CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

2020 Results

CPSP
CANADIAN PAEDIATRIC
SURVEILLANCE PROGRAM

Public Health Agency of Canada
Agence de la santé publique du Canada

Canadian Paediatric Society
Société canadienne de pédiatrie

Mission

To contribute to the improvement of the health of children and youth in Canada by national surveillance and research into childhood disorders that are high in disability, morbidity, mortality, and economic costs to society, despite their low frequency.

Canadian Paediatric Surveillance Program Annual Results

Surveillance is integral to the practice of public health. Public health surveillance, as defined by the World Health Organization, includes the systematic collection, collation, and analysis of data coupled with the timely dissemination of information for assessment and public health response. Integral to its public health mandate, the Canadian Paediatric Surveillance Program (CPSP) is committed to sharing valuable information obtained through its active surveillance of rare diseases and uncommon conditions in Canadian children and youth. Key results of CPSP multi-year studies and one-time surveys are published in this annual report. These results highlight important findings and inform health professionals, researchers, and policy makers in developing strategies to improve the health of children and youth in Canada.

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What is the Canadian Paediatric Surveillance Program?

The Canadian Paediatric Surveillance Program (CPSP) was created in 1996 to study rare diseases and conditions affecting Canadian children and adolescents. It is a joint project of the Public Health Agency of Canada and the Canadian Paediatric Society.

What does the CPSP do?

The CPSP collects and studies information about rare childhood diseases and conditions from paediatricians across Canada.

How does the CPSP work?

Each month, the CPSP asks about 2,800 paediatricians and medical specialists whether they have seen a child or adolescent affected by one of the diseases or conditions that is being studied. If they have, the doctors are asked to let the CPSP know and then answer a few questions about the case.

Information is collected under the authority of the *Public Health Agency of Canada Act* (Section 3(15)) and the *Department of Health Act* (Section 4(2)).

How is the information used?

The CPSP helps us to better understand rare diseases and conditions so that we can improve medical care and health policies for children and adolescents. The CPSP also helps us learn about new health issues so that we can be ready to take action quickly.

How is the information kept safe?

The CPSP follows strict policies and procedures to keep the information that we collect safe and secure and to comply with the federal and provincial laws that apply to our organization. Both physical and technical safeguards are in place, such as storing the CPSP data in a secure facility and limiting access to the data. For more information about CPSP policies and procedures, please visit https://www.cpsp.cps.ca/about-apropos/policies-and-procedures.

Every effort is taken to protect the privacy of patients. We do not collect directly identifying information, such as name, address, or medical record number. We do not contact families or children/adolescents.

Information collected through the CPSP is governed in accordance with Canada's *Privacy Act*.

Am I required to participate?

No, you are not required to participate. If you do not wish to participate, please tell your health care provider. Opting out will mean that your information will not be used as part of the CPSP and will not affect the medical care you receive in any way.

More information is available at:
www.cpsp.cps.ca

Or contact us at: Tel.: 613-526-9397, ext. 239; E-mail: cpsp@cps.ca

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www.cpsp.cps.ca/uploads/publications/What-is-the-CPSP-poster.pdf

Table of Contents

Foreword

Chief Public Health Officer of Canada

Dr. Theresa Tam

The Public Health Agency of Canada (PHAC) is proud of its longstanding partnership with the Canadian Paediatric Surveillance Program (CPSP). For more than two decades, the Program has been providing invaluable information to researchers and health professionals about rare or emerging conditions or injuries in children and youth.

The COVID-19 pandemic has been an unprecedented public health emergency. During this time, effective public health surveillance systems, such as the CPSP, have helped us to keep pace with a novel virus by providing a basis for understanding the new and emerging illnesses associated with it. Our youngest Canadians, while less likely to experience serious illness due to the SARS-CoV-2 infection, have not escaped its direct and indirect impacts.

In 2020, the CPSP met the new and notable challenges of the COVID-19 pandemic while continuing its surveillance efforts in other key areas, such as serious or adverse events due to cannabis exposure in children, acute flaccid paralysis, and life-threatening drug reactions.

It has never been more evident how important global efforts are to address public health challenges. As a member of the International Network of Paediatric Surveillance Units, the CPSP, with over 10,000 paediatricians from around the world, studied and monitored a rare, but serious inflammatory syndrome, temporally associated with the SARS-CoV-2 virus. Information was quickly shared among the global paediatric network, enabling Canadian paediatricians, policy-makers and other health professionals to prepare.

PHAC's collaboration with the Canadian Paediatric Society has been essential to ensuring that the risks to the health of our children and youth, which continue to emerge, will continue to be monitored and understood. The challenges of the pandemic go beyond COVID-19, underscoring the importance of CPSP's wider range of diseases and conditions under surveillance, such as substance-related harms and rare chronic diseases that can be difficult to manage under even the best of circumstances.

This work would not be possible without the approximately 2,800 paediatricians and paediatric sub-specialists across Canada who voluntarily provide their time, insight and knowledge to this Program. Your efforts, during these challenging times, are greatly appreciated. Thank you.

President of the Canadian Paediatric Society

Dr. Sam Wong

As the President of the Canadian Paediatric Society, I am extremely pleased to see how our surveillance programs have contributed such rich and timely data to inform and address Canada's most pressing health concerns in 2020.

Surveillance plays a pivotal role in managing a pandemic. The data collected will help public health officials and front-line care providers understand how the pandemic is evolving, assess the severity of the disease and the risk to Canadian children and youth, and develop the necessary tools to help further prevent the disease's spread. Since the onset of the pandemic, the Canadian Paediatric Surveillance Program (CPSP) has been working in close collaboration with the Public Health Agency of Canada to collect, interpret, and share COVID-19 data.

Enormous thanks are owed to the CPSP's 2,800 dedicated participants. The Program's success relies on their tireless commitment and devoted engagement. Even though the COVID-19 pandemic has put unprecedented demands on hospitals, hospital-based providers, and community physicians, we are grateful to CPSP participants, who continued to reliably submit weekly notifications of cases from across the county. I urge you to continue to follow the CPSP studies and be vigilant for the conditions that are under surveillance to ensure that the CPSP continues to provide the data needed to inform paediatric public health in Canada.

It is, of course, also important during a pandemic to continue collecting surveillance data on other conditions and diseases, especially when the pandemic may have unintended consequences or negative effects on children and youth. Practising in the Northwest Territories, I have certainly seen many of these consequences affect my young patients and their families. As health care providers, we can work together to gain a better understanding of these concerning consequences and how best to help our patients.

On behalf of the Canadian Paediatric Society, I would also like to thank our partners at the Public Health Agency of Canada for their continued support and ongoing collaboration. The strong partnership between the Canadian Paediatric Society and the Public Health Agency of Canada, as well as Health Canada, allows the CPSP to keep providing the necessary data that informs public health efforts and clinical care for our children and youth.

Chair of the Canadian Paediatric Surveillance Program

Dr. Catherine Farrell

As I complete my first year as Chair of the Canadian Paediatric Surveillance Program's (CPSP) Scientific Steering Committee, I am enormously proud of the Program and our achievements in 2020. Responding to the ongoing pandemic has been one of the biggest challenges that our surveillance system has ever faced, and I am so delighted that we rose to, and met, that challenge so admirably.

Reflecting on this most remarkable year, I look back at what the CPSP has achieved, and I realize the true value of having a well-established, robust, national public health surveillance infrastructure in place. The stability and permanence of the CPSP allowed us to quickly mobilize to capture near real-time data on COVID-19 in the paediatric population. The Program was able to adapt as new threats were recognized and address new, critical questions that required answers. The COVID-19 pandemic provided the Program with an opportunity to evaluate its strengths as a surveillance network, allowing us to consider how best to continue to improve, build capacity, and foster resilience in the face of future public health events.

Our exceptionally dedicated COVID-19 study team has analyzed data on hospitalizations associated with SARS-CoV-2 infections, cases in non-hospitalized children with chronic comorbidities, as well as paediatric inflammatory multisystem syndrome/multisystem inflammatory syndrome in children. I invite you to read the preliminary findings of this important study on page 20. This study was groundbreaking, not only because of the topic, but because it is the first CPSP study relying upon weekly reporting in an exclusively electronic format. We are tremendously grateful for the frontline clinicians caring for these patients, who took the time to signal them to the CPSP.

And while COVID-19 was certainly at the forefront of our surveillance efforts in 2020, the Program also initiated three new studies at the beginning of the year. Interim reports on 5q spinal muscular atrophy, micronutrient deficiencies and autism spectrum disorder, and paediatric pulmonary thromboembolism are also included in this report.

On behalf of the CPSP Scientific Steering Committee, and as a paediatrician colleague, I wish to thank everyone involved in the Program—CPSP Scientific Steering Committee members who carefully evaluate each new study proposal, investigators who take the time to carefully analyze and disseminate knowledge on study and survey results, and a special thank you to our 2,800 participants for their continued support and dedication to the CPSP.

Acknowledgements

The key strength of the Canadian Paediatric Surveillance Program (CPSP) is its commitment to improve the health of children and youth in Canada and around the world. This focus would not be possible without the participation of Canadian paediatricians, subspecialists, and other health care providers in the monthly collection of information on rare paediatric conditions, the investigators who design studies and analyse the data to provide knowledge and educational solutions, or the guidance of the Scientific Steering Committee members. We thank them all.

We also thank IMPACT (Immunization Monitoring Program ACTive) centres for their role in verifying the acute flaccid paralysis study data and for their support of the CPSP.

The strong partnership between the Canadian Paediatric Society and the Public Health Agency of Canada allows the program to grow in Canada and to take a leadership role on the international scene.

Funding

Funding for the CPSP is required to support program management. The surveillance program is funded through a combination of government support and unrestricted grants from Canadian charities, research institutions, hospitals, and corporations. All funding is provided to maintain and expand the Program.

We gratefully acknowledge the financial support received in 2020 from the Public Health Agency of Canada's Centre for Surveillance and Applied Research, Health Canada's Marketed Health Products Directorate, and the following non-governmental sources:

- Alberta Children's Hospital Research Institute
- Bethanys Hope Foundation
- CHEO Research Institute
- Psychiatry Endowment Fund, The Hospital for Sick Children

Canadian Paediatric Surveillance Program Scientific Steering Committee

Catherine Farrell, MD (incoming Chair)	Canadian Paediatric Society
Jonathon Maguire, MD (outgoing Chair)	Canadian Paediatric Society
Peter Buck, DVM, MSc	Centre for Food-borne, Environmental and Zoonotic Infectious Diseases, Public Health Agency of Canada
Marie Adèle Davis, MBA	Canadian Paediatric Society
Elizabeth Donner, MD	Canadian Association of Child Neurology (Liaison)
Ciarán Duffy, MB	Paediatric Chairs of Canada (Liaison)
Joanne Embree, MD	IMPACT (Immunization Monitoring Program ACTive) (Liaison)
Sabrina Heyde, JD	Consultant
Krista Jangaard, MD	Canadian Paediatric Society
Carsten Krueger, MD	Canadian Paediatric Society (Resident Representative)
Melanie Laffin Thibodeau, BCom	Canadian Paediatric Society
Joanna Lazier, MD	Canadian College of Medical Geneticists (Liaison)
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Jorge Pinzon, MD	Canadian Paediatric Society
Anne Rowan-Legg, MD	Canadian Paediatric Society
Miriam Santschi, MD	Canadian Paediatric Society
Winnie Siu, MD	Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada
Jill Starkes, MD	Canadian Paediatric Society

In 2020, Dr. Jonathon Maguire completed a six-year term as Chair of the CPSP Scientific Steering Committee. He had previously served on the committee as a representative of the Canadian Paediatric Society and as the interim CPSP Medical Affairs Director. The CPSP Scientific Steering Committee wishes to sincerely thank Jonathon for his dedication to the Program and his valuable expertise on the committee and wish him all the very best in his future endeavours.

About the Canadian Paediatric Surveillance Program

Overview

The Canadian Paediatric Surveillance Program (CPSP) is a joint project of the Public Health Agency of Canada and the Canadian Paediatric Society that contributes to the improvement of the health of children and youth in Canada by national surveillance and research into childhood disorders that are high in disability, morbidity, and economic costs to society, despite their low frequency. The CPSP gathers data from approximately 2,800 paediatricians and paediatric subspecialists each month to monitor rare diseases and conditions in Canadian children.

Objectives

- Maintain an active national surveillance system that monitors low-frequency, high-impact conditions and diseases in Canadian children and youth
- Involve paediatricians, paediatric subspecialists, and other medical professionals in related disciplines in the surveillance of rare conditions that are of public health and medical importance
- Generate new knowledge into rare childhood disorders to facilitate improvements in treatment, prevention, and health-care planning
- Respond rapidly to public health emergencies relevant to Canadian children and youth by initiating rapid one-time surveys and new studies
- Participate in international paediatric surveillance efforts through the International Network of Paediatric Surveillance Units (INOPSU)

Surveillance

- The full surveillance process is summarized in Figure 1 and includes the 3Ds of surveillance: detection, deduction, and dissemination.
- Health surveillance can be defined as: the tracking of any health event or health determinant through the continuous collection of high-quality data (detection); the integration, analysis, and interpretation of the data (deduction) into surveillance products; and the dissemination of those surveillance products to those who need to know (dissemination).

Process

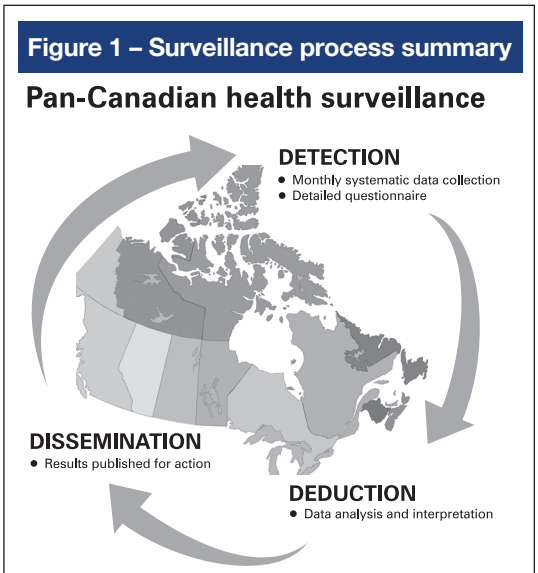
- Study teams from across Canada are encouraged to submit proposals for new studies or one-time surveys that meet the "criteria for submission," available on the CPSP website at www.cpsp.cps.ca/apply-proposez/criteria-for-inclusion-of-studies.
- The CPSP Scientific Steering Committee then reviews the proposals on a biannual basis and selects those of highest medical and public health importance. Proposals are evaluated against set criteria and are subject to comprehensive feedback from the multidisciplinary Scientific Steering Committee, composed of representatives from the Public Health Agency of Canada, the Canadian Paediatric Society, former CPSP investigators, academic clinicians from diverse specialties, and community paediatricians.
- Each month, CPSP participants from across Canada receive a form listing the current conditions under study. Participants notify the program if they have seen any cases that meet the case definitions or have "nothing to report." Participants are encouraged to report all cases, including suspect or probable cases. This sometimes leads to duplicate reporting but avoids missed cases.

CPSP Quick Facts

Did you know?

- The CPSP celebrated its 24th anniversary in 2020.
- The CPSP is comprised of approximately 2,800 dedicated paediatricians and paediatric subspecialists.
- Since its inception, the CPSP has studied 80 rare conditions/diseases and initiated 54 one-time surveys.
- Over 79 peer-reviewed manuscripts on study/survey results have been published in high-impact journals.
- The average monthly response rate is 80%.
- The average detailed questionnaire response rate varies between 80 to 90%.
- By December 2020, 97% of participants committed to receiving their monthly forms electronically.

