CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

2019 Results

Canadian Paediatric Society
Société canadienne de pédiatrie

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

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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Project manager
Melanie Laffin Thibodeau, Manager, Surveillance, CPSP and IMPACT

Scientific review
Charlotte Moore Hepburn, MD, Medical Affairs Director, CPSP and Canadian Paediatric Society

Translation review
Miriam Santschi, MD, Paediatrician, *Centre hospitalier universitaire de Sherbrooke*, Professor, Department of Paediatrics, *Université de Sherbrooke*

Translation
Dominique Paré, C. Tr., Traduction Le bout de la langue inc.

Layout and design
John Atkinson, Fairmont House Design

Editing and production
Una McNeill, CPSP Consultant

Giving CREDIT to our Participants

The Canadian Paediatric Surveillance Program (CPSP) is grateful to our many dedicated participants. The success of our public health surveillance depends on their engagement and continued commitment to the Program.

To show our appreciation, the CPSP is rewarding our loyal participants with a NEW opportunity to earn free Royal College of Physicians and Surgeons of Canada Maintenance of Certification (MOC) Section 3 credits.

How it works

The CPSP is proudly partnering with the Canadian Paediatric Society's online learning portal, Pedagogy. CPSP participants who have reported for all 12 months in 2019 will be offered complimentary registration to the online CPSP module on Pedagogy. The module will feature questions that are related to ongoing or recently completed CPSP studies. By reading the case vignettes and clinical fact sheets in the *2019 CPSP Results*, participants will gain the knowledge necessary to complete the module.

Stay tuned!

Participants will receive a notice in the fall of 2020 when the CPSP module is available online, with clear instructions on how to access their free registration to start earning valuable MOC Section 3 credits.

For more information on Pedagogy visit www.cps.ca/en/ecme.

pedagogy

ONLINE EDUCATION FROM THE CPS

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Foreword

Chief Public Health Officer of Canada

Dr. Theresa Tam

For more than 20 years, the Canadian Paediatric Surveillance Program has provided valuable data to researchers and health professionals. By collecting and monitoring data from thousands of paediatricians and paediatric subspecialists, Canada is able to report cases of rare diseases and conditions affecting Canada's children and youth.

This year, the program has undertaken valuable studies and surveys on a number of issues affecting our youth, including serious adverse events related to recreational cannabis use and vaping-related illness and injury. It also helps to shine a light on paediatric conditions that are not as well known, but represent a disproportionate societal and economic burden. This comprehensive picture provides information for researchers to work better, for health care providers to improve patient care, and for communities to build better programs.

The Public Health Agency of Canada is proud of its long-standing partnership with the Canadian Paediatric Society, and the health care providers across Canada who give their time to provide information and ongoing support. At times when Canada faces rapidly emerging public health challenges, such as COVID-19, the value of this collaboration is abundantly clear. This is an important report that makes vital contributions to the health and future of our youngest Canadians.

President of the Canadian Paediatric Society

Dr. Ellen P. Wood

As the Canadian Paediatric Society's President, I am proud that the Canadian Paediatric Surveillance Program (CPSP) provides Canadians with rich, timely, and cost-effective epidemiological data on rare diseases and conditions. The Canadian Paediatric Society has used the information gathered from CPSP studies and surveys over the years to inform the development or revision of key position statements, to advocate for changes in public health policies affecting children and youth, and to reform critical research questions.

For example, following the 2018 CPSP one-time survey on teething necklaces and bracelets worn by infants and toddlers, the Canadian Paediatric Society advocated directly to Health Canada for the removal of these products from store shelves as they pose significant dangers, including strangulation and choking.

In late 2019, the CPSP worked in close collaboration with Public Health Agency of Canada and Health Canada officials to seek information regarding injuries related to electronic cigarettes. Survey results provided key insights about acute harms occurring to children and youth with exposure to vaping products and will help guide clinician education, public health interventions, and public policy measures to reduce the risks associated with these dangerous products.

The Canadian Paediatric Society also continues to work in close collaboration with the government regarding the safety and availability of paediatric medications in Canada. CPSP studies, including the long-standing adverse drug reactions (ADR) study and the recently launched study on severe adverse events associated with medical cannabis use, provide valuable data to inform drug safety interventions. The CPSP infrastructure also enables the timely communication of critical information to participants on ADRs and potential drug interactions through the monthly ADR Tips.

Just recently, the CPSP demonstrated its ability to respond quickly to the COVID-19 health crisis by adapting its existing platform to allow for the weekly reporting of hospitalized children with COVID-19, as well as those with paediatric inflammatory multisystem syndrome/Kawasaki disease temporally associated with COVID-19, and non-hospitalized cases of COVID-19 in children with chronic conditions. Regular updates will be sent to CPSP participants and the study summary will be in next year's Annual Results.

On behalf of the Canadian Paediatric Society and its Board of Directors, I would like to thank the Public Health Agency of Canada for its ongoing collaboration and support of the CPSP. The strong partnership between the Public Health Agency of Canada and the Canadian Paediatric Society allows the Program to keep providing the data necessary for improving care for children and youth affected by rare conditions and diseases.

I would also like to thank my colleagues across the country for participating in the CPSP. Without your help and insight into these rare conditions, none of this work would be possible!

CPSP Chair

Dr. Jonathon Maguire

The Canadian Paediatric Surveillance Program (CPSP) was busy once again in 2019 tackling important public health issues and emerging concerns facing Canadian children and youth.

With the legalization of cannabis in Canada in late 2018, the CPSP was eager to learn how legalization may impact the health of our youngest citizens. After just over a year of surveillance, early results suggest that accidental consumption of edible cannabis products by children is resulting in injuries requiring emergency care and hospitalization (see page 30). A second multi-year study, this time focusing on serious adverse events with the use of medical cannabis, was launched in December 2019 to provide evidence about the safety of medicinal cannabis for children.

Following a rapid increase in cases of severe lung injury associated with the use of e-cigarettes in the United States in late 2019, the Public Health Agency of Canada, Health Canada, and the CPSP were concerned that Canadian children and youth may be experiencing similar issues. An emergency one-time survey was sent to participants in September 2019 asking them to provide information on cases seen within the last 12 months. The survey was of great interest to CPSP participants and garnered the highest response rate the Program has ever received to a one-time survey. Results can be found on page 36.

The CPSP also undertook two multi-year studies of rare conditions in December 2019 which will assess the incidence and presenting features of paediatric leukodystrophies and the impact and frequency of children and youth who have received a diagnosis of PANDAS/PANS.

Most recently, with the emergence of the COVID-19 pandemic, the CPSP has initiated rapid response surveillance to understand severe COVID-19 illness and complications among children, once again demonstrating the ability of the CPSP to quickly respond to new health concerns.

I would like to take this opportunity to thank our 2800 participants who faithfully report to the CPSP on a monthly basis. To reflect the time and dedication that paediatricians across Canada contribute to the CPSP, we will be offering CPSP participants the opportunity to earn Royal College of Physicians and Surgeons of Canada Maintenance of Certification (MOC) Section 3 credits. For more information on this exciting opportunity, please refer to page 38.

On behalf of the CPSP Scientific Steering Committee and CPSP study and survey teams, thank you to all participants for helping to generate important findings that make an impact on our clinical practice and public health policies.

Acknowledgements

The key strength of the Canadian Paediatric Surveillance Program 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 2019 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:

- Genzyme
- The Chronic Pain Network, a Canadian Institutes for Health Research initiative

CPSP Scientific Steering Committee

Jonathon Maguire, MD (Chair)	Canadian Paediatric Society
Joanna Lazier, MD	Canadian College of Medical Geneticists (Liaison)
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)
Krista Jangaard, MD	Canadian Paediatric Society
Carsten Krueger, MD	Canadian Paediatric Society (Resident Representative)
Melanie Laffin Thibodeau, BCom	Canadian Paediatric Society
Charlotte Moore Hepburn, MD	Canadian Paediatric Society
Paul Muirhead, LLM	Consultant
Jay Onysko, MA	Centre for Surveillance and Applied Research, Public Health Agency of Canada
Jennifer Pennock, MSc	Centre for Immunization and Respiratory Infectious Diseases, Public Health Agency of Canada
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

The CPSP Scientific Steering Committee would like to extend its sincere thanks to Paul Muirhead for his 19 years of valuable service to the committee as an external legal consultant and for his stewardship and guidance on issues of medical ethics and patient confidentiality. We wish Paul the very best in all his future endeavours.

About the Canadian Paediatric Surveillance Program

Overview

The Canadian Paediatric Surveillance Program 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 2800 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

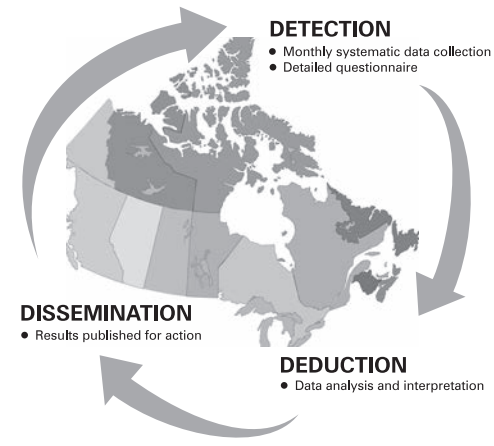
- Study teams from across Canada are encouraged to submit proposals for new studies or one-time surveys that meet the "criteria for submission," available on the CPSP website at www.cpsp.cps.ca/apply-proposez.
- The CPSP Scientific Steering Committee then reviews the proposals on a biannual basis and 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.

CPSP Quick Facts

Did you know?

- The CPSP celebrated its 23rd anniversary in 2019.
- The CPSP is comprised of approximately 2800 dedicated paediatricians and paediatric subspecialists.
- Since its inception, the CPSP has studied 78 rare conditions/diseases and initiated 52 one-time surveys.
- Over 67 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 2019, 84% of participants committed to receiving their monthly forms electronically.

Figure 1 – Surveillance process summary



- 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.
- 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.
- Surveillance totals may not include some groups of 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.

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 2019

Provinces/territories	Reporting rates (%)*	Number of participants†
Alberta (AB)	83	378
British Columbia (BC)	82	280
Manitoba (MB)	84	112
New Brunswick (NB)	91	31
Newfoundland and Labrador (NL)	87	44
Northwest Territories (NT)	—	< 5
Nova Scotia (NS)	90	80
Nunavut (NU)	—	< 5
Ontario (ON)	82	1020
Prince Edward Island (PE)	88	11
Quebec (QC)	78	545
Saskatchewan (SK)	78	61
Yukon (YT)	—	< 5
Canada	**82**	**2569**

* 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 2800. 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 2015–2019

Reporting year	Reporting rates (%)
2015	82
2016	79
2017	83
2018	79
2019	82

TABLE 3 – 2019 detailed questionnaire completion rates as of July 23, 2020

Studies/conditions	Notifications of potential cases*	Pending	% Completion rate
Acute flaccid paralysis	38	0	100
Adverse drug reactions – serious and life-threatening	23	9	72
Complex regional pain syndrome in Canadian children and youth	88	11	89
Congenital Zika syndrome in infants in Canada	< 5	0	—
Frequency and impact of PANDAS/PANS diagnosis*	—	—	—
Incidence trends of type 2 diabetes, medication-induced diabetes, and monogenic diabetes in Canadian children	148	24	86
Infantile and later-onset paediatric Pompe disease (glycogen storage disease type II)	11	0	100
Ophthalmia neonatorum caused by *N gonorrhoeae* or *C trachomatis*	16	5	76
Paediatric-onset leukodystrophies*	—	—	—
Serious adverse events related to cannabis used for medical purposes*	—	—	—
Serious and life-threatening events associated with non-medical (recreational) cannabis use in Canadian children and youth	56	12	82
Severe obesity and global developmental delay in preschool children	49	7	88
Total number of cases (all studies)	**429**	**68**	**87**

* Numbers are suppressed for studies that began in December 2019 and will be reported in the CPSP 2020 Annual Results

Glossary of terms in study results

Reported: Notifications of potential cases received by the CPSP

Reports from Quebec: 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. An interim measure was implemented, asking Quebec participants to defer returning their detailed questionnaires until a new process is defined. Cases notified by Quebec participants after August 1, 2018 are not included in the data analysis, unless they are reported from a centre with project-specific research ethics board approval.

Duplicates: Cases reported by more than one participant

Excluded: Cases not meeting the case definition

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 (outside of centres with 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.

