

The ideal sentinel surveillance system

Richard Platt MD, MSc

Harvard Medical School and Harvard Pilgrim Health Care

HMO Research Network

Centers for Education and Research on Therapeutics (CERT)

Attributes of the ideal system

- Prospectively monitor all aspects of therapeutics for adverse events
- Conduct confirmatory studies
 - Detect rare events in diverse populations
 - Quantify rare events in a reasonable time
 - Conduct *comparative* safety analyses in populations of known composition
 - Identify risk factors for adverse events

The drug safety “tool box”

- Expertise
 - Full use of FDA and other expertise
 - Clinical pharmacology, toxicology, clinical trial design, epidemiology, health services research
- Access to NDA safety data
- Passive surveillance
 - AERS, poison centers
- **Active surveillance**
- Confirmatory toxicology
 - Lab testing
 - Clinical research center

The active surveillance drawer in the safety toolbox

- Claims databases with medical record access
- Electronic medical record data
- Phase 4 clinical trials
- Large simple trials
- Disease-specific networks
 - Liver (DILIN), kidney, SJS, myopathy, lupus, torsades de pointes
- Registries
- Specimen repositories for patients with rare adverse events

Existing linked claims databases

- CDC Vaccine Safety Datalink
 - 8 HMO Research Network Health Plans (includes 4 Kaiser Permanente plans)
 - ~7 million lives. Emphasis on pediatric vaccines.
- FDA post-marketing surveillance contracts
 - HMORN (13 plans including 4 Kaisers, plus separate California Kaiser contract), United, TN/WA Medicaid
 - ~ 20 million lives
- VA system ~6 million lives

All combine data on eligibility / diagnoses /
procedures / pharmacy dispensing.

All are able to review full text medical records.

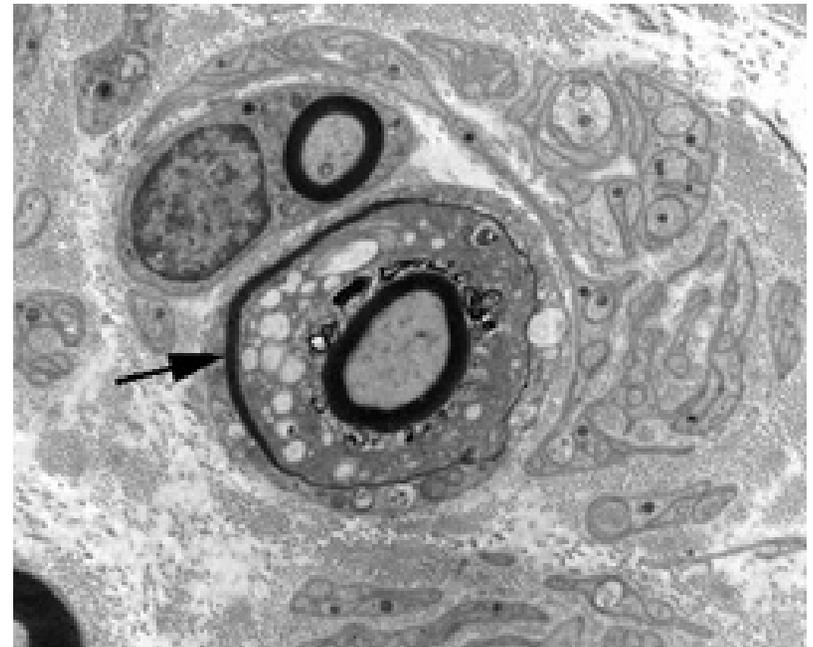
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Does this?



Cause this?



Menactra and Guillain-Barré Syndrome

- Meningococcal conjugate vaccine (Menactra) approved in 2005
- ACIP recommended immunization of all adolescents
- 15 spontaneous reports of Guillain-Barré Syndrome (GBS) within 42 days of immunization through September 2006
- Estimated 5.7 million doses distributed by then
- Questions:
 - Is there excess risk? If yes,
 - How much?
 - Is there a high risk subgroup?

Menactra and GBS – current resources

- Vaccine Safety Datalink is evaluating this.
- After 52 weeks and 98,514 vaccine doses (11,000 person-years), no cases of GBS among vaccinees and 2 in same size control group.
- Background rate: 1-2 cases per 100,000 person-years.
- Conclusion: Need larger population!

Linked claims databases

What else we should have

- Medicare
 - Parts A, B, D
- Medicaid
 - Most large states
- Private health plans

- Need ability to review selected full text medical records!

