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COVID-19 vaccine program surveillance - Part One: Vaccine safety surveillance

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Disclosures

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Outline

- Overview of COVID-19 vaccine program surveillance framework
- Passive vaccine safety surveillance
- Active vaccine safety surveillance using the Canadian National Vaccine Safety (CANVAS) Network

Learning Objectives

- Describe Ontario's COVID-19 vaccine program surveillance framework.
- Understand the systems in place for COVID-19 vaccine safety surveillance
- Describe recent findings from both active and passive surveillance systems that are monitoring COVID-19 vaccine safety in Ontario

COVID-19 Vaccine Program Surveillance in Ontario

- **Background**
  - COVID-19 vaccines are authorized by Health Canada after reviews of randomized clinical trial data
  - Vaccine program implementation in the 'real world' involves broader use of vaccines and in conditions that differ from clinical trials
  - In the setting of scarce vaccine supply, policy and programmatic decisions have been undertaken (delayed second dose interval) that need to be monitored in real time

- **Partners and approach to COVID-19 vaccine surveillance plan development**
  - Ontario Surveillance Subgroup of the COVID-19 Vaccine Task Force Clinical Guidance and Surveillance work stream
  - Environmental scan of existing vaccine surveillance infrastructure in Ontario and Canada
  - Review of other vaccine program surveillance plans (Public Health England, ECCDC, WHO)
  - Linkages with other groups, e.g. Vaccine Surveillance Reference Group of the Canadian Immunity Task Force

COVID-19 Vaccine Program Surveillance

Ontario's COVID-19 vaccine program goals

- Prevent death
- Prevent illness, hospitalization and ICU admission
- Reduce transmission

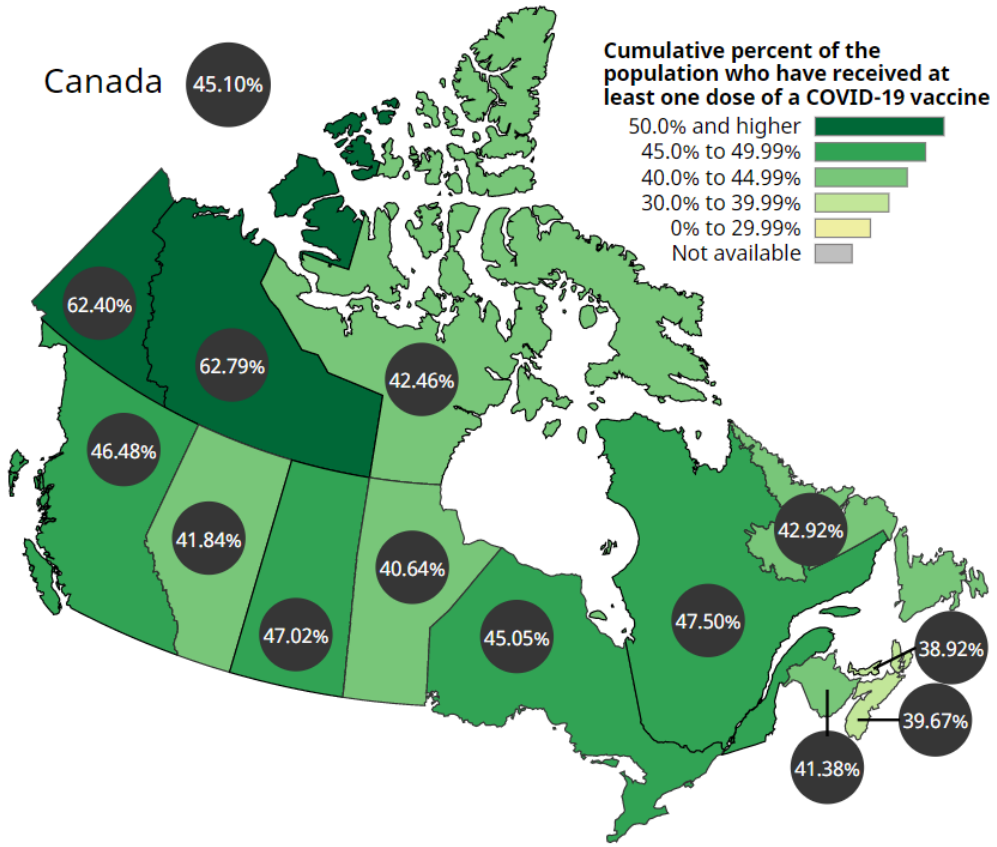
Surveillance components

- Vaccine coverage
- Vaccine safety
- Program impact and vaccine effectiveness
- Viral characterization of cases with vaccine history
- Serosurveillance
- Public confidence

Vaccine Coverage

Objectives:

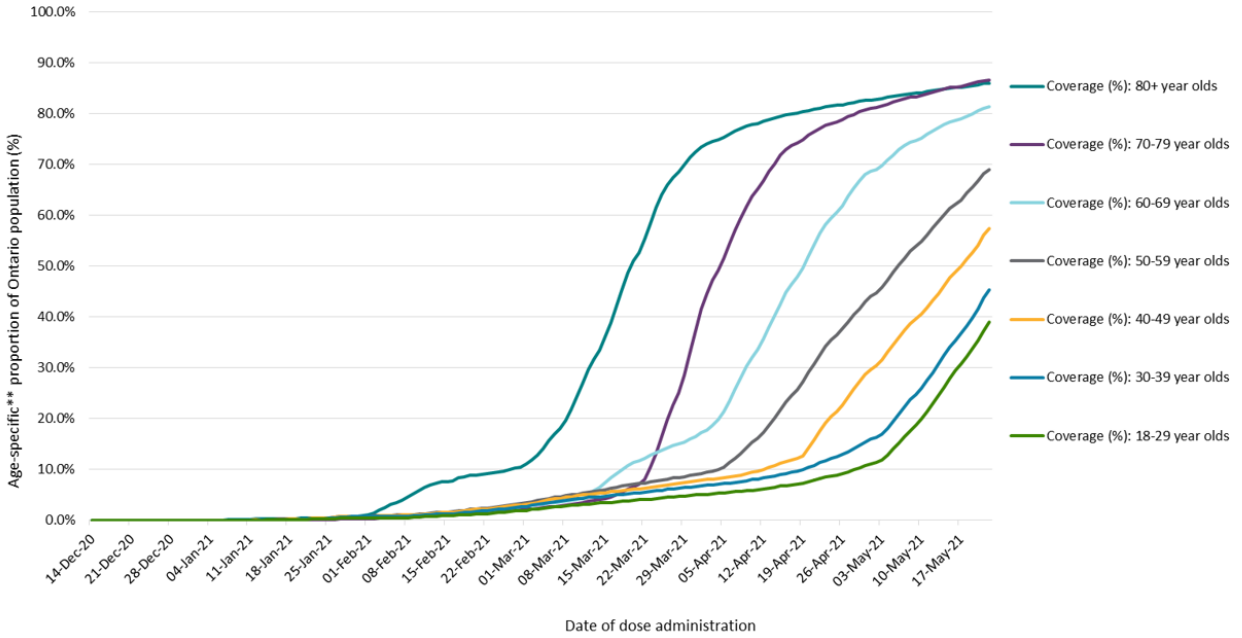
- Monitor coverage of the COVID-19 vaccines overall and among priority groups
- Over time, identify areas or populations at increased risk of outbreaks
- To estimate coverage at multiple points over time, by:
  - Demographics (age group, gender)
  - Vaccine type (Pfizer-BioNTech, Moderna)
  - By dose (dose 1, series completion)
  - By priority group
  - By geography (e.g., PHU)
  - Using small area analysis (e.g. by On-Marg quintile, disease burden at the FSA level, etc.)

