

Fonds de recherche Santé











## Canadian Mother-Child Initiative on Drug Safety in Pregnancy



Anick Bérard PhD FCAHS FISPE

Principal Investigator

Université de Montréal, CHU Ste-Justine









## Medications and Pregnancy

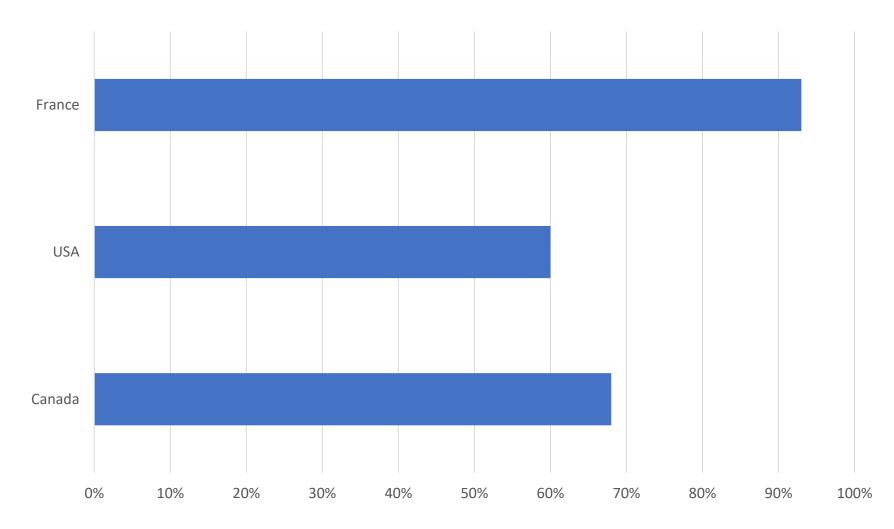


- No randomized controlled trials pre-marketing
- 50% of pregnancies are unplanned
- Maternal age at first pregnancy is increasing worldwide (29 years in Canada)



- Probability of being exposed to medications by inadvertance or to treat a chronic or pregnancy-related condition is high
- In Canada, 68% of pregnant women take at least 1 Rx during pregnancy (Bérard et al., 2022)
- In Québec, 6% of pregnant women are exposed to known teratogens (Kulaga et al., BJOG 2009)
- No risk 0

