Background Incidence Rates of Selected Vaccine Adverse Events of Special Interest in Canada

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Study Ongoing

Administrative details

EU PAS number

EUPAS1000001053

Study ID

1000001053

DARWIN EU® study

No

Study countries

Canada

Study description

The COVID-19 pandemic highlighted the need for timely detection of emerging safety signals for new vaccines and continuous lifecycle monitoring for established vaccines. Background incident rates of adverse events of special interest (AESIs) can facilitate the identification of vaccine safety signals using observed-to-expected analyses. Such analyses were conducted globally in response to safety concerns arising during the COVID-19 vaccine rollout. In Canada, evidence on background incidence rates of AESIs is currently limited to the provinces of British Columbia and Ontario, highlighting the need for national data. As part of a collaboration with the International Coalition of Medicine Regulatory Authorities (ICMRA), CNODES will replicate a DARWIN EU study (EUPAS1000000254) to estimate background incidence rates for selected vaccine AESIs in Canada.

We will conduct a descriptive retrospective cohort study using administrative health databases from 6 provinces. The analysis will be conducted separately for pediatric and adult populations. The study population will include all eligible individuals who were registered for provincial medical services coverage between January 1, 2015, and December 31, 2024 (or the latest date of data availability). We will study the incidence of 5 AESI categories including: Guillain-Barré Syndrome, myocarditis, encephalitis, stroke, and thrombocytopenia; with no prior record of the specific outcome within a 365-day washout window. Incidence rates per 100,000 person-years will be estimated for each AESI. Rates will be stratified by subgroups and will also be age and sex standardized to the European and Canadian populations. Demographic and clinical characteristics of individuals with incident AESIs will be described and compared with individuals without the AESIs matched on age, sex, and calendar time of the event. Three sensitivity analyses will be conducted. Results will be reported by province separately and pooled across provinces.

Study status

Ongoing

Research institutions and networks

Institutions

Lady Davis Institute

First published: 01/02/2024

Last updated: 01/02/2024

Institution

University of British Columbia

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Institution

University of Calgary, Calgary, Canada;

University of Manitoba, Winnipeg, Canada;

Dalhousie University, Halifax, Canada;

ICES, Toronto, Canada;

Saskatchewan Health Quality Council, Saskatoon, Canada

Networks

Canadian Network for Observational Drug Effect Studies (CNODES)

Canada

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Network

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Kristian Filion

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 10/11/2025

Study start date

Actual: 10/11/2025

Date of final study report
Planned: 05/03/2027

Sources of funding

- Other

More details on funding

CNODES is a collaborating core network partner of CoLab, which is funded for query-related activity by Canada’s Drug Agency (CDA-AMC, grant number C222 360).

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Disease epidemiology

Data collection methods:

Secondary use of data

Study design:

Federated, multi-jurisdictional descriptive retrospective cohort study

Main study objective:

This study is a replication of the previous DARWIN EU study (EUPAS1000000254) using data from 6 Canadian provinces. The study has 3 primary objectives:

1. To estimate population level incidence rates of selected AESIs in the general population during 2015 and until the latest data availability, overall and stratified by calendar period based on COVID-19 (pre-, during- and post-pandemic periods), calendar quarter, sex, age groups, sex and age groups, and province.

2. To estimate age and sex standardized incidence rates (to the Canadian and European population) of the selected AESIs in the general population during 2015 and until the latest data availability, stratified by calendar period based on COVID-19 pre-, during- and post-pandemic periods, calendar quarter, sex, and

province.

3. To describe the demographic and clinical characteristics of individuals with incident AESIs and compare these with individuals without the AESIs matched on age, sex and calendar time of the event.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Additional medical condition(s)

Vaccine adverse events of special interest (AESIs)

Population studied

Short description of the study population

The study population will consist of all individuals who were registered for provincial medical services coverage between January 1, 2015, and December 31, 2024 (or the latest date of data availability in each province).