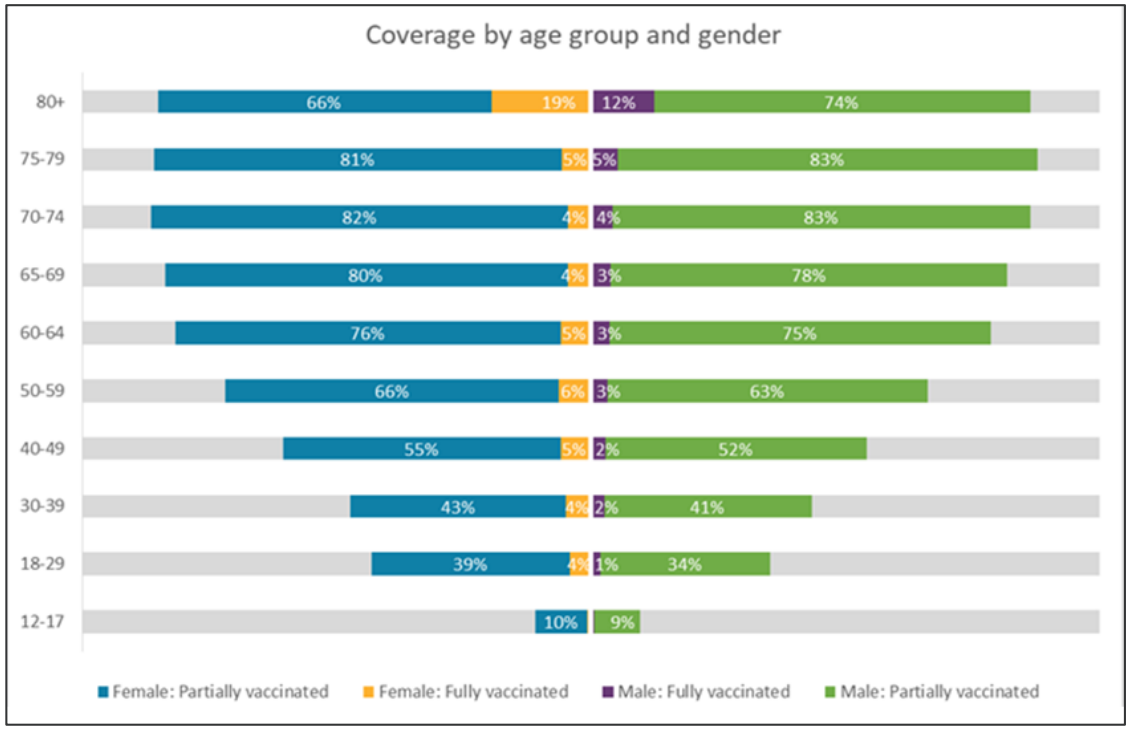


Source: Public Health Agency of Canada. COVID-19 vaccination in Canada [Internet]. Ottawa, ON: Government of Canada; 2021 [modified 2021 May 21; cited 2021 May 27]. Available from: https://health-infobase.canada.ca/covid-19/vaccination-coverage/

COVID-19 Vaccine Coverage by Age

Figure 3. Provincial COVID-19 vaccine coverage estimates (at least one dose) by age group and date*

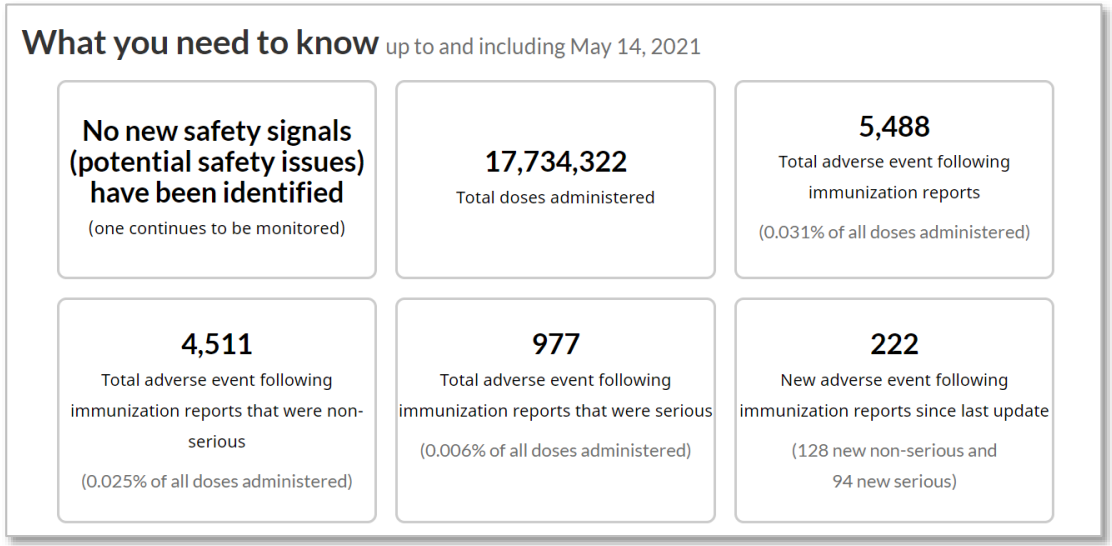




Source: Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 vaccine uptake in Ontario: December 14, 2020 to May 15, 2021 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 May 27]. Available from: https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-vaccine-uptake-ontario-epi-summary.pdf?la=en

Vaccine Safety

- Passive vaccine safety surveillance
  - Adverse Events Following Immunization (AEFIs)
  - Adverse Events of Special Interest (AESIs)
  - Enhanced surveillance
- Active vaccine safety surveillance
  - CANVAS (Surveys of vaccine recipients)
  - IMPACT (Pediatric hospitals)
- Special studies



Source: Public Health Agency of Canada. Reported side effects following COVID-19 vaccination in Canada [Internet]. Toronto, ON: Government of Canada; 2021 [modified 2021 May 21; cited 2021 May 27]. Available from: https://health-infobase.canada.ca/covid-19/vaccine-safety/

