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

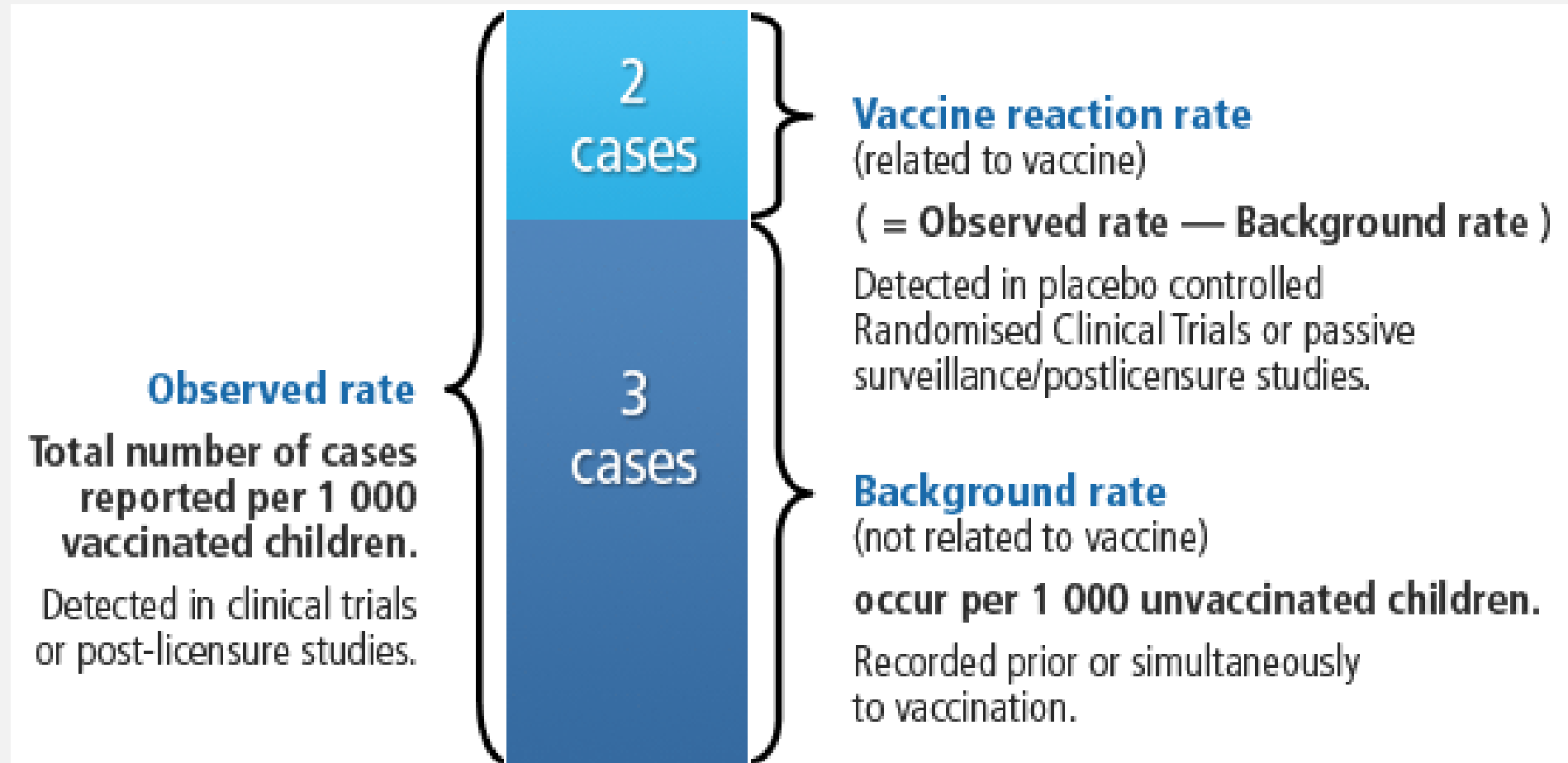# Active, sentinel surveillance

- **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
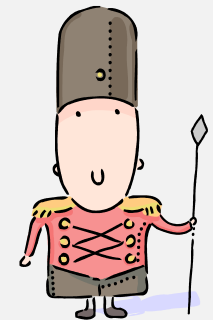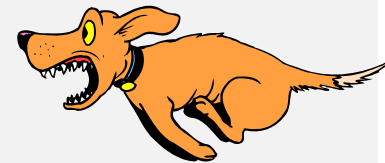
What is a vaccine safety signal?