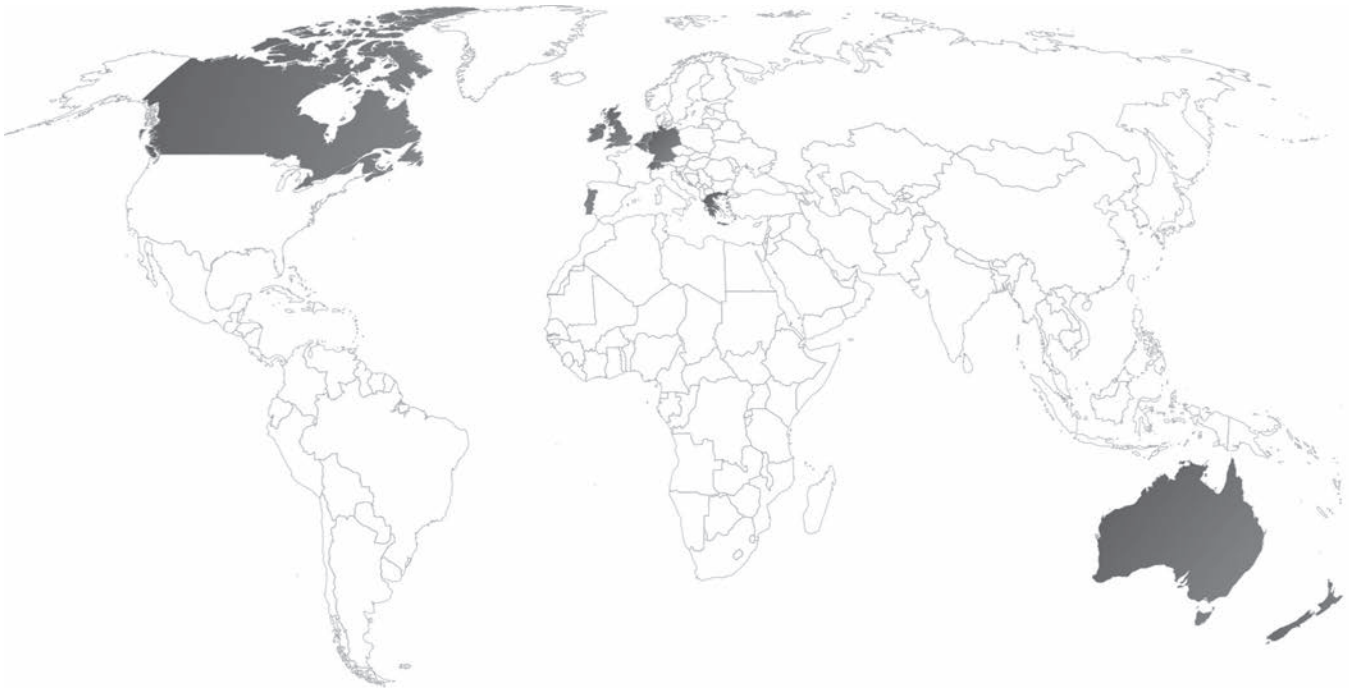
Established in 1998, INOPSU included eight paediatric surveillance units among its active membership in 2019: Australia, Canada, Germany, Ireland, New Zealand, Switzerland, United Kingdom, and Wales.

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 planned 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.

The CPSP is looking forward to the next INOPSU meeting in 2021. During INOPSU meetings, member countries have the opportunity to 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 http://www.inopsu.com/.



Surveillance Studies in 2019

Acute flaccid paralysis

Ongoing study since January 1996


Catherine Dickson

Principal investigator
Catherine Dickson, MD, CM, MSc, FRCPC, Centre for Immunization and Respiratory Infectious Diseases, Public Health Agency of Canada; catherine.dickson@canada.ca

Co-investigator
Ho Mi Fane B

Question

Did Canada maintain its polio-free status in 2019?

Importance

- Acute flaccid paralysis (AFP) surveillance is the cornerstone of monitoring for polio, in light of ongoing transmission of wild poliovirus in a few countries around the world.
- 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.

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 2019

Note: Due to reporting delays, this report represents a snapshot as of January 23, 2020. The total AFP case counts for 2015 to 2018 have been updated with all the confirmed cases that have been reported and are presented in Table 2.

TABLE 1 – AFP cases in 2019

Reported	Reports from Quebec*	Duplicates	Excluded	Pending	Met case definition
22	0	3	2	1	16

* Due to Quebec legislation, cases notified by Quebec participants after August 1, 2018 were not included in the data analysis and detailed case information was not collected, unless reported from a centre with project-specific research ethics board approval. Cases reported through IMPACT centres were included for data analysis in this report.

TABLE 2 – Annual comparison of AFP cases 2015–2018

Year	Total cases
2018	71
2017	32
2016	52
2015	27

In total, 22 reports of sudden onset muscle weakness in children less than 15 years of age were provided to the Public Health Agency of Canada through the CPSP and IMPACT. The vast majority of cases were reported through IMPACT.

Cases that met the case definition

- At the time of analysis, 16 cases were verified as meeting the AFP case definition in 2019; none were assessed as meeting the polio case definition.
- The median time from case onset of paralysis to reporting was 62.5 days and the average was 105 days (range: 22 to 277).

Demographics

- Patient sex was male in the majority of cases.
- Cases ranged in age from younger than 1 year to 14 years, with a median of 2.8 years and a mean of 4.3 years (95% CI 2.3–6.3).

Presentation and diagnosis

- All 16 (100%) cases were hospitalized. Length of stay ranged from 3 to 29 days, for a median of 6 days and a mean of 10 days (95% CI 6–14).
- Eight (50%) cases were diagnosed with Guillain-Barré syndrome. Diagnoses for the remaining 8 (50%) cases included transverse myelitis, acute disseminated encephalomyelitis, unspecified, or unknown.
- The vast majority of cases were up-to-date for their polio vaccinations.
- Seven (44%) cases had stool sample submitted for viral testing. None were positive for polio.

Treatment and outcomes

- Of the 15 (94%) cases with outcomes documented at initial report, all (100%) cases had partially recovered with residual weakness.
- Of the 7 (44%) 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 2019[1]

Number of cases	Incidence rate*	% with adequate stool sample[2]†	% with 60-day follow-up‡
16	0.26	44%	44%

* 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
‡ 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 2019, 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.

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, and Noémie Desmarteaux.

1. Detailed information on WHO surveillance performance indicators can be found at http://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

Ongoing study since January 2004

Sally Pepper

Principal investigator

Sally Pepper, BSc Phm, RPh, Patient Safety Section, Marketed Health Products Directorate, Health Canada; sally.pepper@canada.gc.ca

Question

What serious and life-threatening events suspected to be related to adverse drug reactions (ADRs) in children and youth were reported in 2019?

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.

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 2019

TABLE 1 – ADR cases in 2019

Reported	Reports from Quebec*	Duplicates	Excluded	Pending	Met case definition
14	0	1	0	0	13

* Due to Quebec legislation, cases notified by Quebec participants after August 1, 2018 were not included in the data analysis and detailed case information was not collected, unless reported from a centre with project-specific research ethics board approval.

Cases that met the case definition

- At the time of analysis, 13 suspected serious and/or life-threatening paediatric ADR cases were verified as meeting the case definition in 2019.
- In a small number of cases, more than one product was suspected of causing the adverse reaction.

- The class of health product (using the Anatomical Therapeutic Chemical classification system) most frequently suspected of causing the adverse reactions was antibacterials (seven cases).
- Angiotensin-converting enzyme inhibitors, antiepileptics, anti-inflammatory and antirheumatic products, antimycobacterials, antivirals, and immunosuppressants were each involved in fewer than five cases.

TABLE 2 – Suspect health products in 2019

Class of health product	Name of health product
Angiotensin-converting enzyme inhibitors	Enalapril
Antibacterials	Amoxicillin, ceftriaxone, cloxacillin, vancomycin
Antiepileptics	Perampanel
Anti-inflammatory and antirheumatic products	Ibuprofen
Antimycobacterials	Rifampin
Antivirals	Oseltamivir
Immunosuppressants	Infliximab

Demographics

- Patient sex was male in the majority of cases.
- Cases were fairly evenly distributed across the following age ranges: 0 to 5 years, 6 to 12 years, and 13 to 17 years.

Presentation and diagnosis

- All 13 cases were classified as serious according to the following criteria (more than one cause for classification was provided in some cases): fewer than 5 cases were considered life-threatening, 10 cases required hospitalization, and 5 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 11 cases, with the majority of patients (82%, 9/11) 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 class of health product most frequently suspected of causing adverse reactions in 2019 was antibacterials.
- Since the implementation of the CPSP surveillance for adverse reactions in 2004, the product classes most frequently associated with suspect product reports have been antibacterials for systemic use, antiepileptics, and psychoanaleptics. The most frequently reported suspect drugs in these classes were amoxicillin, carbamazepine, and methylphenidate respectively. No reports meeting the study criteria were received in 2019 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 ADRs to the federal regulator. 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 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

Complex regional pain syndrome in Canadian children and youth

September 2017 to August 2019 – Final report


Krista Baerg

Principal investigator
Krista Baerg, BSN, BA, MD, BScMed, FRCPC, Associate Professor of Pediatrics, University of Saskatchewan, Medical Lead, Interdisciplinary Pediatric Complex Pain Clinic, Department of Pediatrics, Royal University Hospital, Saskatchewan Health Authority - Saskatoon; dr.kbaerg@usask.ca

Co-investigators
Finley GA, Tupper S

Collaborating Canadian paediatric pain clinics: Alberta Children's Hospital, BC Children's Complex Pain Service, Children's Hospital of Eastern Ontario, CHU Sainte-Justine, IWK Health Centre, London Health Sciences Centre, McGill University Health Centre, McMaster Children's Hospital, Saskatchewan Health Authority – Saskatoon, Stollery Children's Hospital, The Hospital for Sick Children

Question

- What are the minimum incidence and geographic distribution of complex regional pain syndrome (CRPS) in the Canadian paediatric population?
- What are the pathways of referral, clinical presentation, diagnostic interventions, and recommended interventions by paediatricians and pain specialists?

Importance

- CRPS is a rare chronic severe pain condition that involves peripheral, central, and autonomic nervous system and immune system mechanisms. It results in significant functional impairment and debilitating symptoms. The persistent and severe pain results in psychological, physical, and neurological structural and functional changes.
- Few interventions for CRPS have been formally evaluated in the paediatric population.
- Variability in the diagnosis and management of CRPS exists.
- Improved knowledge of the incidence and presentation of CRPS in Canada can help promote early detection and diagnosis.

Methodology

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

Case definition

A patient presenting between the ages of 2 and 18 years (up to the 18th birthday) with a new diagnosis of CRPS, meeting the following International Association for the Study of Pain clinical diagnostic criteria:

1. Continuing pain, which is disproportionate to any inciting event
2. Reports at least one symptom in at least three of the following four categories:
   - **Sensory:** hyperesthesia and/or allodynia
   - **Vasomotor:** temperature asymmetry and/or skin color changes and/or skin color asymmetry
   - **Sudomotor/Edema:** edema and/or sweating changes and/or sweating asymmetry
   - **Motor/Trophic:** decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
3. Displays at least one sign at time of evaluation in at least two of the following four categories:
   - **Sensory:** hyperalgesia (to pinprick) and/or allodynia (to light touch and/or temperature sensation and/or deep somatic pressure and/or joint movement)
   - **Vasomotor:** temperature asymmetry (>1°C) and/or skin color changes and/or asymmetry
   - **Sudomotor/Edema:** edema and/or sweating changes and/or sweating asymmetry
   - **Motor/Trophic:** decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)

Exclusion criteria

Presence of another diagnosis that better explains the signs and symptoms

Results – September 2017 to August 2019

TABLE 1 – CRPS cases from September 1, 2017 to August 31, 2019						
Year	**Reported**	**Reports from Quebec‡**	**Duplicates**	**Excluded**	**Pending**	**Met case definition**
2017*	28	—	0	5	6	17
2018	135	5	0	22	39	69
2019†	85	1	1	12	22	49
Total	**248**	**6**	**1**	**39**	**67**	**135**

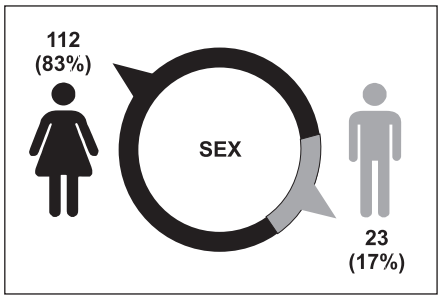
* September 1 to December 31, 2017
† January 1 to August 31, 2019
‡ Due to Quebec legislation, cases notified by Quebec participants after August 1, 2018 were not included in the data analysis and detailed case information was not collected, unless reported from a centre with project-specific research ethics board approval.