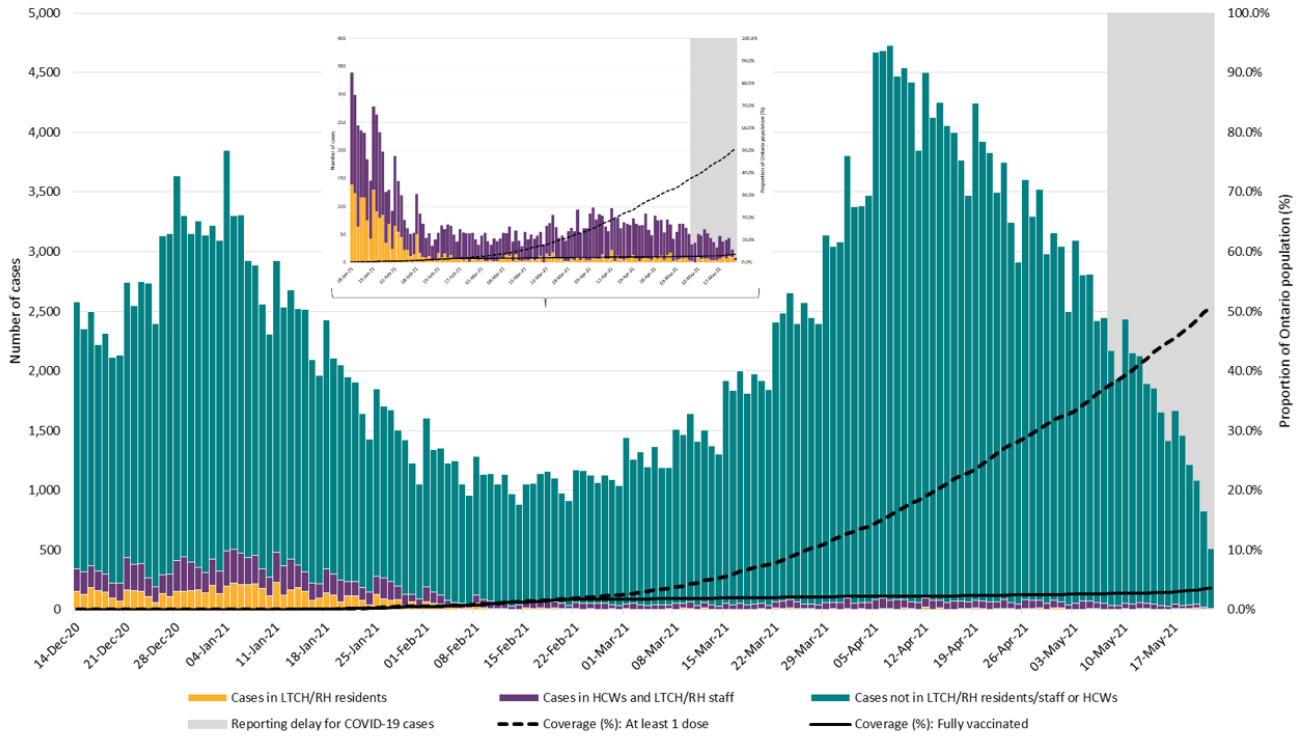
Vaccine Program Impact

- Age-specific trends in COVID-19 incidence and trends in vaccine coverage
- Impact on outbreaks (number, size, duration, etc.)
- Clinical severity among vaccinated and unvaccinated cases

Vaccine Effectiveness

- Against various outcomes: infection, hospitalization, death
- By vaccine related factors (dose number, product) and individual factors (age, sex, comorbidities)

Figure 4. Number of confirmed COVID-19 cases and provincial coverage estimates* by date**



Source: Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 vaccine uptake in Ontario: December 14, 2020 to May 15, 2021 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 May 27]. Available from: https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-vaccine-uptake-ontario-epi-summary.pdf?la=en

Viral Characterization of Cases with Vaccine History

- Descriptive analysis of cases following vaccine (by time since dose/dose number, severity, Variants of Concern (VOC) and mutations of interest)
- Whole genome sequencing

Serosurveillance

- Serosurveillance combines cross-sectional antibody tests with epidemiologic analysis to understand population immunity and has a strong history of use in understanding trends in vaccine-preventable disease susceptibility and immunity.

Public Confidence

- Understanding intention to be vaccinated, knowledge, attitudes and beliefs, barriers and enablers to vaccination with work underway at the national, provincial and local level

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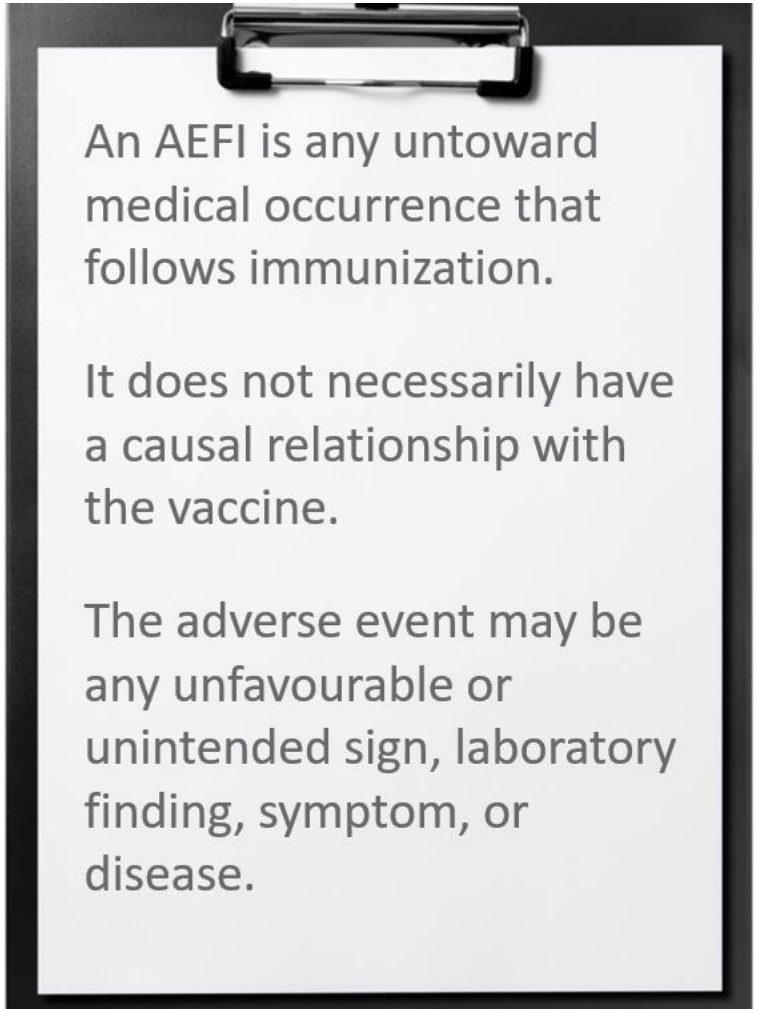
- Dr. Michelle Lloyd (Ontario Health)
- Dr. Allison McGeer (Mount Sinai Hospital)
- Dr. Robin Williams (Ministry of Health, Health Services I&IT Cluster)
- Dr. Sarah Wilson (Public Health Ontario) – Co-Chair
- Dr. Kit Young Hoon (Northwestern Health Unit)

Passive Vaccine Safety Surveillance

What is an AEFI?