## Prevalence of medication use in pregnancy?



## Why study medications in pregnancy?



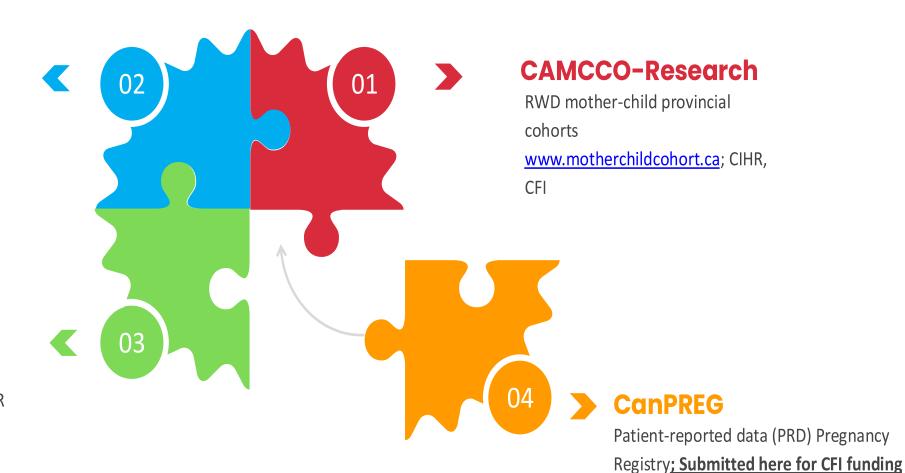
## Building on existing successes

## CAMCCO-Learn Training platform

www.camccol.ca; CIHR, SPOR

#### **CAMCCO-Outreach**

Knowledge dissemination platform www.healthypregnancyhub.ca; CIHR







#### STEERING COMMITTEE

#### AGGREGATE DATA ACCESS COMMITTEE

#### **CANADIAN MOTHER-CHILD COHORTS**

Team Leader: Anick Bérard Co-team Leader: Sherif Eltonsy

Coordinator: Yessica-Haydee Gomez

Projected Sample Size: 4,000,000 mothers & children

Site of aggregate data: CHU Sainte-Justine www.motherchildcohort.ca

Catalogue of cohort variables: Maelstrom Research Database

#### Quebec Nominated PI: **British Columbia** Anick Bérard (team leader) Co-Pls: Co-CPs: **B** Carleton S Bernatsky **G** Hanley E Vinet T Oberlander Site: Site: CHU Ste-Justine - Centre University of British Columbia hospitalier universitaire mèreenfant McGill University **Alberta** Co-PI: **Nova Scotia** P Kaul Co-PI: Mehrabadi A Northern Alberta Clinical Tials & Research Center (NACTRC) **Dalhousie University** Ontario Manitoba Saskatchewan M Walker Co-PIs: Co-PI: S Hawken S Eltonsy (co-team leader) **B Windquist** A Sprague D Chateau Site: Site: Institute of Clinical Evaluative Saskatchewan Health Quality Manitoba Centre for Health Policy Council (HQC) (MCHP) Better Outcomes Registry & Network (BORN) **National and International Collaborators Patient Representative**

Data on 10 million pregnancies, over 8 million children, up to 30 years of follow-up



Drug Safety and Effectiveness Network (DSEN)

Health Canada

FDA Sentinel

#### SteeringCommittee:

- Provicial Ministry of health representatives
- Health Canada representatives
- All PIs



#### Aggregate Data Access Committee:

- Provincial data holder representatives

Dr. Carolina Pineda



## Structure



SA



BC

#### **Provincial Cohort**

- Provincial access
- Provincial-level data
- Individual servers

# QC ON MA

## nadian Institutes Health Research Instituts de recherche en santé du Canada

NS

#### Central repository

- Team access
- Dictionary (provincial- and national-levels)
- Data catalogue

## Ç<sup>2</sup>

- Dictionary
- Codes
- Algorithms

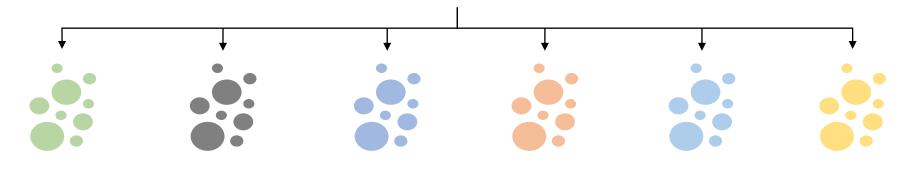
- SAS/R programming
- CDM

#### **Aggregated Data**

- Team access
- Stakeholders access
- National-level data
- Repository

### Website

- Team access
- Stakeholders access
- Global access





AL



#### Linkage procedures within each province

#### Mothers and children date of births

#### **Medical Insurance Claims**

Physician visits, diagnoses (ICD 9-10 codes), procedure codes, medication fillings (calendar date, name of drug (DIN), dosage, duration) sociodemographic data on prescribers, visits to emergency

PIN

#### **Hospitalization Database**

Diagnoses (ICD 9-10 codes) during hospitalization (calendar date), gestational age, procedures, data on delivery or end of pregnancy (spontaneous or planned abortion)