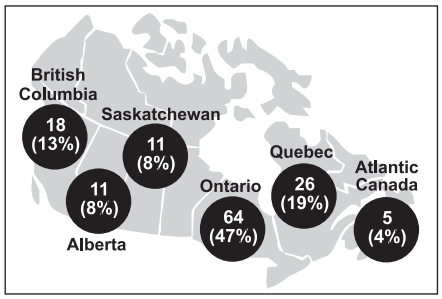
Cases that met the case definition

At the time of analysis, 135 cases were verified as meeting the case definition over the 24 months of the study.

Demographics

- Patient sex was female in 112 (83%) cases and male in 23 (17%) cases.
- The mean age of cases was 11.6 years (range: 6 to 18 years).
- The geographic distribution of cases was: 64 (47%) from Ontario, 26 (19%) from Quebec, 18 (13%) from British Columbia, 11 (8%) from Alberta, 11 (8%) from Saskatchewan, and 5 (4%) from Atlantic Canada.
- The most common population group reported was White (105, 78%).





Presentation and diagnosis

- The average number of months from onset to diagnosis of CRPS was 5.3 months (*SD*=9.7).
- CRPS was diagnosed in a pain clinic in 41 (30%) cases and by a general paediatrician in 15 (11%) cases. In 79 (59%) cases CRPS was diagnosed by another health care professional including paediatric emergency physicians, orthopaedic surgeons, or paediatric rheumatologists.
- Average self-reported pain intensity over the past week was severe in 78 (58%) cases and moderate in 42 (31%) cases.
- The most common inciting/triggering event was trauma/injury in 89 (66%) cases, followed by no known trigger in 29 (21%) cases.
- CRPS presented more commonly in the lower limbs (105, 78%).
- Symptoms were present in the following categories: 116 (86%) cases had sensory symptoms, 114 (84%) vasomotor, 111 (82%) motor/trophic, and 102 (76%) sudomotor/edema.
- Signs were present in the following categories: 119 (88%) cases had motor/trophic signs, 113 (84%) sensory, 90 (67%) vasomotor, and 70 (52%) sudomotor/edema.
- CRPS symptoms had a functional impact on patients in the following areas: 125 (93%) cases experienced an impact on physical activity, 73 (54%) on sleep, 71 (53%) on mood, 69 (51%) on high-level sport, 55 (41%) on family function, 43 (32%) on social activities, and 41 (30%) on school achievement. Seventy-two cases (53%) missed school, and 31/72 (43%) missed less than two weeks.
- The most common conditions reported in CRPS patients' past medical histories included the following: 36 (27%) cases had a mood/anxiety disorder, 34 (25%) had another medical or mental health disorder, 19 (14%) had migraines/headaches, 15 (11%) had a learning disability, 13 (10%) had another pain disorder, 9 (7%) had attention-deficit/hyperactivity disorder, 7 (5%) had hypermobility, and 5 (4%) had a previous diagnosis of CRPS. Less common conditions reported included dysmenorrhea, rheumatologic conditions, and conversion disorder.

Treatment and outcomes

- CRPS patients received the following pain medications and adjuvants: 111 (82%) cases received non-steroidal anti-inflammatory drugs, 87 (64%) acetaminophen, 69 (51%) gabapentinoids, 31 (23%) topicals, 25 (19%) tricyclic antidepressants, 18 (13%)

compounded topicals, 16 (12%) other opioids, 9 (7%) tramadol, 8 (6%) selective serotonin reuptake inhibitors, 7 (5%) regional blocks, and 5 (4%) ketamine. Less commonly reported medications included sodium channel agents, serotonin-norepinephrine reuptake inhibitors, medical marijuana, and bisphosphonates.
- Patients received several complementary therapies including 27 (20%) who received exercise therapy, 17 (13%) chiropractic care, 12 (9%) complementary medicine (e.g., osteopathy, laser therapy), 8 (6%) acupuncture, and 8 (6%) massage therapy.
- CRPS patients received other treatments including 86 (64%) cases who received pain education, 79 (59%) desensitization, 76 (56%) fitness/exercise, 69 (51%) psychological strategies, 49 (36%) graded motor imagery, 47 (35%) bracing ankle/foot orthoses boot, 28 (21%) hydrotherapy, 19 (14%) TENS machine, and 17 (13%) orthotic shoe inserts.
- CRPS patients took nutritional supplements such as vitamin C in 25 (19%) cases, omega-3 in 5 (4%) cases, and other supplements in 8 (6%) cases.
- Patients were most commonly referred to the following health care providers: multidisciplinary pain clinics, physiotherapists, and psychologists. (Note: A paediatric pain clinic commonly involves a paediatrician or anaesthesiologist, nurse, physiotherapist, and psychologist). Patients were also referred to general paediatricians, physiatrists, occupational therapists, psychiatrists, orthopedic specialists, and neurologists.

Study limitations

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

Conclusions

- CRPS affected more females than males and presented more commonly in the lower limbs, consistent with the adult CRPS literature. The majority of patients affected were White.
- The average time from onset to diagnosis of CRPS was 5.3 months (*SD*=9.7). At the time of diagnosis, the majority of CRPS signs and symptoms reported were sensory and motor/trophic.
- Treatment involved a combination of medications, complementary medicines, and therapies.
- The most common services engaged to follow the patient were multidisciplinary pain clinics, physiotherapy, and psychology.
- Once verification of pending cases is complete, the observed minimum incidence rate of CRPS will be determined.

Anticipated study impact

- Study results will identify the minimum incidence of CRPS and highlight current resource needs in Canada.
- The study will identify patient demographics and triggers or risk factors associated with CRPS.
- Results will be used to promote early recognition and treatment to benefit patient recovery.

Publication and dissemination

Canadian surveillance of complex regional pain syndrome in children and youth. Baerg K, Tupper S, Finley GA. Chronic Pain Network Annual Meeting, Hamilton, in September 2017 (poster presentation)

Canadian surveillance of complex regional pain syndrome in children and youth: Results from year 1 of surveillance. Baerg K, Tupper S, Finley GA. Canadian Pain Society 40th Annual Scientific Meeting, Toronto, in April 2019 (poster presentation)

Canadian Paediatric Surveillance Program study of complex regional pain syndrome in children and youth. Baerg K. CRPS symposium, Canadian Pain Society Annual Scientific Meeting, Calgary, in May 2020 (oral presentation) (postponed)

Acknowledgements

Thanks to all the collaborating Canadian paediatric pain clinics, the CPSP, and CPSP participants. We acknowledge Dr. Félix Levesque for his work translating the clinical questionnaires received in French. We gratefully acknowledge funding for this study from the Chronic Pain Network.

Congenital Zika syndrome in infants in Canada

March 2017 to February 2019 – Final report

Shaun Morris

Principal investigators

Shaun Morris, MD, Division of Infectious Diseases, The Hospital for Sick Children; shaun.morris@sickkids.ca

Marianna Ofner, PhD, Public Health Agency of Canada; marianna.ofner@canada.ca

Co-investigators

Bitnun A, Miller S, Moore Hepburn C, Nelson C, Tataryn J

Question

What is the minimum incidence of infants born with congenital Zika syndrome (CZS) in Canada and what is the spectrum of clinical manifestations and abnormalities seen in these infants?

Importance

- In October 2015, an increased incidence of microcephaly was noted in northeastern Brazil. Further investigations noted an increase in severe microcephaly and other neurological disorders among newborns born to mothers with Zika virus infection.
- While severe microcephaly was the first major congenital anomaly linked with Zika virus infection during pregnancy, a wide range of congenital anomalies have been described. As a result of the spectrum of clinical manifestations and abnormalities seen in infants born to Zika virus-infected mothers, the term congenital Zika syndrome has been developed. Importantly, some newborns born to mothers infected with Zika virus have neurological abnormalities with a normal head circumference.
- Surveillance for CZS in Canada through the Canadian Paediatric Surveillance Program (CPSP) started in March of 2017. This project was complementary to the CPSP surveillance for severe microcephaly.

Methodology

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

Case definition

An infant less than 12 months of age who presents with the following criteria:

- Microcephaly, defined as head circumference less than two standard deviations for gestational age and sex according to the standardized reference percentile*
  OR
- Other congenital anomalies and malformations consistent with congenital Zika syndrome including malformations of the central nervous system, such as intracranial calcifications, structural brain or eye abnormalities, or other congenital central nervous system-related abnormalities (not explained by another etiology†)
  AND
- A maternal history that includes an epidemiologic linkage‡ to Zika virus OR a positive or inconclusive Zika virus laboratory test
  OR
- An infant with a positive or inconclusive Zika virus laboratory test

* If there is a case of severe microcephaly suspected to be associated with Zika virus then a questionnaire for the severe microcephaly study and the congenital Zika syndrome study should be completed (i.e., if the case meets both case definitions).

† Other etiologies that should be considered include other congenital infections such as syphilis, toxoplasmosis, rubella, cytomegalovirus, varicella zoster, parvovirus B19, and herpes simplex virus. An assessment of potential genetic and other teratogenic causes of the congenital anomalies should also be considered.

‡ Epidemiological linkage means: travelled to, or resided in, an area with active Zika virus transmission during her pregnancy; OR had unprotected sex during pregnancy with a partner who resided in, or traveled to, an area with active Zika virus transmission.

Unique to this study

A CPSP study examining the incidence and epidemiology of severe microcephaly in Canada took place from June 2016 to May 2018. For cases of severe microcephaly suspected to be associated with Zika virus, CPSP participants were asked to report using both the severe microcephaly questionnaire AND the CZS questionnaire. There was cross-representation of principal and co-investigators on the research teams to ensure that all cases were appropriately identified and analyzed.

Results – March 2017 to February 2019

TABLE 1 – CZS cases from March 1, 2017 to February 28, 2019						
Year	**Reported**	**Reports from Quebec‡**	**Duplicates**	**Excluded**	**Pending**	**Met case definition**
2017*	< 5	—	0	0	0	< 5
2018	< 5	0	0	0	0	< 5
2019†	< 5	0	0	0	0	< 5
Total	**< 5**	**0**	**0**	**0**	**0**	**< 5**

* March 1 to December 31, 2017
† January 1 to February 28, 2019
‡ Due to Quebec legislation, cases notified by Quebec participants after August 1, 2018 were not included in the data analysis and detailed case information was not collected, unless reported from a centre with project-specific research ethics board approval.

Cases that met the case definition
Fewer than five cases of CZS were verified as meeting the case definition in Canada over the study period.

Demographics
As per CPSP policy, case numbers and data for fewer than five cases cannot be presented.

Presentation, diagnosis, treatment, and outcomes
While specific information on this study cannot be presented due to the small number of cases, available literature demonstrates that CZS consists of:
- Severe microcephaly in which the skull has partially collapsed
- Decreased brain tissue with a specific pattern of brain damage, including subcortical calcifications
- Damage to the structures of the eye, including but not limited to macular scarring and focal pigmentary retinal mottling
- Congenital contractures
- Hypertonia

The Public Health Agency of Canada published surveillance data for Zika infections in Canada for the period from June 2015 to December 2018 during which time 582 travel-related cases of Zika virus infection were reported. Studies from other countries show that among completed pregnancies with laboratory evidence of infection with Zika virus, about 6% of fetuses or infants had evidence of Zika-associated birth defects. Among pregnant women with Zika virus infection in the first trimester, about 11% of fetuses or infants had evidence of Zika-associated birth defects.

Study limitations
- Limitations common to all CPSP studies are listed on page 11.
- This study captured only live births.

Conclusions

CZS is rare in Canada. According to the Public Health Agency of Canada, as of December 31, 2018 (the most recent data available), 582 travel-related cases of Zika virus infection had been reported in Canada since June 2015. Fewer than five cases of CZS were verified as meeting the case definition in this CPSP study.

Anticipated study impact

- These data will supplement other data collected via provincial or territorial reportable disease programs.
- A planned future publication will combine data from the CPSP CZS and severe microcephaly studies. Additional planned work will combine CPSP CZS and severe microcephaly data with similar data obtained from national surveillance projects conducted in the United Kingdom, Australia, and New Zealand by collaborators within the International Network of Paediatric Surveillance Units.