- AEFIs can be caused by the vaccine or may occur by chance
- Includes both expected (i.e. listed in product monograph) and unexpected events
- An AEFI is not the same as side effects which are linked to a vaccine by scientific studies

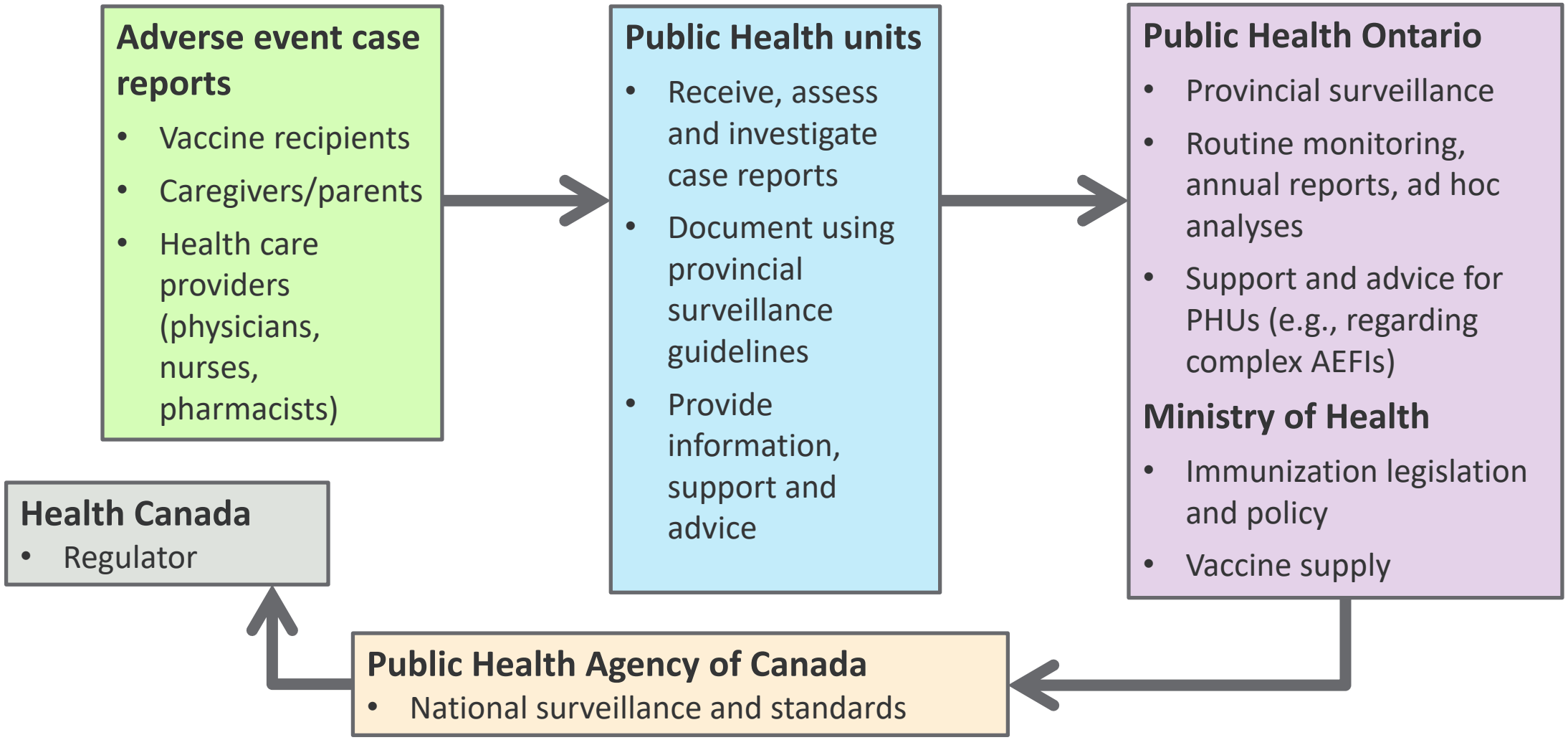
Passive Vaccine Safety Surveillance

- Public health surveillance of AEFIs is a core component of comprehensive vaccine safety surveillance
- In Ontario:
  - Relies on reporting from healthcare provider, vaccine recipients and their parents/caregivers to their local public health unit (PHU)
  - PHUs investigate and report AEFIs into the provincial surveillance system (CCM)
  - Public Health Ontario conducts provincial level analysis of AEFIs reported in CCM
  - Confirmed reports of AEFIs transmitted to the national vaccine safety surveillance system (Canadian Adverse Events Following Immunization Surveillance System [CAEFISS])

Goals of Passive Vaccine Safety Surveillance

- Identify rare events not detected during pre-licensure studies
- Monitor increases in known events
- Identify risk factors/conditions that may promote events
- Identify vaccine safety signals that warrant further assessment or action
  - Changes to the product monograph
  - Changes to counselling as part of informed consent
  - Holds/recalls

Public Health Surveillance Process for AEFIs



COVID-19 Vaccine Safety Surveillance at PHO

- Multi-disciplinary team
  - Epidemiologists:
    - Extract AEFI data, produce reports, ad hoc analysis, signal investigation
  - Nurse Consultants:
    - Daily case-level review, consultation on complex AEFIs, development of resources to support AEFI reporting
  - Public Health Physicians:
    - Consultation on complex AEFIs, advice on vaccine safety issues and re-immunization guidance
- Provincial AEFI surveillance
  - Daily routine monitoring of AEFIs
  - Support to PHU investigations
  - Produce public-facing weekly AEFI summary
  - Transmit AEFI data weekly for inclusion in CAEFISS
  - Contribute to PHAC Vaccine Vigilance Working Group
  - Ad hoc analyses, cluster/signal investigations

PHO Weekly COVID-19 AEFI Report

AEFIs (number and reporting rate):

- Trends over time
- By adverse event type (e.g. local reactions)
- By age/sex and by vaccine product
- Non-serious, serious and medically important events
- Adverse Events of Special Interest (AESI)

Weekly Summary of COVID-19 Vaccine AEFI Reports in Ontario: Dec 13, 2020 to May 22, 2021

