Discussion

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Seattle Symposium on Healthcare Data Analytics

CNODES
CANADIAN NETWORK FOR OBSERVATIONAL DRUG EFFECT STUDIES

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Is Observational Research Useful for Safety Surveillance?

- Madigan: recognize the limitations
  - Operating characteristics derived from RCTs are inappropriate.
  - How much can good design matter?
    - "Clinical judgment" vs. design principles
    - Map observational design to RCTs
    - Time is critical
- Gruber: what is the alternative?
  - Improve data quality
  - Bias analysis, much more generous bounds

Early Detection

- Cook: need *appropriate* methods for signal detection
  - » Use principles from good sequential RCT methods
- React early but not too early
  - » Cost/benefit (both clinical and $)
- What is precise research question?
- Need for validation/confirmatory studies?

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- "Canadian mini-Sentinel" with some twists
- Directed research questions from Health Canada
  - ***Validation***, not detection
  - Usually generated based on initial safety signal
  - Methods specific to the research question
- Distributed data; no common data model
  - Canadian provinces plus CPRD and US MarketScan
- Common protocol/analysis plan
  - Allow for different bias adjustments (within reason) in different sites
  - Allow for *understanding* of heterogeneity
- Meta-analysis if possible

PPIs and Pneumonia

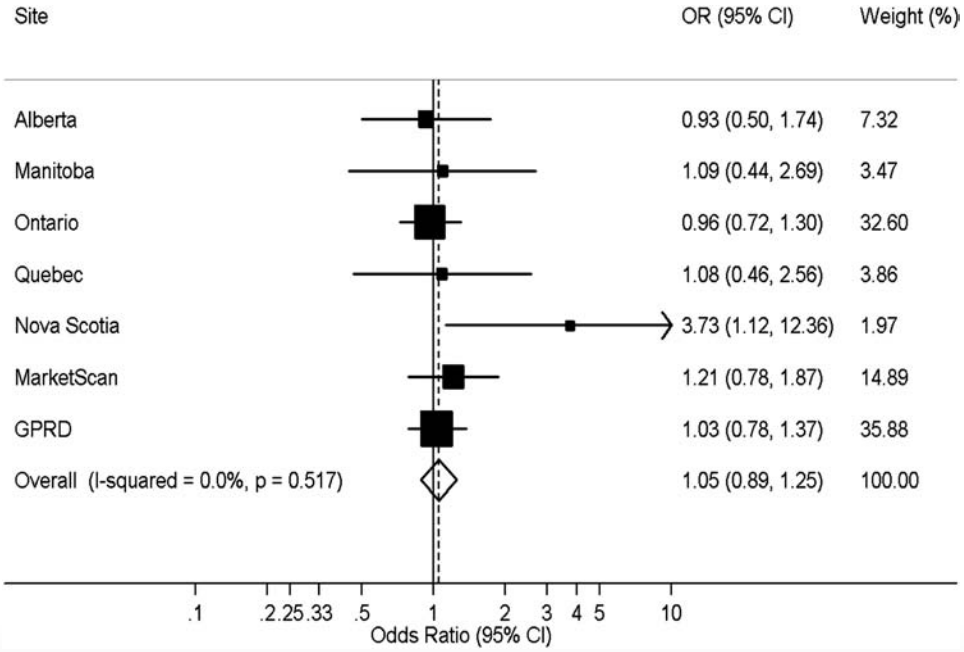
- Conflicting evidence
  - Positive association with short treatment regimens
  - Disappears with longer treatment time
- Problem: subtle protopathic bias
  - Early symptoms similar to GERD
- Solution: restriction to PPI prescribed at same time as NSAID
  - Preventive rather than therapeutic
  - Unconfounded by symptoms

Example

Proton pump inhibitors and the risk of hospitalisation for community-acquired pneumonia: replicated cohort studies with meta-analysis

Kristian B Filion,[1] Dan Chateau,[2] Laura E Targownik,[3] Andrea Gershon,[4] Madeleine Durand,[5] Hala Tamim,[6] Gary F Teare,[7] Pietro Ravani,[8] Pierre Ernst,[1] Colin R Dormuth,[9] the CNODES Investigators

- Very restricted sample
- Conclusion: no association
  - » Associations re-appear in unrestricted cohort



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Bottom Line

- We need to learn from observational data
- But we need to better recognize the limitations
  - More work on operating characteristics in controlled conditions
  - Better practice at the *design* stage
  - Better estimation of the *true* uncertainty

Questions

- What CAN we do?
- No choice but to make observational studies better
  - Learn the operating characteristics
  - Or make our conclusions more appropriate?
- Should we do more or different trials?
  - Seems like David's arguments apply to them too…
  - Can we make them large enough to learn about safety?
  - Pragmatic trials?
  - Registry trials?
    - Rigor of a trial, speed and efficiency of an observational data analysis
    - Feasibility? Cost?

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