Publication and dissemination

Incidence of congenital Zika syndrome and other causes of severe microcephaly in Canada; results from the Canadian Paediatric Surveillance Program. Morris SK, Ofner M, Demarsh A, Nelson C, Bitnun A, Miller S, Shevell M, Moore A, Tataryn J, Evans J, Zipursky A, Moore-Hepburn C. World Congress of the Society for Pediatric Infectious Diseases, Manila, Philippines in November 2019 (oral presentation)

Zika virus: What does a physician caring for children in Canada need to know? Robinson JL, Canadian Paediatric Society Infectious Diseases and Immunization Committee. *Paediatr Child Health* 2017:22(1):48–51 (practice point)

Acknowledgements
The investigators and the CPSP would like to thank all physicians who have reported cases to this study.

Incidence trends of type 2 diabetes, medication-induced diabetes, and monogenic diabetes in Canadian children

June 2017 to May 2019 – Final report


Shazhan Amed

Principal investigators

Shazhan Amed, MD, MSc.PH, FRCPC, Clinical Associate Professor, University of British Columbia, Paediatric Endocrinologist, BC Children's Hospital; samed@cw.bc.ca

Jill Hamilton, MD, MSc, FRCPC, Professor, University of Toronto, Paediatric Endocrinologist, The Hospital for Sick Children; jill.hamilton@sickkids.ca

Elizabeth Sellers, MD, MSc, FRCPC, Professor, University of Manitoba, Paediatric Endocrinologist, Winnipeg Children's Hospital; esellers@exchange.hsc.mb.ca

Co-investigators

Bienek A, Hadjiyannakis S, Henderson M, Nour M, Pinto T, Wicklow B

Question

- What is the minimum incidence of non-type 1 diabetes mellitus (NT1DM) and its subtypes (type 2 diabetes [T2D], medication induced diabetes [MID], and monogenic diabetes) in Canada?
- What are the 10-year minimum incidence trends of NT1DM and its subtypes in Canada?
- What are the risk factors, clinical characteristics, and diabetes-related complications associated with childhood-onset T2D?

Importance

- The incidence of childhood-onset T2D is increasing. With Canadian data on the incidence of T2D in children and youth from 2006 to 2008, this second Canadian Paediatric Surveillance Program (CPSP) study will provide national incidence trend data over a 10-year period.
- This surveillance study will produce the first-ever 10-year incidence trends for other forms of NT1DM including MID and monogenic diabetes.

Methodology

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

Case definition

A new or revised* diagnosis of non-type 1 diabetes (NT1DM) in a patient less than 18 years of age with clinical features that are **not** consistent with classic type 1 diabetes (defined as a child with symptomatic acute hyperglycemia).

* A revised diagnosis occurs when a child previously diagnosed with type 1 diabetes mellitus receives a "revised" diagnosis of non-type 1 diabetes based on clinical progression and/or results of investigations.

Diabetes is defined based on the Diabetes Canada Guidelines:
- Fasting plasma glucose (FPG) ≥ 7.0 mmol/L† or
- Random plasma glucose ≥ 11.1 mmol/L† or
- Two-hour plasma glucose ≥ 11.1 mmol/L† after a standard oral glucose tolerance test

† Requires a second, confirmatory test if child is asymptomatic

Clinical features suggestive of non-type 1 diabetes mellitus are listed below:
a) Obesity (body mass index >95th percentile for age and gender)
b) Family history of type 2 diabetes in a first- or second-degree relative(s)
c) Belonging to a high-risk ethnic group (e.g., Indigenous, Black, Latin American, South-Asian)
d) A history of exposure to diabetes *in utero* (diagnosed before or during pregnancy)
e) Acanthosis nigricans

f) Polycystic ovarian syndrome
g) Diabetes in a person with a syndrome often associated with type 2 diabetes (Prader-Willi syndrome)
h) Diabetes in a non-obese patient with at least one first-degree relative with diabetes
i) Diabetes diagnosed in a neonate/infant less than 6 months of age
j) Minimal or no insulin requirement with a normal or near normal A1c level (4–6%) one year after diagnosis
k) A diagnosis of diabetes while on medical therapy with a known diabetogenic medication (e.g., glucocorticoids, L-asparaginase, cyclosporine, tacrolimus, atypical antipsychotic, anticonvulsant)

Exclusion criteria
Do not report patients with cystic fibrosis-related diabetes, pregnant teenagers with gestational diabetes, and patients in critical care settings requiring **short-term** insulin therapy for stress hyperglycemia.

Unique to this study
Reporting physicians had the option of accessing free specialized pancreatic autoantibody testing accessed via the Barbara Davis Center for Childhood Diabetes (Denver, Colorado) if they felt that the additional testing would help with the classification of diabetes subtype, and did not have access to this testing via their provincial laboratory services. This part of the study was not conducted through the CPSP and required patient consent.

Results – June 2017 to May 2019

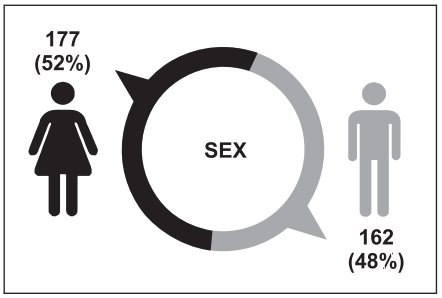
TABLE 1 – NT1DM cases from June 1, 2017 to May 31, 2019

Year	Reported	Reports from Quebec‡	Duplicates	Excluded	Pending	Met case definition
2017*	149	—	11	18	24	96
2018	281	2	11	23	79	166
2019†	136	6	5	7	41	77
Total	**566**	**8**	**27**	**48**	**144**	**339**

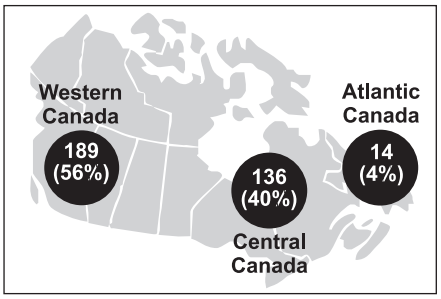
* June 1 to December 31, 2017
† January 1 to May 31, 2019
‡ Due to Quebec legislation, cases notified by Quebec participants after August 1, 2018 were not included in the data analysis and detailed case information was not collected, unless reported from a centre with project-specific research ethics board approval.

Cases that met the case definition
At the time of analysis, 339 cases were verified as meeting the case definition for NT1DM from June 1, 2017 to May 31, 2019.

Demographics
- Patient sex was female in 177/339 (52%) cases and male in 162/339 (48%) cases.
- Population groups were indicated for 337 cases with the majority of cases being from the following groups: 152 (45%) Indigenous, 83 (25%) White, and 34 (10%) South Asian (Bangladeshi, Punjabi, Sri Lankan, Indian).
- The geographic distribution of cases was as follows: 189 (56%) from Western Canada, 136 (40%) from Central Canada, and 14 (4%) from Atlantic Canada.



Presentation and diagnosis
- The 339 cases were assigned a final classification of diabetes subtype by the research team: 265 (78%) cases were T2D, 52 (15%) were MID, 10 (3%) were monogenic diabetes, and 12 (4%) were indeterminate.
- Patients were asymptomatic in 154/331 (47%) cases.
- Polyuria was present at diagnosis in 151/331 (46%) cases and polydipsia in 143/331 (43%) cases.
- Diabetic ketoacidosis (DKA) was described in 28/337 (8%) cases. Hyperglycemic hyperosmolar state (HSS) was described in 5/331 (2%).



Treatment and outcomes
- Insulin was initiated in 185/334 (55%) cases and metformin in 166/334 (50%) cases.
- Almost 70% (229/334) of cases were provided with diet/lifestyle modification counselling.

Study limitations
- Limitations common to all CPSP studies are listed on page 11.
- In some cases, insufficient clinical information was provided to accurately assign a diagnosis of diabetes subtype.

Conclusions

- Sex-specific differences in NT1DM presentation were not observed.
- Indigenous peoples were disproportionately affected by NT1DM, accounting for 45% of the cases reported.
- Nearly half of NT1DM cases were asymptomatic at presentation.
- Approximately 10% of cases presented with DKA and/or HHS.
- Classification of the pending NT1DM cases is ongoing. Once classification is complete, the observed minimum incidence rates of NT1DM and its subtypes (T2D, monogenic diabetes, MID) will be determined and compared to the previous CPSP study from 2006 to 2008.

Anticipated study impact

- Study results will provide minimum incidence rates and trends in childhood-onset NT1DM and its subtypes based on Canada's unique ethnic, cultural, and geographic characteristics.
- Results will help define childhood-onset T2D risk factors and clinical characteristics, and will describe diabetes-related complications.
- By replicating the first CPSP study on NT1DM, this subsequent study can help determine whether the epidemiology of childhood-onset T2D is changing related to demographics, clinical presentation, and severity — information that is critical to designing prevention and treatment programs that meet the specific needs of the populations affected.

Publication and dissemination

Non-type 1 diabetes. Amed S, Sellers E. Canadian Paediatric Society Annual Conference, Quebec City, in May 2018 (oral presentation)

Acknowledgements
The study team would like to thank clinical fellow, Trisha Patel and research coordinator, Aysha Ayub.

Infantile and later-onset paediatric Pompe disease (glycogen storage disease type II)

October 2017 to September 2019 – Final report

Eugenio Zapata Aldana

Principal investigators

Craig Campbell, MD, Department of Neurology, Paediatrics, University of Western Ontario, London Health Sciences Centre; craig.campbell@lhsc.on.ca

Eugenio Zapata Aldana, MD, Genetics, Department of Neurology Paediatrics, London Health Sciences Centre; eugenio.zapataaldana@lhsc.on.ca

Co-investigators

Brunel-Guitton C, Chakraborty P, McMillan H, Mitchell J, Roth J, Rupar T, Tarnopolsky M, Turner L

Question

- What is the clinical presentation of infantile and later-onset paediatric Pompe disease in Canada?
- What are the minimum incidence and minimum prevalence of infantile-onset and later-onset paediatric Pompe disease in Canadian children and adolescents?

Importance

- The classic manifestations in congenital and adult-onset Pompe disease have been well characterized, but it is critical to understand the full spectrum of symptoms and clinical characteristics associated with infantile and juvenile-onset paediatric Pompe disease in order to start prompt management and treatment.
- The incidence and prevalence of infantile and juvenile-onset paediatric Pompe disease in Canadian children and adolescents are unknown.
- Raising awareness among Canadian paediatricians about infantile and juvenile-onset Pompe disease in Canadian children and adolescents is important to ensure that the disease is considered appropriately in the differential diagnosis for children presenting with proximal weakness, hypotonia, respiratory insufficiency, and/or high serum creatine kinase.
- Early diagnosis and treatment are critical for infants with Pompe disease. Study results may provide evidence to support the addition of Pompe disease to the list of diseases for newborn screening.

Methodology

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

Case definition

A patient (new or previously diagnosed) of less than 18 years old meeting the following criteria:

1. **Genetic criteria:** Pathogenic mutations affecting both *GAA* genes (encodes the acid alpha-glucosidase protein) as determined by sequence analysis or deletion/duplication analysis

   AND/OR

2. **Biochemical criteria:** Measurement of acid alpha-glucosidase (GAA) enzyme activity performed on one or more of:
   - Dried blood spot GAA enzyme activity assay
   - Whole blood GAA enzyme activity assay
   - Skin biopsy (fibroblast culture) GAA enzyme activity assay
   - Muscle biopsy GAA enzyme activity assay

Exclusion criteria

Clinical evidence of proximal muscle weakness without genetic or biochemical confirmation of disease

Unique to this study

Although Canadian Paediatric Surveillance Program (CPSP) studies classically capture minimum incidence rates, this study also aimed to capture the prevalence of infantile and later-onset paediatric Pompe cases in Canada.

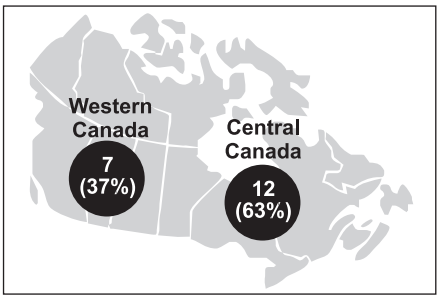
Results – October 2017 to September 2019

TABLE 1 – Infantile and later-onset Pompe cases from October 1, 2017 to September 30, 2019						
Year	**Reported**	**Reports from Quebec‡**	**Duplicates**	**Excluded**	**Pending**	**Met case definition**
2017*	1	—	0	0	0	1
2018	13	0	1	0	1	11
2019†	11	0	0	0	4	7
Total	**25**	**0**	**1**	**0**	**5**	**19**

* October 1 to December 31, 2017
† January 1 to September 30, 2019
‡ Due to Quebec legislation, cases notified by Quebec participants after August 1, 2018 were not included in the data analysis and detailed case information was not collected, unless reported from a centre with project-specific research ethics board approval.