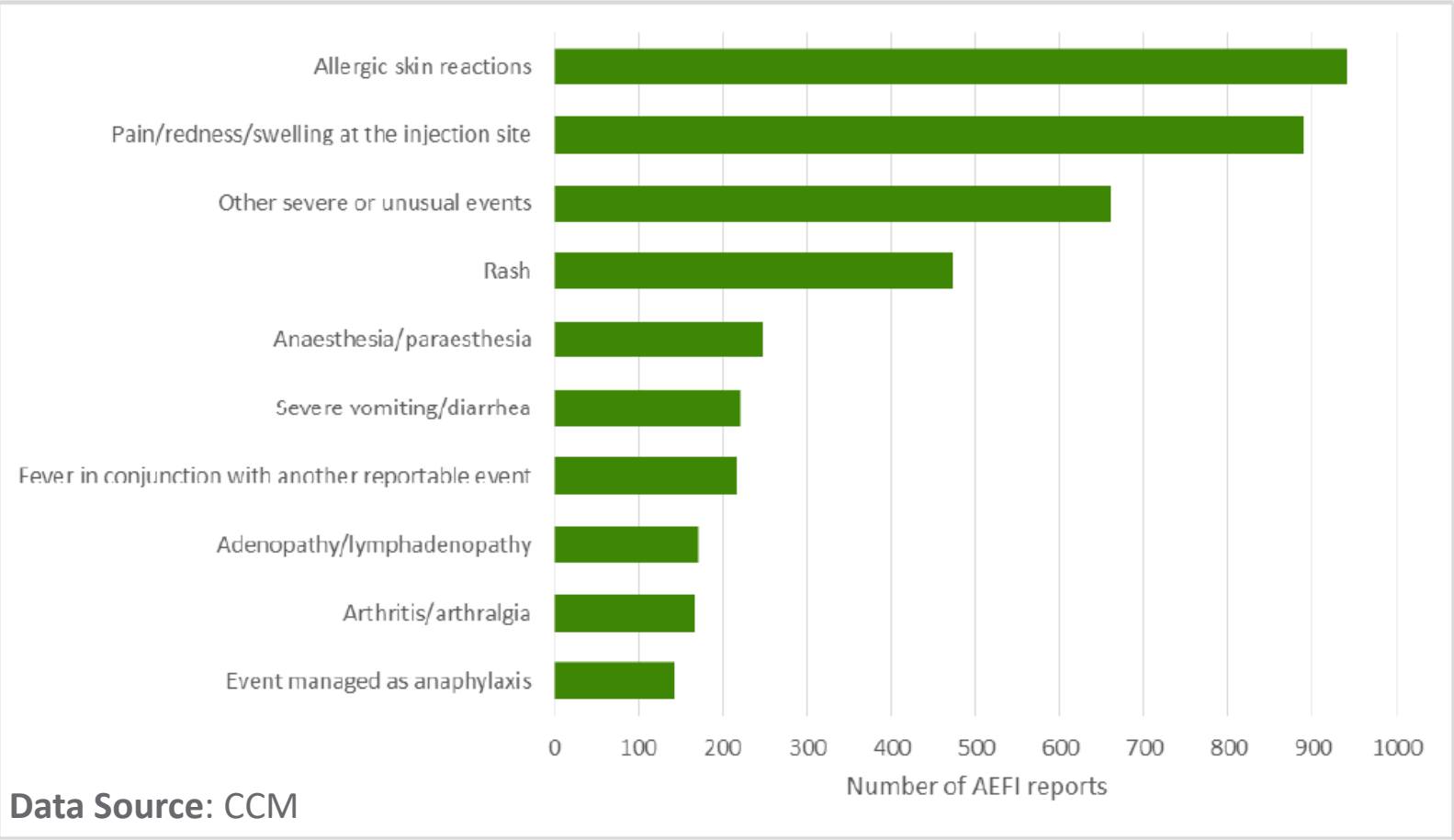
3,569 AEFI reports

- Following 8,069,397 doses of COVID-19 vaccine administered
- Reporting rate of 44.2 per 100,000 doses administered
- 0.04% of all doses administered

- Non-serious events
  - n=3,429, 96.1% of total AEFIs
- Serious events
  - n=140, 3.9% of total AEFIs

Source: Ontario Agency for Health Protection and Promotion (Public Health Ontario). Weekly summary: adverse events following immunization (AEFIs) for COVID-19 in Ontario: December 13, 2020 to May 22, 2021 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 May 27]. Available from: https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-aefi-report.pdf?la=en

Top 10 Most Frequently Reported Adverse Events for all COVID-19 Vaccines in Ontario: Dec 13, 2020 to May 22, 2021



Data Source: CCM

Most commonly reported adverse events:

- Allergic skin reactions n=941, 26.4% of reports
- Pain/redness/swelling at the injection site n=890, 24.9% of reports

Source: Ontario Agency for Health Protection and Promotion (Public Health Ontario). Weekly summary: adverse events following immunization (AEFIs) for COVID-19 in Ontario: December 13, 2020 to May 22, 2021 [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 May 27]. Available from: https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-aefi-report.pdf?la=en

In-depth Analyses, Signal Investigations, Enhanced Surveillance

- Enhanced epi summary of anaphylaxis in Ontario published in March
  - Validated and documented an observed level of anaphylaxis that was increased compared to usual AEFI reporting (while still rare)
  - Applied Brighton Collaboration case definition to all events managed as anaphylaxis

- Other examples:
  - Lot specific questions
  - Events associated with specific products (e.g., delayed injection site reactions following Moderna vaccine)

- Enhanced surveillance
  - Thrombosis with Thrombocytopenia Syndrome (TTS)/Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) following COVISHIELD/AstraZeneca vaccine

AEFI Surveillance in Action: TTS/VITT Events

March

- Reports of blood clots with low platelets (thrombocytopenia) with AstraZeneca vaccine seen in Europe
- International monitoring for this adverse event

April

- Raising awareness among providers to look out for this event and report to public health
- Enhanced surveillance directive issued by PHO to capture these events for provincial surveillance
- Expedited reporting of these events to PHAC

April-May

- Case finding definition (Brighton Collaboration and PHAC) for "Thrombosis with Thrombocytopenia Syndrome" (TTS) or "Vaccine-Induced Immune Thrombotic Thrombocytopenia" (VITT)
- Ongoing case finding and information sharing with surveillance partners

May

- Increase in reports of TTS/VITT seen in passive vaccine safety surveillance system
- Ontario announces pause on first dose of AstraZeneca vaccine out of an abundance of caution due to increased reports, increased and reliable supply of mRNA vaccines and downward trend in cases

Canadian National Case Definition for TTS

- Adapted from the Brighton Collaboration case finding definition
- Any patient presenting with both new onset of: 1) thrombocytopenia, **AND** 2) venous or arterial thrombosis (as defined by the Brighton Collaboration), with:
  - No known exposure to heparin within 100 days before symptom onset
  - No other underlying condition or explanation for the condition
  - Onset within 6 weeks (42 days) of vaccination

- Subtyping based on anti-platelet 4 antibody status
  - Anti-PF4 positive/**VIPIT**/**VITT**– either screening binding assay or functional assay positive
  - Anti-PF4 pending – screening binding or functional assay pending
  - Anti-PF4 negative – negative functional assay
  - Anti-PF4 unknown – not ordered or unknown if tests were ordered

Task Force for Global Health, Brighton Collaboration. Interim case definition of thrombosis with thrombocytopenia syndrome (TTS) [Internet]. Decatur, GA: Task Force for Global Health; 2021 [cited 2021 May 27]. Available from: https://brightoncollaboration.us/thrombosis-with-thrombocytopenia-syndrome-interim-case-definition/