Menactra and GBS – health plan study

- Cohort study in 4 health plans with 40+ million members. Intended to complement VSD study
- Use claims to identify:
 - Demographic information
 - Eligible person-time
 - Immunizations
 - Potential cases of GBS
- Review medical records of potential cases
 - Adjudication by expert panel
- Report to FDA, CDC, manufacturer, public

Coming soon: CERTs Health Plan Consortium for Public Health

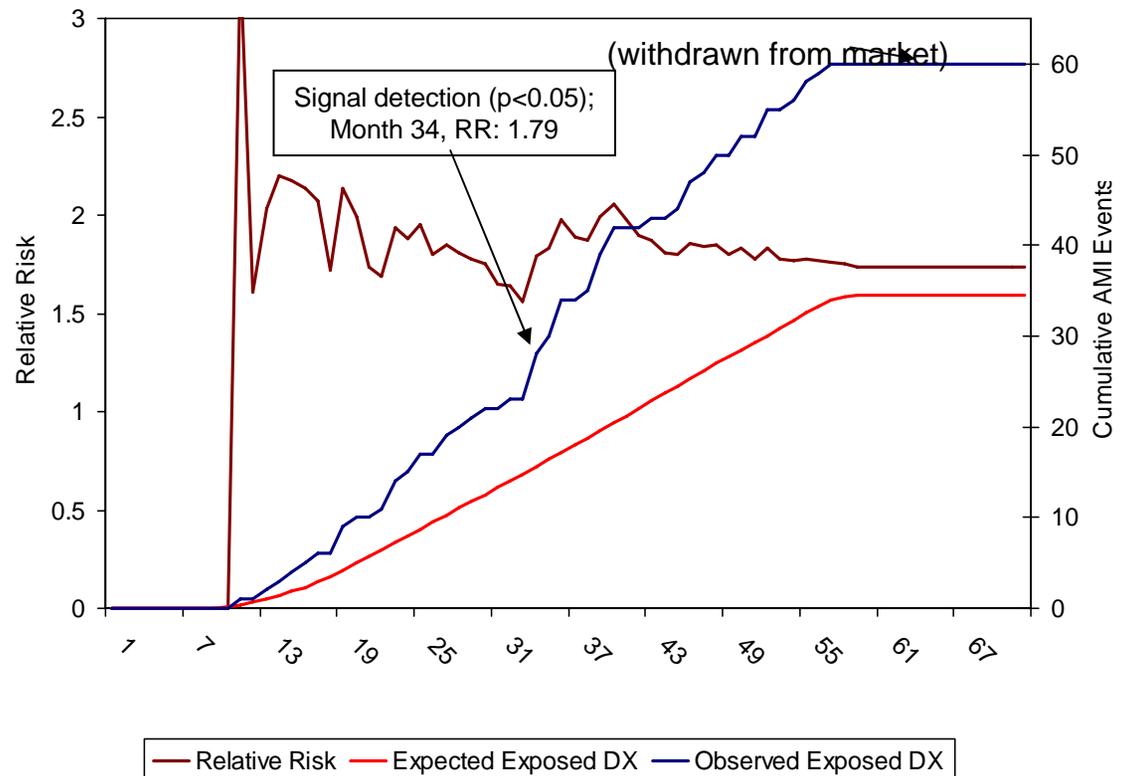
- Goal: Improve the safety and safe use of marketed vaccines and prescription drugs by studying their use in large populations of health plan members
- Target population: 100 million
- A planned activity of the Centers for Education and Research on Therapeutics (CERTs)
 - Created under Congressional mandate to be a trusted national resource in therapeutics
 - Administered by AHRQ in consultation with FDA
 - Accepted processes for administering public-private partnerships

CERTs Health Plan Consortium for Public Health – Aims

- Timely risk identification and quantification
 - Prospective signal detection for all new therapeutics; both routine and customized analyses
 - Detailed assessment of specific questions
- Identification of potentially unsafe use of preventive therapeutic agents
- Other topics, subject to Board approval

Rofecoxib and myocardial infarction – observing 7 million

- Relative risk rapidly stabilized between 1.5 and 2
- Signal occurred after 28 heart attacks among new users of drug
- Would have occurred by 2nd or 3rd month if 100 million people had been observed



Base population: 7 million. Comparator: naproxen. Adjusted for age, sex, and health plan.

CERTs Health Plan Consortium for Public Health – Structure and governance

- Public-private partnership
 - CERTs, health plans, federal agencies, foundations, industry, academic community
- Broadly representative governing board
- Research limited to public health priorities
 - determined by Board with input from Council of Stakeholders
- Specific research topics can be proposed by any agency, group, or individual
 - Must have agreement of at least one federal agency

CERTs Health Plan Consortium for Public Health – Data sources

- Health plans' claims data
 - Standard format files: eligibility, demographics, diagnoses, procedures, drug dispensing
 - Pre-processed to allow rapid queries via re-usable data tools
 - Updated at regular intervals
 - Ongoing quality checking
- Access to full text medical records as needed
- Potential to include other data
 - Laboratory test results
 - Electronic medical record information

Any health plan can opt in/out of specific uses

CERTs Health Plan Consortium for Public Health – Transparency

- Study protocols available for public comment before they are finalized
- Protocols available to public when study commences
- Results placed in public domain

CERTs Health Plan Consortium for Public Health – Confidentiality / Privacy

- Protection for individuals via HIPAA privacy regulations and federal human research rules
- Protection of health plans' identities and proprietary data

CERTs Health Plan Consortium for Public Health – Funding

- Infrastructure requires core funding
- Individual projects will require separate funding

CERTs Health Plan Consortium for Public Health

- Existing health plan data allow substantial enhancement of timeliness, power, and efficiency of post-marketing studies of therapeutics
- This information can/should complement other sources – Medicare/Medicaid, VA, Vaccine Safety Datalink