

COVID-19

- 1) Hospitalized patients with acute COVID-19**
- 2) Hospitalized patients with paediatric inflammatory multisystem syndrome/Kawasaki disease temporally associated with COVID-19**
- 3) Non-hospitalized patients with acute COVID-19 AND chronic comorbid conditions**

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Background

The human coronaviruses can cause a range of human illness from mild upper respiratory tract infections to severe and potentially fatal disease; notably from severe acute respiratory syndrome coronavirus-1 (SARS-CoV-1) and Middle East respiratory syndrome coronavirus (MERS). In late 2019, a novel coronavirus, now named SARS-CoV-2, first emerged in Hubei Province in China. In contrast to SARS-CoV-1 and MERS, SARS-CoV-2 is easily transmitted person to person in the community and has now spread to nearly every country in the world. In February 2020 the World Health Organization (WHO) named the human



disease caused by SARS-CoV-2 COVID-19 and on March 11, 2020 WHO declared COVID-19 to be a global pandemic.

To date the majority of cases of severe COVID-19 have been described in adults over the age of 60 and with underlying co-morbidities including obesity, hypertension, and diabetes. However, as the pandemic progresses, it is becoming increasingly clear that the spectrum of illness is wider than originally described and that younger individuals can also have severe COVID-19 disease, including death.

The spectrum of COVID-19 illness in children, and what groups of children may be at higher risk for severe disease, is not well described. The purpose of this study is to use the Canadian Paediatric Surveillance Program (CPSP) to provide timely information to public health officials and practising providers related to paediatric patients (up to age 18) hospitalized with microbiologically confirmed COVID-19, as well as to describe characteristics associated with non-hospitalized children (up to age 18) with microbiologically confirmed cases of COVID-19 who are considered to be potentially at “high risk,” due to very young age or an underlying complex medical condition. Information on epidemiology, clinical presentation, and outcomes will be collected.

This surveillance study also aims to capture critical information on the epidemiology of the rare paediatric inflammatory multisystem syndrome (PIMS) that is temporally associated with COVID-19. Since the first cases of PIMS were described in April 2020, multiple jurisdictions, primarily those hardest hit by the COVID-19 pandemic, have reported a small number of children presenting with an acute inflammatory illness and signs of circulatory compromise. Clinical features include persistent fever, symptoms suggestive of complete or incomplete Kawasaki disease, and/or toxic shock. Little is known about this important paediatric presentation and the global community is working to better understand, diagnose, and manage this serious illness. A public health alert was issued by the CPSP on May 14, 2020 outlining what was known about PIMS as of that date, and urging participants to maintain a high index of suspicion when caring for children.

This study is being conducted in partnership with the International Network of Paediatric Surveillance Units (INOPSU). At the conclusion of the data collection period, the Canadian paediatric experience with COVID-19 will be compared with other international jurisdictions (including, but not limited to, the United Kingdom, Switzerland, and New Zealand). While case definitions for PIMS are rapidly evolving and vary across jurisdictions, efforts were made to align to ensure capture of similar populations as well as parallel data elements.

Methods

Leveraging the infrastructure of the CPSP, approximately 2,800 paediatricians and paediatric subspecialists who are actively practising in Canada will receive a weekly electronic reporting form. Participants will be asked to voluntarily indicate if they have encountered a new case, meeting the case definition, within the prior 7 days. Clinicians who report encountering a case will be directed to complete a detailed questionnaire online.

In the May 14, 2020 CPSP Public Health Alert, participants were made aware of the plan to expand the case definition to include cases of PIMS.

Physicians who have encountered a patient meeting the case definition more than 7 days



ago, and have not yet reported it, will be able to enter the case at any point. Weekly surveillance will continue until public health officials declare that epidemic SARS-CoV-2 in Canada has passed.

At the close of the study, case numbers collected via the CPSP will be compared with case numbers reported via other platforms, specifically case numbers reported by provincial public health laboratories/public health authorities.

Participants will also be asked if they would be willing to be contacted within 12-months for the purpose of following reported cases longitudinally, as long-term outcomes and adverse events are of great public health and scientific interest. Participating in the follow-up component of the study will be optional and will occur outside of the CPSP platform.