Figure 1 – Surveillance process summary



- Participants who have seen a case are sent a detailed clinical questionnaire to complete and return to the CPSP.
- Once the detailed questionnaire is returned to the CPSP, it is stripped of all unique identifiers and sent to the investigators for data analysis. All notifications of potential cases are assessed against the case definition. Duplicates or cases that don't meet the case definition are excluded.
- It is important to note that CPSP studies use anonymized data from patient charts; the study investigators have no direct contact with individual patients.
- The study team is responsible for data analysis, and for ensuring that a solid knowledge translation plan is in place to disseminate the results in a timely and effective manner.
- Study results are published annually and acted upon to improve the health of Canadian children and youth. For example, CPSP study results help to warn of emergent public health issues, identify safety hazards, mobilize knowledge on rare diseases/conditions, and inform new policies and guidelines.

Limitations of surveillance

As with any voluntary reporting surveillance system, the CPSP recognizes that its surveillance has some limitations, including the following:

- Reporting on minimum incidence rates can under-represent events in the population.
- Some cases may present to family doctors or other health care practitioners and not to paediatricians.
- Surveillance totals may not include some children, such as those who live in rural or remote areas who are less likely to receive timely specialist care.
- Some data elements (e.g., laboratory investigations, pre-existing medical conditions) may not be available in the patient chart at the time of reporting and therefore may be absent from the surveillance totals.
- Data from Quebec are incomplete. Due to Quebec legislation, cases reported from that province can only be included in the data analysis when reported from a centre with project-specific research ethics board approval.
- Since the start of the COVID-19 pandemic, with the unprecedented demands being placed on front-line health care providers, it is possible that some cases may have gone unreported.

Despite these limitations, surveillance serves an important purpose and provides rich clinical data that allows for a better understanding of the rare childhood diseases/conditions under study.

Response rates

The CPSP's average national monthly response rate is 80% and the average detailed questionnaire completion rate varies between 80 to 90%.

TABLE 1 – Initial response rates (%) and number of participants for 2020

Provinces/territories	Reporting rates (%)*	Number of participants†
Alberta (AB)	84	375
British Columbia (BC)	84	298
Manitoba (MB)	81	117
New Brunswick (NB)	78	36
Newfoundland and Labrador (NL)	87	47
Northwest Territories (NT)	—	< 5
Nova Scotia (NS)	81	88
Nunavut (NU)	—	< 5
Ontario (ON)	82	1053
Prince Edward Island (PE)	91	10
Quebec (QC)	77	566
Saskatchewan (SK)	78	67
Yukon (YT)	—	< 5
Canada	**81**	**2662**

* The CPSP national monthly reporting rate averages 80%. Every effort is made to maximize reporting, and annual response rates are subject to change due to delays in reporting.

† The total number of individual CPSP participants is approximately 2,800. However, in this table, the number of CPSP participants in Canada is calculated based on both individual and group reporting. When a group designate responds to the CPSP on behalf of group members, it is counted as one response.

TABLE 2 – National initial response rates 2016–2020

Reporting year	Reporting rates (%)
2016	79
2017	83
2018	79
2019	82
2020	81

TABLE 3 – 2020 detailed questionnaire completion rates as of August 20, 2021*

Studies/conditions	Notifications of potential cases	Pending	% Completion rate
5q spinal muscular atrophy	23	9	61
Acute flaccid paralysis†	38	0	100
Adverse drug reactions – serious and life-threatening	21	4	81
COVID-19†§	932	—	—
Frequency and impact of PANDAS/PANS diagnosis‡	25	5	80
Micronutrient deficiencies and autism spectrum disorder	28	7	75
Ophthalmia neonatorum caused by *N gonorrhoeae* or *C trachomatis*	9	0	100
Paediatric-onset leukodystrophies‡	22	3	86
Paediatric pulmonary thromboembolism	16	2	88
Serious adverse events related to cannabis used for medical purposes‡	< 5	1	—
Serious and life-threatening events associated with non-medical (recreational) cannabis use in Canadian children and youth	78	12	85
Severe obesity and global developmental delay in preschool children	< 5	0	—
Total number of cases (all studies)	**1197**	**43**	**85**

* The numbers in this table were compiled later than those contained in the individual study reports and hence may differ because of delayed case reporting or case analysis.
† Includes case notifications from Quebec from centres with project-specific research ethics board approval. For all other studies, case notifications from Quebec were excluded.
‡ Includes reports from December 1, 2019 to December 31, 2020
§ The data collection methodology for this study was different, as described in the study report, and as such, the completion rate is not presented.

Glossary of terms in study results

Reported: Notifications of potential cases received by the CPSP

Duplicates: Cases reported by more than one participant

Excluded: Cases not meeting the case definition and cases reported from Quebec institutions without project-specific research ethics board approval

In mid-2018, the CPSP became aware of a change in Quebec legislation that affected the ability of the Program to collect detailed information from physicians who practise in that province. The Ministère de la Santé et des Services sociaux approved the continued collection of CPSP case notifications (including date of birth and sex) from paediatricians and subspecialists in Quebec. More detailed case-level information for CPSP studies may also be collected in Quebec from institutions with project-specific research ethics board approval. Therefore, cases notified by Quebec participants after August 1, 2018 are included in the data analysis only if they are reported from an institution with CPSP project-specific research ethics board approval.

Pending: Detailed questionnaires not received or not yet verified as meeting the case definition

Met case definition: Cases verified as meeting the case definition, excluding duplicate case reports, cases failing to meet the case definition, cases pending verification, and cases reported from Quebec from institutions without project-specific research ethics board approval

International Network of Paediatric Surveillance Units

The CPSP offers an opportunity for international collaboration with other paediatric surveillance units worldwide, through the International Network of Paediatric Surveillance Units (INOPSU). The network provides a successful and easily accessible platform for international surveillance. No other network enables international comparisons of demographics, diagnoses, treatments, and outcomes for rare childhood conditions.

Established in 1998, INOPSU's membership includes many paediatric surveillance units from around the world, from Canada to New Zealand. Many of the paediatric surveillance units have been collecting data on rare childhood conditions for 20 years or more. Over 300 rare conditions have been studied to date, including rare infectious and vaccine-preventable diseases, mental health disorders, child injuries, and immunological conditions. The network encompasses approximately 10,000 child health care providers who voluntarily contribute data on these rare diseases every month.

Joint collaborative studies are seen as an important method of advancing the knowledge of uncommon childhood disorders around the world. For example, collaborative work is taking place to combine the data from the CPSP's congenital Zika syndrome and severe microcephaly studies with data from similar national surveillance projects conducted in the United Kingdom, Australia, and New Zealand.

During INOPSU meetings, member countries can highlight their surveillance program activities, explore innovative study ideas of interest to the network, discuss knowledge translation and joint publication opportunities, as well as strategize on how best to maintain active engagement of participants.

More information on INOPSU can be found at www.inopsu.com.

Surveillance Studies in 2020

5q spinal muscular atrophy

Study duration: January 2020 to December 2021


Jean K. Mah

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Questions

- What is the minimum incidence of 5q spinal muscular atrophy (SMA) in children in Canada?
- What is the age at onset of symptoms and the age at time of genetic confirmation of disease?
- What therapeutic interventions are used in the treatment of children with SMA across Canada?

Importance

- SMA is the leading genetic cause of infant death and the second most common autosomal recessive disorder.
- SMA types 1, 2, and 3 are childhood onset diseases. Patients with SMA type 1 present before 6 months of age, with severe muscle weakness, hypotonia, and areflexia leading to progressive feeding and respiratory insufficiency. Affected infants are not able to sit and often die before their second birthday if untreated. Patients with SMA type 2 are symptomatic before 18 months of age and can sit but are unable to stand or walk unassisted; orthopedic and respiratory complications are common and the condition can be associated with reduced life expectancy. Patients with SMA type 3 present after 18 months of age with the ability to walk unassisted; progressive weakness may result in loss of independent ambulation, but a normal life span can be expected.
- A growing number of effective therapies for SMA are now available. Understanding the minimum incidence, disease presentation, and current care practices will help inform strategies to improve the standard of care for children with SMA in Canada.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/current-studies.

Case definition
Any patient with a new genetically confirmed case of SMA (type 0 – 3) from birth to 18 years of age. The majority (96%) of 5q SMA cases are due to homozygous deletion of exon 7 (and exon 8) of the SMN1 gene; mutations of one SMN1 allele plus a deletion or mutation of SMN1 on the other allele can be found in the remaining 3–4% of cases.

Exclusion criteria
Excludes patients with other causes of developmental delay, hypotonia, or weakness (such as genetic or acquired causes of myopathies, muscular dystrophies, neuropathies, neuromuscular junction transmission defects, and central nervous system disorders) or non-5q SMA (such as distal SMA, SMA with respiratory distress, and other genetic or acquired motor neuron diseases).

Unique to this study
This study aims to estimate the minimum annual incidence of SMA using multiple sources, including a) the Canadian Paediatric Surveillance Program (CPSP); b) molecular genetics laboratories in Canada; and c) the Canadian Neuromuscular Disease Registry.

Results – January to December 2020

TABLE 1 – 5q SMA cases in 2020				
Reported	**Duplicates**	**Excluded**	**Pending**	**Met case definition***
11	0	0	0	11

* Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis.

Cases that met the case definition

At the time of analysis, all 11 cases reported in 2020 were verified as meeting the case definition.

Demographics

- The median age of cases was 12 months (IQR 6–21).
- Patient sex was male in most cases.
- The geographic distribution of cases was: five (45%) cases from Ontario and the remaining cases from Atlantic Canada and Western Canada.

Presentation and diagnosis

- Diagnosis was confirmed by genetic testing in all 11 (100%) cases.
- In 10 (91%) cases there was no known family history of SMA.
- The 11 reported cases included SMA types 1, 2, and 3.
- The majority of SMA type 1 cases were diagnosed at 5 to 6 months of age, with a mean of three months between symptom onset and diagnosis.
- The majority of SMA type 2 cases were diagnosed between 9 to 22 months of age, with a mean of eight months between symptom onset and diagnosis.
- The majority of SMA type 3 cases were diagnosed between 22 to 42 months of age, with a mean of 18 months between symptom onset and diagnosis.
- The most common presenting symptoms included a delayed motor milestone in 7 (64%) cases and hypotonia in 7 (64%) cases. Muscle weakness was reported in fewer than five cases.

Treatment and outcomes

Eight (73%) cases received nusinersen.

Study limitations

Limitations common to all CPSP studies are listed on page 11.

Conclusions

- On average, diagnosis was delayed after the onset of symptoms by three months for SMA type 1, by eight months for type 2, and by 18 months for type 3.
- Early recognition and newborn screening may reduce diagnostic delay and enable early treatment.

Anticipated study impact

- Details on patient function, health status, and access to health services will be examined.
- Results will help advance the care and health outcomes of children with SMA.

Acute flaccid paralysis

Study duration: Ongoing study since January 1996

Catherine Dickson

Principal investigator

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Co-investigators

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Question

Did Canada maintain its polio-free status in 2020?

Importance

- Poliomyelitis is targeted for eradication, with only two countries having ongoing wild poliovirus transmission. Acute flaccid paralysis (AFP) surveillance is the cornerstone of monitoring for polio and is critical for documenting the absence of poliovirus circulation required for countries to declare polio-free status.
- Canada conducts AFP surveillance in children under 15 years of age, in accordance with World Health Organization (WHO) recommendations and standards of practice.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/current-studies.

Case definition

Acute onset of focal weakness or paralysis characterized as flaccid (reduced tone) without other obvious cause (e.g., trauma) in a child less than 15 years of age. Transient weakness (e.g., post-ictal weakness) does not meet the case definition.

Unique to this study

Cases are captured through both the Canadian Paediatric Surveillance Program (CPSP) and Canada's Immunization Monitoring Program ACTive (IMPACT) based in 12 tertiary care paediatric centres. Of the cases reported from Quebec, only AFP cases reported by Quebec IMPACT centres are eligible for data analysis in this report.

Results – January to December 2020

Note: Due to reporting delays, this report represents a snapshot as of May 11, 2021. The total AFP case counts for 2016 to 2020 have been updated with all the confirmed cases that have been reported and are presented in Table 2.

TABLE 1 – AFP cases in 2020

Reported	Duplicates	Excluded	Pending	Met case definition*
33	3	2	1	27

* Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis, unless reported from a centre with project-specific research ethics board approval. Cases reported through the following centres were included in the data analysis for this report: CHU Sainte-Justine, Montreal Children's Hospital, and CHU de Québec-Université Laval and Centre mère-enfant Soleil.

TABLE 2 – Annual comparison of AFP cases 2016–2020

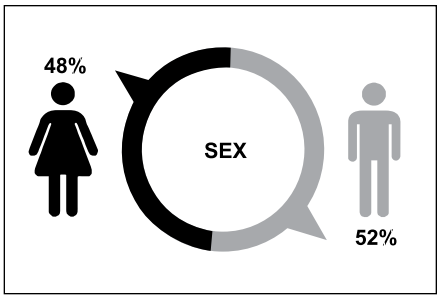
Year	Total cases
2020	27
2019	34
2018	72
2017	32
2016	52

Cases that met the case definition

- In total, 33 reports of sudden onset muscle weakness in children younger than 15 years of age were provided to the Public Health Agency of Canada. All reports were reported through IMPACT.
- At the time of analysis, 27 cases were verified as meeting the AFP case definition in 2020; none were assessed as meeting the polio case definition.
- The median time from case onset of paralysis to reporting was 87 days and the average was 96 days (range: 11– 300).

Demographics

- Fifty-two percent of the cases were male and 48% were female.
- Cases ranged in age from younger than 1 year to 14 years, with a median of 4.9 years and a mean of 6.3 years (95% CI 4.6–8.0).



Presentation and diagnosis

- All 27 (100%) cases were hospitalized. Length of stay ranged from 2 to 69 days, with a median of 8 days and a mean of 12 days (95% CI 7–18).
- Ten (37%) cases were diagnosed with Guillain-Barré syndrome. Diagnoses for the remaining 17 (63%) cases included transverse myelitis, acute disseminated encephalomyelitis, acute inflammatory demyelinating polyradiculoneuropathy, ataxia, other types of myelitis, or the diagnosis was unspecified or unknown.
- Twenty-three (85%) cases were up-to-date for their polio vaccinations.
- Thirteen (48%) cases had stool sample submitted for viral testing; 10 (37%) of these had samples taken within 14 days of paralysis onset. None were positive for polio.

Treatment and outcomes

- All cases had outcomes documented at initial report, of which 25 (93%) cases had partially recovered with residual weakness.
- Of the 9 (33%) cases with clinical outcomes reported at least 60 days after the onset of paralysis or weakness, the vast majority had partially recovered.

TABLE 3 – Measure of Canada's performance against WHO AFP surveillance performance indicators in 2020[1]

Number of cases	Incidence rate*	% with adequate stool sample[2†]	% with 60-day follow-up‡
27	0.45	37%	33%

* Per 100,000 population in those less than 15 years of age - target is 1.0 AFP case per 100,000
† Target is at least 80% of cases have adequate stool sampling within 14 days of paralysis onset
‡ Target is at least 80% have follow-up examination for residual paralysis at least 60 days after onset

Study limitations

- Limitations common to all CPSP studies are listed on page 11.
- Stool samples in patients with AFP are sometimes difficult to obtain due to the nature of the patient's symptoms, including constipation. Additionally, rapid availability of advanced diagnostic testing often identifies the diagnosis prior to the collection of the stool sample.

Conclusions

- Although Canada did not meet the WHO performance indicators for national AFP surveillance in 2020, there was sufficient evidence to suggest that no polio cases occurred in Canada.
- AFP surveillance in Canada is conducted through a sensitive and active surveillance system that allows prompt and appropriate investigation of AFP cases to detect polio. Polio is a reportable disease in every province and territory, and is nationally reportable.

Anticipated study impact

Canada's polio-free status remains intact, as assessed annually by Canada's National Certification Committee for Polio Eradication.

Acknowledgements
The investigators would like to thank everyone who participated in collecting the data. They would also like to acknowledge the excellent work of Susan Squires, Francesca Reyes Domingo, Brigitte Ho Mi Fane, and Jamal Ahmadian-Yazdi.

1. Detailed information on WHO surveillance performance indicators can be found at https://polioeradication.org/polio-today/polio-now/surveillance-indicators/
2. Adequate stool sample refers to one stool sample taken within 14 days of paralysis onset.