Age groups

- **Paediatric Population (< 18 years)**
  - Neonate
    - Preterm newborn infants (0 – 27 days)
    - Term newborn infants (0 – 27 days)

    - Infants and toddlers (28 days – 23 months)
    - Children (2 to < 12 years)
    - Adolescents (12 to < 18 years)
- **Adult and elderly population (≥18 years)**
    - Adults (18 to < 65 years)
        - Adults (18 to < 46 years)
        - Adults (46 to < 65 years)
    - Elderly (≥ 65 years)
        - Adults (65 to < 75 years)
        - Adults (75 to < 85 years)
        - Adults (85 years and over)

Study design details

Setting

The analysis will be conducted separately in pediatric and adult populations. Due to data availability, Alberta will contribute only to the adult cohort. In each case, the study population will consist of all individuals in that age group who were registered for provincial medical services coverage at any time in the study period, defined as January 1, 2015, to December 31, 2024 (or the latest date of data availability in each province). A minimum lookback period (continuous health plan enrollment) of 365 days will be required to ensure adequate capture of incident AESIs events and measurement of covariates.

Incidence of AESIs will be estimated overall and within calendar periods (annual and quarterly). Individuals will be eligible to contribute person-time to the at-risk population for each AESI provided that they have no prior record of that specific outcome within a prior 365-day washout window. For each outcome,

follow-up (cohort entry) will begin on the latest of: the study start date (January 1, 2015), the date on which individuals have sufficient prior data availability (365 days), or the date on which they fulfil the 365-day washout window. Individuals will be followed up until the earliest of: occurrence of the AESI (event date), death, loss of provincial coverage, the day of exceeding the specified age range (in age-group specific analysis), or the end of the study period (December 31, 2024, or the latest date of data availability). Individuals will be allowed to enter the outcome-specific cohort multiple time provided they meet all the eligibility criteria.

Comparators

Not applicable

Outcomes

We will assess the incidence of 5 AESI categories evaluated in the DARWIN EU study: Guillain-Barré Syndrome, myocarditis, encephalitis, stroke, and thrombocytopenia. In the primary analysis, outcomes will be defined using inpatient and emergency department (where available) data only. In provinces with access only to inpatient data, outcomes will be defined using those data. Where feasible, outcomes will be defined using both broad and narrow case definitions.

Data analysis plan

In each province, the incidence rate for each AESI will be calculated as the number of cases per 100,000 person-years at risk during the study entire study period, excluding the COVID-19 pandemic period, in order to avoid its influence on the baseline rates of these outcomes, and 95% confidence intervals will be estimated using the Poisson distribution. Using data from the same period as the overall rates, incidence rates will be stratified by the following subgroups: calendar year, calendar quarter, time period relative the COVID-19 pandemic

(pre-: 2015-2019; during: 2020-2022; and post-: 2023 to latest available data), sex, age group (pediatric cohort: 0-12 and 13-17; adult cohort: 18-29, 30-39, and so on to ≥ 80 years), and sex and age group. All incidence rates will be further age and sex standardized to the Canadian and European populations by the direct method.

For each incident AESI cohort, demographic and clinical characteristics of cases will be summarized. To contextualize these characteristics, each case will be matched 1:1 to individuals without the AESIs on age, sex, and calendar time of the event. Characteristics between the AESI and matched cohorts will be compared using standardized mean differences.

Three sensitivity analyses will be conducted. First, as in the DARWIN EU study, different case definitions for selected AESIs (encephalitis and ischemic stroke) will be applied to assess the impact of varying sensitivity and specificity. Second, rates will be estimated in Manitoba and Ontario using data only from the post-pandemic period, as this may better represent the current baseline rates of these AESIs. Third, a 90-day washout window for AESIs will be used in Manitoba and Ontario for closer alignment with the DARWIN EU study. If necessary, these sensitivity analyses will be conducted in the remaining provinces.

Results will be reported for each province separately and pooled using random-effects meta-analyses to provide national baseline rates.

Documents

Study, other information

ICMRA AESI HMA-EMA Registration Appendix_2026.07.07.pdf (110.57 KB)

DARWIN EU study (EUPAS1000000254)

Link to project page on CNODES website.

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s), other

Canadian provincial administrative health databases

Data sources (types)

Administrative healthcare records (e.g., claims)

Pharmacy dispensing records

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Unknown