood tests.** Clinical guidelines from NICE recommend that health care providers order bloodwork and/or imaging procedures to potentially determine causes of symptoms and rule out other illnesses as the cause of people's symptoms.[4]
- **intensive care in hospitals and/or ICUs.** Cohort studies (including 1 preprint) found that about 17% of people who had been hospitalized for COVID-19 during the acute phase returned to the emergency department and 10% were re-hospitalized.[34,153] An estimated 70% to 80% of children with MIS-C may require admission to a pediatric ICU.[48]
- **nutritionist services.** Education in nutrition may be needed to treat muscle loss and frailty from severe acute illness, as well as specific post–COVID-19 symptoms such as nausea or diarrhea.[87]
- **lung transplantations.** There may be an increase in demand for lung transplantations due to the severe damage COVID-19 can cause to the lungs.[154]

Health Equity

In Canada and around the world, health equity has been an issue since before the onslaught of the COVID-19 pandemic, as discrimination and stigma based on factors such as ethnicity, sex and/or gender, and socioeconomics impacts people's health.[155] Many people experiencing vulnerabilities, such as people from diverse ethnic backgrounds and lower-income households, were at higher risk of being infected with COVID-19.[84,155] Thus, these groups may

also have a high proportion of people with post–COVID-19 condition. Other groups at risk include people with disabilities, people experiencing homelessness or housing instability, or people living in correctional facilities.[97] Furthermore, these groups may be disproportionately impacted by post–COVID-19 condition, as they may be more likely to:

- work in jobs without sick leave and/or extended health benefits, and thus struggle to access needed treatment, which could lead to worsened health and greater health inequities
- struggle more financially if they or someone in their household becomes unable to work full-time
- find it challenging to access health services
- be misdiagnosed or have their post–COVID-19 symptoms dismissed (e.g., due to anxiety).[53,54]

Some approaches suggested by the CDC and health policy researchers to address these inequities have been to:

- allocate resources to raise awareness of post–COVID-19 condition among marginalized groups and increase access to needed services[97]
- provide training to health care providers surrounding sensitivity to and awareness of stigma, empathy, and the importance of completing a full clinical evaluation[97]
- implement a primary care–based model to improve access to specialized services typically only covered by private insurance (e.g., physiotherapy)[84]
- ensure services are easy to navigate (e.g., providing information in clear plain language) and culturally sensitive (e.g., being available in multiple languages or have interpreters available, culturally relevant and appropriate treatment plans)
- require minimal appointments to avoid interrupting work for those who do not have access to paid sick leave or who may live far from the clinic
- use telemedicine for easier scheduling, easier collection of information including symptoms (e.g., people can complete forms on their smartphones or computers in their free time at home or between work), and improve access (e.g., not requiring people to drive to a distant clinic).[95,113]

As services are rolled out, they will need to continually be evaluated for any accessibility barriers and ensure that people are receiving high-quality, cost-effective, and culturally appropriate care.[84]

Patients' Perspectives and Experiences

Access to Care and Care Navigation

Although post–COVID-19 condition is now acknowledged as an issue by WHO and researchers, many people may be struggling to receive recognition of their condition and access appropriate care.[51,120] In a Canadian survey that ran in May of 2021, some participants reported health care professionals dismissing their symptoms and other people who received attention from their health care providers reported difficulties accessing care.[51] Because of diagnostic uncertainty, it may be challenging for people with post–COVID-19 condition to know where to seek care and for health care providers to know when and how to provide treatment. Providing health care services navigation support to people with suspected post–COVID-19 condition may be needed to prevent overwhelming hospitals or other health

care services. Similarly, raising awareness about post–COVID-19 condition among health care providers and providing clear guidelines for self-management, testing, and treatment options may also help address challenges related to care navigation. Outlining care pathways may make care navigation simpler, less time-consuming, and less stressful for both health care providers and people with post–COVID-19. Systems may also need to consider how to minimize waiting times for receiving care.[156]

Quality of Life and Daily Activities

In addition to post–COVID-19 condition having an impact on people's health, it could impact their quality of life (QoL) and daily living. A systematic review and meta-analysis reported that post–COVID-19 condition was associated with lower health-related QoL, particularly in people who had been admitted to the ICU and people experiencing fatigue.[157] Approximately one-third of people in Canada who had been hospitalized for COVID-19 reported reduced QoL 3 months after symptom onset.[158] A prospective cohort study from Germany has suggested that lower QoL could continue for up to 12 months after symptom onset.[33]

Reduced QoL could result from a variety of factors, such as general poorer health (e.g., fatigue) or cognitive difficulties such as memory difficulties and brain fog even among young people who had mild acute illness.[30,159] These symptoms could result in:

- limitations in day-to-day activities (e.g., being able to engage in social activities or hobbies, requiring assistance for personal care)[10,25,160,161]
- reduced ability to care for children and/or dependents[7]
- reduced ability to work full-time (i.e., switching from full-time to part-time or taking leave from work), leading to financial stress, in particular for people who are less financially stable.[22,51] Estimates based on surveys of people self-reported to have post–COVID-19 who were working before their illness suggest that between 44% and 68% of people faced challenges to their work, either through reduced hours, taking leave, or not working.[22,162] One study reported that people with suspected post–COVID-19 condition were significantly more likely to not return to full-time work compared to people who developed COVID-19 but were able to recover within 12 weeks.[22]

Post–COVID-19's impact on people's ability to return to work could have important implications for health and economic equity. While preliminary studies of rehabilitation programs indicate improved health outcomes for those who had been hospitalized, it is not known if rehabilitation helps people return to work more quickly.[88] Providing guidance and resources for people with post–COVID-19 condition and their educational institutes and workplaces may help to alleviate these difficulties. Studies that measure disability-adjusted life-years and quality-adjusted life-years will also likely be needed to better understand the burden of post–COVID-19 condition and help to quantify which treatment and management protocols are most clinically effective and cost-effective.

Continuing Engagement

Patient support and self-help groups, including COVID Long-Haulers Canada and Long COVID Kids (which has groups in the US, UK, and Canada) are active.[8,163,164] People with post–COVID-19 condition have reported that these support groups have been invaluable in providing support and validation about their condition, and continue to help raise public awareness.[53,165,166] Advocacy groups are also calling on governments to set up working groups to address the needs of people with post–COVID-19 condition, commission urgent research, establish multidisciplinary clinics, ensure health care providers are able to provide appropriate

treatment, and assess economic implications including providing long-term sick leave, financial support, and employer awareness.[166]

Implications for Children

Similar to adults, children with post–COVID-19 condition could experience a lower QoL through:

- being unable to engage in physical activities or only enjoying them occasionally and often having symptoms worsen afterwards[46]
- lowered self-esteem due to their symptoms (e.g., rash) and inability to engage in activities with their peers
- being unable to attend school full-time or at all, which in turn can lead to poorer physical and mental health, as well as poorer academic performance.[44,85,165] This may be an issue especially for children and adolescents without access to supports (e.g., private tutoring) and may lead to greater inequalities that extend into adulthood (e.g., lowered chance to attend higher education, poorer job prospects).[167]

As of the time of writing (September 2021), COVID-19 vaccines are not approved for children younger than 12 in Canada. Although uptake of vaccines by adults may help to reduce the spread of COVID-19, children can be at risk of infection, especially as public health restrictions ease in many jurisdictions. In addition to the risk of children being infected and developing post–COVID-19 condition or MIS-C, their family and communities are also at risk.

An additional consideration about post–COVID-19 in children is related to developing back-to-school policies that allow children to safely return to school. It is unknown if and to what extent children may develop post–COVID-19 condition through asymptomatic spread in the school setting, especially among unvaccinated children younger than 12 years.[168] Many children and families are keen to return to full-time, in-person teaching, without the disruptions from the past school year that led to academic, psychological, and social development losses for children and adolescents, particularly those from marginalized and/or low-income families.[169] However, considerations will likely be needed to minimize the risks of COVID-19 infection and post–COVID-19 condition to children, their families, and communities. Protective measures including mask-wearing, ventilation, regular testing, small class sizes, and spaced classrooms could help to reduce these risks.[168]

Final Remarks

It has become increasingly clear that a significant portion of people who recover from acute COVID-19 will need care for weeks or months. Post–COVID-19 condition is a new area of research and evidence is still emerging. While many trials and reviews on the condition have been registered and are under way, it will take months and years before a clear picture of post–COVID-19 condition's cause(s) and natural history is available, as well as what constitutes the most clinically effective and cost-effective treatment and management options. Notable gaps in the evidence include a lack of health economics studies (e.g., the estimated costs that post–COVID-19 condition will put on the health care system and the costs and benefits of different care models, social support, and support systems for people with post–COVID-19 condition) and studies assessing children with post–COVID-19 condition. As jurisdictions in Canada and across the world continue to monitor the emerging

evidence base, increasing recognition about post–COVID-19 condition, improving reporting about its prevalence, and addressing the research gaps can help to better prepare and equip health systems.[170]

Moving forward, addressing health equity issues and engaging with people with post–COVID-19 condition will also likely be key. Collaborating with patient advocates has allowed researchers and health care providers to learn a great deal about post–COVID-19 condition, from its very existence to its range of complex symptoms. Continuing to involve a diverse range of people with lived experiences will help to develop a better understanding of post–COVID-19 condition and allow for the development of care that addresses their health and well-being.

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