PIN

## Birth and Death Certificate Data

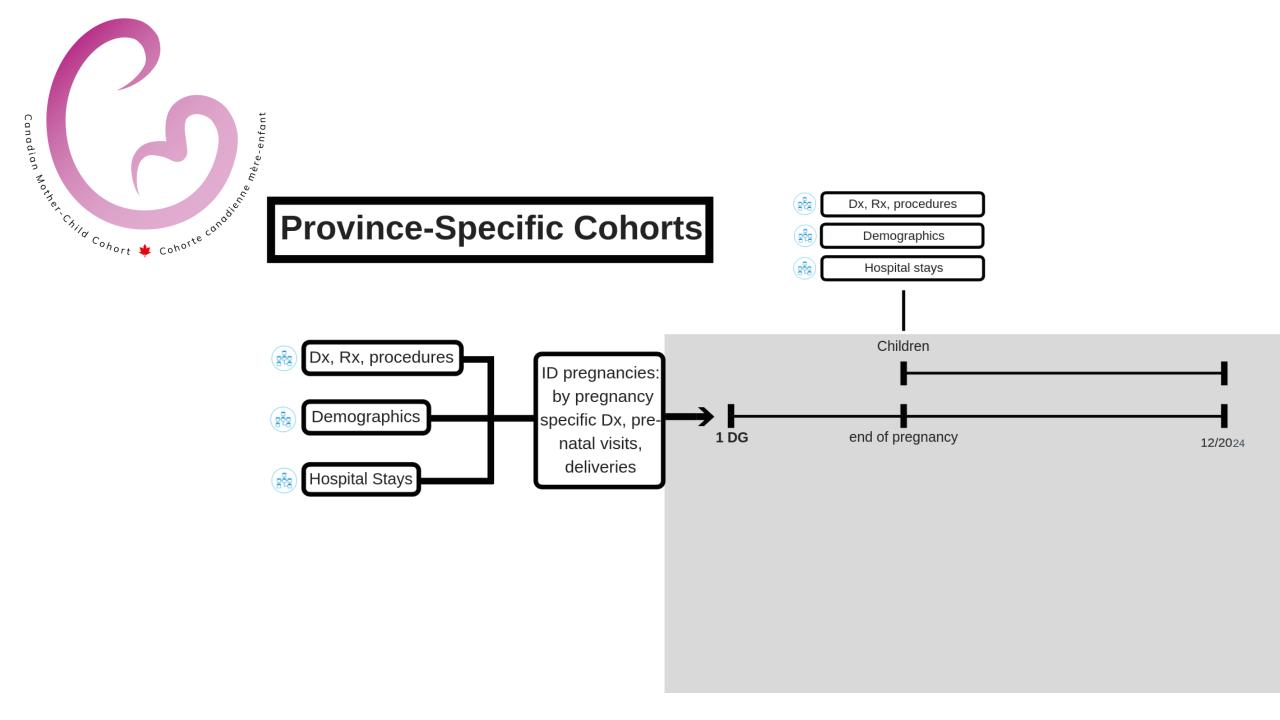
Data on child (gestational age at birth, birth weight), marital status of mother, education level, race-ethnicity

#### Province – Specific mother-child cohort

#### LEGEND

ICD 9-10: International Classification of Diseases 9<sup>th</sup> and 10<sup>th</sup> Revisions; DIN: Drug Identification Number; PIN: Unique Personal identification number for mothers and children within each province.

Confidentiality
Anonymized data
Secure Server



#### RESEARCH ARTICLE

### The Canadian Mother-Child Cohort Active Surveillance Initiative (CAMCCO): Comparisons between Quebec, Manitoba, Saskatchewan, and Alberta

Anick Bérard 1,2,3\*, Padma Kaul<sup>4,5</sup>, Sherif Eltonsy<sup>6</sup>, Brandace Winquist<sup>7</sup>, Dan Chateau<sup>6,8</sup>, Steven Hawken<sup>9,10,11</sup>, Ann Sprague<sup>12</sup>, Mark Walker<sup>9,10,11,12,13</sup>, Sasha Bernatsky<sup>14</sup>, Michal Abrahamowicz<sup>15</sup>, Cristiano Soares de Moura<sup>16</sup>, Évelyne Vinet<sup>14</sup>, Bruce Carleton<sup>17</sup>, Gillian Hanley<sup>18</sup>, Tim Oberlander<sup>19</sup>, Odile Sheehy<sup>2</sup>, Yessica Haydee Gomez<sup>2</sup>, Jessica Gorqui<sup>1,2</sup>, Anamaria Savu<sup>5</sup>