Cases that met the case definition

- At the time of analysis, 19 incident and prevalent cases of infantile and later-onset paediatric Pompe disease were verified as meeting the case definition from October 1, 2017 to September 30, 2019.
- During the two-year surveillance period, fewer than five incident cases were reported.



Demographics

- Patient sex was male in the majority of cases.
- Age ranges were as follows: 8 (42%) cases were 0 to 5 years of age; 7 (37%) cases were aged 6 to 12 years; and the remaining cases (21%) were older than 13 years of age.
- Population group was reported as White in 60 percent (11/19) of cases.
- The geographic distribution of cases was 12 (63%) from Central Canada and 7 (37%) from Western Canada.
- In thirteen (68%) cases, the reported child was the first known case in the family.

Presentation and diagnosis

- The age range of symptom onset was 0 to 13 years. Eleven (58%) cases had symptoms before the age of 12 months.
- Twelve (63%) cases were diagnosed within a year of symptom onset.
- Twelve (63%) cases presented with high serum creatine kinase levels.
- The most frequent signs or symptoms prior to the clinical diagnosis included the following: 11 cases with cardiomyopathy, 10 cases with hypotonia, 8 cases with proximal weakness of the legs, 7 cases with proximal weakness of the arms, and 7 cases who were never able to crawl.
- Multiple methods were used for the diagnosis of Pompe disease, but the most used were blood enzyme analysis through dried blood in 12 (63%) cases and Sanger targeted gene sequencing in 7 (37%) cases. Biochemistry and genetic analyses were performed mostly in laboratories in Central and Western Canada.

Treatment and outcomes

Enzyme replacement therapy (ERT) was available for 15 (79%) cases after the diagnosis. Of the patients who received ERT, nine (60%) reported clinical improvement.

Study limitations

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

Conclusions

- During the 24-month study, fewer than five incident cases were reported. Given the annual live birth rate in Canada, this data suggests that the incidence of infantile and later-onset paediatric Pompe disease is substantially lower than what is reported in the literature. However, caution should be taken before making firm conclusions or calculating true incidence or prevalence rates from a two-year surveillance period for this exceptionally rare disease. The number of cases reported will be validated against numbers reported by the clinical diagnostic laboratories across Canada.
- Close to 60% of cases had symptoms before 12 months of age and were diagnosed within a year of symptom onset. Most cases presented with high serum creatine kinase levels and the most frequently reported signs or symptoms were cardiomyopathy, hypotonia, proximal weakness of the arms and/or legs, and inability to crawl.
- A significant proportion of identified prevalent cases treated with ERT demonstrated its effectiveness, as reported by the participating health care providers.

Anticipated study impact

Knowledge translation will include comparative data of minimum disease prevalence against what is reported in the literature. Information will be distributed to relevant knowledge users across Canada.

Acknowledgements
We would like to thank Rhiannon Hicks and Riley Young for all their help with the CPSP Pompe study.

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

November 2018 to October 2020

Jesse Papenburg

Principal investigators

Andrée-Anne Boisvert, MD, Department of Paediatrics, CHU de Québec, Faculty of Medicine, Université Laval; andree-anne.boisvert.1@ulaval.ca

Jesse Papenburg, MD, MSc, Infectious Diseases Division, Department of Paediatrics, and Division of Microbiology, Department of Laboratory Medicine, Assistant Professor of Paediatrics, Montreal Children's Hospital; jesse.papenburg@mail.mcgill.ca

Co-investigators

Aho J, Darling E, Moore DL, Mulholland C, Perreault T

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 National Disease Surveillance System (NDSS); 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.

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 NDSS.

Results – November 2018 to December 2019

TABLE 1 – ON cases from November 2018 to December 2019					
Reported	**Reports from Quebec***	**Duplicates**	**Excluded**	**Pending**	**Met case definition**
12	0	0	3	0	9

* Due to Quebec legislation, cases notified by Quebec participants after August 1, 2018 were not included in the data analysis and detailed case information was not collected, unless reported from a centre with project-specific research ethics board approval.

Cases that met the case definition
At the time of analysis, nine cases of ON were verified as meeting the case definition since surveillance started in November 2018.

Demographics
For the nine confirmed cases, the mean age at presentation was 16.4 days (median 13 days, range: 4 to 34 days).

Presentation and diagnosis
- Conjunctival/ocular discharge was present in all cases (9/9).
- Conjunctival/ocular erythema was present in 8/9 cases.
- Conjunctival and/or peri-ocular swelling was present in 6/9 cases.
- Microbiological specimens were positive for *C trachomatis* in six cases.

Prevention, treatment, and outcomes
- All cases received optimal treatment as per current guidelines.
- There was no evidence of complications/sequelae such as corneal ulcers, ocular perforation, or pan ophthalmitis.
- The nine confirmed cases included reports from jurisdictions that mandate erythromycin ointment, jurisdictions where use is routine with informed consent, and jurisdictions where use is routine unless the decision is made to opt out. At this stage in the data collection, no clear trend related to the policy context and administration of ocular prophylaxis is evident.
- In some cases, the mothers received adequate STI screening and treatment during pregnancy; however, others had prenatal care without being screened or did not have access to prenatal care.

Study limitations
Limitations common to all Canadian Paediatric Surveillance Program (CPSP) studies are listed on page 11.

Conclusions
- This CPSP study will continue until October 2020 and monitor the number of GON and CON cases that are reported to the Program.
- Further data analysis is required.

Anticipated study impact
- This study will provide valuable clinical and epidemiological information on cases of ON across Canada, as ON is no longer a nationally notifiable disease.
- Information on infection rates can be used to understand the effect of current neonatal ocular prophylaxis practices on disease rates, and may inform future clinical recommendations and/or public health policy changes.

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

September 2018 to October 2020


Richard E. Bélanger

Principal investigators

Richard E. Bélanger, MD, Department of Paediatrics, Centre mère-enfant Soleil—CHU de Québec—Université Laval; richard.belanger@chudequebec.ca

Christina Grant, MD, Division of Adolescent Medicine, Department of Paediatrics, McMaster University; chgrant@mcmaster.ca

Co-investigators

Abramovici H, Acker A, Ammerman SD, Gingras N, Laroche J, Moore Hepburn C, Yates R

Collaborator: Dirk Huyer, MD, Chief Coroner for Ontario

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 two-year time period following cannabis legalization?

Importance

- There is currently no scientific data describing the impact of cannabis legalization on the health of Canadian children and youth.
- Data provided by this study will be used to assess the impact of cannabis legalization in the paediatric population.

Methodology

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

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 2019

TABLE 1 – Serious and life-threatening events associated with non-medical cannabis use cases in 2019

Reported	Reports from Quebec*	Duplicates	Excluded	Pending	Met case definition
51	10	0	1	4	36

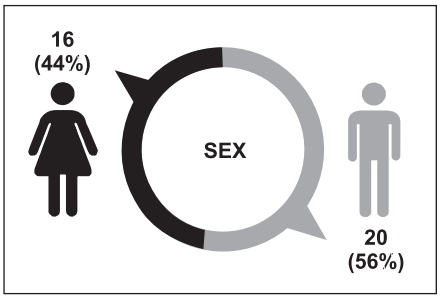
* Due to Quebec legislation, cases notified by Quebec participants after August 1, 2018 were not included in the data analysis and detailed case information was not collected, unless reported from a centre with project-specific research ethics board approval.

Cases that met the case definition

- In total, 51 cases of cannabis related exposure were reported through the Canadian Paediatric Surveillance Program (CPSP) network in 2019.
- At the time of analysis, 36 cases of serious and life-threatening events associated with non-medical cannabis use were verified as meeting the case definition in 2019.

Demographics

- Among confirmed cases, 16 (44%, 95% CI 29–62) were female and 20 (56%, 95% CI 39–71) were male.
- The mean age was 9.7 years with a median of 9.4 years.



Presentation and diagnosis

- The most common case presentation was unintentional injury due to cannabis exposure in 15 cases (42%, 95% CI 26–59), followed by gastrointestinal problems in 8 cases (22%, 95% CI 11–40), and cannabis related disorder (DSM-5) in 5 cases (14%, 95% CI 6–30).
- A third of all cases (12/36, 33%, 95% CI 19–51) were aged 12 years or younger and presented with unintentional injury due to accidental ingestion of edible cannabis products (e.g., gummies, chocolate).
- All eight cases with gastrointestinal problems were between 13 to 18 years old and presented with cannabis hyperemesis syndrome.

Treatment and outcomes

- The vast majority of cases were hospitalized (34/36, 94%, 95% CI 79–99): 29/34 cases (85%, 95% CI 68–94) as inpatients and 6/34 cases (18%, 95% CI 8–35) were admitted to the intensive care unit (more than one location of hospitalization was given for some cases).
- Medical treatment was received by 28 cases (78%, 95% CI 61–89) in the form of ventilation assistance, IV fluids, observation in hospital, antiemetics, etc. Of these cases, 13 (46%, 95% CI 28–66) also received mental health treatment (e.g., psychiatry consultation, referral to a social worker).

Study limitations

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

Conclusions

- A third of cases were 12 years of age or younger with unintentional injury due to accidental ingestion of edibles. This trend will be monitored as the study continues, especially in light of the recent legalization and regulation of cannabis edible products in Canada (October 2019).
- More time is required to determine the impact of the new legislation, since edible cannabis products did not become available for purchase through the legal market until late December 2019 or later.

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 policies and further regulation related to non-medical cannabis.
- The information from this study may be adapted for public education materials.

Publication and dissemination

A green light for advocacy efforts by paediatricians around cannabis use. Bélanger R, Grant C. Canadian Paediatric Society Annual Conference, Toronto, in June 2019 (oral presentation)

Acknowledgements

Thank you to Anna-Maria Frescura, Health Canada, for all 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

February 2018 to January 2020

Geoff Ball

Principal investigators

Geoff Ball, PhD, RD, Professor, Department of Pediatrics, University of Alberta; gdball@ualberta.ca

Catherine Birken, MD, MSc, FRCPC, Professor, Department of Paediatrics, University of Toronto; catherine.birken@sickkids.ca

Co-investigators

Bélanger S, Bridger T, Chanoine JP, Gibson W, 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

Question

- 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.

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.

   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 – January to December 2019

TABLE 1 – SO and GDD cases in 2019

Reported	Reports from Quebec*	Duplicates	Excluded	Pending	Met case definition
42	9	1	6	10	16

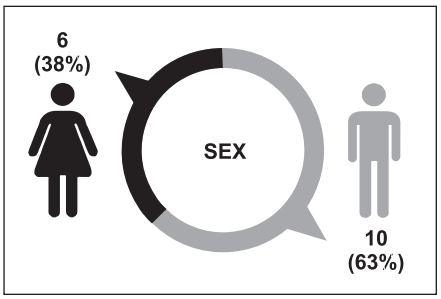
* Due to Quebec legislation, cases notified by Quebec participants after August 1, 2018 were not included in the data analysis and detailed case information was not collected, unless reported from a centre with project-specific research ethics board approval.

Cases that met the case definition

At the time of analysis, 16 cases of comorbid SO and GDD were verified as meeting the case definition in 2019.

Demographics

- Patient sex was male in 10 (63%) cases and female in 6 (38%) cases.
- The mean age of the cases was 3.2 years (*SD*=1.2).
- The geographic distribution of cases was: 11 (69%) from Ontario and the remaining cases from other provinces/territories.
- Population groups were as follows: 8 (50%) cases were White and the remaining cases were Métis, Black, First Nations, Latin American, and South Asian.



Presentation and diagnosis

- Cases had a mean BMI z-score of 4.4 (*SD*=1.1).
- 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*=1.6).
- The mean age of first weight concern was 1.9 years (*SD*=1.3).
- The most common comorbidity was autism spectrum disorder (5/16, 31%).
- The most frequently reported health problems were school and/or behavioural problems (7/16, 44%) and high blood pressure (5/16, 31%).
- Genetic tests were ordered for 14 (88%) cases, including 12 (75%) microarrays.
- Central nervous system imaging was ordered for 6 (38%) cases.

