Post-COVID-19 condition (long COVID)

CPSP
CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

PROTOCOL

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Background

Post-COVID-19 condition, or long COVID, is emerging as an important burden to societies and health care systems (1). Since the World Health Organization declared the coronavirus disease 2019 (COVID-19) global pandemic in March 2020, over 255 million people have been infected worldwide and new infections continue at a significant rate (2). A proportion of people with COVID-19 continue to suffer from persistent symptoms. This condition, commonly referred to as 'long COVID', may last for months or longer and can significantly impact daily functioning. First described in adults, long COVID is estimated to affect greater than 10% of adults infected with SARS-CoV-2, and is now recognized to also affect children and youth (3, 4). There is growing concern about the public health and economic consequences of long COVID. However, there is limited data on the incidence, presentation, and burden in children and youth.

Currently, there is no one accepted case definition of long COVID, which has also been called 'long haul COVID', 'post-acute sequelae of COVID-19', 'post-COVID-19 condition', and 'post-COVID-19 syndrome'. Case definitions from national and international bodies have begun to converge and include the following elements: 1) history of probable or confirmed SARS-CoV-2 infection, 2) persistent or new symptoms that have lasted for at least two months, and 3) symptoms not explained by an alternate diagnosis. It has also been noted that symptoms commonly include fatigue, shortness of breath, cognitive dysfunction,

sleep disturbance, arthralgia, and headache, and can impact daily functioning and lead to a decline in quality of life (5, 6, 7).

Based on emerging clinical experience, long COVID has a major impact on the health of children and youth and its clinical management is resource intense. While the pathophysiology and optimal management plan is poorly understood, the symptoms are multi-system and often require care from medical, rehabilitation, and psychological specialties (8).

Despite the significant impact of long COVID on children and youth, robust data about long COVID in children is sparse. No Canadian studies have been published. A large study based on patient self-report in the United Kingdom estimated that 1 to 2% of children with COVID-19 had symptoms which persisted for at least eight weeks (9). Other studies, however, have estimated a higher incidence, ranging from 4% to 27% (10, 11, 12). One study of long COVID in children reported that 36% of children with long COVID experienced severe limitations in daily function (4). The true incidence, range of symptoms, and exact burden of illness in children and youth remain unclear.

The 'Canadian Pediatric Long COVID Network' has been formed to address clinical, knowledge dissemination, and scholarship needs around this new condition in children and youth. The network includes paediatric generalists, specialists, and allied health team members (rehabilitation and neuropsychology) working in academic and community settings who are involved in the care of children with long COVID in 14 cities across Canada. Members of the Canadian Pediatric Long COVID Network will serve as co-investigators on this study and champion its success and knowledge dissemination.

A Canadian Paediatric Surveillance Program (CPSP) study on long COVID will provide critical information to advance the management of this condition for Canadian children and youth. The incidence and clinical characteristics of long COVID in children and youth in Canada is unknown and the burden of this illness in children in Canada has not been described. Based on early reports in the literature and clinical experiences managing children with long COVID, the resource utilization for each patient is significant and a better understanding of the extent and nature of this new condition in children is required so that health care systems may better prepare to support their recovery.

Methods

Through the established methodology of the CPSP, approximately 2800 paediatricians and paediatric subspecialists in Canada will receive a monthly electronic reporting form. Participants will be asked to voluntarily indicate if they have encountered a new case of long COVID, meeting the case definition, within the prior 30 days. Clinicians who report encountering a case will be directed to complete a detailed questionnaire online.

Participants will also be asked if they would be willing to be contacted within 12 months for the purpose of following reported cases longitudinally.

Participating in the follow-up component of the study will be optional and will occur outside of the CPSP platform.

Case definition

Report any patient less than 18 years of age (up to the 18th birthday) who meets both of the following criteria:

1) Experiencing one or more new or persistent symptoms after recovery from acute COVID-19 (proven by laboratory testing and/or highly suspected based on clinical history)

AND

2) Symptom(s) have persisted for at least eight (8) weeks

Objectives

1) Estimate the minimum incidence of long COVID in children and youth in Canada
2) Describe characteristics of children and youth with long COVID in Canada, specifically demographic features, nature of acute COVID-19 illness, family history of long COVID, and pre-existing co-morbidities
3) Describe clinical features of long COVID at presentation to paediatric care, specifically the nature and duration of symptoms at presentation and the impact on the child's participation in daily activities

Duration

September 2022 to August 2024

Expected number of cases

The current incidence of long COVID in children and youth in Canada is unknown.

