Vaccine Safety Surveillance

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Disclosure Statement

• I have no affiliation (financial or otherwise) with a pharmaceutical, medical device or communications organization

• I am a member of the National Advisory Committee on Immunization and the BC Immunization Committee
Objectives

• Describe active and sentinel surveillance approaches for monitoring and evaluating vaccine safety in Canada
• Understand what a vaccine safety signal is and how it is detected
Active, sentinel surveillance

- **Active:** Outreach to detect cases or stimulate case reporting
  - Active case searching of hospital records, laboratory reports, discharge summaries, etc.

- **Sentinel:** Monitoring in selected groups/populations
  - Group represents entire population
  - Standard case definitions and protocols
What is a vaccine safety signal?

- Increase in reports of a specific type of AEFI after a specific vaccine suggesting a new potentially causal association or change in severity and frequency of a known AEFI
  - Cluster of AEFI in a certain region or associated with a certain vaccine
  - Reports of a new type of AEFI
  - Unexpected increase in known AEFI with new or established vaccine program
  - Concern about vaccine quality reported by manufacturer
- Temporal events
Is the event occurring at a higher than expected rate after vaccination?

Post-marketing surveillance systems in Canada

- Canadian Adverse Event Following Immunization Surveillance System
  - Mandatory reporting from vaccine manufacturers (<5%)
  - Passive surveillance through public health from provinces/territories
  - Active sentinel surveillance of selected adverse events leading to pediatric hospitalization

- Canadian National Vaccine Safety Network (CANVAS)
  - Active participant-based reporting of AEFI after influenza vaccination
Canadian Immunization Monitoring Program Active

- 12 pediatric tertiary care centers, conducting active surveillance for select serious adverse events following immunization (AEFIs) since 1991 for children 0-16 years
- Current network:
  - Covers over 90% of tertiary care pediatric beds
  - Referrals from all provinces, territories
- Nurse monitors actively scan hospital admissions for conditions under surveillance, review chart and vaccine records
- AEFIs reported to PHAC and local public health
- In 2021, funded monitor for COVID-19 targets at 13 centers (3 in Ontario)
IMPACT AEFI Surveillance Targets

- AEFI
  - Seizures (febrile, non-febrile)
  - Encephalopathy/itis, ADEM
  - Myelitis
  - GBS and other Acute Flaccid Paralysis
  - Thrombocytopenia
  - Intussusception
  - Miscellaneous

- COVID (2020-2022)
  - Myocarditis/pericarditis
  - Multisystem inflammatory syndrome in children
IMPACT AEFI Surveillance

• IMPACT accounted for 4% of AEFI reports in national passive surveillance in children < 18 years of age from 2005–2012

• >50% of all serious AEFI reports (70–90% of neurologic AEFI)

Source: Nooshin Ahmadipour Public Health Agency of Canada
IMPACT AEFI Highlights

• Over 16 publications on vaccine safety:
  • Benign outcome of ITP after MMR
  • Reduced risk of seizures, HHE with aP
  • Absence of encephalopathy cases after aP
  • Post-immunization rate of GBS
  • Evaluation of Brighton Collaboration seizures definition in surveillance
  • Kawasaki disease following immunization

Publication List: https://www.cps.ca/en/impact
IMPACT: Challenges & Limitations

• Only catches the “tip of the iceberg” – AEFI/VPDs severe enough to require hospitalization

• Immunization history often difficult to obtain:
  • No national immunization schedule or registry
  • Information in chart usually incomplete

• Case identification dependent on local testing and admitting practices

• Labour-intensive: ~6000 cases screened to identify 100–120 reportable AEFIs annually
CANVAS-COVID and Influenza: Surveillance

- Over 1 million participants enrolled
  - BC, YT, AB, QC, ON, NS, PEI participating
  - Age group, vaccine type, health status, previous COVID Infection
- Online survey captures health events in first week after vaccination
- Survey captures severe health events:
  - Cause work/school absenteeism
  - Prevent daily activities
  - Require a medical visit
- Control survey of unvaccinated controls captures health events over 7 day period
- Telephone follow up for medically attended events

Bettinger et al. BMJ Open 2021

www.CANVAS-COVID.ca
CANVAS-COVID Results

- Weekly results summaries provided to federal and provincial public health
- CANVAS-COVID website: high level summary updated weekly
- Various signals investigated throughout campaign
- Safety of COVID vaccines in adults
- Safety of mRNA vaccines in pregnant people
- Safety of COVID vaccines in people previously infected with COVID

![CANVAS-COVID: Monitoring the safety of COVID-19 vaccines in Canada](https://www.CANVAS-COVID.ca)

**Total Number of Persons Enrolled in the Study:** 1,833,666

- Vaccination dose received and survey completed:
  - DOSE 1 survey completed: 931,317
  - DOSE 2 survey completed: 498,808

Participant-based ACTIVE surveillance

strengths

• Real-time surveillance
• Relatively low-cost
• Can be adapted to capture different types of AEFI or for different vaccines

challenges

• Patient self-report without medical validation may lead to incorrect diagnosis
• Small populations with low power to detect rare outcomes
• Respondents may not be representative of general population
Signal detection: example

- IMPACT detected 3 deaths in First Nations/Inuit infants associated with BCG vaccine
- Deaths due to disseminated BCG
- All 3 cases had immunodeficiencies

- Prompted review of IMPACT BCG vaccine complications in 2002

Signal evaluation: Deaths after BCG

Observed rate for dissemination was 205 per million FNI, 150x higher than expected

**Result:** Routine use of BCG limited to communities with ongoing active TB disease, with neg HIV screening and no risk factors for PID

Deeks et al, PIDJ, 2005
Conclusions

• Vaccine safety is closely monitored at all stages of development and after introduction in general population

• Active surveillance identify and investigate vaccine safety signals
  • With appropriate control group/background rate determine if the observed event rate is higher than the background rate

• Measuring temporal events does NOT mean causation
Questions