Sentinel Initiative

Methods for Signal Refinement in Active Medical Product Surveillance

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Sentinel Initiative

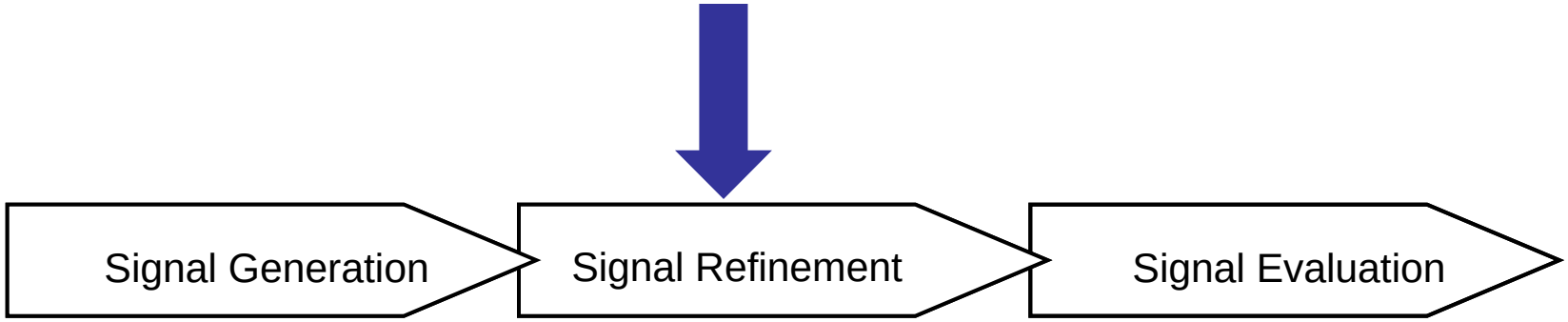
- Develop a national electronic safety monitoring system
  - Strengthen FDA's ability to monitor postmarket performance of medical products
  - Enable FDA to access existing automated healthcare data by partnering with data holders (e.g., insurance companies with large claims databases, owners of electronic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

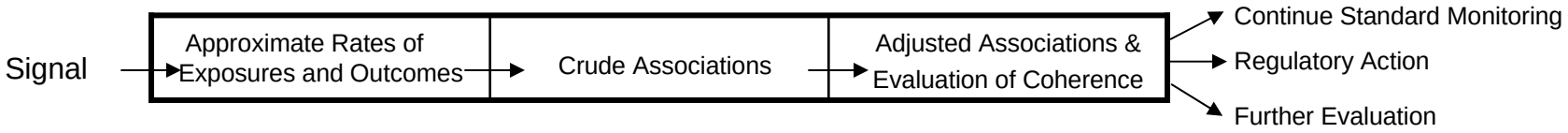


- Signal generation includes a collection of methods for identifying potential associations between medical products and health outcomes of interest (HOIs)
- Signal refinement is a process for evaluating the magnitude and clinical significance of a suspected association
- Signal evaluation consists of 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
- Concern emerges after product has been marketed for a period of time

Potential steps in signal refinement



FDA's challenge…

Determine the boundaries of signal refinement

- If the goal of a Sentinel System evaluation is to produce actionable information using active surveillance methods, what extent of evaluation will result in an answer that is "good enough"?

Finding a balance between timeliness, resource needs, and confidence in the result

Crude measure of association

- Can be calculated quickly
- Subject to a host of biases

Adjusted measure of association

- May address many biases
- Protocol writing is time consuming
- Approaches to adjust for confounding may be resource intensive

Charge for the day

- Help FDA sort through potential high level approaches for systematizing the evaluation of the many safety signals that will need attention
- Delineate data resource needs to facilitate timely active surveillance evaluations
- Describe approaches that balance confidence in the evaluation results with timeliness and efficient use of resources