Adverse drug reactions – serious and life-threatening

Study duration: Ongoing study since January 2004

Sally Pepper

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Question

What serious and life-threatening events suspected to be related to adverse drug reactions (ADRs) in children and youth were reported in 2020?

Importance

- Only a minority of prescribed pharmaceuticals on the market in North America have been tested in paediatric patients, and most of them are used without the benefit of adequate and/or specific guidance on safety or efficacy in this population.
- Post-marketing surveillance is essential for detection of ADRs, and contributes to the ongoing monitoring of the benefit-risk profile of health products used in children.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/current-studies.

Case definition

Serious and life-threatening adverse drug reactions* in an infant or child up to the age of 18 years, associated with the use of prescription, non-prescription, biological (immunoglobulin) products, complementary medicines (including herbals), and radiopharmaceutical products.

* Noxious and unintended severe response to a drug, which occurs at any dose and results in emergency observation, hospitalization, persistent or significant disability, or death

Exclusion criteria

Reactions to medical devices, blood products, (platelets, red cells and single-donor plasma), vaccines, poisonings or self-administered overdoses

Unique to this study

Significant results for the ADR study contribute to the monthly ADR Tips distributed by the Canadian Paediatric Surveillance Program (CPSP).

Results – January to December 2020

TABLE 1 – ADR cases in 2020

Reported	Duplicates	Excluded	Pending	Met case definition*
10	0	1	0	9

* Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis.

Cases that met the case definition

- At the time of analysis, nine suspected serious and/or life-threatening paediatric ADR cases were verified as meeting the case definition in 2020.
- In a small number of cases, more than one product was suspected of causing the adverse reactions.
- The classes of health products, as classified using the Anatomical Therapeutic Classification (ATC) system, most frequently suspected of causing the adverse reactions were antibacterials and antiepileptics.

- Antiadrenergic agents, anti-inflammatories, antineoplastic agents, corticosteroids, and immunosuppressants were each involved in fewer than five cases.

Demographics

- Patient sex was female in the majority of cases.
- Cases were reported from each of the following age ranges: 0 to 5 years, 6 to 12 years, and 13 to 17 years.

TABLE 2 – Suspect health products in 2020

Class of health product	Name of health product
Antiadrenergic agents, centrally acting	Clonidine
Antibacterials	Amoxicillin, sulfamethoxazole/trimethoprim
Antiepileptics	Lamotrigine, phenytoin, valproic acid
Anti-inflammatory and antirheumatic products	Naproxen
Antineoplastic agents	Pegaspargase, rituximab
Corticosteroids	Prednisolone
Immunosuppressants	Azathioprine

Presentation and diagnosis

- All nine cases were classified as serious according to the following criteria (more than one cause for classification was provided in seven reports): fewer than five cases were considered life-threatening; eight cases required hospitalization; six cases were considered to be medically important (defined as a case that may not be immediately life-threatening or result in death/hospitalization but may jeopardize the patient or require intervention to prevent one of these other outcomes from occurring).
- The majority of the adverse reactions described skin and subcutaneous tissue disorders. This finding is consistent with the trend seen for all reports received through the CPSP since the initiation of the study in 2004.
- The majority of the reports described reactions generally documented in the approved Canadian product monograph or other drug information references.

Treatment and outcomes

- No deaths were reported.
- The outcome was known in all nine cases, with all patients experiencing a full recovery.

Study limitations

- Limitations common to all CPSP studies are listed on page 11.
- All adverse reactions to health products are considered suspicions as a definite causal association often cannot be determined. The true incidence of adverse reactions is unknown because they remain under-reported and total patient exposure is unknown.

Conclusions

- The classes of health products most frequently reported in 2020 as suspected of causing adverse reactions were antibacterials and antiepileptics.
- Since the implementation of the CPSP surveillance for adverse reactions in 2004, the product classes most frequently associated with suspect products have been antibacterials for systemic use, antiepileptics, and psychoanaleptics. The most frequently reported suspect drugs in these classes are amoxicillin, carbamazepine, and methylphenidate respectively. No reports meeting the study criteria were received in 2020 for carbamazepine and methylphenidate.

Anticipated study impact

- Health Canada recognizes the need to strengthen information related to paediatric health, as the use of medications to treat children is increasing, and the safety and efficacy of these medications may be significantly different in paediatric patients than in adult patients.[1, 2] The ongoing sharing of safety information through voluntary reporting of ADRs from various sources, such as the CPSP, is valuable to Health Canada as it contributes to ongoing monitoring of the benefit-risk profile of health products used in children and can thus result in the implementation of risk mitigation measures.
- In acknowledgement of the importance of safety information provided by ADR reporting, Health Canada has implemented Vanessa's Law, an amendment to the Food & Drugs Act that requires certain health care institutions to identify and report serious adverse drug reactions and medical device incidents to the federal regulator (for more information, visit: https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting/mandatory-hospital-reporting/education/module-1.html). A key objective of mandatory reporting is to improve the quality and quantity of serious ADR reports, and to expand on the real-world data available to monitor the safety of health products used in children.

Acknowledgements

The assistance of Lynn Macdonald and Heather Morrison is greatly appreciated.

1. Klassen TP, Hartling L, Craig JC, et al. Children are not just small adults: the urgent need for high-quality trial evidence in children. *PLoS Medicine* 2008;5(8):1180-2
2. Abi Khaled L, Ahmad F, Brogan T, et al. Prescription medicine use by one million Canadian children. *Paediatr Child Health* 2003;8(A):6A-56A

COVID-19

Study duration: Ongoing study since April 2020


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Questions

- What is the spectrum of disease, and what are risk factors for severe disease, from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children in Canada?
- What is the spectrum of disease, and what are the clinical features of paediatric inflammatory multisystem syndrome (PIMS)/ multisystem inflammatory syndrome in children (MIS-C) temporally associated with coronavirus disease 2019 (COVID-19)?

Importance

- COVID-19 is caused by SARS-CoV-2, a novel coronavirus that spread rapidly around the world in 2020 causing a global public health emergency. While severe disease in children is less common than in adults and the elderly, the spectrum of acute illness and the comorbid conditions that increase the risk for severe disease, remain poorly understood.
- SARS-CoV-2 has also been associated with a post-infectious hyperinflammatory syndrome referred to as both PIMS and MIS-C. Little is known about this important, but rare, complication of SARS-CoV-2 infection in children. There is an urgent need to refine current diagnostic approaches as well as to better understand the response to current therapies.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/current-studies.

Case definition

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 (C-reactive protein [CRP], erythrocyte sedimentation rate [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
- Obesity
- Congenital heart disease
- Immunocompromising medications (high-dose steroids,* chemotherapy, biologics, immunomodulators)
- Solid organ transplant
- Primary or secondary immunodeficiency
- Sickle cell disease or other chronic hematologic condition
- Tracheostomy
- Inflammatory bowel disease or other chronic gastrointestinal or liver disease
- Asthma
- Chronic lung disease
- Chronic renal disease
- Solid tumor or hematologic malignancy
- Bone marrow transplant
- Chronic neurologic or neurodevelopmental condition
- Diabetes
- Chronic rheumatologic or autoimmune disease
- Genetic/metabolic disease

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

Unique to this study

Unique aspects of this study include three separate case definitions, weekly surveillance using entirely electronic data capture, and the size and scope of the co-investigator team.

Results – April to December 2020

Note: This report includes 2020 cases notified before February 2, 2021.

TABLE 1 – COVID-19 cases from April 1 to December 31, 2020

Reported	Duplicates	Excluded	Pending	Met case definition*
822	109	60	59	594

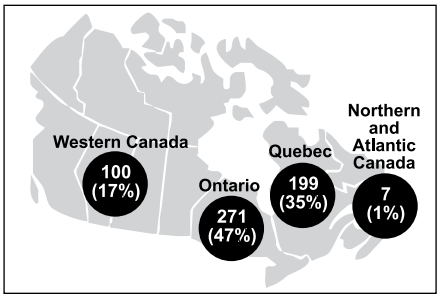
* Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis, unless reported from a centre with project-specific research ethics board approval. Cases reported through the following centres were included in the data analysis for this report: CHU Sainte-Justine, Montreal Children's Hospital, CHU de Sherbrooke, and CHU de Québec-Université Laval and Centre mère-enfant Soleil.

Cases that met the case definition

- In total, 594 cases met at least one study case definition, including 254 cases hospitalized with confirmed SARS-CoV-2 infection, 156 cases hospitalized with PIMS, and 200 non-hospitalized cases with confirmed SARS-CoV-2 infection who either had a chronic comorbid condition or were less than 1 year of age.
- Eight cases simultaneously met the case definitions for hospitalized patients with SARS-CoV-2 infection and PIMS, while another eight cases reported to the PIMS study also retrospectively met the case definition of non-hospitalized patients with SARS-CoV-2 infection.

Demographics

- Hospitalized cases with SARS-CoV-2 infection were most often younger than 1 year of age (94/250; 38%), followed by those 13 to 17 years of age (72/250; 29%).
- Non-hospitalized cases with SARS-CoV-2 infection were most often younger than 1 year of age (104/199; 52%), followed by those 6 to 12 years of age (36/199; 18%).
- PIMS cases were most often 1 to 5 years of age (71/155; 46%), followed by those 6 to 12 years of age (43/155; 28%).
- Across all case definitions, the geographic distribution of cases was as follows: 271/577 (47%) from Ontario, 199/577 (35%) from Quebec, 100/577 (17%) from Western Canada, and 7/577 (1%) from either Atlantic or Northern Canada.



Presentation and diagnosis

- Among the hospitalized cases with SARS-CoV-2 infection, 134/251 (53%) were admitted for care related to symptoms of COVID-19, 103/251 (41%) were admitted for care unrelated to COVID-19, and 14/251 (6%) were admitted for social/humanitarian or infection control purposes.
- The most common symptoms among cases from both acute COVID-19 case definitions were fever (235/390, 60%), cough (148/390, 38%), and runny nose (132/390, 34%).
- The most common clinical features among PIMS/MIS-C cases were rash (119/156; 76%), bilateral bulbar conjunctival injection without exudate (113/156, 72%), and changes in the lips/oral cavity (106/156, 68%).

Treatment and outcomes

- COVID-19 therapies (i.e., biologics, hydroxychloroquine, remdesivir) were administered to 6/254 (2%) of hospitalized cases with SARS-CoV-2 infection.
- The most common treatments for PIMS cases were immunoglobulin (143/156, 92%) and aspirin (136/156, 87%).
- Admission to an intensive care unit was required by 45/246 (18%) hospitalized cases with SARS-CoV-2 infection and 30/153 (20%) hospitalized PIMS cases.
- Some form of respiratory or hemodynamic support was required by 51/254 (20%) hospitalized cases with SARS-CoV-2 infection and 28/156 (18%) hospitalized PIMS cases.
- Across all case definitions, fewer than five children were reported to have died, none of whom had PIMS.

Study limitations

Limitations common to all Canadian Paediatric Surveillance Program studies are listed on page 11.

Conclusions

- Hospitalizations for acute COVID-19 infection in children remain uncommon in Canada, with only 53% of children hospitalized with SARS-CoV-2 infection admitted for care related to COVID-19.
- There were more hospitalized PIMS/MIS-C cases (n=156) than those hospitalized for symptoms of acute COVID-19 (n=134), suggesting that this post-inflammatory syndrome is as important to monitor as acute COVID-19 in children.

Anticipated study impact

These data will inform both clinical care and policy-related decisions about children and COVID-19.

Publication and dissemination

Canadian Paediatric Surveillance Program commentary on hospitalizations from COVID-19 among children in Canada [Internet]. Kakkar F, Moore Hepburn C, Drouin O, Morris SK; on behalf of the Canadian Paediatric Surveillance Program COVID-19 study team. Ottawa: Canadian Paediatric Society; 2020 Sep. Available from: www.cpsp.cps.ca/uploads/publications/CPSP_COVID-19_Commentary_September_2020.pdf

COVID-19, The Road to Recovery: Preliminary Results of the CPSP Study. Morris S, Tam T, Korczak D. Canadian Paediatric Society Virtual Learning Session, in September 2020 (oral presentation and panel discussion)

Acknowledgements

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Frequency and impact of PANDAS/PANS diagnosis

Study duration: December 2019 to November 2021


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Question

What is the frequency and impact of applying the diagnostic label of PANDAS (paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection)/PANS (paediatric acute-onset neuropsychiatric syndrome) in Canadian children?

Importance

- PANDAS/PANS is an acute, debilitating neuropsychiatric syndrome with significant impacts on children, families, and health care utilization.
- There are challenges in the application of the current PANDAS/PANS diagnostic criteria and the true frequency of the diagnosis is unknown.
- Practice patterns related to the clinical assessment and treatment of paediatric patients diagnosed with PANDAS/PANS in Canada are poorly understood.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/current-studies.

Case definition

Any child between the ages of 3 years and 18 years (up to the 18th birthday), seen in the previous month who has received* the diagnostic label of PANDAS or PANS.

* The diagnosis was given by any health care provider (generalist, specialist, subspecialist, allied health care provider, or complementary/alternative health care provider) or a family member.

Unique to this study

- Unlike traditional Canadian Paediatric Surveillance Program (CPSP) studies that identify and examine characteristics associated with a specific and confirmed disease or condition, this study attempts to define the minimum incidence of children who have received the diagnostic label of PANDAS or PANS (as applied by a medical professional or by a family member). It is the diagnostic label, and not the diagnosis, per se, that is under active study.
- This study included targeted outreach to certain specialist/subspecialist groups (including child psychiatrists, paediatric neurologists, and paediatric rheumatologists) as well as specialized clinics known to be referral centres for suspected PANDAS/PANS cases.

Results – December 2019 to December 2020

TABLE 1 – Cases of PANDAS/PANS diagnosis from December 1, 2019 to December 31, 2020

Reported	Duplicates	Excluded	Pending	Met case definition*
21	0	0	0	21

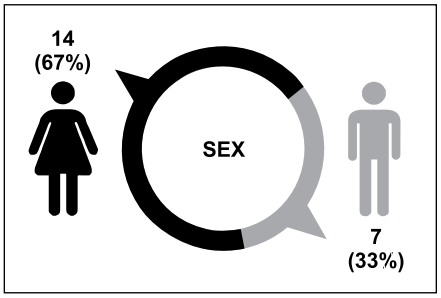
* Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis.

Cases that met the case definition

At the time of analysis, 21 children and youth were verified as meeting the case definition of having received the diagnostic label of PANDAS or PANS from December 1, 2019 to December 31, 2020.

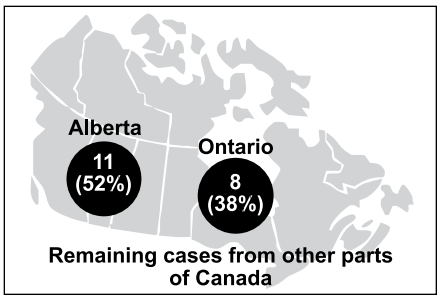
Demographics

- Two thirds (14/21, 67%) of cases were female.
- The mean age of cases was 10 years.
- Most cases were from Alberta (11/21, 52%) and Ontario (8/21, 38%).



Presentation and diagnosis

- Thirteen (62%) cases had one or more pre-existing condition, with the most common being attention-deficit/hyperactivity disorder (7/21, 33%).
- Most cases presented with at least one neurobehavioral (20/21, 95%) or obsessive-compulsive (18/21, 86%) feature or abnormal movement (12/21, 57%).
- The most frequently reported symptoms were anxiety (17/21, 81%), emotional lability (17/21, 81%), irritability (16/21, 76%), tics (12/21, 57%), aggression (11/21, 52%), ordering/list making/rituals (7/21, 33%), and fear of contamination (6/21, 29%).
- In 71% (15/21) of cases, the pace of symptom onset was gradual, with a reported progression from no symptoms to severe symptoms over a period of greater than 48 hours.