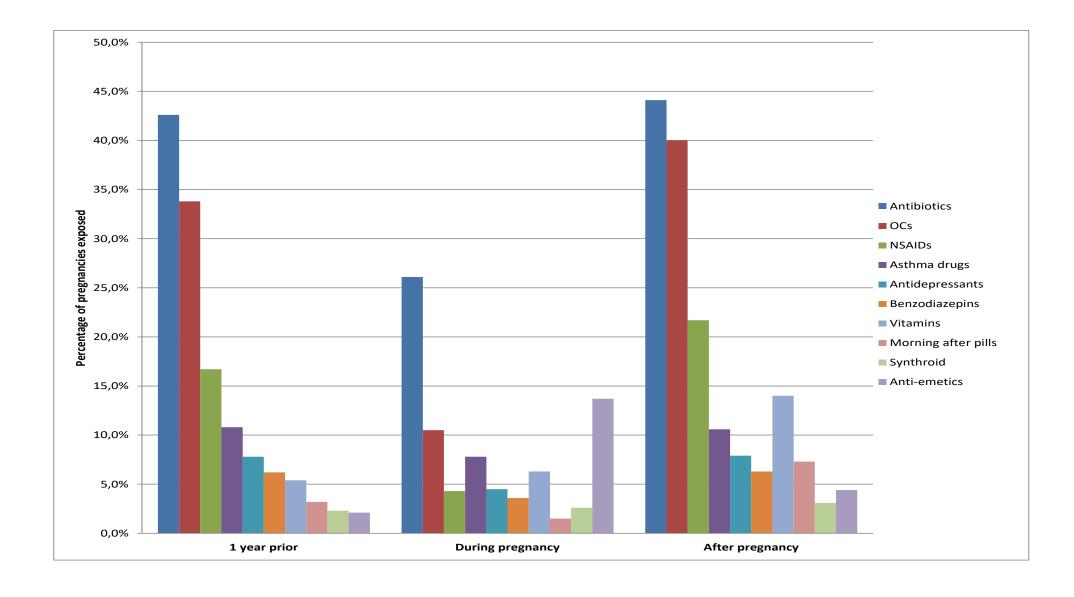
Citation: Bérard A, Kaul P, Eltonsy S, Winquist B, Chateau D, Hawken S, et al. (2022) The Canadian Mother-Child Cohort Active Surveillance Initiative (CAMCCO): Comparisons between Quebec, Manitoba, Saskatchewan, and Alberta. PLoS ONE 17(9): e0274355. https://doi.org/10.1371/journal.pone.0274355

**Editor:** Rodrigo Romao, Dalhousie University, CANADA



PLOS ONE | https://doi.org/10.1371/journal.pone.0274355 September 20, 2022





## Active Risk Identification and Analysis (ARIA)



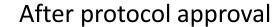
Detection of New and Unsuspected Potential Safety Concerns Level 1

Descriptive Analyses, Unadjusted Rates Level 2

Adjusted Analyses with Sophisticated Confounding Control



Sequential Adjusted
Analyses with Sophisticated
Confounding Control



- Signal ID: 1-2 months
- Level 1: 3-4 months
- Level 2: 6 months
- Level 3: 12 months





### Completed studies

frontiers | Frontiers in Pharmacology

TYPE Original Research PUBLISHED 12 November 2024 DOI 10.3389/fphar.2024.1469552

www.nature.com/scientificreports

Check for updates

#### **scientific** reports



The Canadian Mother-Child Cohort Active Surveillance Initiative (CAMCCO): Comparisons between Quebec, Manitoba, Saskatchewan, and Alberta

Anick Bérard. 1.2.3\*, Padma Kaul<sup>4,5</sup>, Sherif Eltonsy<sup>6</sup>, Brandace Winquist<sup>7</sup>, Dan Chateau<sup>6,8</sup>, Steven Hawken<sup>9,10,11</sup>, Ann Sprague<sup>12</sup>, Mark Walker<sup>9,10,11,12,13</sup>, Sasha Bernatsky<sup>14</sup>, Michal Abrahamowicz<sup>15</sup>, Cristiano Soares de Moura<sup>16</sup>, Évelyne Vinet<sup>14</sup>, Bruce Carleton<sup>17</sup> Gillian Hanley18, Tim Oberlander19, Odile Sheehy2, Yessica Haydee Gomez2 Jessica Gorgui<sup>1,2</sup>, Anamaria Savu<sup>5</sup>