Treatment and outcomes

- The most common reporting physician's role was consulting endocrinologist in 6 (38%) cases and consulting paediatrician in 5 (31%) cases.
- Other clinicians/services involved in patient care included: general paediatricians in 13 (81%) cases; 11 (69%) cases each of speech therapists, dietitians, and family physicians; and 10 (63%) cases each of developmental programs, geneticists, and social workers.
- Challenges reported in caring for children with SO and GDD included coordination of care and the family's geographic distance from health services.

Study limitations

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

Conclusions

- In the cases reported in 2019, concerns about SO among children with GDD were recognized at approximately 1.9 years of age.
- Overall, the demographic characteristics and presentation of cases reported in 2019 were similar to those reported in 2018.
- Genetic testing, including microarray, was ordered in most cases, which is consistent with current guidelines.
- Multidisciplinary services were provided often; however, coordination of care and geography were perceived challenges that had a negative impact on health service delivery.

Anticipated study impact

- This study will be the first to establish the minimum incidence of SO and GDD in preschool children in Canada.
- The study will help 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.

Acknowledgements

We wish to thank Nicole Gehring (University of Alberta) and Stephan Oreskovich (The Hospital for Sick Children) for their help with the CPSP study on severe obesity and global developmental delay in preschool children.

One-Time Surveys

Paediatric cholesterol screening and treatment in Canada: Practices, attitudes, and barriers

February 2019


Michael Khoury

Principal investigators
Michael Khoury, MD, Division of Pediatric Cardiology, Stollery Children's Hospital, University of Alberta; khoury1@ualberta.ca

Sarah de Ferranti, MD, MPH, Department of Cardiology, Boston Children's Hospital; Sarah.DeFerranti@cardio.chboston.org

Co-investigators
Birken C, Gill P, Harris K, Mackie A, McCrindle B, McLaughlin T, Rodday AM, Wong P

Question

What are the practices, attitudes, and perceived barriers related to paediatric lipid screening and treatment among Canadian paediatricians?

Importance

- Familial hypercholesterolemia (FH) has a population prevalence of approximately 1:250 and results in lifelong elevations in low-density lipoprotein cholesterol (LDL-C), leading to accelerated atherosclerosis (starting in childhood) and premature cardiovascular disease (CVD).
- As children with FH are typically asymptomatic, recommendations have been made in the United States for universal paediatric lipid screening.
- Knowledge of the current practices, attitudes, and barriers related to paediatric lipid screening and treatment in Canada are currently unknown.

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.

Unique to this survey

The survey specifically targeted those caring for 9- to 11-year-old children. Analysis focused on paediatricians who reported providing primary care as part, or all, of their practice.

Results

The survey response rate was 28% (759/2742), including 236 primary-care-providing paediatricians with a mean duration of practice of 18 years (*SD*=13).

Lipid screening and management practices

- The vast majority of primary-care-providing paediatricians (93%, 215/230) reported that they do not perform routine lipid screening for healthy children.
- Screening practices were more common for youth with specific risk factors or at-risk conditions, such as overweight/obesity, hypertension, diabetes, and a family history of premature CVD.

TABLE 1 – Lipid screening practices for 9-to 11-year-old children with different risk factors			
Risk factors	**n**	**Never/rarely/some of the time**	**Usually/most/all of the time**
Healthy children	230	215 (93%)	15 (7%)
Overweight/obesity	235	46 (20%)	189 (80%)
At-risk race/ethnicity	225	155 (69%)	70 (31%)
Chronic cardiometabolic condition (e.g., hypertension, diabetes)	220	30 (14%)	190 (86%)
Family history of premature CVD	217	87 (40%)	130 (60%)
Family history of high cholesterol	215	61 (28%)	154 (72%)

TABLE 2 – Lipid screening and management practices for a child aged 9 to 11 years with LDL-C of 5.2mmol/L (ideal <2.8mmol/L) persisting despite dietary and lifestyle changes			
Lipid Practices	**n**	**Never/rarely/some of the time**	**Usually/most/all of the time**
Start statin	220	184 (84%)	36 (16%)
Refer to dietician	220	23 (10%)	197 (90%)
At-risk race/ethnicity	224	47 (21%)	177 (79%)

Attitudes towards paediatric lipid screening and management

- Only 34% (72/210) of respondents agreed or strongly agreed that all children should receive cholesterol screening. Half of respondents (50%, 107/213) felt that screening all children would result in unnecessary and costly follow-up.
- Three quarters (75%, 167/223) of respondents agreed or strongly agreed that statins were appropriate for children 9 to 11 years old with elevated LDL-C (>5 mmol/L) despite lifestyle changes. However, a significantly lower proportion would start statin therapy themselves in a child with persistent severe elevations in LDL-C.

Perceived barriers

- Almost half (49%, 114/233) of respondents felt that a major barrier to the screening and treatment of paediatric lipid disorders was a lack of relevant Canadian paediatric lipid guidelines.
- Other barriers reported included a lack of access to the following: professionals who address behaviour change (68%, 153/224), physical activity opportunities or programs (52%, 120/233), dietary/nutrition specialists (45%, 96/215), and paediatric lipid specialists (35%, 77/219).

Survey limitations

- Limitations common to all CPSP surveys are listed on page 11.
- While the response rate is somewhat low, it is in keeping with previous CPSP one-time surveys. The practice patterns, attitudes, and perceived barriers of respondents may be different than non-respondents.
- The presented results are specifically for paediatricians providing primary care. The survey did not include family physicians, who provide most of the primary care for Canadian youth.
- The self-reported practice patterns may not be consistent with true clinical practice.

Conclusions

- Primary-care-providing paediatricians infrequently perform universal paediatric lipid screening for otherwise healthy 9- to 11-year-old children. Rather, they are more likely to perform selective screening based on the presence of existing risk factors or conditions.
- Management of severe dyslipidemia includes appropriate dietician and specialist referral. The majority of respondents support the use of statins when clinically indicated.
- Key barriers limiting the screening and management of paediatric lipid disorders by primary-care-providing paediatricians include a lack of relevant Canadian guidelines and poor access to specialists and services.

Anticipated survey impact

The survey findings will inform the development of a Canada-specific paediatric lipid screening statement and contribute to knowledge translation tools for Canadian primary-care providers.

Publication and dissemination

Child and adolescent lipid screening and management. Khoury M, Wong J, Wong P. Canadian Paediatric Society Annual Conference, Vancouver, in June 2020 (seminar) (postponed)

Vaping-related illness and injury

September 2019

Nicholas Chadi

Principal investigator

Nicholas Chadi, MDCM, MPH, Adolescent and Addiction Medicine, Department of Paediatrics, CHU Sainte-Justine, Clinical Assistant Professor, Université de Montréal; nicholas.chadi.hsj@ssss.gouv.qc.ca

Co-investigators

Beno S, Moore Hepburn C, Richmond S, Thompson W

Question

- Over the preceding 12 months, how often did Canadian paediatricians observe cases of illness or injury related to the routine use of vaping devices (i.e., direct inhalation or second-hand exposure), ingestion (i.e., drinking) of e-liquids and/or other vaping substances, and malfunction of vaping devices (e.g., explosion, fire)?
- Are paediatricians comfortable discussing vaping-related health risks with youth and families?

Importance

- According to the 2018–19 Canadian Student Tobacco, Alcohol and Drugs Survey, 20% of high school students had used an e-cigarette in the past 30 days, an increase from 10% in 2016–17.
- Given the rapidly changing rates of vaping in Canada, timely data is essential to understand the landscape of injuries and serious illnesses related to children and adolescents' exposure to vaping products in Canada.

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.

Results

The survey response rate was 42% (1131/2693).

Respondent demographics and comfort discussing vaping-related health risks

- Survey responses were received from across the country and almost all participants (99%, 1126/1131) reported their practice specialty. Of those, over half (57%, 637/1126) were general paediatricians and 42% (475/1126) were paediatric subspecialists.
- Of the eighty-eight percent (990/1131) of respondents who reported their comfort level in discussing potential vaping-related health risks with youth and families, 31% (307/990) felt somewhat or very uncomfortable discussing vaping-related health risks.

Overall vaping-related illness and injury

- Respondents reported 88 cases of vaping-related illness and injury in children and youth in the preceding 12 months.
- Twenty-eight cases resulted in visits to the emergency room, 22 cases required hospitalization, and 13 cases were admitted to the intensive care unit. In some cases, treatment was sought in multiple locations.
- Where patient outcome was known, 31% (16/51) had ongoing health issues.

Serious illness or injury following routine use of vaping device

- Respondents reported 71 cases of illness or injury related to the routine use of a vaping device (i.e., direct inhalation or second-hand exposure) including 40 (56%) males and 31 (44%) females.
- Of these cases, 68% (48/71) were older than 15 years of age, with the majority exposed through direct inhalation.
- All cases involving children 9 years old and under resulted from second-hand exposure.
- Access to the vaping device was reported in 49/71 (69%) of cases. Of those, 34/49 (69%) patients owned the device and 17/49 (35%) patients obtained the device from a friend or family member. Some cases reported multiple means of access to the device.
- The vaping substance(s) contained in the e-liquid was known for half (51%, 36/71) of the cases. For those cases reporting specific substances, nicotine was most commonly mentioned.

- The patient's health complaint(s) was reported for 65/71 (92%) cases. Of the injuries and illnesses reported, 38/65 (58%) cases involved respiratory distress/lung injury, 13/65 (20%) cases had symptoms of acute nicotine toxicity and 8/65 (12%) cases reported central nervous system depression. Other injuries and illnesses reported included mouth/throat irritation and/or burn, abdominal pain, and nausea/vomiting. In some instances, multiple complaints were reported for the same case.
- Treatment location was reported for 57/71 (80%) cases, with more than one location per patient recorded in some cases. The majority of cases were treated in the emergency room and/or on a hospital ward; 12/57 (21%) cases required intensive care unit admission.
- Patient outcome was reported for 44/71 (62%) cases. Of those, 31/44 (70%) patients fully recovered and 13/44 (30%) patients had ongoing health issues.

Ingestion of e-liquids and/or other vaping substances

- Survey respondents reported 13 cases of illness or injury related to the ingestion (i.e., drinking) of e-liquids and/or other vaping substances, including 8 (62%) females and 5 (38%) males.
- There was an equal number of intentional and unintentional ingestions. Intentional ingestions were more common among youth 15 years of age and older while unintentional ingestions were more common in younger children 1 to 4 years of age.
- The type of substance ingested was reported in 6/13 (46%) cases. Of those, cannabis, nicotine and flavouring were the most commonly reported substances.

Injury secondary to malfunction of vaping device

- Survey respondents reported fewer than five cases of injuries resulting from the malfunction of a vaping device (e.g., explosion, fire).
- The majority of cases involved youth 15 through 18 years of age.
- The majority of injuries were due to battery malfunction or electrical fire.

Survey limitations

- Limitations common to all CPSP surveys are listed on page 11.
- Given that data was collected from multiple providers, duplicate cases cannot be identified and it is possible that some cases were counted more than once. However, data was checked for potential overlap using respondents' postal codes and demographic characteristics and no overlap was found.
- Survey participants were paediatricians and paediatric subspecialists; therefore, results did not include cases that were seen or managed by non-paediatricians.
- Data collection relied on physician voluntary reporting of cases which was subject to recall bias.

Conclusions

- Survey results revealed that injuries and illnesses associated with the use of vaping products are occurring in Canada. Respondents reported 88 cases of vaping-related illness and injury in the preceding 12 months.
- The most common illness/injuries associated with the routine use of a vaping device were lung injury or respiratory distress.
- Twenty-eight cases resulted in visits to the emergency room, 22 cases required hospitalization, and 13 cases were admitted to the intensive care unit. In some cases, treatment was sought in multiple locations.
- Thirty-one percent (16/51) of cases had ongoing health issues.
- Thirty-one percent (307/990) of respondents reported feeling somewhat uncomfortable or very uncomfortable discussing vaping-related health risks with youth and families, suggesting there is an opportunity for training and education for those who care for children and youth who may be exposed to vaping products.

Anticipated survey impact

- Survey results provide insights about acute harms associated with vaping product exposure among children and youth. These insights can help guide improvements in clinical practice and public health interventions to reduce risks associated with vaping products.
- Survey results on harms related to vaping products will be shared with provincial and federal policy and regulatory departments.
- This survey also provides important preliminary data laying the groundwork for more in-depth, epidemiological prevention and intervention studies.