Treatment and outcomes

- In the majority of cases, there was no microbiologically confirmed group A streptococcal (GAS) infection or other documented infection, either at symptom onset (13/21, 62%) or at symptom exacerbation (14/21, 67%).
- Two thirds (14/21, 67%) of cases reported having had five or more health care visits since the onset of symptoms and over one third (8/21, 38%) of cases were involved with more than five different health care providers.
- Significant negative impacts were reported in the following domains since symptom onset: new or increased intra-family stress, mental health concerns, or conflict (18/21, 86%); school absences (12/21, 57%); withdrawal from social activities/friends (9/21, 43%); and decline in school achievement (7/21, 33%).
- Despite a minority of cases having microbiologically confirmed GAS infection, antibiotic treatment course for GAS infection (17/21, 81%) and antibiotic prophylaxis for GAS infection (9/21, 43%) were routinely administered.
- The most common anti-inflammatory/immune modulating treatment prescribed was non-steroidal anti-inflammatory drugs (9/21, 43%).
- Psychological treatment and psychotropic medication were provided in 38% (8/21) and 57% (12/21) of cases, respectively.
- Clinicians most often reported feeling “uncertain” about the diagnosis of PANDAS/PANS, while families most commonly reported that they “strongly believed” the diagnosis.

Study limitations

Limitations common to all CPSP studies are listed on page 11.

Conclusions

- There was high health care utilization among patients who received a diagnostic label of PANDAS/PANS, including a significant number of health care visits, diagnostic tests, treatments (including antibiotics in the absence of documented GAS infection), as well as care by multiple health care providers.
- Psychological therapies and psychotropic medications for behavioural or mental health symptoms were not consistently prescribed to patients with a PANDAS/PANS diagnosis.
- Preliminary results suggest a high level of discordance in diagnostic certainty between clinicians and families.

Anticipated study impact

- This study will improve the understanding of how frequently the PANDAS/PANS diagnosis is being applied to children in Canada and will help to describe the clinical features of children receiving the diagnosis and the associated burden for children, families, health care providers, and the health care system.
- Study results will impact awareness, education, and clinical practice related to PANDAS/PANS.

Micronutrient deficiencies and autism spectrum disorder

January 2020 to December 2022

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Question

- In Canadian children and youth with autism spectrum disorder (ASD), what is the minimum incidence of specific micronutrient deficiencies (vitamin A deficiency/xerophthalmia; scurvy; severe, symptomatic vitamin D deficiency; and severe iron deficiency anemia)?
- What clinical characteristics, use of health care services, and health complications are associated with micronutrient deficiencies in Canadian children and youth with ASD?

Importance

- The incidence of micronutrient deficiencies in Canadian children and youth with ASD is unknown.
- Better understanding the burden of serious micronutrient deficiencies in Canadian children and youth with ASD will inform anticipatory guidance, screening, and prevention strategies in this population.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/current-studies.

Case definition

All children and youth less than 18 years of age (up to their 18th birthday) with autism spectrum disorder **AND** a new diagnosis of one or more of the following micronutrient deficiencies:

- Vitamin A deficiency/xerophthalmia
- Scurvy
- Severe, symptomatic vitamin D deficiency
- Severe iron-deficiency anemia

The patient's autism spectrum disorder must have been diagnosed by a general paediatrician, developmental paediatrician, psychiatrist, or psychologist. Definitions for the micronutrient deficiencies and laboratory reference ranges can be found in Appendix 1 of the study protocol.

Results – January to December 2020

TABLE 1 – Micronutrient deficiency and ASD cases in 2020

Reported	Duplicates	Excluded	Pending	Met case definition*
33	1	14	8	10

* Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis.

Cases that met the case definition

- At the time of analysis, 10 children and youth with micronutrient deficiency and ASD were verified as meeting the case definition from January 1, 2020 to December 31, 2020.

- The majority of patients met the case definition for only one of the four micronutrient deficiencies under surveillance; however, some patients had more than one of the deficiencies. Among the 10 patients, there were 14 diagnoses of micronutrient deficiency.
- Of the four specific micronutrient deficiencies under surveillance, scurvy was the most common (8 cases). The other micronutrient deficiencies were reported less frequently (in decreasing order, with no group having more than five cases: severe, symptomatic vitamin D deficiency; severe iron deficiency anemia; and vitamin A deficiency/xerophthalmia).

Demographics

- The majority of patients were male.
- The median age of patients was 8.6 years (range 4.3–12.9 years).
- Most patients (7/10, 70%) were from Ontario, with the remainder from other provinces.

Presentation and diagnosis

- All patients (10/10, 100%) were deemed to have a restricted diet/limited food repertoire. In all cases (10/10, 100%), the reporting physician attributed the restricted diet/limited food repertoire to the patient himself/herself (e.g., picky eater, unwilling to try new foods) rather than other factors (e.g., diagnosed food allergies, parental choice, food insecurity).
- In 89% of patients (8/9), the total number of different foods in the patient's diet was less than 10.
- Half of the patients (5/10, 50%) were reported as being non-verbal (i.e., using no spoken language or only a few spoken words).
- Very few patients had medical conditions other than ASD, and none had food allergies/intolerances diagnosed by a medical professional.
- It was uncommon for patients to be receiving vitamins, herbals and/or supplements at the time of micronutrient deficiency diagnosis.
- Half of the patients (5/10, 50%) had a height and weight measured at the time of micronutrient deficiency diagnosis. Based on the reporting physician's classification of weight status or growth measurements, most patients were of normal/healthy weight (7/9, 78%) and no patients were underweight.
- In 7/10 (70%) patients, the micronutrient deficiency was first diagnosed by a general paediatrician.
- In patients with scurvy, arthralgia/limp/abnormal gait/inability to bear weight was the most common presenting symptom (6/8, 75%).

Treatment and outcomes

- Half of the patients (5/10, 50%) were admitted to hospital due to their micronutrient deficiency, either for investigations leading to diagnosis or for management. The median duration of admission was nine days (range 6–21 days).
- Of the five patients admitted to hospital, the majority underwent an invasive procedure as part of their diagnostic workup (e.g., bone marrow aspiration, general anesthetic for imaging).
- All patients (10/10, 100%) were treated via administration of enteral vitamins.
- No deaths were reported. Other serious, permanent sequelae were very infrequently reported, although the timing of reporting may limit respondents' ability to comment on long-term effects of micronutrient deficiencies.

Study limitations

- Limitations common to all Canadian Paediatric Surveillance Program studies are listed on page 11.
- Given the relatively small number of reported cases and the relatively brief duration of surveillance, these results should be interpreted with caution; this CPSP study will continue until December 2022.

Conclusions

- From January to December 2020, 10 children and youth with ASD were verified as meeting the case definition for one or more of the following: vitamin A deficiency/xerophthalmia; scurvy; severe, symptomatic vitamin D deficiency; or severe iron deficiency anemia.
- These 10 cases of micronutrient deficiency and ASD suggest that:
  - Very restricted diet/limited food repertoire is common in cases of micronutrient deficiency, and this dietary restriction is related to the preferences and choices of the child or youth.
  - Weight status and micronutrient status are not synonymous; a child or youth with a micronutrient deficiency may not be underweight.
  - Hospital admission and invasive investigations are not uncommon in children and youth with ASD and micronutrient deficiency.

Anticipated study impact

- This study is the first to evaluate the incidence of micronutrient deficiencies in Canadian children and youth with ASD.
- Ongoing surveillance will help to identify clinical characteristics, use of health care services, and health complications associated with micronutrient deficiencies in Canadian children and youth with ASD.
- Results will inform anticipatory guidance, screening, and prevention strategies in this population.

Publication and dissemination

'Rare' micronutrient deficiencies may be more common in children with ASD. Kinlin LM. *Canadian Paediatric Society News*, Fall/Winter 2019, page 5. www.cps.ca/uploads/publications/CPSNews%28fall-winter19%29.pdf

Acknowledgements
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Ophthalmia neonatorum caused by *N gonorrhoeae* or *C trachomatis*

Study duration: November 2018 to October 2020 – Final report

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Question

- What is the minimum incidence of ophthalmia neonatorum (ON) caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis* in Canada?
- Do rates of ON caused by *N gonorrhoeae* or *C trachomatis* differ in jurisdictions with mandatory ocular prophylaxis versus those without?

Importance

- ON is neonatal conjunctivitis that occurs within the first month of life. *C trachomatis* and *N gonorrhoeae* have been reported to account for up to 40% and 1% of ON cases respectively, according to the most recent data available from the United States (as of the early 2000s).
- Without preventive measures, gonococcal ophthalmia neonatorum (GON) occurs in 30 to 50% of infants exposed during delivery; without treatment, the disease may progress rapidly and cause severe consequences. Infants born to women with untreated chlamydia infection at delivery have a 30% to 50% risk of developing chlamydial ophthalmia neonatorum (CON).
- Ocular prophylaxis for ON with erythromycin is mandatory in some provinces.
- In 2015, a Canadian Paediatric Society position statement recommended the discontinuation of mandatory ocular prophylaxis for ON because of the questionable efficacy of erythromycin. The position statement advocated for the enhancement of routine sexually transmitted infection (STI) screening and treatment programs for pregnant women and for babies exposed to *N gonorrhoeae* and *C trachomatis* at birth.
- Concerns about the current effectiveness of STI screening and treatment programs for pregnant women include the worry that discontinuation of erythromycin ocular prophylaxis could result in increased rates of GON and CON.
- Gonorrhea and chlamydia infections in children less than 1 year of age are notifiable through the Canadian Notifiable Disease Surveillance System (CNDSS); however, ON is no longer a notifiable disease at the federal level. This has raised concerns about the ability to monitor the effect of changing policies on rates of ON.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/concluded-studies.

Case definition

Any patient less than 28 days of age (4 weeks) at onset of symptoms, with clinical features of ophthalmia neonatorum including at least one of the following:

- Conjunctival/ocular erythema
- Conjunctival/ocular discharge
- Conjunctival and/or peri-ocular swelling

AND

N gonorrhoeae isolated in culture or identified by nucleic acid amplification test in specimens from the eye, blood, CSF, or other sterile site

OR

C trachomatis isolated in culture or identified by nucleic acid amplification test in specimens from the eye, nasopharynx, or other respiratory tract specimen

Exclusion criteria

- Positive microbiology test for *C trachomatis* or *N gonorrhoeae* without any associated clinical abnormality
- Ophthalmia neonatorum associated with another microorganism

Unique to this study

Case numbers will be compared to case numbers collected via the CNDSS.

Results – November 2018 to October 2020

TABLE 1 – ON cases from November 1, 2018 to October 31, 2020

Year	Reported	Duplicates	Excluded	Pending	Met case definition‡
2018*	<5	0	<5	0	<5
2019	9	0	4	0	5
2020†	7	0	<5	0	<5
Total	**19**	**0**	**7**	**0**	**12**

* November 1 to December 31, 2018
† January 1 to October 31, 2020
‡ Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis.

Cases that met the case definition

At the time of analysis, 12 cases of ON were verified as meeting the case definition from November 1, 2018 to October 31, 2020.

Demographics

For the 12 cases, the mean age at onset of symptoms was 10 days (median 9 days, range 2–22 days).

Presentation and diagnosis

- Conjunctival/ocular discharge was present at presentation in all 12 (100%) cases.
- Conjunctival/ocular erythema was present at presentation in 11 (92%) cases.
- Conjunctival and/or peri-ocular swelling was present at presentation in 9 (75%) cases.
- Microbiological specimens were positive (either by culture or by polymerase chain reaction) for *C trachomatis* in 9 (75%) cases.

Policy context and administration of ocular prophylaxis

- Ocular prophylaxis is mandated by law in Ontario, Alberta, and Prince Edward Island; 7 (58%) cases of ON came from these provinces. Nine other provinces/territories have policies recommending, but not mandating, prophylaxis. The 5 (42%) remaining cases were from these jurisdictions.
- Six (50%) cases did not receive ocular prophylaxis with erythromycin ointment at birth. For the remaining 6 (50%) cases, data was either not available or prophylaxis was given as per provincial recommendations.

Prevention, treatment, and outcomes

- Seven of the 12 (58%) cases had maternal STI screening once during pregnancy, either during the first, second, or third trimester of pregnancy. When screening was positive, treatment was given in accordance with established guidelines in all cases.
- All cases of ON reported to the Canadian Paediatric Surveillance Program (CPSP) received optimal treatment as per treatment guidelines.
- There were no reported complications/sequelae, such as corneal ulcers, ocular perforation, or pan ophthalmitis, among the 12 cases.

Study limitations

Limitations common to all CPSP studies are listed on page 11.

Conclusions

- As initially anticipated, the minimum incidence of ON caused by *C trachomatis* was higher than that caused by *N gonorrhoeae*. The minimum incidence rates for ON with laboratory-confirmed *C trachomatis* or *N gonorrhoeae* infection in Canada (excluding Quebec) were 1.56 and 0.52 per 100,000 live births respectively (based on birth statistics for 2018–2019 from Statistics Canada).
- In 2018, the most recent year for which data are available, the CNDSS reported 12 cases of *C trachomatis* infection and 5 cases of *N gonorrhoeae* infection in infants less than one year of age (mean numbers of cases for the preceding five years were 20.6 cases of

C. trachomatis and 3.4 cases of *N gonorrhoeae*). Incidence rates for 2018 were calculated to be 3.22 and 1.34 per 100,000 live births for *C trachomatis* and *N gonorrhoeae* respectively. Lower case numbers were reported to the CPSP than to the CNDSS and the incidence rates calculated from the CPSP data are also lower than those calculated from the CNDSS data. The lower numbers reported to the CPSP are partially explained by the following: the CNDSS data includes all infections from *C trachomatis* and *N gonorrhoeae* (e.g., *C trachomatis* respiratory tract infections), not just ON; the CNDSS data includes data from Quebec; and cases may have been reported to the CNDSS by physicians other than paediatricians.

- Despite existing provincial policies regarding the use of ocular prophylaxis at birth, study findings revealed that half of ON cases did not receive prophylaxis. However, due to the low number of cases, assumptions about policy impact cannot be drawn. It should be noted that there was a shortage of erythromycin ophthalmic ointment for neonatal use throughout the period of this surveillance.

Anticipated study impact

- This study provided valuable clinical and epidemiological information on cases of ON across Canada (except Quebec), as ON is no longer a nationally notifiable disease.
- The number of cases of ON was too low to infer the effect of current neonatal ocular prophylaxis practices on disease rates, as it is a rare disease. Consequently, it is difficult to use these data to inform future clinical recommendations and/or public health policy changes.

Paediatric-onset leukodystrophies

Study duration: December 2019 to November 2022


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Questions

- What is the minimum incidence of paediatric-onset leukodystrophies (LD) in Canada?
- What are the patterns of presentation, clinical features, comorbidities, and diagnostic journeys of children and youth with different types of LD?

Importance

- Determining the minimum incidence of paediatric-onset LD in Canada will provide information that will help with more effective planning of services to children and youth with this condition, and help families and health care practitioners more effectively advocate for this vulnerable group of patients.
- By determining the proportion of children with each specific LD, diagnostic protocols and educational programming can be developed to enhance clinical care.
- This study will be foundational for the development of national and international collaborative studies on the natural history and pathobiology of LD, which will serve as a step towards future therapeutic developments.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/current-studies.