Montreal, Montreal, Quebec, Canada, 3 Faculty of Medicine, Université Claude Bernard Lyon, 1, Lyon, Epidemiology, College of Medicine, University of Saskatchewan, Saskatoon, Canada, 8 Research School of Population Health, Australian National University College of Health and Medicine, Canberra, Australia, of Medicine, Department of Clinical Epidemiology, McGill University, Montréal, Québec, Canada, 17 Divisio of Translational Therapeutics Department of Pediatrics, Faculty of Medicine, University of British Columbia, Vancouver, Canada, 18 Department of Obstetrics & Gynaecology, University of British Columbia, Vancouver Department of Pediatrics, Vancouver, British Columbia, Canada

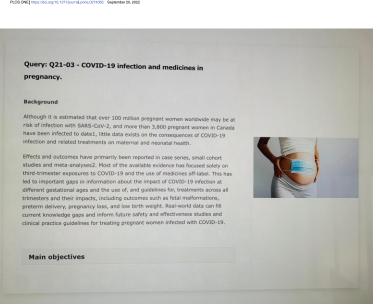
1 Research Center, CHU Sainte-Justine, Montreal, Quebec, Canada, 2 Faculty of Pharmacy, University of France, 4 Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada, 5 Canadian VIGOUR Center, University of Alberta, Edmonton, Alberta, Canada, 6 College of Pharmacy, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada, 7 Community Health and 9 Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada, 10 Institute of Clinical Evaluative Sciences, uOttawa Site, Ottawa, Ontario, Canada, 11 School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, Ottawa, Ottario, Canada, 12 Better Outcomes Registry & Network (BORN) Ontario, Ottawa, Ontario, Canada, 13 Department of Obstetrics, Gynecology and Newborn Care, The Ottawa Hospital, Ottawa, Ontario, Canada, 14 Divisions of Rheumatology and Clinical Epidemiology, McGill University Health Centre, Canada, 15 Department of Epidemiology and Biostatistics, School of Global & Population Health, McGill University, Montreal, Quebec, Canada, 16 Faculty British Columbia, Canada, 19 University of British Columbia, School of Population and Public Health



#### OPEN ACCESS

Citation: Bérard A. Kaul P. Eltonsy S. Winquist B. Chateau D, Hawken S, et al. (2022) The Canadian Mother-Child Cohort Active Surveillance Initiative (CAMCCO): Comparisons between Quebec, Manitoba, Saskatchewan, and Alberta. PLoS ONE 17(9): e0274355. https://doi.org/10.1371/journal

Editor: Rodrigo Romao, Dalhousie University



#### **Health Canada advisory impacts** on the prevalence of oral codeine use in the Pediatric Canadian population: comparative study across provinces

O. Sheehy<sup>1</sup>, S. Eltonsy<sup>2</sup>, S. Hawken<sup>3,4,5</sup>, M. Walker<sup>3,4,6,7,8,9</sup>, P. Kaul<sup>10</sup>, B. Winquist<sup>11</sup>, O. Barrett<sup>12</sup>, A. Savu<sup>10</sup>, R. Dragan<sup>13</sup>, M. Pugliese<sup>3,14</sup>, S. Bernatsky<sup>15</sup>, J. Gorgui<sup>1</sup> & A. Bérard<sup>1,16,17</sup>

Health Canada (HC) has, since 2013, issued safety alerts restricting the use of codeine-containing drugs among breastfeeding women and children/adolescents under 18 years of age. These products are linked to breathing problems among ultra-rapid CYP2D6 metabolizers and early use of opioid can lead to future opioid misuse. Using a multi-province population-based cohort study, we estimate the impact of federal safety alerts on annual rates of codeine use in the Canadian pediatric population. We analyzed data from 8,156,948 children/adolescents in five Canadian provinces between 1996 and 2021, using a common protocol. Children/adolescents were categorized as: ≤ 12 years (children) or > 12 years (adolescents). We defined codeine exposure by ≥ 1 prescription filled for codeine alone or combined with other medications. For both age categories, we obtained province-specific codeine prescription filling rates per calendar year by dividing the number of children/adolescents with ≥ 1 codeine prescription filled by the number of person-time. Annual rates of codeine use per 1000 persons vary by province from 3.0 (Quebec) to 10.1 (Manitoba) in children, and from 5.5 to 51.3 in adolescents. After the 2013 HC advisory, exposure decreased in all provinces (adjusted level change from - 0.6 to -18.4%) in children and from -2.1 to -17.9% in adolescents after the 2016 advisory. Annual rates declined over time in all provinces, following HC safety alerts specific to each of the two age categories.