Understanding that there are many variables with the COVID-19 pandemic that are difficult to predict, our group has used the following approximation to estimate the expected number of cases: A recent study from the United Kingdom that prospectively followed children with symptomatic acute COVID-19 estimated approximately 1% will develop symptoms lasting greater than eight weeks (9). Our group used this number in our estimation as the denominator used in this study (children in a largely outpatient setting) fit most closely with our expected patient population. In the first two years of the pandemic, there were approximately 348,000 children with microbiologically proven acute COVID-19 in Canada (13). Assuming that up to 40% of these cases were asymptomatic, 1% of symptomatic cases would result in approximately 1000 children affected by long COVID per year in Canada. Based on the current experience in the Canadian Pediatric Long COVID Network, however, it is anticipated that the number of children who will be affected significantly enough to seek medical care from a paediatrician will be lower. Further, the impact of vaccination will likely decrease the number of new infections in Canada. Therefore, it is

estimated that fewer than 200 cases of long COVID will be reported per year through the CPSP.

Study limitations

With voluntary reporting surveillance systems, the reporting on minimum incidence rates can have limitations, including under-representation of the disease in the population. It is possible that some groups of children will be missed, for example, those who live in rural or remote areas as they may be less likely to receive timely specialist care. There may be children with long COVID who seek care from health care providers other than paediatricians who will not be captured in this study. Additionally, case-level surveillance data is extracted from patient charts following the clinical encounter. Data elements, including details of history, physical examination, and relevant components of the diagnostic assessment not collected as part of routine care, will be absent from the surveillance totals.

To encourage voluntary reporting during a time when the health care system is strained, every effort has been made to ease and streamline reporting, and to ensure that only the most essential data elements are collected.

Despite its limitations, surveillance serves a very important purpose. This surveillance will help define the minimum incidence, clinical presentation, and characterization of long COVID in children in Canada.

Ethical approval

- Health Canada and Public Health Agency of Canada Research Ethics Board
- Quebec legislation allows for the collection of case notifications from Quebec paediatricians and subspecialists (including the reporting of cases identified by CPSP participants, with the age and sex of the infant/child/youth). Collection of detailed case-level information for CPSP studies, however, is only permitted from Quebec institutions with project-specific research ethics board approval in place.

Analysis

The analysis will be mainly descriptive.

Objective 1: The minimum incidence of long COVID and the 95% confidence interval will be estimated for the time interval of the CPSP study period. The numerator for the estimate will be the number of cases of long COVID identified through the CPSP during the study period. The denominator for the estimate will be the sum of the total number of children and youth infected with SARS-CoV-2 in the provinces and territories participating in the CPSP during the study period (available at https://health-infobase.canada.ca/covid-19/epidemiological-summary-covid-19-cases.html). We will also estimate yearly incidences of long COVID for more recent time periods and by sex.

Objectives 2 and 3: Demographic and clinical presentation characteristics will be summarized using descriptive statistics (means with standard deviations or medians with interquartile range for continuous variables and percentages for categorical variables).

Knowledge translation

To increase awareness about the extent of this condition in children in Canada and the need for resource allocation to support their recovery, knowledge translation activities will be conducted through established networks and relationships, including the Canadian Pediatric Long COVID Network, local institutions, public health units, provincial ministries of health and advisory boards (e.g., Ontario COVID-19 Science Advisory Table), Children's Healthcare Canada, the Public Health Agency of Canada, and the Canadian Paediatric Society. Results from this CPSP study will be presented at continuing medical education events, online webinars for practising paediatricians (e.g., Children's Healthcare Canada webinar), clinical and scientific meetings (e.g., Canadian Paediatric Society annual conference) and social media. Study findings will be published in a peer-reviewed journal.

The results of this study will also serve as the foundation for future work examining the outcomes and optimal management of this condition.

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