Case definition

Report any new patient less than 18 years of age (up to the 18th birthday) who meets one of the following three case definitions:

- 1) HOSPITALIZED with acute COVID-19 (i.e., microbiologically confirmed SARS-CoV-2)
- 2) HOSPITALIZED with paediatric inflammatory multisystem syndrome (PIMS)/Kawasaki disease temporally associated with COVID-19, defined as:
 - Persistent fever (>38 degrees Celsius for 3 or more days) and elevated inflammatory markers (CRP, ESR, or ferritin)

AND one or both of the following:

- Features of Kawasaki disease (complete or incomplete)
- Toxic shock syndrome (typical or atypical)

AND

- No alternative etiology to explain the clinical presentation
(**Important note: Patients should be reported regardless of SARS-CoV-2 status**)
- 3) NON-HOSPITALIZED with acute COVID-19 (i.e., microbiologically confirmed SARS-CoV-2) AND at least one of the following chronic comorbid conditions:

< 12 months of age	Asthma
Obesity	Chronic lung disease
Congenital heart disease	Chronic renal disease
Immunocompromising medications (high-dose steroids,* chemotherapy, biologics, immunomodulators)	Solid tumor or hematologic malignancy
Solid organ transplant	Bone marrow transplant
Primary or secondary immunodeficiency	Chronic neurologic or neurodevelopmental condition
Sickle cell disease or other chronic hematologic condition	Diabetes
Tracheostomy	Chronic rheumatologic or autoimmune disease
Inflammatory bowel disease or other chronic gastrointestinal or liver disease	Genetic/metabolic disease

* Equivalent to at least 2 mg/kg or 20 mg/day of prednisone for at least 2 weeks

Objectives

Primary objective

- 1) Define the minimum incidence of hospitalization, intensive care unit (ICU) admission, and death from COVID-19 in children in Canada.

Secondary objectives

- 1) Identify the incidence of specific serious complications in children hospitalized with COVID-19 in Canada.
- 2) Identify underlying medical conditions and risk factors that increase the likelihood of severe disease from COVID-19 in children in Canada.
- 3) Identify the incidence and key clinical features of PIMS temporally associated with COVID-19
- 4) Compare the Canadian paediatric COVID-19 experience with that of other paediatric surveillance units around the world.

Duration

April 1, 2020 until public health officials declare that epidemic SARS-CoV-2 in Canada has passed.

Expected number of cases

This study aims to establish the minimum national incidence of hospitalization for COVID-19 in paediatric patients, as well as to establish the burden of illness amongst non-hospitalized paediatric patients with a significant co-morbid condition. The study also aims to establish the minimum national incidence of hospitalized paediatric patients with PIMS temporally associated with COVID-19. The sample size will be determined by the number of cases identified using the described surveillance methodology.

Data available from China, and more recent data published by the Centers for Disease Control and Prevention in the United States, suggests that paediatric COVID-19 cases might be less severe than cases in adults. From the most recent United States data, 1.7% of cases (when age was indicated) were in patients less than 18 years. The total burden associated with COVID-19 will be determined by the success of current (and future) public health measures designed to prevent transmission of SARS-CoV-2. In total, the anticipated number of cases will be less than 500. However, case numbers will be tracked closely throughout the study period. Should case reporting exceed 500 cases within the study period, a review of the case definition and detailed questionnaire will be completed by the study team.

The incidence of PIMS is currently unknown, but it is hypothesized that the incidence may parallel the burden of acute SARS-CoV-2 in the community, and may peak several weeks after the apex of the epidemiologic curve in each jurisdiction. As above, case numbers will be tracked closely throughout the study period.

Study limitations

As with any voluntary reporting surveillance system, the CPSP recognizes that 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. 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.

During the pandemic, it is possible the demands on the health care system, and especially front-line care providers, will not allow for voluntary reporting. Every effort has been made to ease and streamline reporting, and to ensure that only the most essential data elements are collected. Efforts to align with other national surveillance and research endeavors have also been made.

Despite its limitations, surveillance serves a very important purpose and provides rich clinical data that will allow a better understanding of the impact of COVID-19 in Canadian children and youth. This surveillance will help define high-risk populations to inform targeted prevention, prophylaxis, and therapeutic plans, as therapies for SARS-CoV-2 become available. This surveillance will also help define the incidence, clinical presentation, and risk factors associated with PIMS temporally associated with COVID-19.

Ethical approval

- Health Canada and the Public Health Agency of Canada's Research Ethics Board
- The Hospital for Sick Children Research Ethics Board

Analysis and publications

The analysis in this study will be mainly descriptive. Data extracted will include vital outcome, underlying risk factors, epidemiologic exposures, clinical course, treatment, and intensive care admission.

Baseline and demographic characteristics will be summarized using descriptive statistics (means with standard deviations for continuous variables and percentages for categorical variables). Basic comparisons will be made based on age (older or younger than 1 year) and underlying high-risk conditions. Chi-square or Fisher's Exact test will be used to compare categorical variables, as appropriate. Unpaired t-tests or Wilcoxon rank-sum tests will be used to compare continuous variables that are normally and non-normally distributed respectively.