Sentinel Initiative

Statistical and Epidemiological Issues in Active Medical Product Surveillance

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Sentinel Initiative

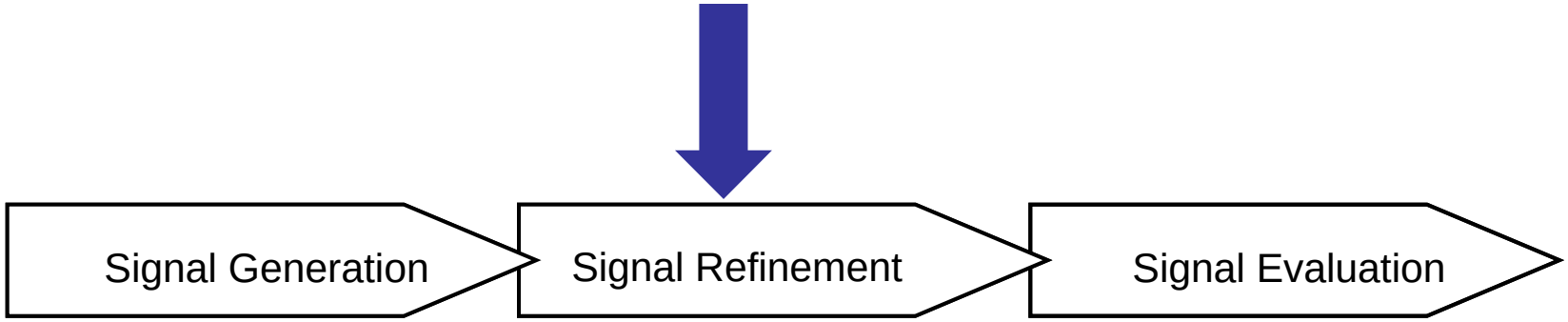
- Develop a national electronic safety monitoring system
  - Strengthen FDA's ability to monitor postmarket performance of medical products
  - Enable FDA to access existing automated healthcare data by partnering with data holders (e.g., insurance companies with large claims databases, owners of electronic health records, others)

- Will augment, not replace, existing safety monitoring systems

Potential Capabilities of Sentinel

- Safety issues may be identified and evaluated in near real-time
- Sentinel may expand current capacity for evaluating safety issues
  - Improved access to subgroups, special populations
  - Improved access to long-term data
- Active surveillance may identify an increased risk of common AEs (e.g., MI, fracture) that health care providers may not suspect are related to medical products

Definitions



- Signal generation includes a collection of methods for identifying potential associations between medical products and health outcomes of interest (HOIs)
- Signal refinement is a process for evaluating the magnitude and clinical significance of a suspected association
- Signal evaluation consists of the implementation of a formal epidemiological analysis to more definitively establish or refute causality between exposure to a medical product and the health outcome of interest

Scenarios included in signal refinement

- Concern emerges prior to marketing
  - Safety concern observed in premarket development program
  - Theoretical safety concern
    - based on serious side effects of medical products, in general
    - based on serious side effects occurring in a drug or product class
- Concern emerges after product has been marketed for a period of time

Mini Sentinel

Harvard Pilgrim Healthcare

- Develop the scientific operations needed for the Sentinel Initiative.
- Create a coordinating center with continuous access to automated healthcare data systems, which would have the following capabilities:
  - Provide a "laboratory" for developing and evaluating scientific methodologies that might later be used in a fully-operational Sentinel Initiative.
  - Offer the Agency the opportunity to evaluate safety issues in existing automated healthcare data system(s) and to learn more about some of the barriers and challenges, both internal and external.

Progress to Date – Methods Core

- Framework for safety surveillance methods and a prioritized list of gaps
- Regression methods applicable for sequential surveillance programs
- Case only methods, e.g., cross-over designs, utilizing time-varying covariates
- Enhance methods for application of high dimensionality propensity score confounder adjustment

Planned methods projects for Year 2

- Enhance Year 1 taxonomy with lessons learned from Year 1 methods projects
- Developing a framework for examining the validity of the results of a signal refinement activity
- White paper on methods to evaluate impact of FDA regulatory actions
- PRISM:
  - Methods for use in active vaccine safety surveillance (unanticipated and non-prespecified adverse events)
  - Causal inference in sequential analysis