OMOP and Mini-Sentinel Collaborations Supporting Routine Prospective Surveillance

Jennifer Nelson[1], Mini-Sentinel
David Madigan[2], OMOP

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1. Group Health Research Institute and University of Washington
2. Columbia University

Some history…

- OMOP began its activities in 2007
  - Characterize the effectiveness of different epidemiological and statistical methods for estimating the effects of medical products using large-scale observational data
- Mini-Sentinel got underway at the end of 2009
  - Create an active surveillance system, including routine prospective safety monitoring, for FDA-regulated medical products using electronic health care data
- Key area of shared interest and research
  - Developing and evaluating methods for active surveillance
  - Identify and address barriers and challenges

Methodological challenges

- All the usual observational study biases…and more
- New purpose
  - Rapid detection of safety signals as product uptake occurs
  - Scaled up to monitor many, diverse medical products
- New setting (not a research environment)
  - Unpredictable uptake rate, composition of users over time
  - Distributed data environment, constrains analytics
- New data sources
  - Data are dynamic, data quality needs constant study
  - Heterogeneity across sites is large, must be addressed

Collaborative methods vision

- Leaders from both OMOP and Mini-Sentinel involved in crafting the original Mini-Sentinel methods agenda
  - Methods for generating hypotheses
  - Methods for refining and testing hypotheses
  - Methods to evaluate and improve method performance
- Mini-Sentinel investigators have spent 3 years systematically implementing aspects of this plan
- One such activity was led by OMOP and helped evaluate and push forward self-controlled methods for use in Mini-Sentinel

Self-controlled methods workgroup

- Open methods questions in safety surveillance setting
  - When are self-controlled methods advantageous over other designs?
  - What extensions are desirable (e.g., Bayesian, multi-drug)?
  - What is the opportunity for multi-drug outcome-focused active surveillance *vs* surveillance of a target drug?
- Specific working group aims
  - Describe key differences, strengths, and limitations of self-controlled case series (SCCS) *vs* case-crossover designs
  - Overview the usage of case-based designs in published studies
  - Assess OMOP's multi-drug SCCS and other new SCCS developments
  - Make recommendations to Mini-Sentinel

Other Mini-Sentinel methods work groups

- How can we systematize and expedite the selection of an appropriate surveillance design?
- What data and analysis methods are best-suited for use in Mini-Sentinel's distributed data setting?
- How can sequential testing methods be best adapted to achieve rapid detection while minimizing errors?
- What methods should be conducted to further evaluate a signal generated by routine surveillance?

Current status: Mini-Sentinel

- Mini-Sentinel work has culminated in development of a Routine Prospective Surveillance plan and methods
  - OMOP leaders have participated in this work
- Designed to conduct semi-automated, prospective surveillance to complement protocol-based evaluations
  - Less resource intensive, less control of systematic biases
  - Ability to generate potential signals for further assessment
- Created a methods toolbox, diverse and flexible options
  - Some are methods or variants of those assessed by OMOP
  - Includes self-controlled, matching, regression approaches

Current status: OMOP

- Completed two large-scale experiments to evaluate competing methods for estimating the effects of medical interventions
- Developed a process for choosing the optimal customized analytic method for a given context
- Developed approaches for calibrating p-values and confidence intervals to deliver correct the correct Type I error rate and coverage properties
- Developed a Bayesian framework for synthesizing empirical evidence

Current status: Joint Collaborations

- Since June 2012: Mini-Sentinel developing and testing code for use in Routine Prospective Surveillance
  - Continued participation by and input from OMOP
- Sept 2012: Joint OMOP/Mini-Sentinel meeting
  - Synthesized prior work, generated ideas for future joint work
  - Ideas leverage experience and expertise of OMOP and Mini-Sentinel and improve Routine Prospective Surveillance plans
- Oct-Dec 2012: FDA input obtained, ideas refined
- Early January 2013: OMOP/Mini-Sentinel leaders met again with FDA to select topic to be pursued together
  - Design and implement a methods performance evaluation

Performance evaluation plans

- Review existing evaluation work
  - Current suite of OMOP experimental results
  - Simulation evaluations conducted within Mini-Sentinel
- Identify key gaps in of the performance of existing Routine Prospective Surveillance methods
- Develop an evaluation framework and metrics to assess these unanswered performance aspects
- Identify appropriate setting to conduct the evaluation
- Design and implement the performance evaluation to address these gaps using the developed metrics

Next steps

- Continued participation by OMOP in Mini-Sentinel's existing Routine Prospective Surveillance group
- New joint working group has been formed to develop the scope of work, timeline, and required resources for the OMOP/Mini-Sentinel method performance evaluation project
- Specific OMOP/Mini-Sentinel research projects getting underway