Case definition

All children and youth less than 18 years of age (up to their 18th birthday) with a new diagnosis of a leukodystrophy, defined as a genetically* determined disorder characterized by primary involvement of the white matter. Disorders characterized as leukodystrophies include, but are not limited to, the following (non-exhaustive list):

- Pol-III related disorders (4H syndrome (hypomyelination, hypodontia, and hypogonadotropic hypogonadism))
- 18q minus syndrome
- X-linked adrenoleukodystrophy (X-ALD)
- Adult-onset leukodystrophy with neuroaxonal spheroids and pigmented glia (including hereditary diffuse leukoencephalopathy with spheroids, HDLS, and pigmentary type of orthochromatic leukodystrophy with pigmented glia, POLD)
- Aicardi-Goutières syndrome (AGS)
- Alexander disease (AxD)
- Autosomal dominant leukodystrophy with autonomic disease (ADLD)
- Canavan disease
- Cerebrotendinous xanthomatosis (CTX)
- Chloride ion channel 2 (ClC-2) related leukoencephalopathy with intramyelinic oedema
- eIF2B related disorder (vanishing white matter disease or childhood ataxia with central nervous system hypomyelination (CACH))
- Fucosidosis
- Globoid cell leukodystrophy (Krabbe disease)
- Hypomyelination with atrophy of the basal ganglia and cerebellum (H-ABC)
- Hypomyelination with brainstem and spinal cord involvement and leg spasticity (HBSL)
- Hypomyelination with congenital cataract (HCC)

- Leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL)
- Leukoencephalopathy with thalamus and brainstem involvement and high lactate (LTBL)
- Megalencephalic leukoencephalopathy with subcortical cysts (MLC)
- Metachromatic leukodystrophy (MLD) and its biochemical variants
- Oculodentodigital dysplasia
- Pelizaeus-Merzbacher disease (PMD)
- Pelizaeus-Merzbacher-like disease (PMLD)
- Peroxisomal biogenesis disorders (including Zellweger, neonatal adrenoleukodystrophy, and infantile Refsum)
- Polyglucosan body disease (PGBD)
- RNAse T2 deficient leukoencephalopathy
- Sialic acid storage disorders (Salla disease, infantile sialic acid storage disease and intermediate form)
- Single enzyme deficiencies of peroxisomal fatty acid beta oxidation (including only D-bifunctional protein deficiency; sterol carrier protein X (SCPx) deficiency; peroxisomal acyl-CoA-oxidase deficiency)
- Sjögren-Larsson syndrome
- SOX10-associated PCWH: peripheral demyelinating neuropathy, central dysmyelinating leukodystrophy, Waardenburg syndrome, and Hirschsprung disease

* For information on the availability of and access to genetic testing in your region, refer to the list of study principal investigators/co-investigators at the beginning of the study protocol and contact the one who is located closest to your practice.

Results – December 2019 to December 2020

TABLE 1 – Paediatric-onset leukodystrophy cases from December 1, 2019 to December 31, 2020

Reported	Duplicates	Excluded	Pending	Met case definition*
16	0	0	0	16

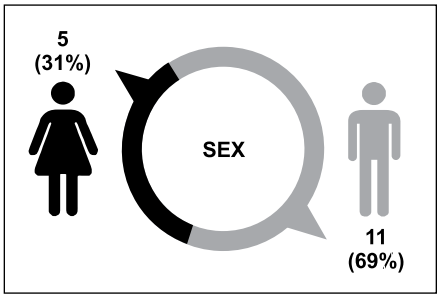
* Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis.

Cases that met the case definition

At the time of analysis, 16 cases of paediatric-onset LD were verified as meeting the case definition from December 1, 2019 to December 31, 2020.

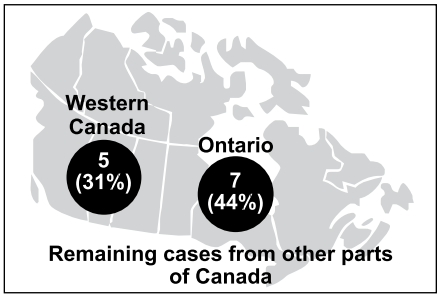
Demographics

- Patient sex was reported as 11 (69%) males and 5 (31%) females.
- The geographic distribution of cases was 7 (44%) from Ontario, 5 (31%) from Western Canada, and the remaining cases from other parts of Canada.



Presentation and diagnosis

- The most common symptoms at presentation included the following: 8 (50%) cases with global developmental delay, 7 (44%) with developmental regression, 6 (38%) with abnormal muscle tone, 6 (38%) with feeding issues, 5 (31%) with seizures, and 5 (31%) with behavioural changes.
- The following LD diagnoses were reported: metachromatic leukodystrophy, globoid cell leukodystrophy (Krabbe disease), Alexander disease, Pelizaeus-Merzbacher disease, X-linked adrenoleukodystrophy, and L-2 hydroxyglutaric acid.
- LD diagnoses were made most frequently via whole exome sequencing (5/16, 31%). The remaining cases were diagnosed using chromosomal microarray, single gene testing, family history, by unknown means, or the diagnosis had not yet been confirmed genetically.
- LD diagnoses were made on average 13.2 (SD 26.6) months after presentation to medical attention.



Treatment and outcomes

- Patients required between 4 to 10 health care providers for their multidisciplinary care.
- Reporting physicians said, in their opinion, the most important challenges to caring for children with leukodystrophies included the following: medical and psychosocial complexity, the need for multiple specialists, a lack of experience with these disorders, access to specialists, and lack of awareness of clinical care guidelines.

Study limitations

- Limitations common to all Canadian Paediatric Surveillance Program studies are listed on page 11.
- Due to COVID-19 restrictions, in-person patient visits and access to diagnostic tests may have been limited.

- The LD diagnoses reported in this study to date represent the classic forms and not the wide range of diagnoses currently known—this may have influenced the time from presentation to medical attention to confirmation of diagnosis. Recognizing that rarer types of LD can take much longer to diagnose than many of the cases in this study, which have classic clinical and magnetic resonance imaging (MRI) presentations, the average time from presentation to medical attention to confirmation of diagnosis of 13 months may be an underestimate.

Conclusions

- Once presenting to medical attention, diagnosis of more common paediatric leukodystrophies takes an average of 13 months. While patients with paediatric-onset LD receive indicated health care services once they present to medical attention, early diagnosis allows for optimal management. Disease-specific treatments (e.g., bone marrow transplant, gene therapy), where available, can be provided once a genetic diagnosis is obtained.
- These conditions continue to be challenging to manage for both the patient and the health care provider due to the patient's medical complexity and the need for multiple subspecialists.

Anticipated study impact

- Study results will assist with developing knowledge translation activities to educate child health care providers about the types of LD, the various presentations, and needs of children with LD. Increasing awareness about the current diagnostic journey of children and youth with LD, may lead to improvements in timely diagnosis and early implementation of potential therapies.
- The collaboration of interested paediatricians and subspecialists from across the country in this study may set the foundation for expanding the Canadian Paediatric Genetically-determined White Matter Diseases Network and creating LD centres of excellence across Canada, in collaboration with health care decision makers. Ultimately, this work may lead to the development of a prospective Canadian LD registry to study longitudinal cohorts and determine natural history, morbidity, and mortality rates of LD.
- Study results could contribute to the development of standardized clinical management guidelines for LD relevant to the Canadian population.

Paediatric pulmonary thromboembolism

Study duration: January 2020 to December 2021

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Questions

- What is the minimum incidence of pulmonary thromboembolism in the Canadian paediatric population and what are the demographics and geographic distribution of cases?
- What are the clinical presentation, risk factors, and short-term outcomes of paediatric pulmonary thromboembolism?
- What diagnostic modalities and therapeutic interventions are chosen by clinicians?

Importance

- Pulmonary thromboembolism is a rare but life-threatening event, with very little known about the epidemiology and presenting characteristics in the paediatric population.
- Variability exists in diagnosis and management.
- Improved knowledge of the incidence, presentation, and risk factors of paediatric pulmonary thromboembolism can help to promote early detection and diagnosis, and to improve management and outcomes for patients.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/current-studies.

Case definition

Any patient up to their 16th birthday with a new diagnosis of confirmed or suspected pulmonary thromboembolism. Pulmonary thromboembolism is defined as in situ thrombus or embolism, including fragments and fat embolism, situated anywhere in the pulmonary arterial circulation from the right ventricle (RV), through the outflow tract, to the peripheral and subsegmental regions of the pulmonary arteries. Report patients including, but not limited to, asymptomatic patients, post-operative patients, pregnant or recently pregnant patients, and deceased patients.

Confirmed pulmonary thromboembolism – patient fulfills one of four criteria:

1. Pulmonary thromboembolism diagnosed on computerized tomography (CT) pulmonary angiography **OR** conventional pulmonary angiography **OR** magnetic resonance imaging/magnetic resonance pulmonary angiography
2. Ventilation–perfusion (V/Q) scan reporting high probability of pulmonary thromboembolism
3. Echocardiogram demonstrating thrombus in the RV **OR** outflow tract **OR** main pulmonary artery/branch pulmonary arteries **OR** in transit
4. Pulmonary thromboembolism identified on autopsy

Suspected pulmonary embolism – patient fulfills one of two criteria:

1. Clinical suspicion of pulmonary thromboembolism **AND** V/Q scan reporting intermediate probability of pulmonary thromboembolism
2. Clinical suspicion of pulmonary thromboembolism **AND** echocardiogram demonstrating RV dysfunction with no other explanation

Results – January to December 2020

TABLE 1 – Paediatric pulmonary thromboembolism cases in 2020

Reported	Duplicates	Excluded	Pending	Met case definition*
17	<5	7	<5	<5

* Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis.

Cases that met the case definition
At the time of analysis, fewer than five cases were verified as meeting the case definition in 2020.

Demographics
As per Canadian Paediatric Surveillance Program (CPSP) policy, case numbers and data for fewer than five cases cannot be presented.

Presentation, diagnosis, treatment, and outcomes
Although specific information on this study cannot be presented at this time due to the small number of cases, existing literature indicates that:

- pulmonary thromboembolism presents with non-specific symptoms, the most common of which are dyspnea, pleuritic chest pain, tachypnea, tachycardia, and hypoxia;
- most cases of pulmonary thromboembolism are associated with the presence of at least one risk factor, including the presence of a central venous catheter and/or deep vein thrombosis. Other factors in combination may pose cumulative risk;
- computerized tomography pulmonary angiogram (CT-PA) is increasingly used for diagnosis; and
- evidence for therapeutic interventions is largely extrapolated from adult data.

Study limitations
- Limitations common to all CPSP studies are listed on page 11.
- This study was limited to patients up to their 16th birthday. An amendment has been accepted by the research ethics board to allow for broadening the case definition to include patients up to their 18th birthday, with retrospective reporting allowed for cases identified since study onset.

Conclusions
More time is required to estimate true minimum incidence rates. A greater number of reported cases will allow for more accuracy in describing presentation, risk factors, diagnostics, treatment, and outcomes.

Anticipated study impact
- This study will provide Canadian-specific data on the epidemiology, presentation, and outcomes of paediatric pulmonary thromboembolism, and how clinicians diagnose and manage this condition.
- This information may be useful for the development of a practice point for clinicians.

Acknowledgements
Thank you to Julien Gallant, Research Coordinator, Department of Paediatric Critical Care, IWK Health Centre for his involvement in this study's start-up, analysis, and reporting.

Serious adverse events related to cannabis used for medical purposes

Study duration: December 2019 to November 2022

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Questions

- What are the clinical characteristics of serious adverse events (SAEs) related to cannabis used for medical purposes in children, including indications for use and concomitant medications?
- How were SAEs associated with intentional cannabis exposure identified and managed?
- What are the outcomes following SAEs related to authorized and unauthorized cannabinoid or cannabis used for medical purposes in Canadian children and adolescents?

Importance

- While Health Canada has not approved any product containing cannabinoids for use by children or youth, medical cannabis is currently used for a variety of conditions, including nausea and vomiting in children with cancer, drug-resistant seizure disorders, and refractory spasticity.
- There is little real-world data on SAEs in Canadian children using cannabis products for medical/therapeutic purposes and limited knowledge about what products, indications, and adverse events are associated with paediatric cannabinoid use.
- There is also limited scientific evidence on the clinical characteristics, management, and outcomes following SAEs in children and youth exposed to medical cannabis.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/current-studies.

Case definition

Any serious or life-threatening adverse event* in a child up to 18 years of age related to the intentional use of cannabis for medical purposes.† Report an adverse event even if there is not certainty it is related to the use of cannabis. Include any cannabis product from a licensed producer or private producer (home grown) such as dried cannabis to be smoked or vaporized, oils to be ingested or applied topically, and cannabis products taken by any other route of administration.

* A serious or life-threatening adverse event is defined as a noxious and unintended severe response to a drug which occurs at any dose and results in emergency observation, hospitalization, persistent or significant disability, or death.

† Cannabinoids or cannabis used for medical purposes is defined as intentional cannabis use for any self-reported (or parent reported) health reasons, with or without physician authorization.

Exclusion criteria

- Adverse events resulting from recreational cannabinoid/cannabis use
- Adverse events resulting from accidental/unintentional cannabinoid/cannabis exposure (even if being used medicinally by another individual in the home)

Results – December 2019 to December 2020

TABLE 1 – SAEs related to cannabis used for medical purposes cases from December 1, 2019 to December 31, 2020				
Reported	**Duplicates**	**Excluded**	**Pending**	**Met case definition***
<5	0	0	0	<5

* Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis.

Cases that met the case definition

Fewer than five cases were verified as meeting the case definition in Canada from December 1, 2019 to December 31, 2020.

Demographics

As per Canadian Paediatric Surveillance Program (CPSP) policy, case numbers and data for fewer than five cases cannot be presented.

Presentation, diagnosis, treatment, and outcomes

Specific information on this study cannot be presented due to the small number of cases.

Study limitations

Limitations common to all CPSP studies are listed on page 11.

Conclusions

- Fewer than five cases were reported and verified as meeting the case definition in the first 13 months of this CPSP study.
- This study will continue until November 2022 and case reporting will be encouraged and promoted on social media via the Canadian Paediatric Society and the Canadian Childhood Cannabinoids Clinical Trials (C4T).

Anticipated study impact

- This study will provide Canadian-specific paediatric data on the clinical characteristics, management, and outcomes of patients following SAEs related to authorized and unauthorized cannabinoid or cannabis used for medical purposes.
- The information from this study will be shared directly with Health Canada and may be adapted for professional and public education materials.

Acknowledgements

The investigators would like to thank the physicians who reported cases for this study.

Serious and life-threatening events associated with non-medical (recreational) cannabis use in Canadian children and youth

Study duration: September 2018 to August 2022

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Question

- What is the minimum incidence of serious and life-threatening events associated with non-medical cannabis use in Canadian children and youth?
- What are the clinical presentations and associated medical needs of children and youth presenting with serious and life-threatening events related to non-medical cannabis exposure?
- Are there changes in the incidence of serious and life-threatening events during the four-year period following cannabis legalization?

Importance

- There is currently limited scientific data quantifying the impact of cannabis legalization on the health of Canadian children and youth.
- Data provided by this study will be used to assess the health impacts of cannabis legalization in the paediatric population.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/current-studies.

Case definition

Any child or adolescent less than 18 years of age (up to the 18th birthday) presenting with a new health condition or a deteriorating chronic/previously diagnosed condition resulting in either hospitalization (inpatient, intensive care unit, psychiatric), permanent disability, or death, which was likely primarily caused by the use of cannabis for non-medical (recreational) purposes.

This includes either intentional or unintentional exposure to cannabis in a child or adolescent, or a condition resulting from use by another individual, such as a friend or a parent/caregiver, who is under the influence of cannabis.

Exclusion criteria

- A condition resulting from cannabis use for non-medical purposes during pregnancy/breastfeeding
- A condition resulting from cannabis use for medical purposes

Results – January to December 2020

TABLE 1 – Serious and life-threatening events associated with non-medical cannabis use cases in 2020

Reported	Duplicates	Excluded	Pending	Met case definition*
78	2	16	12	48

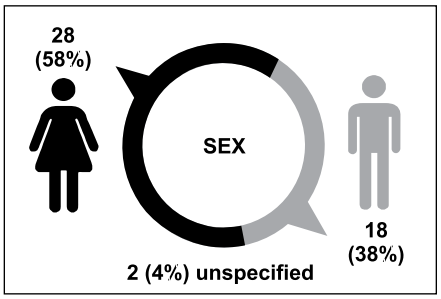
* Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis.

Cases that met the case definition

- In total, 78 cases of recreational cannabis-related exposure were reported through the Canadian Paediatric Surveillance Program (CPSP) in 2020.
- At the time of analysis, 48 cases of serious and life-threatening events associated with non-medical cannabis use were verified as meeting the case definition in 2020. In comparison, 11 cases met the case definition from September to December 2018, and 36 cases met the case definition in 2019.