#### ( Check for updates

#### OPEN ACCESS

Mohammed Salahudeen, University of Tasmania, Australia

> Boulenouar Mesraoua Weill Cornell Medicine-Qatar, Qatar Klára Fekete. University of Debrecen, Hungary

Sherif Eltonsy. sherif.eltonsy@umanitoba.ca

RECEIVED 24 July 2024 ACCEPTED 31 October 2024 PUBLISHED 12 November 2024

Peymani P, Berard A, Winquist B, Kaul P, Sheehy O, Lavu A, Leong C, Falk J, Delaney JA Kowalec K, Ng M, Ruth C, Aboulatta L Alessi-Severini S, Dragan R, Derksen S Barrett O. Shams G and Eltonsy S (2024) Trends of antiseizure medication utilization among pregnant people in four Canadian provinces from 1998 to 2023; a study from the Canadian mother-child cohort active surveillance initiative (CAMCCO). Front. Pharmacol. 15:1469552 doi: 10.3389/fphar.2024.1469552

© 2024 Peymani, Berard, Winquist, Kaul, Sheehy, Lavu, Leong, Falk, Delaney, Kowalec, Ng, Ruth, Aboulatta, Alessi-Severini, Dragan, Derksen, Barrett, Shams and Eltonsy. This is an open-access article distributed under the terms ons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms

Trends of antiseizure medication utilization among pregnant people in four Canadian provinces from 1998 to 2023; a study from the Canadian mother-child cohort active surveillance initiative (CAMCCO)

Payam Peymani<sup>1</sup>, Anick Berard<sup>2,3</sup>, Brandace Winquist<sup>4</sup>, Padma Kaul<sup>5,6</sup>, Odile Sheehy<sup>2</sup>, Alekhya Lavu<sup>1</sup>, Christine Leong<sup>1,7</sup>, Jamie Falk<sup>1</sup>, Joseph A. Delaney<sup>1.8</sup>, Kaarina Kowalec<sup>1.9</sup>, Marcus Ng10, Chelsea Ruth11,12, Laila Aboulatta1, Silvia Alessi-Severini 1.12, Roxana Dragan 12, Shelley Derksen 12, Olesya Barrett<sup>13</sup>, Golnaz Shams<sup>14</sup> and Sherif Eltonsy<sup>1,15</sup>\*

<sup>1</sup>College of Pharmacy, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, MB, Canada, <sup>2</sup>Research Center, CHU Sainte-Justine, Montreal, QC, Canada, <sup>5</sup>Faculty of Pharmacy, University of Montreal, Montreal, QC, Canada, <sup>4</sup>College of Medicine, University of Saskatchewan, Saskatoon, SK, Canada, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB, Canada, Canadian VIGOUR Center, University of Alberta, Edmonton, AB, Canada, 7Department of Psychiatry, College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, MB, Canada, ® Department of Medicine and Epidemiology, University of Washington, Seattle, WA, United States, 9Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden, 10 Section of Neurology, Max Rady College of Medicine, University of Manitoba, Winnipeg, MB, Canada, 11Departmen of Pediatrics and Child Health, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, MB Canada, 12 Manitoba Centre for Health Policy, Winnipeg, MB, Canada, 13 Alberta Health Services Edmonton, AB, Canada, 14Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran, 15Children's Hospital Research Institute of Manitoba, Winniped, MB, Canada

Background: Epilepsy management during pregnancy is crucial for both the mother and fetus. The use of antiseizure medications (ASMs) during pregnancy requires careful consideration due to their potential effects on maternal and

#### **On-going studies:**

ASM and Neurodevelopment (Eltonsy et al., CIHR; Bérard et al., CIHR)

Risk management program (Bérard et al., CIHR)

Treatment of cardiovascular comorbidity in pregnancy (Malhamé et al., CIHR)

PregTrial (Dayan/Bérard et al., CIHR)