Overview of Events in Ontario and Canada

- TTS/VITT in Ontario (as of May 22, 2021):
  - 16 TTS events reported as confirmed following **first dose** of AstraZeneca/COVISHIELD, of which 13 are VITT
  - Reporting rate of TTS based on 16 reports is 2.0 per 100,000 first doses administered (approximately 1 in 50,000)
  - Reporting rate of VITT (as a subtype of TTS) based on 13 reports is 1.6 per 100,000 first doses administered (approximately 1 in 61,000)
  - One report of death recorded in CCM that occurred in an individual with VITT. The investigation is ongoing and a cause of death has not been determined at this time.
  - Ontario reporting rate for TTS/VITT similar to national estimate for VITT following COVISHIELD (1/55,000)

PHO Resources

Resources to support AEFI reporting

- Infectious Disease Protocol, Appendix B (*updated April 2021*)
- Ontario AEFI Reporting Form (*updated May 2021*)
- Adverse Events of Special Interest (AESI) for COVID-19 Vaccine Surveillance (*Updated May 2021)*

Reports

- Weekly AEFI Report
- Enhanced Epidemiological Summary: Anaphylaxis

Knowledge products

- How Vaccine Safety is Monitored in Canada
- Vaccine Regulatory Approval Process in Canada

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- Tara Harris

Canadian National Vaccine Safety Network (CANVAS):

COVID-19 Vaccine Safety Surveillance

Matthew P. Muller, MD, PhD

Medical Director, IPAC, St. Michael's Hospital

Ontario Site Lead, CANVAS

CANVAS

- CANVAS vaccine surveillance in Canada since 2009 focused on:
  - H1N1 pandemic influenza vaccines (2009) [1]
  - Seasonal influenza vaccines (2010 - 2020) [2]
  - Meningococcal vaccine B vaccine (2014) [3]
- CANVAS uses an active surveillance method with a control group
- For influenza vaccines CANVAS recruits >50,000 participants / year
- Vaccine safety data shared with public health and published

(1) De Serres G et al. PLoS One 2012:7(7)
(2) Bettinger JA. Euro Surv 2020;25(22)
(3) Langley JM. Vaccine 2016;34

CANVAS-COVID – Background

- The COVID-19 pandemic has led to an unprecedented effort to develop safe and effective vaccines
- This effort has paid off with four Health Canada approved vaccines that demonstrated safety and efficacy in phase III trials
- The success of efforts to end the pandemic requires the achievement of herd immunity via vaccination – and that requires public trust
- Vaccine safety surveillance (and clear communication about AEFI risks) is a key factor that is required to build and maintain this trust

CANVAS-COVID – Objectives

- To identify the incidence of health events associated with COVID-19 vaccination by vaccine, demographics and health-related factors including populations not studied in Phase III trials [(1)]
  - Pregnant or breast-feeding
  - Immuno-compromised patients and those with auto-immune disease
  - Prior COVID-19
- To identify the incidence of health events that are severe
  - Interrupt daily activities including attendance at work or school
  - Require a medical assessment
- To determine if events are more common in vaccinees vs. controls

1. Bettinger JA et al. BMJ Open 2021 (in press)

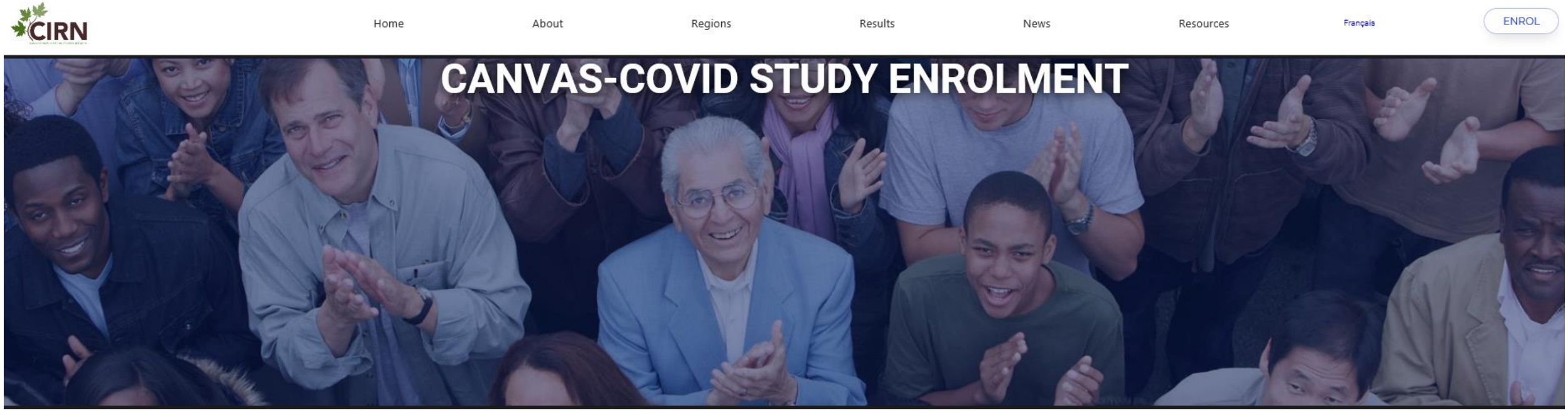
Methods - Recruitment

- Recruitment occurring in 7 P&T accounting for >75% of the Canadian population (ON, BC, AB, Que, NS, PEI and Yukon)
- Recruitment approach varies by Province
- In Ontario through collaboration between CANVAS-COVID, PHO, MOH and COVAX we have implemented an automated recruitment method
  - Vaccinees asked to consent to receive research emails via COVAX
  - If 'yes' you receive an email from the Canadian Immunization Research Network (CIRN) about CANVAS-COVID within 24 hours
  - Email links you to the CANVAS website at www.CANVAS-COVID.ca
  - On the website you can consent and enroll in CANVAS
- Goal: 240,000 participants per vaccine product

Methods – Control Recruitment

- Controls must be unvaccinated
- Recruiting from
  - Previous CANVAS flu participants
  - CANimmunize participants
  - Anyone else who wants to participate and is unvaccinated

www.CANVAS-COVID.ca



The CANVAS-COVID Study

The **Canadian National Vaccine Safety (CANVAS) Network** is a national platform that monitors vaccine safety after vaccines are approved for use. We are monitoring the safety of the COVID-19 vaccines in Canada and we need YOUR help.

Using a web-based survey we will collect information about whether or not health events occur after receiving COVID-19 vaccines. We will also collect health events from people who have not received a COVID-19 vaccine.

How to Enrol

If you want to participate, please register for the study by selecting the button to the right that applies to you (whether you have received a COVID-19 vaccine or you have not). If you haven't received the vaccine, you can still participate in the non-vaccinated (control) survey. If you join under the non-vaccinated group, you may later re-join the vaccinated group once you've received the vaccine.