Demographics

- Patient sex was female in 28 (58%, 95 CI 44–72) cases, male in 18 (38%, 95 CI 25–52) cases, and in 2 (4%, 95 CI 1–16) cases sex was not indicated.
- The mean age was 5.7 years with a median of 4.6 years. The majority of cases were 12 years of age and younger (42/48, 88%).



Presentation and diagnosis

- The most common primary case presentation was poisoning/intoxication due to unintentional cannabis exposure (28/48, 58%, 95 CI 44–72). The majority of these cases (25/48, 52%, 95 CI 38–66) were 12 years and younger and had ingested edible cannabis products. Cannabis-infused gummies were, by far, the most mentioned edible product ingested.
- Other case presentations included cannabis use disorder (DSM-5) (15/48, 31%, 95 CI 19–46), neurologic problems (9/48, 19%, 95 CI 10–33), and gastrointestinal problems including cannabis hyperemesis syndrome (6/48, 13%, 95 CI 6–26). Eleven cases (23%, 95 CI 13–37) reported more than one primary presenting condition.
- Seventy-one percent of all cases, regardless of age, had ingested cannabis in the form of edible products (34/48, 71%, 95 CI 56–82). In almost one third of these cases, the cannabis products were reported to have been acquired from a legal source (11/34, 32%).
- Consistent with data from previous years, in the majority of cases the source of cannabis was unknown by the reporting physician (29/48, 60%, 95 CI 46–74).

Treatment and outcomes

- The vast majority of cases were hospitalized (47/48, 98%, 95 CI 86–100): 40/48 cases (83%, 95% CI 69–92) were admitted as inpatients, 6/48 cases (13%, 95% CI 6–26) were admitted to the intensive care unit, and for one case this information was missing.
- Physical treatment was received by 30 cases (63%, 95% CI 48–75) in the form of ventilation assistance, intravenous fluids, etc. Fourteen cases (29%, 95% CI 18–44) received mental health treatment (e.g., psychiatry consultation, referral to a social worker), either exclusively or in addition to physical treatment.

Study limitations

Limitations common to all CPSP studies are listed on page 11.

Conclusions

- Serious and life-threatening events associated with non-medical cannabis use are occurring among children and youth in Canada, with 48 cases reported in 2020. More than two thirds (71%) of these cases had ingested cannabis in the form of edible products.
- Over half (52%) of reported cases were 12 years of age or younger with unintentional injury due to accidental ingestion of cannabis edibles. This trend will be monitored as the study continues, especially in light of the recent legalization of cannabis edible products in Canada (October 2019).
- More time is required to determine the impact of the new legislation, and specifically the new regulations associated with edible cannabis products, since edible products did not become available for purchase through the legal market until late December 2019.

Anticipated study impact

- This study will provide Canadian-specific data on the impact of cannabis legalization on the health and well-being of children and youth. This data may be used to inform public policies and additional and/or revised regulations related to non-medical cannabis.
- The information from this study may be adapted for public education materials.

Acknowledgements

Thank you to Anna-Maria Frescura, Health Canada, for her involvement in the analysis of the data relating to this project and the writing of this preliminary report.

Severe obesity and global developmental delay in preschool children

Study duration: February 2018 to January 2020 – Final report

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Questions

- What is the minimum incidence of severe obesity (SO) and global developmental delay (GDD) in preschool children in Canada?
- What are the age of onset, risk factors, and health care utilization associated with SO and GDD in Canadian preschoolers?

Importance

- To date, no Canadian studies have examined comorbid SO and GDD in children.
- Understanding the incidence and risk factors of SO and GDD is necessary to develop effective management strategies and inform health system planning.

Methodology

The complete protocol can be accessed at www.cpsp.cps.ca/surveillance/concluded-studies.

Case definition

Any new case of a child ≤5 years of age with:

1. Severe obesity, defined as body mass index (BMI) ≥99.9th percentile according to references developed by the World Health Organization and the Canadian Pediatric Endocrine Group. The absolute cut-offs by age and sex can be accessed in the study protocol at www.cpsp.cps.ca/surveillance/concluded-studies.

   AND

2. Global developmental delay, defined as a significant delay in two or more developmental domains, including: Gross motor, Fine motor, Speech/language, Cognitive, Social/personal, Delay in activities of daily living

Unique to this study

An infographic was created to raise awareness of the study and was disseminated through existing research and clinical networks (e.g., Team to Address Bariatric Care in Canadian Children, Women and Children's Health Research Institute, Maternal Infant Child and Youth Research Network). The infographic was designed to encourage Canadian Paediatric Surveillance Program (CPSP) participants to report cases meeting the case definition.

Results – February 2018 to January 2020

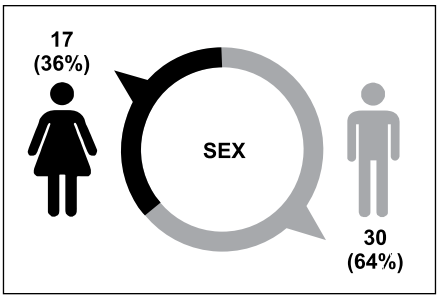
TABLE 1 – SO and GDD cases from February 1, 2018 to January 31, 2020

Year	Reported	Duplicates	Excluded	Pending	Met case definition‡
2018*	39	1	20	0	18
2019	49	2	19	0	28
2020†	<5	0	0	0	<5
Total	**89**	**3**	**39**	**0**	**47**

* February 1 to December 31, 2018
† January 1 to 31, 2020
‡ Due to Quebec legislation, any cases notified by Quebec participants were counted in the Reported column, but detailed case information was not collected and these cases were excluded from the data analysis.

Cases that met the case definition

In total, 47 cases of comorbid SO and GDD were verified as meeting the case definition from February 1, 2018 to January 31, 2020.



Demographics

- Patient sex was male in 30 (64%) cases and female in 17 (36%) cases.
- The mean age of the cases was 3.5 years (SD=1.2).
- The geographic distribution of cases was: 22 (47%) from Ontario and the remaining cases were from various other provinces.

Presentation and diagnosis

- Cases had a mean BMI z-score of 7.2 (SD=3.6).
- The majority of cases presented with at least three significant delays in the defined domains and the mean age of GDD diagnosis was 2.7 years (SD=1.4).
- The mean age of first weight concern was 2.5 years (SD=1.3).
- Health problems included snoring and/or sleep apnea (20/47, 43%), school and/or behavioural problems (17/47, 36%), and asthma or recurrent wheezing (10/47, 21%). In 34% (16/47) of cases, the patient also had a diagnosis of autism spectrum disorder.
- Genetic tests were ordered for 30 (64%) cases, including 27 (57%) microarrays.
- Central nervous system imaging was ordered for 12 (26%) cases.

Treatment and outcomes

- The most common reporting physician's role was consulting paediatrician in 22 (47%) cases.
- Other clinicians/services involved in patient care included: general paediatricians in 39 (83%) cases and family physicians in 32 (68%) cases; dietitians in 35 (75%) cases; and speech therapists in 33 (70%) cases.
- The biggest challenges reported in supporting children with SO and GDD included family dynamics and difficulties accessing appropriate services and resources.

Study limitations

Limitations common to all CPSP studies are listed on page 11.

Conclusions

- The minimum incidence of SO and GDD was 3.3 cases per 100,000 children aged 5 years and under per year, which is likely an underestimate.
- The age of onset for weight concerns and GDD diagnosis was between 2.5 to 2.7 years of age.
- Genetic testing, including microarray, was ordered in most cases, which is consistent with current guidelines.
- Multidisciplinary services were provided often; however, difficulties accessing services and resources were perceived to be a challenge that had a negative impact on health service delivery.

Anticipated study impact

- This study is the first to report the minimum incidence of SO and GDD in preschool children in Canada.
- The study helped to identify patient demographics, age of onset, risk factors, and health care service use associated with SO and GDD.
- Results will be used to promote early recognition and treatment of comorbid conditions and improve paediatric providers' awareness of SO and GDD among Canadian preschoolers.

Publication and dissemination

Severe obesity and global developmental delay in preschool children: Findings from a Canadian Paediatric Surveillance Program study. Gehring ND, Ball GDC, Bélanger S, Bridger T, Chanoine JP, Gibson WT, Hadjiyannakis S, Haines J, Hamilton J, Haqq A, Henderson M, Ho J, Irvine B, Legault L, Luca P, Maguire J, McPherson A, Morrison K, Wahi G, Weksberg R, Zwaigenbaum L, Birken CS. University of Alberta's Pediatric Research Day, virtually, in April 2021 (poster presentation)

Severe obesity and global developmental delay in preschool children: preliminary findings from a Canadian Paediatric Surveillance Program study. Gehring ND, Ball GDC, Bélanger S, Bridger T, Chanoine JP, Gibson WT, Hadjiyannakis S, Haines J, Hamilton J, Haqq A, Henderson M, Ho J, Irvine B, Legault L, Luca P, Maguire J, McPherson A, Morrison K, Wahi G, Weksberg R, Zwaigenbaum L, Birken CS. 8th Conference on Recent Advances in the Prevention & Treatment of Childhood and Adolescent Obesity, virtually, in October 2020 (poster and oral presentation)

Acknowledgements

We wish to thank Nicole Gehring (University of Alberta) for all of her work leading the day-to-day activities for this study.

One-Time Surveys

Interim Federal Health Program

January 2020

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Questions

- What is the current understanding of, and utilization by, Canadian paediatricians of the Interim Federal Health Program (IFHP)?
- Is there an association between physician demographics and IFHP registration and knowledge of the program?

Importance

- Refugee and refugee claimant children in Canada are entitled to health insurance coverage under the IFHP.
- Providers have reported limited understanding of who and what is covered by the IFHP as well as challenges with reimbursement and registration.
- While coverage for medical and allied health services should be provided under the IFHP, there is concern that eligible children may not be accessing necessary services because of lack of registered IFHP providers or limited provider understanding.

Methodology

A one-time survey was sent to paediatricians and paediatric subspecialists through the Canadian Paediatric Surveillance Program (CPSP). The survey tool can be accessed at www.cpsp.cps.ca/surveillance/one-time-surveys.

Unique to this survey

The survey tool was reviewed by Immigration, Refugees and Citizenship Canada prior to its circulation to CPSP participants.

Results

- The survey response rate was 37% (1006/2753).
- All odds ratios were adjusted for specialty (general versus subspecialist), province, living in a large urban centre (Vancouver, Calgary, Edmonton, Winnipeg, Toronto, Ottawa, or Montreal), practice setting (academic hospital, community hospital, or private office), number of IFHP-eligible patients seen, and registration status.

Who provided care to IFHP-covered patients?

- Just over half of respondents (52%, 526/1006) had provided care to IFHP-eligible patients in the previous six months. Of those, the majority had provided care to between 0 to 5 patients (58%, 303/526) or 6 to 19 patients (27%, 140/526).
- The majority of those who had provided care to IFHP-eligible patients were in Ontario (46%, 241/526) and Quebec (23%, 119/526).

What factors were associated with being a registered IFHP provider?

- Of the 526 respondents who had provided care to refugee or refugee claimant children and adolescents in the previous six months, only 139 (26%) were registered IFHP providers.
- After odds ratio adjustment, providers practising outside of Ontario had lower odds of being registered compared to those in Ontario (Quebec OR 0.49, 95% CI 0.28–0.85; Prairies OR 0.43, 95% CI 0.22–0.84; and British Columbia OR 0.10, 95% CI 0.13–0.79).

- Providers in academic teaching hospitals had lower odds of being a registered IFHP provider compared to those not in academic teaching hospitals (OR 0.51, 95% CI 0.27–0.97).
- Living in a large urban centre (Vancouver, Calgary, Edmonton, Winnipeg, Toronto, Ottawa, or Montreal) was not associated with registration status.
- Of those respondents who were not registered, 70% (188/268) indicated that they did not know they had to register, and 30% (79/268) did not know how to register.
- Of those with unknown registration status, 69% (81/118) indicated they provided care to refugee or refugee claimant children and adolescents regardless of their registration status and 25% (30/118) indicated they were compensated for the care they provide to IFHP-eligible patients regardless of their registration status.

What factors were associated with knowledge about services covered by the IFHP?

- Only 10% (52/526) of those who had provided care to IFHP-eligible patients in the previous six months could identify all six services eligible for coverage under the IFHP.
- None of the following factors had any significant association with knowledge of the IFHP: specialty, years in practice, practice location (academic hospital, community hospital, and private office), practice in a large urban centre, and number of IFHP-eligible patients seen.
- After adjustment, knowledge of IFHP-covered services was associated only with registration status (OR 1.92, 95% CI 1.09–3.37).

Survey limitations

- Limitations common to all CPSP studies are listed on page 11.
- Social desirability bias may have contributed to participants over-reporting their registration status and knowledge.

Conclusions

Registration rates for the IFHP are low and understanding of the program is poor amongst Canadian paediatricians. This remains true even amongst paediatricians who have recently provided care to IFHP-eligible patients.

Anticipated survey impact

- Upon study publication, the results of this survey will be used to advocate for increased IFHP registration rates among paediatric providers with an eye to improving health care access for eligible patients.
- Survey results will be communicated with stakeholders including Immigration, Refugees and Citizenship Canada, residency programs, and the Canadian Paediatric Society.

Publication and dissemination

Interim Federal Health Program (IFHP): Survey of access and utilization by pediatric health care providers. Leps C, Monteiro J, Suleman S. Canadian Paediatric Society Annual Conference, virtually, in June 2021 (poster presentation)

Acknowledgements
Thank you to the CPSP for survey funding via the Resident Surveillance Grant.

Maintenance of Certification Section 3 Credit Case Vignettes

Note: Multiple choice questions for these Maintenance of Certification (MOC) Section 3 case vignettes will be available in the fall of 2021 via the Canadian Paediatric Society's online learning portal, Pedagogy. For more information on Pedagogy visit www.cps.ca/en/ecme.

References: Available upon request from the Canadian Paediatric Surveillance Program

5q spinal muscular atrophy

Jean K. Mah, MD, Pediatric Neurology, University of Calgary, Alberta Children's Hospital

Clinical case

A 2.5-month-old boy presents to a paediatric neurologist after being referred by his family physician for hypotonia and muscle weakness. He was born at term after an unremarkable pregnancy, with a birth weight of 3.2 kg. He went home on the second day after birth with no feeding or breathing issues. His check-up at 6 weeks of life was remarkable for decreased central and peripheral tone and a significant head lag. Currently he smiles, coos, fixes, and follows. He remains breastfed and receives vitamin D daily. His first immunization went well. Family history is unremarkable.

On exam, the patient appears alert, with normal growth parameters for age, and stable vital signs. He has no birthmark, dysmorphic features, murmurs, lymphadenopathy, or organomegaly. His chest is clear and his spine is normal. Cranial nerves II to XII appear intact; he has no ptosis, strabismus, or fasciculation. Motor exam reveals prominent head lag and slip-through on vertical suspension. He has reduced spontaneous movement in his lower extremities more than upper extremities due to diffuse weakness, with decreased muscle bulk. Deep reflexes are absent throughout, with up-going plantar responses. Primitive reflexes, including root, suck, and grasp, are weakly present; he has no Moro or Gallant response. He withdraws from tactile stimulation.

Recent investigations, including a complete blood count, serum electrolytes, glucose, creatinine, liver enzymes, creatine kinase, and thyroid stimulating hormone, were normal. An expedited molecular genetic test confirms a diagnosis of spinal muscular atrophy (SMA) type 1, with homozygous deletion of exon 7 and 8 of *SMN1*, and 2 copies of *SMN2*.

What a clinician needs to know

Presentation and diagnosis

SMA is a severe neuromuscular disease associated with progressive muscle atrophy and paralysis. A known autosomal recessive disorder, most cases are due to homozygous deletions of the *SMN1* gene on chromosome 5q11-13 that encodes for the survival motor neuron (SMN) protein. Having higher copy numbers of a nearby *SMN2* gene is associated with a milder phenotype, as it can express some (~10%) of the full-length SMN protein that is essential for diverse cellular functions.