- 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?

Observed rate

Total number of cases reported per 1 000 vaccinated children.

Detected in clinical trials or post-licensure studies.

2 cases

Vaccine reaction rate
(related to vaccine)

(= Observed rate — Background rate)

Detected in placebo controlled Randomised Clinical Trials or passive surveillance/postlicensure studies.

3 cases

Background rate
(not related to vaccine)

occur per 1 000 unvaccinated children.

Recorded prior or simultaneously to 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 AEFIs 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)
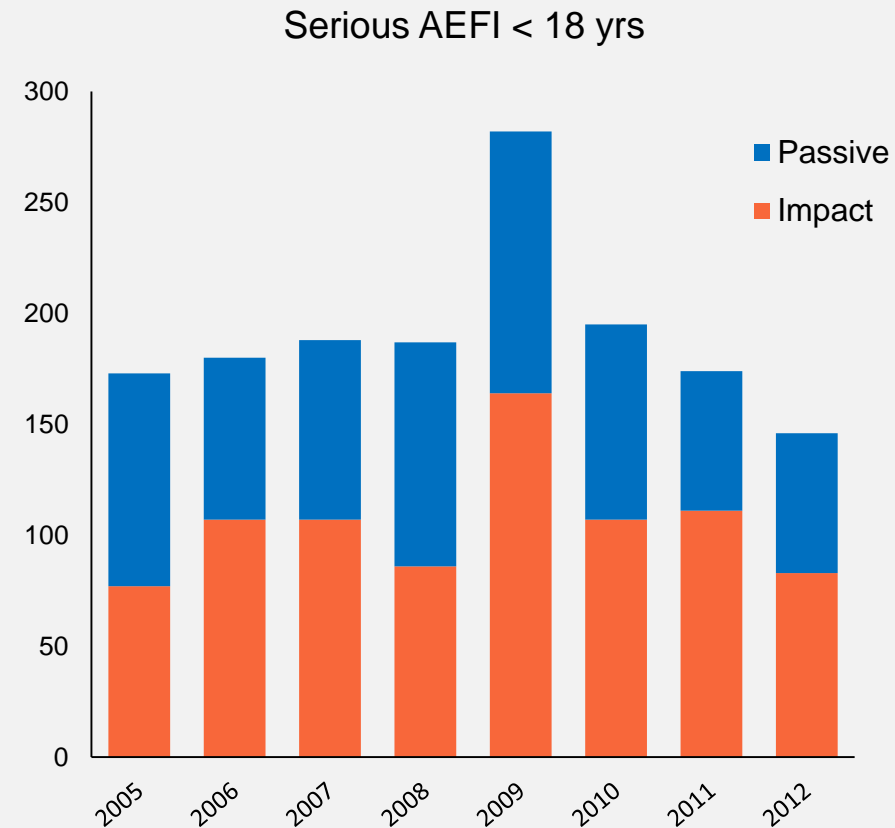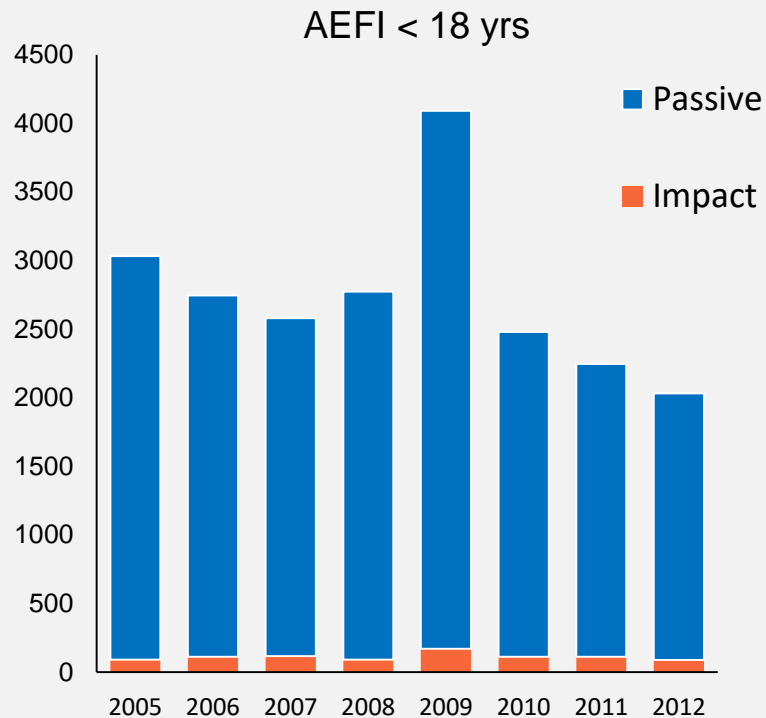