You will then be directed to select your Province of residence and you will need to provide your first name, email address and telephone number. If you have been vaccinated we will need to know your vaccination date and vaccine product.

Enrol Here

Have You Received the COVID-19 Vaccine?

I have had the COVID-19 vaccine

I haven't had the COVID-19 vaccine

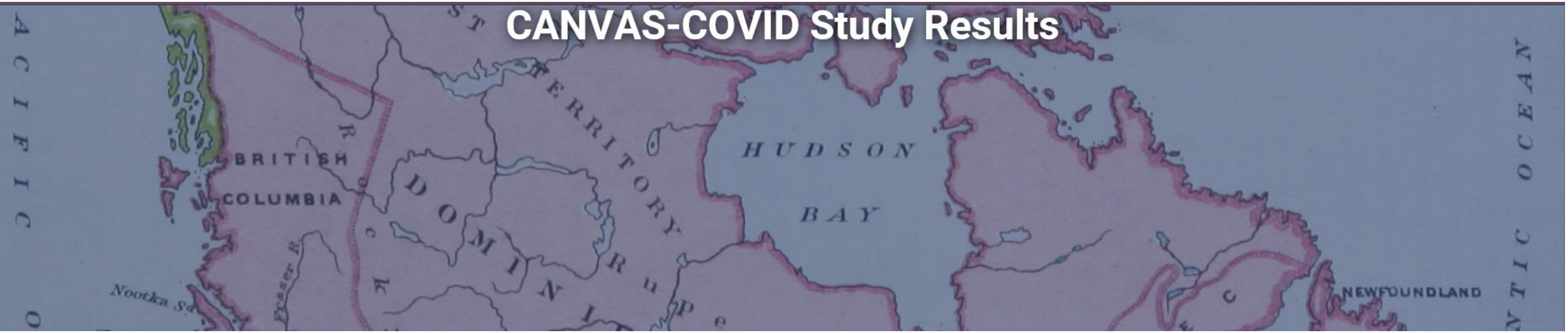
Methods – Data Collection

- Vaccinees receive email surveys to collect AEFI information
- Surveys are done one week after each dose and 6 months after vaccination is completed
- Participants that report an ‘health event’ severe enough to require a medical assessment are contacted by phone to review the AEFI
- Can add a manual trigger for phone interviews or extra survey if specific AEFI suspected
- Controls (Retroactive and Proactive) – surveyed at one week, one month and six months

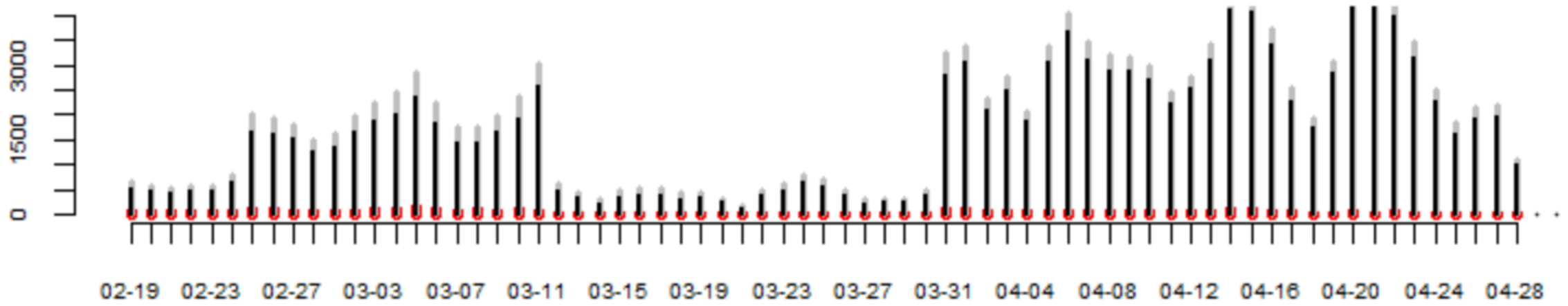
Health Events, Severe Health Events, AEFI

- In CANVAS – health events are those events that follow vaccination within a defined period – they may or may not be caused by the vaccine
- Severe health events are those that result in
  - Missing work or school
  - Interruption of daily activities
  - Need for a medical assessment
- To determine if these are AEFI requires comparison with controls
- Severe health events that meet public health criteria are reported to the local public health department for assessment