SMA is subdivided into several clinical subtypes based on the age of symptom onset and the maximum attainable gross motor function. Type 1 SMA constitutes approximately 60% of all SMA at birth, followed by type 2 (30%), and type 3 (10%). Infantile-onset SMA (type 1, non-sitters) presents before 6 months of age with hypotonia, muscle weakness, and paradoxical breathing pattern due to involvement of the intercostal muscles; progressive bulbar and respiratory insufficiency leads to death before the second birthday if untreated. Similarly, children with type 2 (sitters, non-walkers) and type 3 (walkers) SMA have hypotonia and proximal weakness leading to delayed motor milestones, with less bulbar and respiratory involvement. All types of SMA are associated with significant disability as well as increased burden of care for the family and high economic costs for society.

SMA should be suspected in any bright and alert infant/child with motor developmental delay and lower motor neuron signs on exam, including hypotonia, symmetrical weakness, muscle wasting, and reduced or absent deep tendon reflexes. Molecular genetic testing is the recommended first line of investigation; the absence of both *SMN1 copies* provides diagnostic confirmation of SMA.

Other causes of lower motor neuron weakness should be excluded based on a careful history and physical exam. Additional investigations such as electromyography/nerve conduction study, serum creatine kinase, and a neuromuscular gene panel may be

required to rule out genetic or acquired disorders such as myopathies, muscular dystrophies, neuropathies, neuromuscular junction transmission defects, or other motor neuron diseases.

Prevention, treatment, and management

Early recognition of clinical manifestations and diagnosis of SMA are critical for timely access to new disease-modifying treatments. For children with suspected SMA, an urgent paediatric neurology referral is recommended to expedite genetic testing and a treatment plan. Referral to a genetics clinic is essential for family counselling. Regular follow-up by a multidisciplinary program, including both physical therapy and respiratory therapy, is essential to ensure optimal outcomes. Respiratory management is especially important for children with early-onset SMA. Pulmonary care should be proactive, and should include therapies to optimize airway clearance and respiratory function. Updated standard of care recommendations for SMA are available to inform care and management of affected individuals.[1, 2]

Recently, several SMA therapies have been approved by Health Canada, including the following: a) nusinersen, an antisense oligonucleotide given intrathecally to modify *SMN2* splicing and increase survival motor neuron (SMN) protein; b) onasemnogene abeparvovec, an adeno-associated virus vector-based *SMN1* gene therapy, given as a one-time intravenous infusion; and c) risdiplam, an oral *SMN2* splicing modulator. Notably, the best outcomes, with normal or nearly normal motor function, are achieved when treatments are given to infants before the onset of symptoms. Population-based newborn screening programs based on validated molecular methods have been shown to be reliable and effective in enabling pre-symptomatic diagnosis and early treatment of infants with SMA. Newborn screening for SMA is currently available in Ontario; other provinces will hopefully follow as part of a national newborn screening strategy.

1. Mercuri E, Finkel RS, Muntoni F, Wirth B, Montes J, Main M, et al. Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. Neuromuscul Disord 2018;28(2):103–15
2. Finkel RS, Mercuri E, Meyer OH, Simonds AK, Schroth MK, Graham RJ, et al. Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics. Neuromuscul Disord 2018;28(3):197–207

Mandatory reporting of serious adverse drug reactions and medical device incidents by hospitals

Sally Pepper, BScPhm, RPh, Patient Safety Section, Marketed Health Products Directorate, Health Canada

Clinical case

A 10-year-old girl is undergoing treatment at a paediatric hospital for a pulmonary exacerbation of cystic fibrosis. She has been prescribed a 14-day course of piperacillin/tazobactam and tobramycin. Complete blood count (CBC) is normal at initiation of therapy. On day five of therapy, a drop in platelets is noted from 210 x 10^9/L on the previous day to 181 x 10^9/L. Over the next few days, the platelet count continues to fall (145 x 10^9/L on day six, 80 x 10^9/L on day eight, 57 x 10^9/L on day nine, and 23 x 10^9/L on day 10). Over the same period, the patient also experiences a drop in hemoglobin and white blood cells, with respective nadirs of 69 g/L and 3.9 x 10^9/L. Therapy is stopped 10 days after initiating the antibiotics. She receives treatment with platelets and a packed red blood cell (RBC) transfusion. The patient's stay in hospital is prolonged until the laboratory values return to normal. An adverse drug reaction (ADR) to piperacillin/tazobactam and tobramycin is suspected.

What a clinician needs to know

As part of regulatory amendments to the *Food and Drugs Act*, new measures were introduced by the federal government to improve Health Canada's ability to collect post-market safety information and to facilitate appropriate action when a serious risk to health is identified. The *Protecting Canadians from Unsafe Drugs Act*, more commonly known as Vanessa's Law, grants Health Canada new powers including the requirement for mandatory reporting of serious ADRs and medical device incidents (MDIs) by health care institutions. The mandatory reporting requirement came into effect on December 16, 2019.

Mandatory reporting of serious ADRs and MDIs by hospitals provides critical safety information, augmenting the mandatory reporting by manufacturers and the multiple voluntary reporting systems already in place to support safety monitoring after a drug or medical device receives market authorization in Canada. These reports are an important source of data for identifying emerging safety issues or for further characterization of known risks. The reports may provide information for shared learning, including warnings and advisories that Health Canada publishes for health care providers and patients. They may also contribute to the improvement of the safety of products through risk mitigation activities such as changes to the product monograph or recalls.

Who is required to report?

The mandatory reporting regulations apply to all hospitals. Outpatient clinics, if they are legally part of the hospital, even if physically separate from the hospital, are also included. Clinics that are not legally part of a hospital are not subject to the regulations. Health care sites and organizations that are outside the scope of the definition of a hospital, including private clinics or long-term care facilities (e.g., nursing homes), should continue to report on a voluntary basis.

How can individual physicians participate in ADR and MDI reporting?

Individual health care providers should continue to report ADRs and MDIs on a voluntary basis to Health Canada at www.health.gc.ca/medeffect. Serious ADRs should also be reported by participants of the Canadian Paediatric Surveillance Program through their monthly reporting form (www.cpsp.cps.ca/uploads/studies/adverse-drug-reactions-protocol.pdf).

What is a serious ADR and what is an MDI?

A serious ADR is a noxious and unintended response to a drug that occurs at any dose and that:

- requires inpatient hospitalization or prolongation of existing hospitalization,
- causes congenital malformation,
- results in persistent or significant disability or incapacity,
- is life-threatening, or
- results in death.

ADRs that require intervention to prevent any of the outcomes listed in the above definition would also be considered serious. Examples of such events include treatment in an emergency room for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

An MDI is an incident related to a failure of a medical device or a deterioration in its effectiveness, or any inadequacy in its labelling or in its directions for use that has led to the death or a serious deterioration in the state of health of a patient, user, or other person, or could do so were it to recur.

Hospitals are not required to establish causality between the drug or medical device and the event; the information to be submitted by the hospital to Health Canada only needs to represent the suspicions of a health care professional that a serious ADR or MDI has been observed. The same is true for individual health care providers. Physicians should report any suspected ADR or MDI, even if they are not certain if the product or medical device caused the adverse reaction, or if some of the reporting details are not available.

What products are in the scope of these regulations?
The mandatory reporting requirements for hospitals apply to therapeutic products, including:
- Pharmaceuticals (prescription and non-prescription drugs)
- Biologic drugs (biotechnology products, blood products with a Drug Identification Number, plasma proteins, and certain vaccines)
- Radiopharmaceutical drugs
- Disinfectants
- Medical devices
- Drugs for an urgent public health need

The term medical device covers a wide range of health and/or medical instruments used in the treatment, mitigation, diagnosis or prevention of a disease or abnormal physical condition.

Medical devices are classified into Class I (lowest risk) to Class IV (highest risk) and all classes are included in mandatory reporting by hospitals. Examples are:
- Class I – hospital beds, wheelchairs, leg prostheses
- Class II – infusion sets, syringes, tracheostomy tubes, urethral catheters
- Class III – infusion pumps, anesthesia gas machines, intrauterine devices
- Class IV – pacemakers, defibrillators, breast implants, bone grafts

Hospitals are not required to report on:
- Semen and ova
- Cells, tissues, and organs
- Blood and blood components
- Vaccines used under a routine immunization program of a province or territory
- Natural health products
- Cannabis
- Drugs and devices used under the Special Access Program for drugs, for clinical trials, or investigational testing for medical devices

When must hospitals report?
The regulations require hospitals to report serious ADRs or MDIs in writing to Health Canada within 30 calendar days of first documentation of the serious ADR or MDI within the hospital.

Information "within the control of the hospital"
The regulations require hospitals to report all documented serious ADRs and MDIs where the required information is within the control of the hospital. Information that is within the control of the hospital is information that would be reasonably accessible within the hospital. While hospitals should take all reasonable steps to retrieve the required information to complete as thorough a report as possible, there is no requirement to do further investigation to obtain the information. Clinicians may choose to inform the patient and/or family that the ADR or MDI will be reported to Health Canada.

Tips for recognizing a serious ADR or MDI
Serious harm from a drug or from a medical device can be mistaken for a symptom of a disease, or a sign of disease progression. A high level of suspicion, clinical awareness, and patient dialogue are key components in identifying a serious ADR or MDI. Consider a serious ADR or MDI if there is:
- an unexpected change in the patient's clinical condition,
- a new health problem for the patient,
- a need for urgent additional therapies, procedures, or surgeries,
- a sudden need for a rescue drug (e.g., naloxone, epinephrine, glucagon), or
- a medical order for an acute change to therapy (e.g., abrupt discontinuation).

In this clinical vignette, is the hospital required to report?
Yes, the hospital is required to report the events of thrombocytopenia, leukopenia, and low hemoglobin suspected to be associated with the use of piperacillin/tazobactam and tobramycin in the case of the 10-year-old child. The hospital must report because the:
- Event required administration of platelets and packed RBCs to prevent life-threatening harm
- Event was associated with the prolongation of the hospitalization
- ADR meets the criteria for "serious"

Submitting reports to Health Canada
The reporting forms for serious ADRs and MDIs, together with instructions and additional information on mandatory reporting, are available on the Health Canada website:
- Serious ADR reporting form
- MDI reporting form

Micronutrient deficiencies and autism spectrum disorder

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Clinical cases

Case 1: An 8-year-old boy with autism spectrum disorder (ASD) presents to the emergency department with eye complaints in the absence of antecedent trauma. He is non-verbal but his parents perceive that he has had bilateral eye pain and decreased visual acuity for two weeks.

On exam by an ophthalmologist, there is xerosis (dryness) of the cornea and conjunctiva, with a foamy patch of conjunctiva consistent with a Bitot's spot. Visual acuity is hand motion only. Based on ophthalmologic findings, the patient is diagnosed with xerophthalmia. Vitamin A deficiency is confirmed when serum vitamin A level is reported (0.1 mcmol/L). The patient's diet consists almost exclusively of carbohydrates and chicken nuggets, with no fruits or vegetables. His vitamin A deficiency and xerophthalmia are attributed to inadequate vitamin A intake. Treatment is initiated based on World Health Organization guidelines.

Case 2: A 4-year-old boy with ASD is seen in an outpatient paediatric clinic because of food selectivity. His diet consists of cow's milk (950 ml daily) and fruit purees. He refuses meat and has essentially no intake of iron-rich foods. He has been accepting a children's multivitamin daily.

On examination, the patient's height and weight plot at the 40th and 30th percentiles, respectively. There is no tachycardia, hypotension, or other signs of hemodynamic instability. General physical exam is unremarkable. A microcytic anemia is identified on blood work (hemoglobin 72 g/L, mean corpuscular volume 52 fL). Hypochromia, microcytosis, polychromasia, and mild pencil forms are found on blood smear. Ferritin is 4 mcg/L. C-reactive protein (CRP) is not elevated. A ferrous iron preparation is started for treatment of severe iron-deficiency anemia. The boy's parents are counselled about reducing cow's milk intake and encouraging iron-rich foods.

What a clinician needs to know

Food refusal, limited dietary repertoire, and high-frequency single food intake are common in children and youth with ASD. These feeding problems may lead to micronutrient deficiencies and associated clinical syndromes. Xerophthalmia (secondary to vitamin A deficiency) and anemia (secondary to iron deficiency) are described here. Other syndromes associated with nutritional deficiency have been reported in the context of ASD (e.g., scurvy secondary to vitamin C deficiency, and rickets secondary to vitamin D deficiency), but are not covered in these case vignettes.

Presentation

Xerophthalmia is the spectrum of ophthalmologic disease caused by vitamin A deficiency. An important public health problem worldwide, it is uncommon in North America. Characterized by extreme dryness of the cornea and conjunctiva, manifestations include Bitot's spots (areas of desquamated, keratinized epithelium on the conjunctiva) and, in more severe cases, corneal ulceration and keratomalacia (softening and liquefaction of the corneal stroma). Because of a role in photoreception at the retina, vitamin A deficiency also causes night blindness and retinopathy. Xerophthalmia may present with a variety of eye symptoms and signs, including night blindness, pain, epiphora (tearing), and decreased visual acuity. Clinicians should maintain a high index of suspicion in patients with ASD, limited dietary repertoire, and any ophthalmologic complaint.

Iron-deficiency anemia (IDA) occurs when there is a state of insufficient total body iron, such that hematopoiesis cannot be maintained. More than 1.5% of Canadian infants and children are affected. There are no universal definitions of IDA severity, although a hemoglobin <80 g/L has been used to define severe IDA. Mild to moderate IDA most commonly presents without symptoms in a well-nourished child. Children with severe IDA may present with lethargy, irritability, poor feeding, tachypnea, and pallor; however, clinicians should note that pallor appears to be a poor diagnostic indicator until hemoglobin is very low (<50 g/L). Given that IDA is not always clinically apparent—and there is no Canadian recommendation for routine screening—risk factors for iron deficiency should be carefully assessed. Key risk factors include prolonged bottle use, excess intake of cow's milk, infrequent consumption of meat or iron-rich alternatives, and obesity.

Diagnosis

Xerophthalmia is diagnosed based on clinical findings. Biochemical evidence of vitamin A deficiency is supportive, but may be delayed based on reporting times for serum vitamin A assays.

IDA is diagnosed via laboratory measurements reflective of low hemoglobin concentration (anemia), low mean corpuscular volume (microcytosis), low reticulocyte count (hypoproduction), and inadequate iron stores to meet physiologic needs (iron deficiency). Numerous laboratory indices of iron deficiency are available (e.g., serum ferritin, serum iron, transferrin saturation, reticulocyte hemoglobin content), although all can be affected by factors other than iron status. Ferritin appears to be the single "best test" for identifying iron deficiency in adults, and some paediatric experts rely primarily on ferritin levels for diagnosis of iron deficiency in children. Clinicians should know, however, that ferritin is an acute phase reactant and may be falsely elevated in the setting of inflammation. If CRP is elevated, a normal or high ferritin should be interpreted with caution. Reticulocyte hemoglobin content is not affected by inflammation, but may be low in thalassemia trait and may not be available in all laboratories.

Complications and treatment

Xerophthalmia can result in irreversible vision loss and is therefore a medical emergency. Management is based on the World Health Organization treatment schedule, with three age-specific doses of oral vitamin A: immediately at diagnosis, the next day and at least two weeks later. For children and youth >12 months of age, 200,000 IU of vitamin A are given per dose. Ophthalmology may recommend adjunct treatments including lubricating eye drops and topical antibiotics for treatment or prevention of secondary bacterial infection.