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 2020 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

Incidence trends of type 2 diabetes, medication-induced diabetes, and monogenic diabetes in Canadian children

Trisha Patel, MD, FRCPC, Paediatric Endocrinology Fellow, BC Children's Hospital

Elizabeth Sellers, MD, MSc, FRCPC, Professor, University of Manitoba, Paediatric Endocrinologist, Winnipeg Children's Hospital

Jill Hamilton, MD, MSc, FRCPC, Professor, University of Toronto, Paediatric Endocrinologist, The Hospital for Sick Children

Shazhan Amed, MD, MSc.PH, FRCPC, Clinical Associate Professor, University of British Columbia, Paediatric Endocrinologist, BC Children's Hospital

Clinical case

A 15-year-old, previously healthy male, presents with polyuria and polydipsia to his family physician. There is no fever or infection. His random blood glucose is 12 mmol/L and he has glucosuria. His urine ketones are negative. The mother's pregnancy history revealed no gestational diabetes. He was born at term. His birth weight was 3.2 kg. Past medical history is significant for a learning disability. He takes no medications. His family is of European descent and there is no consanguinity. His mother has diabetes, diagnosed at 24 years of age and she requires insulin therapy. His maternal grandfather was also diagnosed with type 2 diabetes and has been treated with insulin since diagnosis (age at diagnosis is unknown). This gentleman developed diabetes nephropathy at 50 years of age.

On examination, the boy's height is 174.5 cm (76th percentile), weight is 65 kg (76th percentile), and body mass index is 21.3 kg/m^2 (72nd percentile). His blood pressure is normal. Systemic examination is unremarkable, including no acanthosis nigricans. Further investigations are requested to delineate diabetes subtype: hemoglobin A1c is 6.8%, GAD65 antibody is negative, fasting blood glucose is 7.6 mmol/L, fasting insulin is 61 pmol/L, fasting C-peptide is 400 pmol/L (normal 325–1050), and high-sensitivity C-reactive protein (CRP) is low. Blood glucose monitoring is initiated at home. Blood glucose levels are: fasting 5.6–6.1 mmol/L, before meals 5.3–8 mmol/L, and 2-hour post-prandial 7.1–9 mmol/L. Monogenic diabetes is suspected. Initially, he is managed with diet and lifestyle changes. Genetic testing confirms a pathogenic variant in the *HNF1A* gene, consistent with a diagnosis of MODY-3. Due to persistent hyperglycemia, low-dose gliclazide is prescribed and he tolerates it well.

What a clinician needs to know

Monogenic diabetes is caused by single gene variants and accounts for 1–6% of paediatric diabetes. Monogenic diabetes includes neonatal diabetes, syndromic diabetes, and maturity-onset diabetes of the young (MODY). A defect in the development or function of beta cells, resulting in reduced insulin secretion, underscores the pathophysiology of MODY.

Presentation and diagnosis

Similar to type 1 or type 2 diabetes, individuals with MODY can present with weight loss, fatigue, polydipsia, polyuria, and nocturia. Thus, patients may be misdiagnosed as having type 1 or type 2 diabetes. Features that suggest MODY include: 1) a family history of diabetes affecting two generations (e.g., one affected parent and another first-degree relative of that affected parent); 2) absence of islet autoantibodies, especially if measured at diagnosis; 3) low insulin requirements and/or measurable C-peptide levels (indicating endogenous insulin secretion) at least five years post-diagnosis; 4) lack of acanthosis nigricans on physical examination and/or other clinical features of metabolic syndrome; and 5) absence of severe or generalized obesity.

At least 14 genes have been linked to a MODY-like phenotype. Although MODY is primarily familial due to heterozygous dominant variants in these genes, sporadic de novo variants have been reported. The most common subtypes are MODY-3 (*HNF1A*) and MODY-2 (*GCK*), accounting for approximately 70% of all cases, followed by MODY-1 (*HNF4A*) and other rarer subtypes. Molecular genetic testing confirms a diagnosis of MODY. MODY gene panels are offered by speciality laboratories in the United States and the United Kingdom. If a specific subtype is suspected, targeted gene analysis is preferred, and it is available in Canada.

Types of MODY and treatment

MODY-2 patients are usually asymptomatic and present with mildly elevated fasting glucose (5.5–8.5 mmol/L). Minimal post-prandial hyperglycemia may occur (8.6 mmol/L). This condition remains stable over time and diabetes-related complications are rare. Pharmacologic treatment is not required.

MODY-1 and MODY-3 patients share some similarities. With beta cell function decline over time, patients typically present during adolescence or young adulthood. Initially, fasting blood glucose can be normal but post-prandial hyperglycemia and/or an abnormal response after the two-hour oral glucose tolerance test are observed. Eventually, patients develop fasting hyperglycemia and become symptomatic. Diabetes-related complications commonly occur. Suspicious features for MODY-1 include low triglyceride, high low-density lipoprotein (LDL) cholesterol, low high-density lipoprotein (HDL) cholesterol, large-for-gestational age at birth, and a history of neonatal hyperinsulinemic hypoglycemia. Characteristics unique to MODY-3 include glycosuria at blood glucose <10 mmol/L, low high-sensitivity CRP, and normal or increased HDL cholesterol. Diet and lifestyle management may suffice initially, but the majority need pharmacologic treatment. Sulfonylureas are the most effective therapy and offer better glycemic control than insulin.

MODY-5 patients similarly present during adolescence and young adulthood. Renal developmental disorders (e.g., renal cysts, renal dysplasia), genital tract anomalies, hyperuricemia, and abnormal liver function tests are extra-pancreatic features of MODY-5. Exocrine pancreatic function can be impaired as well, evidenced by reduced fecal elastase. The genetic basis of MODY-5 is *HNF1B* variants. Patients with MODY-5 are less responsive to sulfonylureas, and insulin treatment is often initiated early.

With increased awareness and heightened suspicion for MODY, clinicians can provide timely diagnosis, appropriate treatment, and genetic counselling. Involvement of endocrinology, medical genetics, and other specialty services (e.g., nephrology) ensures comprehensive medical care for MODY patients.

Infantile and later-onset paediatric Pompe disease (glycogen storage disease type II)

Craig Campbell, MD, Department of Neurology, Paediatrics, University of Western Ontario, London Health Sciences Centre

Eugenio Zapata Aldana, MD, Genetics, Department of Neurology Paediatrics, London Health Sciences Centre

Clinical case

A nine-year-old female presents with a six-month history of progressive fatigue and exercise intolerance. Her developmental history reveals normal motor milestones. Her medical history includes three visits to the emergency room in the last two years due to "shortness of breath". These episodes were diagnosed as possible asthma exacerbations; however, a lack of response to bronchodilators was noted. Her physical examination is significant for generalized low muscle bulk, scapular winging, moderate thoracolumbar scoliosis, and weakness of the hip flexors. Testing shows she has a high serum creatine kinase (CK) of 1300 U/L.

What a clinician needs to know

Typical presentation

Infantile Pompe disease is characterized by profound hypotonia and muscle weakness, failure to thrive, respiratory distress, feeding difficulties (macroglossia, tongue weakness, poor oral-motor skills), hepatomegaly, and myopathic facies (where the face appears expressionless with sunken cheeks, bilateral ptosis, and inability to elevate the corners of the mouth due to muscle weakness). Cardiac manifestations include left ventricular hypertrophy and cardiomyopathy. Cognition is normal.

Later-onset Pompe disease can present any time in childhood or adulthood. Muscle weakness is the most common feature, accompanied with high serum CK levels and/or exercise intolerance due to respiratory insufficiency. Patients also may have scoliosis, gastrointestinal involvement (hepatomegaly and irritable bowel-like symptoms), chronic pain, and joint contractures.

Diagnosis

The differential diagnosis depends on the clinical presentation. The differential diagnosis for infantile-onset Pompe disease should include severe congenital muscle disorders, such as spinal muscular atrophy type 1, Danon disease, systematic primary carnitine deficiency, and glycogen storage disease types III and IV, along with congenital myopathies and congenital muscular dystrophies. For later-onset Pompe disease, the differential diagnosis includes limb-girdle muscular dystrophy, Duchenne muscular dystrophy, juvenile dermatomyositis, and glycogen storage disease types V or VI.

The diagnosis is based on clinical manifestations together with measured acid alpha-glucosidase in dry blood spot and/or Sanger sequencing of the *GAA* gene. Other clinical diagnostics that can be helpful include the following: an electromyography (EMG), which classically demonstrates a myopathic pattern; a total body muscle magnetic resonance image (MRI), which typically shows early tongue involvement; and a muscle biopsy, which demonstrates glycogen accumulation in membrane-bound vesicles as well as abundance of glycogen with periodic acid-Schiff (PAS) staining.

Treatment and management

Performing a rapid and accurate diagnosis is imperative for prompt management with the objective to improve the cardiac, respiratory, and motor function, and most importantly, to increase survival. The management is multidisciplinary with multiple paediatric subspecialties involved including: neurology/neuromuscular medicine, cardiology, respirology, gastroenterology, orthopedics, and genetics.

Enzyme replacement therapy can improve cardiac and respiratory function, and prolong survival in patients with infantile Pompe disease, as well as improve muscle strength, pulmonary function, and survival in patients with later-onset Pompe disease.

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

Andrée-Anne Boisvert, MD, Department of Paediatrics, CHU de Québec, Faculty of Medicine, Université Laval

Jesse Papenburg, MD, MSc, Infectious Diseases Division, Department of Paediatrics, and Division of Microbiology, Department of Laboratory Medicine, Assistant Professor of Paediatrics, Montreal Children's Hospital

Clinical case

A 6-day-old boy presents in the emergency room with eye discharge. At examination, bilateral conjunctival erythema and purulent discharge are noticed. Eyelid swelling is also noted. No fever was documented, either at home or at the hospital. Antibiotics (cefotaxime and azithromycin) are started after cultures are drawn. Ocular erythema and swelling resolve within 48 hours. The nucleic acid amplification test (NAAT) of ocular discharge comes back positive for *Chlamydia trachomatis*. A three-day course of azithromycin is completed. No sequela or complications are noticed at follow-up. The mother was referred to her doctor for assessment and adequate treatment for her and her sexual contact.

What a clinician needs to know

Ophthalmia neonatorum or neonatal conjunctivitis is defined as conjunctivitis occurring in the first 4 weeks of life. Previously, this term referred only to cases caused by *Neisseria gonorrhoeae*, but the definition has evolved to include any conjunctivitis in this age group. Conjunctivitis could be caused by a bacterium (e.g., *N gonorrhoeae*, *C trachomatis*, staphylococcus species, a streptococcus species, a *Haemophilus* species or other Gram-negative bacterial species), a virus (e.g., herpes simplex, adenovirus, enteroviruses), or by noninfectious causes such as mechanical (e.g., blocked tear ducts), chemical, or irritative.

Presentation and diagnosis

Neonatal conjunctivitis presents with eyelid swelling and erythema, and can be unilateral or bilateral. Further investigations are needed to confirm the cause and orient treatment. Consultation with an ophthalmologist may be needed to assess ocular involvement. Regular bacterial culture of eye secretions, including gram stain are useful. Culture on selective media for *N gonorrhoeae* could be added. However, NAAT is a more sensitive and rapid test than culture for *N gonorrhoeae* and *C trachomatis*. Blood and cerebrospinal fluid cultures should be considered as per clinical presentation (e.g., fever, change in behaviour). Information about maternal screening during pregnancy should be gathered for *N gonorrhoeae*, *C trachomatis*, HIV, syphilis, and hepatitis B serologies. Other investigations may be needed as per risk factors or clinical findings.

Prevention and treatment

An effective preventive measure for gonococcal and chlamydial infections is to screen, treat, and retest the pregnant woman before the baby is born. Ocular prophylaxis is also used to prevent neonatal conjunctivitis. In Canada, only erythromycin eye ointment (0.5% erythromycin base) is available and must be given as per provincial/territorial regulations. Without preventive measures, gonococcal neonatal conjunctivitis occurs in 30 to 50% of infants exposed during delivery and infants born to women with untreated chlamydia infection at delivery have a 30% to 50% risk of developing chlamydial neonatal conjunctivitis.

After the specimen has been sent to the laboratory, antibiotic treatment should be started empirically until microbiological results are available. Recommended dosages for optimal coverage of gonococcal neonatal conjunctivitis are one dose of ceftriaxone 25 to 50 mg/kg intravenously or intramuscularly, not to exceed 125 mg, or cefotaxime 25 to 50 mg/kg/day divided in two to three doses (based on patient age). For chlamydial neonatal conjunctivitis, use erythromycin 50 mg/kg/day divided in four doses for 14 days or azithromycin 20 mg/kg/day for three days. The mother and her sexual contact should also be referred for assessment and treatment.