CANVAS-COVID Study Results

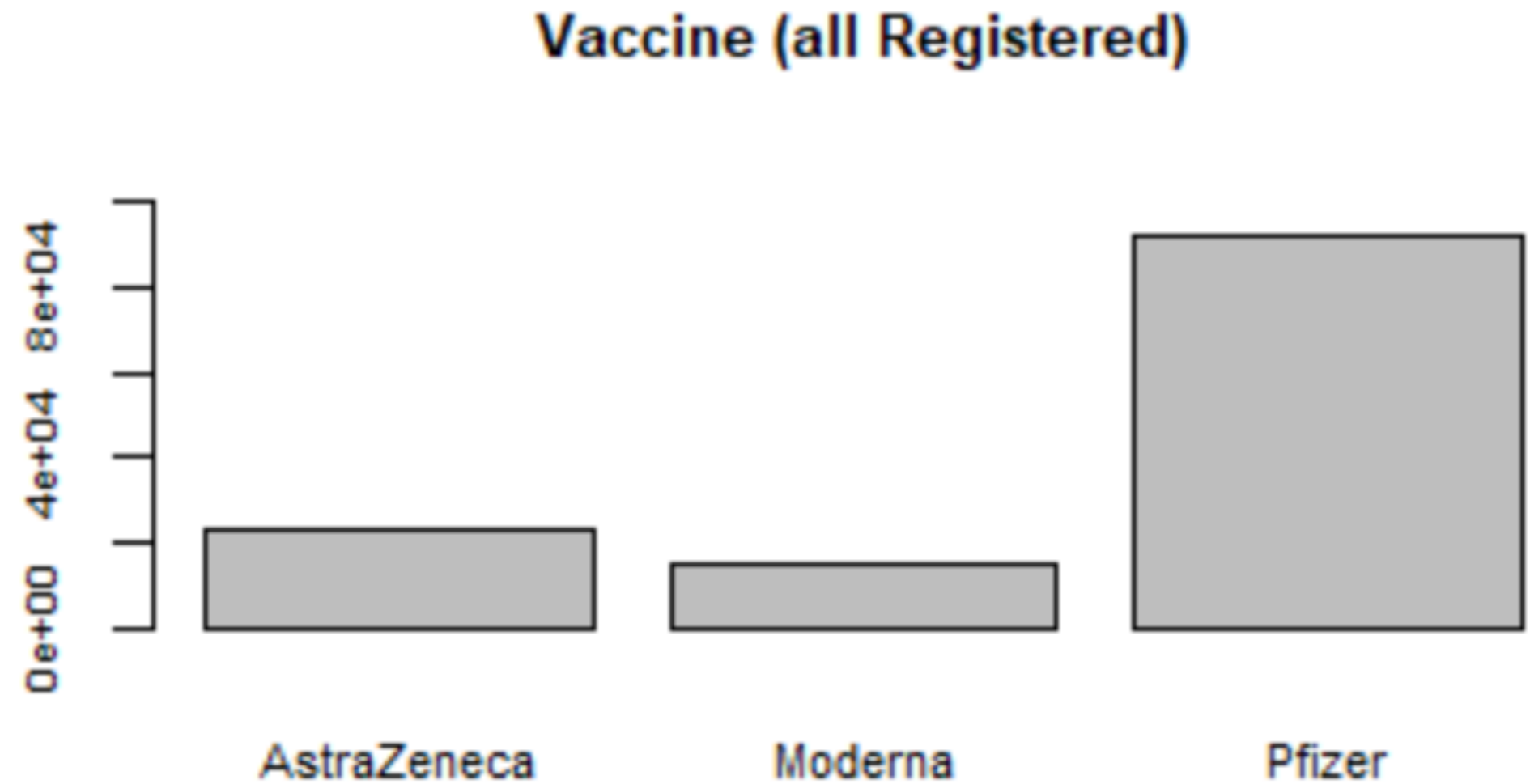


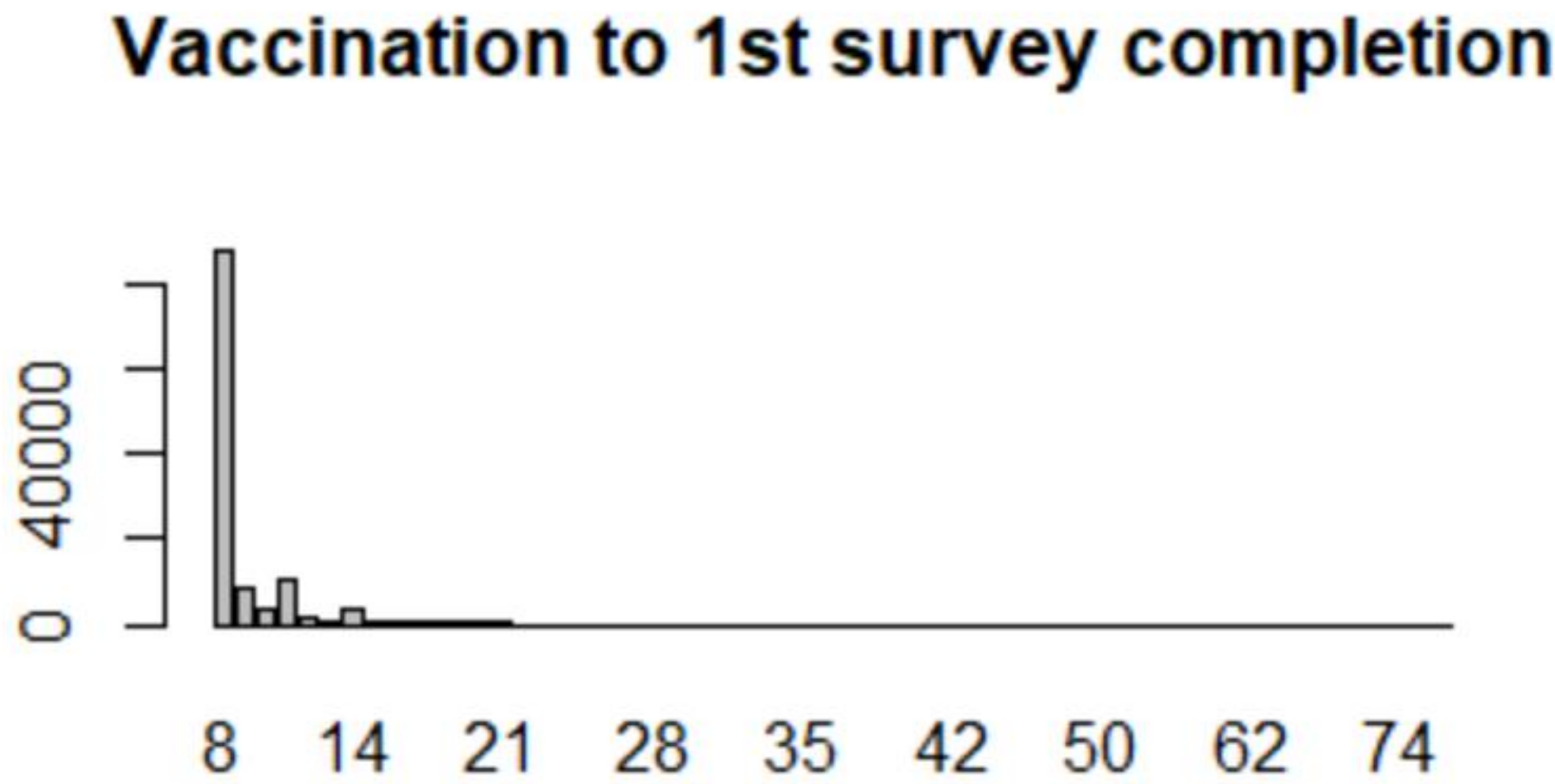
Number of Participants Registered (grey) and Completed Dose 1 (black) and dose 2 (red) surveys



Some Ontario Data

- Total enrolled: >260,000
- Controls: >8000
- Immunocompromised: >5000
- Pregnant or breast feeding: >1500
- Prior COVID-19: >1600


Vaccine (all Registered)
0e+00
4e+04
8e+04
AstraZeneca
Moderna
Pfizer


Vaccination to 1st survey completion
0
40000
8
14
21
28
35
42
50
62
74

Total persons enrolled in study

Vaccination dose received and survey completed:

DOSE 1
survey completed
538,278

DOSE 2
survey completed
4,440

People experiencing **local reaction**:

48%

Injection site pain/swelling/redness

Other health events that occurred after dose 1:

9%

of people developed a new health event within 7 days of receiving their first dose

43,212 out of 538,278 doses

4%

of people developed a new health event within 7 days that **prevented daily activities/ work/required a medical visit**

22,409 out of 538,278 doses

Other health events that occurred after dose 2:

14%

of people developed a new health event within 7 days of receiving their second dose

600 out of 4,440 doses

8%

of people developed a new health event within 7 days of receiving their second dose that **prevented daily activities/work/required a medical visit**

350 out of 4,440 doses

Most frequent other health events reported:

4.4%

Systemic Symptoms

(fever, fatigue, muscle ache, feeling unwell)

1.8%

Nausea, vomiting, diarrhea

CANVAS-COVID Conclusions

- Active screening via CANVAS is providing rapid data on vaccine safety and supporting public health passive surveillance
- Adapted from CANVAS flu surveillance – but scaled up!
- Will provide data on understudies groups (e.g. pregnant women) excluded from phase III studies
- Provides long (>6 month) follow up for AEFI
- Preliminary results consistent with Phase III study data re: common AEFI post initial dose
- More data will be available soon as dose 2 numbers increase

Acknowledgements

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