IMPACT

Canadian Immunization Monitoring Program, ACTive
Programme canadien de surveillance active de l'immunisation

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)

AEFI < 18 yrs

Serious AEFI < 18 yrs
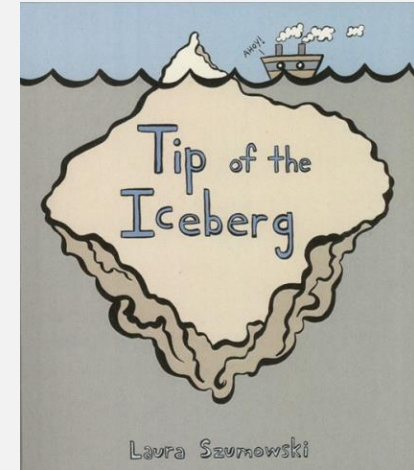
IMPACT AEFI Highlights

- 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

Tip of the Iceberg

Laura Szumowski

IMPACT

Canadian Immunization Monitoring Program, ACTive
Programme canadien de surveillance active de l'immunisation

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

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

Results as of: September 7, 20227

CANVAS-COVID:
Monitoring the safety of COVID-19 vaccines in Canada

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**

Sadarangani et. al. Lancet ID 2022, Bettinger et. al. CID 2022, Bettinger et al. Eurosurv 2015, 2019

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

UBC

BC Children's Hospital
Research Institute

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

Scheifele DW, et al. Can Commun Dis Rep (CCDR) 1998; 24:69-72

Signal evaluation: Deaths after BCG

TABLE 2. Summary of Disseminated BCG Infection Cases, 1993–2003

Case	Year of Diagnosis	Case Details	Underlying Immunodeficiency	Case Outcome
1	1993	FNI child vaccinated at 3 d of age in Manitoba, multiple infections	SCID	Fatal
2	1996	FNI child vaccinated at 3 d of age in Manitoba, multiple infections	HIV infection	Fatal
3	1996	FNI child vaccinated at 3 wk of age in Alberta, multiple infections	IFN-γ receptor deficiency	Fatal
4	1997	FNI child vaccinated at 1 d of age in Manitoba, multiple infections	SCID	Fatal
5	1998	FNI child vaccinated at birth in NWT, child died after bone marrow transplant	SCID	Fatal
6	1999	Child vaccinated in Iran in 1993, developed disease 6.5 yr later	Combined immunodeficiency	Recovered
7	2003	FNI child vaccinated at 2 d of age in Manitoba, multiple infections	SCID	Fatal

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