## Real World Data...

#### **Strengths**

- Larger and more diverse study population
- High statistical power
- Decrease selection bias
- Historical data over decades
- Study rare events/outcomes
- Target rial emulation

#### Limitations

- Data is collected for nonresearch purposes and outcomes may not be validated
- Inadequate or missing information
- Data access and privacy concerns

Launch – November 2024

CHUSJ Gala Excellence et Reconnaissance (May 30<sup>th</sup> 2025)

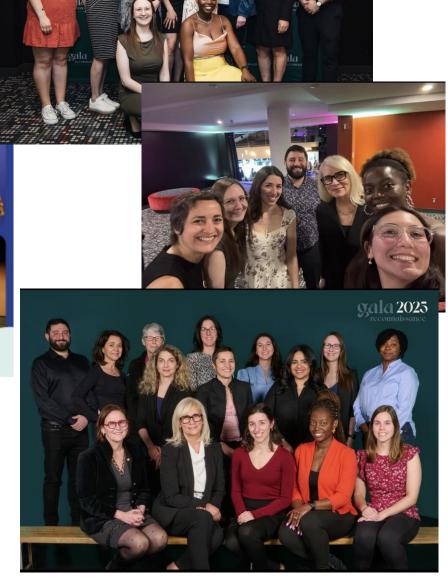














51 sheets; 35 ressources; Collaborations with ANSM, MothertoBaby, EPI-PHARE, MotherSafe

www.hubgrossesseensante.ca www.healthypregnancyhub.ca

## CAMCCO-Outreach team: 76 academics; 46 graduate students/fellows; 7 decision-makers; 16 knowledge users; 2,000 people with lived experiences

Chaque grossesse est unique; elle a son environnement, ses symptômes, ses défis qui varient d'une personne à l'autre et même d'une grossesse à l'autre. Dans certains cas, prendre un médicament est la meilleure chose à faire pour la santé de maman et donc celle du héhé

Plus de 3 personnes enceintes sur 4 prennent des médicaments, mais l'information sur leur sécurité durant cette période est souvent limitée. Nous sommes convaincus et convaincus qu'en ayant toute l'information nécessaires, chaque personne aura les outils pour discuter avec son équipe soignante et prendre une décision éclairée pour une GROSSESSE en SANTÉ.

C'est pourquoi nous avons regroupé une équipe de plus de 70 chercheuses et chercheurs nationaux et plus de 2 000 personnes ayant une expérience vécues afin d'offrir de l'information accessible fondée sur des données scientifiques.

Que vous soyez futur parent, membre d'une équipe professionnelle en santé périnatale ou personne curieuse, ce site changera la façon de vous informer sur les **médicaments durant la grossesse** pour vous soutenir dans votre choix.













Un peu, beaucoup, passionnément, à la foli...que!













#### Can Acetaminophen (Tylenol®) **During Pregnancy Affect Baby's Brain Development?**

#### What Are Brain Development Disorders?

It includes conditions that affect how the brain grows and works, making it harder for a person to:

- - move
- communicate handle emotions

#### What Did We Do?

Our team looked at ALL the research on the effect of



acetaminophen during pregnancy on baby's brain development.

#### What Does Science Say?

lack now increased risk 🕲 of Language Delay



Trouble with learning to talk and understand words on time.

\$5,000 pregnancies from 5 studies.



thinking. remembering, and tearning.

7,500 pregnancies from 2 studies.



#### What Did We Find?

Right now, studies show no clear link between acetaminophen use in pregnancy and problems with baby's brain development.

More research in the future can help to confirm this.

#### Research Is Great, But It's Not Perfect

Limits of research can make it difficult to be sure about the effects because:



Difficult to know the exact amount of acetaminophen taken during pregnancy, so the effect of dose is unclear.

Different tools are used to evaluate a child's brain development, making study results difficult to compare.



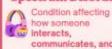
People take acetaminophen for many reasons, making it difficult to tell if effects are from the medication, the illness, or other factors.



Condition that makes it hard to focus, sit still, and control actions. 2,5 millions pregnancies from 4 studies.

of ADHD

No increased risk of Autism Spectrum Disorder



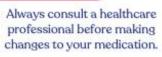
interacts, communicates, and behaves.