Complications

Complications are seen mainly with *N gonorrhoeae* due to corneal involvement. Ulceration with resultant scarring or endophthalmitis could also be sequelae of gonococcal neonatal conjunctivitis, leading to visual impairment. Conjunctival scarring and corneal micro pannus are seen less frequently with chlamydial neonatal conjunctivitis. Non ocular complications can also be seen as *C trachomatis* pneumonia and joint involvement with *N gonorrhoeae.*

Paediatric cholesterol screening and treatment in Canada: Practices, attitudes, and barriers

Michael Khoury, MD, Division of Pediatric Cardiology, Stollery Children's Hospital, University of Alberta

Sarah de Ferranti, MD, MPH, Department of Cardiology, Boston Children's Hospital

Clinical case

An otherwise healthy 10-year-old girl presents to your office for a routine health maintenance visit. On family history, she and her parents are uncertain regarding the extent and timing of cardiovascular disease in the family, but the father has been on statin therapy since young adulthood for "high levels of the bad cholesterol". A non-fasting lipid screening assessment is done and she is found to have a low-density lipoprotein cholesterol (LDL-C) level of 5.2 mmol/L (ideal <2.8 mmol/L). The patient is not obese, is on no medications, and has no other known medical concerns.

After confirming the laboratory result with a fasting assessment, the patient is referred to a dietician and lifestyle recommendations are made. In follow-up four months later, the LDL-C remains elevated at 5.2 mmol/L. The patient is referred to a paediatric lipid specialist. After ruling out secondary causes of paediatric dyslipidemia, the patient is diagnosed with probable heterozygous familial hypercholesterolemia (FH) and is commenced on atorvastatin at 10 mg once per day. Four weeks later, a repeat fasting lipid assessment reveals an LDL-C of 2.9 mmol/L.

What a clinician needs to know

FH is an autosomal co-dominant disorder that results in marked lifelong elevations in LDL-C and premature coronary artery disease. FH is common; present in its heterozygous form in about 1:250 individuals, and even more prevalent in certain ethnic groups such as French Canadians. Because FH results in lifelong dyslipidemia, identification in childhood is feasible. Despite its high prevalence and ease of detection, FH is underdiagnosed, with an estimated 90% of cases remaining undetected.

Presentation and diagnosis

Selective lipid screening on the basis of a family history of premature cardiovascular disease (defined as cardiovascular disease in a man <55 years of age and woman <65 years of age) misses approximately 30 to 60% of cases. Early identification of severe dyslipidemia in youth is important, as a number of clinical trials have demonstrated that early statin treatment from childhood can slow or even reverse atherosclerotic progression and may effectively normalize cardiovascular disease risk in those with FH. Recognizing the benefits associated with early identification, the 2011 National Heart, Lung, and Blood Institute Expert Panel (endorsed by the American Academy of Pediatrics and supported by the 2018 American Heart Association/American College of Cardiology cholesterol guidelines) advised universal non-fasting lipid screening for *all* children at 9 to 11 years of age and again between 17 to 21 years of age. At present, there are no Canadian guidelines advising on paediatric lipid screening.

In the evaluation of a child with severe dyslipidemia, secondary causes of dyslipidemia should be ruled out, including specific medications (such as corticosteroids and estrogen-containing contraceptives), hepatic disease, endocrine disorders such as hypothyroidism and diabetes mellitus, inflammatory disorders such as systemic lupus erythematosus, renal disorders such as chronic renal disease or nephrotic syndrome, acute viral or bacterial infections, among other potential causes. Investigations should be guided on the basis of the clinician's suspicion from the history and physical examination. FH can either be diagnosed via clinical diagnosis or by definitive genetic testing. A number of diagnostic criteria for FH exist, including the widely used Dutch Lipid Clinic Network criteria and recently published Canadian clinical criteria. In the Canadian criteria, the presence of severe elevations in LDL-C (≥4 mmol/L) in the setting of a positive family history of a first-degree member with premature cardiovascular disease or high LDL-C implies "probable" FH. The detection of a causative DNA mutation, the presence of tendon xanthomas, or LDL-C ≥8.5 mmol/L yields a diagnosis of "definite" FH. Systemic manifestations, including cutaneous xanthomas, are typically not present in children with heterozygous FH. Early diagnosis and appropriate therapy from childhood can slow or even reverse atherosclerotic progression and normalize risk in this high-risk population.

Treatment and management

Statin use in the paediatric population effectively lowers LDL-C and slows atherosclerotic progression (measured non-invasively) with short- and medium-term safety established. Specifically, the incidence of statin-associated severe liver or muscle toxicity is exceedingly rare and liver and muscle enzyme measures do not appear different between youth receiving statins and those who are not. Statin use has not been shown to impact growth, pubertal development, or cognition in children. In adults, statin use is associated with a mildly increased risk of type-2 diabetes mellitus. Whether this risk translates to children who receive lower doses of statins and have lower baseline risks for type 2 diabetes mellitus, remains to be studied. On the basis of the evidence to date, accumulated from numerous clinical trials, the advantages of statin use in youth, particularly for FH, appears to outweigh any potential risks. Statins are typically considered in children with persistent elevations in LDL-C ≥4.1 mmol/L, despite appropriate dietary and lifestyle modifications for four to six months. For patients with high-level risk factors or conditions including, but not limited to, severe obesity, diabetes mellitus, and/or hypertension requiring medications, statin use is often considered for LDL-C remaining ≥3.4 mmol/L. Referral to a paediatric lipid specialist should be considered at the time of consideration of statin therapy or for patients presenting with marked elevations in LDL-C (≥6.5 mmol/L).

Serious and life-threatening events associated with non-medical (recreational) cannabis use

Richard E. Bélanger, MD, Department of Paediatrics, Centre mère-enfant Soleil - CHU de Québec - Université Laval

Anna-Maria Frescura, Epidemiologist, Office of Drug Research and Surveillance, Controlled Substances and Cannabis Branch, Health Canada

Christina Grant, MD, Division of Adolescent Medicine, Department of Paediatrics, McMaster University

Clinical case

A 17-year-old male presents in the emergency department experiencing recurring episodes of acute nausea, intractable vomiting, and abdominal pain. This is his third visit to the emergency department in the past six months with a similar presentation. The patient notes that symptoms alleviate with very hot showers, which are repeated several times a day. Nausea and abdominal pain start a few days prior to bouts of vomiting. A thorough medical and social history reveals that the patient is a frequent and heavy cannabis user (2 g of marijuana smoked on a nearly daily basis). Cannabis use was initiated two years prior to the initial emergency department visit and has gradually increased over time. The patient also consumes alcohol on a regular basis, sometimes concurrently with cannabis, but did not indicate the use of any other psychoactive substances.

After ruling out other underlying conditions, a diagnosis of cannabis hyperemesis syndrome (CHS) is determined. While the patient's laboratory workup lacks electrolyte disturbances, the patient still needs treatment for dehydration. He is counselled to discontinue cannabis use to avoid a recurrence of symptoms. To help with the potential cessation of his cannabis use, the adolescent is referred to a local substance abuse program.

What a clinician needs to know

CHS is a syndrome of cyclic vomiting typically seen in patients with chronic cannabis use. The association between recurrent episodes of vomiting and cannabis consumption was first described in 2004 and diagnostic criteria were developed in 2016 as part of the Rome IV criteria for gastrointestinal disorders. With the recent legalization and regulation of cannabis in Canada, and the parallel increase in cannabis availability, it is anticipated that CHS incidence may increase. Paediatric CHS has been reported in a small number of published cases, but is thought to be under reported given the high prevalence of cannabis use among youth. Fatal cases of CHS in young adults have been reported.

Presentation and diagnosis

Patients with CHS typically present with abdominal pain, cyclical bouts of uncontrollable nausea and vomiting, and dehydration, following quasi-daily use of cannabis, minimally several times a week, for several months. Symptoms are temporarily relieved with hot showers or baths, which are repeated frequently. The progression of CHS symptoms can be divided into three phases: 1) pre-emetic (early morning nausea, abdominal pain), 2) hyperemetic (intense and persistent nausea and vomiting up to five times per hour, abdominal pain, dehydration, frequent hot showers), and 3) recovery (return to wellness, regain of weight, regular bathing habits). CHS symptoms may take up to a week to abate.

Diagnosis of CHS is typically established through a thorough medical history, physical examination, and by ruling out other more prevalent causes of nausea and vomiting. While laboratory and radiological tests are regularly performed, endoscopic studies should not be the norm before attribution of CHS. Patients with CHS can develop nonspecific electrolyte disturbances, but they are not always present. Standard urine drug screens, not mandatory in the evaluation of CHS, include immunoassays that detect delta-9 tetrahydrocannabinol (THC) metabolites, primarily THC carboxylase.

Patient history includes screening for the following; demographic risk factors (e.g., adolescent, male gender); the onset, frequency, and progression of the patient's vomiting; the use of hot showers or baths; substance use; and any comorbidities. Physicians should be sensitive to the fact that patients may be hesitant to disclose their cannabis/substance use and should ensure that patients are aware that confidentiality will be honored. Physical examination, while centred on the abdomen, should also include a complete neurological evaluation as well as looking for clinical signs of dehydration.

According to the Rome IV diagnostic criteria, in order to confirm the diagnosis of CHS, symptoms must be present for several months. This underscores the chronic and recurrent nature of the condition, as well as the importance of considering other medical conditions during the diagnosis process. For adolescents presenting with a chronic history of vomiting, the possibility of an eating disorder should be investigated. Moreover, CHS shares many clinical features with cyclic vomiting syndrome

(CVS); therefore, CVS should also be considered. While CVS lacks a history of both chronic and heavy cannabis use, one must remember that patients with CVS may use cannabis intermittently, in an effort to tame their nausea and vomiting. And for all patients, it is important to remember that some adolescents may refrain from openly discussing their cannabis use, even after having established a secure space for discussion.

Treatment

Treatment of CHS mainly involves supportive therapy with fluid resuscitation. Standard antiemetic medications and benzodiazepines are usually of no help. The therapeutic value of intravenous haloperidol and capsaicin creams remains to be clarified. The focus of CHS treatment should include both symptom relief and education and support regarding cannabis cessation. Cannabis abstinence is currently the only known strategy for full recovery.

Publications 2017–2019

Published papers related to studies and one-time surveys

(For a complete list with hyperlinks, see www.cpsp.cps.ca/publications/published-papers-related-to-studies.)

Adrenal suppression

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Rh sensitization
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National

Cannabis
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Complex regional pain syndrome
Canadian surveillance of complex regional pain syndrome in children and youth: Results from year 1 of surveillance. Baerg K, Tupper S, Finley GA. Canadian Pain Society 40th Annual Scientific Meeting, Toronto, in April (poster)

Neonatal abstinence syndrome
Neonatal abstinence syndrome: Variation and barriers in care in Canada. Puvitharan D, Dow K, Lacaze-Masmonteil T, Do M, Nelson C, Little J, Khurshid F. Canadian Paediatric Society Annual Conference, Toronto, in June (poster)

Procedural skills
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Rh sensitization
Canadian Infants Affected by Rh Sensitization: A 2-year National Surveillance Study. Baker JM. University of Toronto, Divisions of Hematology & Hematopathology 12th Annual Academic Day, Toronto, in April (poster)

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Neonatal abstinence syndrome
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Self-harm
Near-fatal suicide attempts among Canadian youth: A CPSP study. Mitchell RHB, Ani C, Cyr C, Irvine J, Joffe A, Skinner R, Stang A, Wong S, Yao X, Korczak DJ. International Summit on Suicide Research, Miami USA, in October (poster)

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.
- The CPSP is effective at monitoring low-frequency, high-impact diseases and conditions encountered by general paediatricians and paediatric subspecialists.

Track record

- The average monthly response rate from approximately 2,800 paediatricians is 80%.
- The average detailed questionnaire response rate varies between 80% to 90%.

Themes of interest

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.

Public health policies and legislation: Results have informed the total ban on baby walkers and the promotion of booster seats to prevent lap-belt syndrome.

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 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 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, Chief of Pediatrics, Children's Hospital of Eastern Ontario; Professor and Chairman, Department of Pediatrics, Faculty of Medicine, University of Ottawa; 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:

Canadian Paediatric Society
Melanie Laffin Thibodeau, Manager, Surveillance
2305 St. Laurent Blvd., Suite 100
Ottawa ON K1G 4J8
Tel.: 613-526-9397, ext. 239
Fax: 613-526-3332
cpsp@cps.ca
www.cpsp.cps.ca

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