IDA, when severe, can result in heart failure and, rarely, death. Evidence also suggests an association between IDA and stroke, particularly cerebral sinovenous thrombosis, in otherwise healthy young children. Beyond short-term health sequelae, iron deficiency in early life has been linked to cognitive and functional impairments in adulthood. Although the importance of treatment is generally recognized, there is relatively little evidence guiding management in the paediatric population. Standard practice is oral iron therapy (2 to 6 mg elemental iron/kg/day) for three to six months; traditionally-used ferrous iron preparations (e.g., ferrous fumarate, ferrous sulfate) appear to be more effective than newer polysaccharide iron complex preparations. Dietary modifications and follow-up to ensure treatment response are important components of management. Intravenous iron is generally considered a second-line treatment but may be indicated in specific circumstances (e.g., malabsorption, intolerance of oral iron with persistent anemia). Red blood cell transfusion is sometimes used in severe IDA, although there are no formal guidelines pertaining to indications for transfusion. Typically, transfusion would be considered in cases of very low hemoglobin (<50 g/L) or hemodynamic instability. If transfusion therapy is deemed to be indicated, clinicians should carefully consider volume and rate, mindful of the risk of transfusion-associated circulatory overload.

Paediatric pulmonary thromboembolism

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Clinical case

A 15-year-old girl, with no significant past medical or surgical history, presents to the emergency department with a one-day history of chest pain and dyspnea. She has no fever, cough, or other infectious symptoms. Over the past month, she has had increasing shortness of breath on exertion, for which she was prescribed a salbutamol metered-dose inhaler without effect. She has a past medical history of dysmenorrhea and has been taking oral contraceptives for six months.

On examination, the patient is afebrile and her respiratory rate is 30 breaths per minute, oxygen saturation is 93%, heart rate is 120 beats per minute, and blood pressure is 90/60. Her weight is 90 kg. Heart sounds are normal; breath sounds are diminished bilaterally. Laboratory investigations include a normal complete blood count and electrolytes, with blood gas showing respiratory alkalosis (pH 7.5) and hypocapnia (pCO_2 30 mmHg). D-dimer is >4,000 ng/ml. Her electrocardiogram shows tachycardia and nonspecific ST-segment changes. Her chest radiograph shows infiltrates to the left lower lobe with a small effusion. Echocardiogram shows reduced right ventricular function and mild to moderate tricuspid regurgitation. A computerized tomography (CT) pulmonary angiogram demonstrates a filling defect, confirming the diagnosis of pulmonary embolism.

The patient is transferred to the intensive care unit where she receives fluids and unfractionated heparin for five days before transitioning to low-molecular-weight heparin. She is counselled on safe contraception alternatives and provided with weight management strategies prior to being discharged home with hematology follow-up.

What a clinician needs to know

Pulmonary thromboembolism (PTE) is a rare but potentially life-threatening event. Occlusion of the pulmonary blood vessels results in right-sided heart failure and reduced systemic cardiac output. Due to the rarity and non-specific clinical presentation of PTE, delays in diagnosis and treatment are common and rates of post-mortem diagnosis are high.

Presentation and diagnosis

In children, the clinical presentation of PTE is often non-specific or masked by underlying disease, with the most common symptoms being dyspnea and pleuritic chest pain. Signs include tachypnea, tachycardia, hypoxia, and occasionally cough or hemoptysis. Severe cases may present in shock or cardiac arrest.

Paediatric cases have a bimodal age distribution, with most cases occurring in infants less than 1 year of age or in adolescents. Nearly all cases are associated with at least one risk factor and many cases are associated with more than one. Risk factors include the presence of an indwelling central venous catheter, congenital heart disease, congenital (e.g., prothrombin mutation, factor V Leiden) or acquired (e.g., oncologic diagnosis, nephrotic syndrome) prothrombotic disorders, sickle cell disease, and sepsis. Immobilization, recent surgery, and trauma are also risk factors; however, in isolation, they are rarely responsible for pulmonary embolism in infants and children. Hormone-based contraception is rarely identified as the sole risk factor, but it increases the risk of thromboembolism in combination with other factors, such as obesity. Many cases of PTE are associated with the presence of a deep vein thrombosis (DVT) and a history of prior thrombotic events.

Diagnostic criteria validated in adults are not reliable in children, with a high false-positive rate. The clinical utility of the D-dimer and other biomarkers is uncertain. Chest X-ray occasionally shows infiltrates or pleural effusion, but is most useful in excluding other conditions. Electrocardiogram typically shows sinus tachycardia and rarely right ventricular strain.

Pulmonary angiography has previously been considered the gold standard for diagnosis, but CT pulmonary angiogram is more commonly used due to its accuracy and less invasive nature. PTE may be diagnosed by ventilation/perfusion (V/Q) scintigraphy, or magnetic resonance imaging (MRI). Although echocardiogram is not routinely used for diagnosis, it may be useful in unstable patients. Right heart failure from elevated pulmonary pressures may result in right ventricular dilatation, interventricular septum motion abnormalities, and tricuspid regurgitation.

Prevention, treatment, and management

Most patients whose signs and symptoms are recognized early and who receive prompt treatment for PTE survive with good outcomes. Early consultation with paediatric subspecialists (e.g., critical care, hematology) is recommended. Evidence for therapeutic interventions is extrapolated from adult data. Therapeutic options include systemic thrombolytic therapy with recombinant tissue plasminogen activator or anticoagulation with unfractionated or low-molecular-weight heparin, transitioning to vitamin K antagonist

after achieving therapeutic anticoagulation. Occasionally, catheter-assisted embolectomy may be used to administer local thrombolytic agents. Surgical embolectomy is indicated for sub-massive/massive PTE in patients who have failed or have contraindications to thrombolysis, and patients in shock who require immediate intervention. Inferior vena cava filters may be used when DVT is present and anticoagulation is contraindicated due bleeding risk.

Paediatric patients with PTE should undergo investigations to assess for DVT, and sometimes a thrombophilia workup is indicated. Development of an unprovoked DVT and PTE in a paediatric patient suggests a prothrombotic disorder, particularly when family history is positive. It is important to counsel patients regarding modifiable risk factors (e.g., physical activity, weight management, smoking cessation) prior to discharge. Physical activity has not been shown to increase the risk of thrombus progression or recurrent pulmonary embolism and may reduce the risk of post-thrombotic syndrome. Risk of thrombosis associated with hormone-based contraceptive therapy is significantly increased among women with prothrombotic disorders. Alternate forms of contraceptive therapy should be recommended. The duration of anticoagulant therapy can be reassessed after three months of treatment, taking into account the results of any investigations performed to detect a prothrombotic disorder.

Serious adverse events related to cannabis used for medical purposes

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Clinical case

A 15-year-old female presents to a general paediatric clinic with persistent lower back pain that inhibits her ability to exercise, disrupts her sleep, and impairs her concentration at school. She has been experiencing this pain for the past 15 months. A comprehensive medical workup excludes all organic causes. Her past medical history is significant for attention-deficit/hyperactivity disorder (ADHD) for which she has been prescribed lisdexamfetamine (Vyvanse) and for major depressive disorder for which she has been prescribed fluoxetine (Prozac). Both medications have been prescribed for approximately two years. She is referred to a paediatric physiotherapist, but her pain continues. At a follow-up appointment she mentions that recreational cannabis decreases her lower back pain and asks you to provide access to medical cannabis. After consulting with colleagues, and after careful review of the evidence, the patient is told about the risks and uncertainties associated with medical cannabis, is encouraged to continue with physiotherapy, and is referred to a psychologist for cognitive behavioural therapy.

At a subsequent visit, the patient says that she went to a local medical cannabis clinic and received authorization for an oral cannabis oil product containing cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC). She has been taking the recommended dose of the authorized cannabis oil for the last three months and reports that, since starting the cannabis product, her back pain and sleep have improved. However, she has lost 12% of her bodyweight and reveals that her appetite is much decreased. She experienced decreased appetite when first prescribed her stimulant medication for ADHD, but her food intake has now drastically decreased; she reports skipping lunch and dinner, and only feeling minimally hungry for breakfast. She denies snacking, other substance or laxative use, diarrhea, or deliberate attempts to lose weight. She also reports difficulty concentrating and a loss of interest in school activities. Her physical exam is notable for bradycardia, with a resting heart rate of 48 beats per minute, and an orthostatic change in heart rate equal to 20 beats per minute. She is admitted to the hospital for weight stabilization, monitored feeding, and consultation with both adolescent medicine and psychiatry. She is advised to discontinue using cannabis products for pain relief due to a suspected drug-drug interaction.

What a clinician needs to know

Safety considerations and potential adverse effects associated with medical cannabis

The cannabis plant contains more than 400 chemicals, including up to 100 different bioactive cannabinoids. The two most prevalent cannabinoids in the cannabis plant are CBD and THC. Outside of drug resistant epilepsy, there is little evidence supporting the efficacy of cannabis for paediatric patients despite widespread use and advocacy from industry groups and online parent communities. Adverse events and drug-drug interactions with cannabis products are common and providers should be aware of these risks.

THC is the primary psychoactive compound in cannabis. Potential negative effects from THC include the risk of neuropsychiatric events, impaired cognition, and sedation. Withdrawal syndromes and dependence have been reported but are not well characterized in children using cannabis for medical purposes. Further, the effect of THC can be heightened or limited through drug-drug interactions, and THC can increase the toxicity of concomitant medications by limiting their metabolic pathways (mostly CYP3A4 and CYP2C19). CYP2C9 polymorphisms lead to decreased metabolic function and increased THC bioavailability, and may increase the likelihood of adverse effects.

CBD is the second most prevalent cannabinoid. The safety of CBD is often assumed given that it is widely accessible, has received regulatory approval (Epidiolex®), and lacks the euphoric, psychoactive properties of THC. CBD, however, has intrinsic pharmacologic effects including the potential for increased transaminase elevations and hypersensitivity reactions. Given CBD use among patients with complex conditions and treatment regimens, as well as its expanded consumer availability, awareness of potential safety issues associated with CBD is also needed. The use of CBD products should be discussed with patients and families including the lack of evidence for long-term safety. In trials of Epidiolex® (cannabidiol) in children with Lennox-Gastaut syndrome or Dravet syndrome, the most commonly reported adverse events (reported by 10% or more of participants and greater than placebo) included somnolence, decreased appetite, diarrhea, transaminase elevations, fatigue, malaise, asthenia, rash, insomnia, sleep disturbances, and infections.

Importantly, both THC and CBD have effects on common biological targets implicated in drug metabolism (e.g., cytochrome P450 enzymes) and excretion (e.g., P-glycoprotein); therefore, the potential for drug-drug interactions with commonly used medications, such as stimulants, antibiotics, chemotherapies, antiretrovirals, and some antidepressants, is high. General clinical recommendations of reducing substrate doses, monitoring for adverse events, and finding alternative therapy should be considered, especially in medically complex patients. Recommendations include CBD dose reductions with strong CYP3A4 and CYP2C9 inhibitors (e.g., fluoxetine) and

consideration for dose increases if given with strong CYP3A4 or CYP2C19 inducers. When co-administering CBD with other substrates for CYP2C19 (e.g., clobazam), a dose reduction may also be considered. Dose adjustments are also recommended for individuals with hepatic impairment. These effects should be considered in the risk-benefit assessment of CBD therapy.

Weight loss is not uncommon among patients taking lisdexamfetamine or medical cannabis products, and is likely a result of decreased appetite. To complicate matters, other medications, such as fluoxetine, which increases cannabinoid levels through CYP2C19 inhibition, may further decrease appetite and increase weight loss. Although decreased appetite is a common indication for medical cannabis use, particularly for cancer and HIV/AIDS patients, CBD has been known to decrease appetite in other populations. Weight loss or the underlying decreased appetite could complicate treatment, change how other medications are absorbed, or lead to vitamin or mineral deficiencies.

Treatment and management

The 2021 International Association for the Study of Pain (IASP) Presidential Task Force on Cannabis and Cannabinoid Analgesia position statement,[1] does not currently endorse general use of cannabis and cannabinoids for pain relief in children due to the lack of high-quality clinical evidence. Cannabinoids such as THC and CBD should be considered a medically active substance, and treated like standard prescription products, with a thorough discussion of both risks and benefits with patients and families. Given the increasing availability and use of medical cannabis products in the paediatric population, physicians need to be aware of the possible adverse effects of cannabinoids to monitor for, and mitigate, known risks. Regardless of the cannabis source (authorization or not), actions such as starting with low-dose therapy, monitoring, and carefully up-titrating to effect ("start low and go slow") should be promoted to paediatric patients choosing medical cannabis. In general, THC-dominant products should be avoided whenever possible and smoking routes discouraged.

There are animal data suggesting potential harms following cannabinoid exposures in pregnancy and lactation; therefore, counselling female patients on contraception may be appropriate. Cannabis products can impair driving and patients should be advised not to drive a vehicle or operate heavy machinery for a minimum of six hours following cannabis product use. Appropriate documentation about product selection, adverse effects, and perceived benefits should be included in patient records to foster transparency and improve care.

CBD has a complex pharmacokinetic and pharmacodynamic profile with the potential to interact with other medications and medical conditions. It is not, contrary to popular belief and anecdote, a biologically inert compound. Health care providers should be aware of the potential for drug-drug interactions and adverse events with CBD and monitor and manage patients accordingly. Paediatric patients using cannabis under clinical supervision should be screened for potential adverse events and drug-drug interactions between CBD, other pharmacotherapies, and their underlying conditions. Increased awareness of the potential for adverse events is also needed among the lay public who are recreational cannabis users or who use recreational cannabis for medical purposes.

1. IASP Presidential Task Force on Cannabis and Cannabinoid Analgesia. International Association for the Study of Pain Presidential Task Force on Cannabis and Cannabinoid Analgesia position statement. *PAIN* July 2021;162:S1-S2. doi: 10.1097/j.pain.0000000000002265. https://journals.lww.com/pain/Citation/9000/International_Association_for_the_Study_of_Pain.98086.aspx

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COVID-19
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Canadian Paediatric Surveillance Program

New Study and One-Time Survey Opportunities

The opportunity

- Benefit from the CPSP's well-established, timely, cost-effective, and internationally recognized surveillance platform.
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Including examples of successful CPSP studies

- Rare diseases (including genetic, metabolic, or rare acquired conditions)
  - Congenital myotonic dystrophy
  - Medium-chain acyl-coenzyme A dehydrogenase deficiency
- Rare complications of more common diseases
  - Adrenal suppression with glucocorticoid therapy
  - Serious adverse events associated with complementary and alternative medicine
- Emerging infections
  - COVID-19
  - Lyme disease
- Threats to public health and safety
  - Vaping
  - Neonatal abstinence syndrome
  - Teething necklaces and bracelets worn by infants and toddlers

Study success factors

- A study or condition with an incidence of less than 500 cases per year
- A multidisciplinary study team, with national representation
- Local champions who encourage study reporting at their institutions

Study impact

Knowledge translation: Studies have been published in high-impact, peer-reviewed journals; the CPSP is well known and recognized by prominent editorial boards.

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Professional medical guidelines: Results have informed guidelines such as the Canadian Paediatric Society position statements on neonatal hyperbilirubinemia and medical assistance in dying.

Public health promotion and education: Results have informed efforts to prevent vitamin D deficiency rickets and the use of e-cigarettes in those under the legal age to use conventional tobacco products.

CPSP
CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

"As the Paediatric Chairs of Canada representative to the CPSP Scientific Steering Committee, I have witnessed the extraordinary ability of the CPSP to bring together study investigators from across paediatric disciplines and across Canada in the study of rare paediatric diseases. For conditions that are high in disability, morbidity, mortality, and economic costs to society, despite their low frequency, national surveillance to capture case-level data is essential. On behalf of the Scientific Steering Committee, I would like to extend a sincere thank you to the thousands of CPSP participants who contribute to the Program. We are truly fortunate to have such a robust paediatric surveillance program in Canada."

Ciarán M. Duffy, MB, BCh, MSc, FRCPC, FRCPI; Professor, Department of Pediatrics, Faculty of Medicine, University of Ottawa; Past CPSP Steering Committee representative, Paediatric Chairs of Canada

For more information, please call us at 613-526-9397 ext. 239, e-mail cpsp@cps.ca or visit www.cpsp.cps.ca.

For more information on the Canadian Paediatric Surveillance Program or to obtain a French version of this report, please contact:

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