2.5 millions prograncies from 2 studies.



movement and coordination skills.

[4] 35,000 pregnancies from 3 studies.



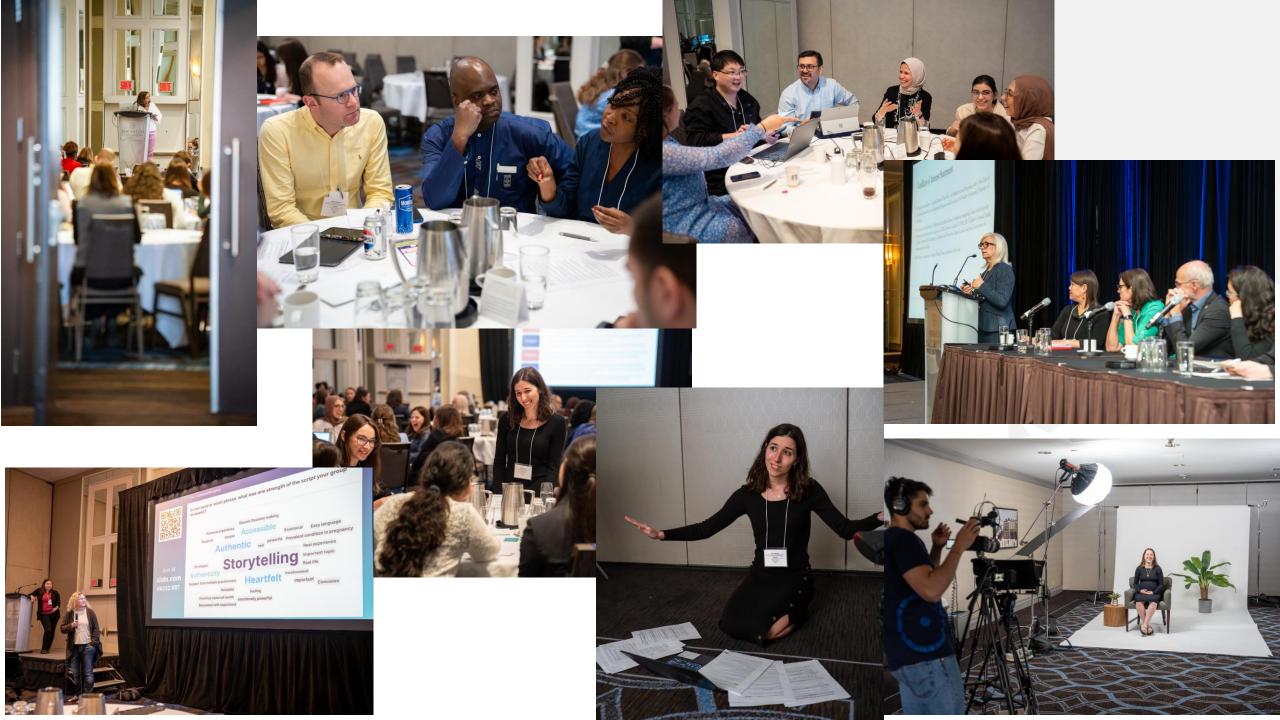












**◄** LinkedIn

Publication de Canadian Institutes of Health R...

## Canadian Institutes of Health Research • Suivre

3 j · 🕙

Are medications safe to take during pregnancy? A quick Google search might tell you to avoid them all, but that's not always true.

The Healthy Pregnancy Hub is tackling misinformation with trusted, research-backed resources – from fact sheets to videos – to help pregnant individuals make informed decisions about their health.

https://cihr-irsc.gc.ca/e/54363.html? hsid=d2d92720-a06e-4900-b5aee5aea77913ab&utm\_medium=facebook&utm\_s ource=canadian+institutes+of+health+research

**OO** 31

9 partages













## The Society of Obstetricians and Gynaecologists of Canada

12 650 abonnés 4 sem. • • •

The SOGC was present at the Canadian National Perinatal Research Meeting (CNPRM) last week in ... plus

#### Afficher la traduction







Montreal



Thank you!

anick.berard@umontreal.ca www.motherchildcohort.ca www.camccol.ca

https://healthypregnancyhub.ca/