Methods for Signal Refinement

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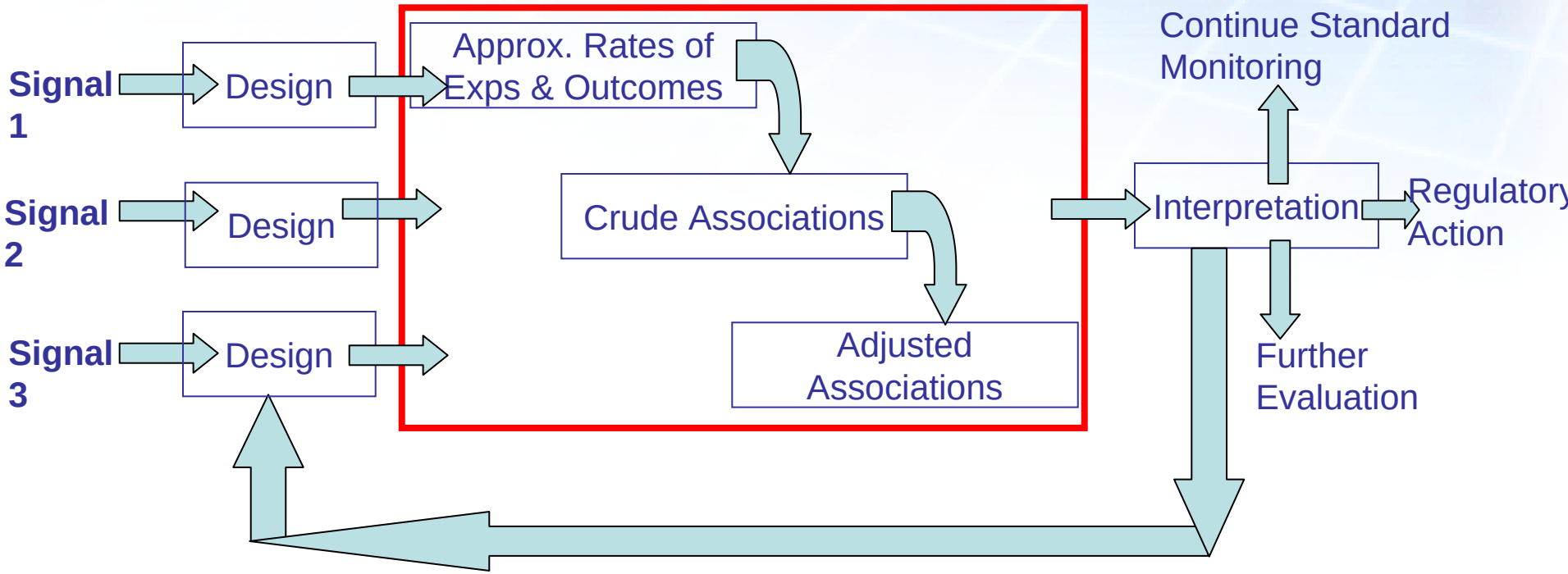
Steps in Signal Refinement



Signal 1: Product + Outcome = Known Drug-related AE (agranulocytosis, Stevens-Johnson, hepatic failure)
Signal 2: Product + Outcome = Possible mechanism of action or toxicity, minimal existing data
Signal 3: Product + Outcome = Common medical condition that may be part of disease process
Signal 4: …

Key Goals/Process Attributes – "Refinement" Stage

- **Definition of Cohort/Exposure**
- **Nature of Product-Outcome pair will drive design and implementation of Signal Refinement workflow**
  - Frequency? Severity? Background/expected rates in that disease?
- **Agreed definition of "outcome"?**
- **Session II: Strengths of Observational Data to address?**
  - Administrative claims? EMR?
  - Existing registries, prospective trials?
- **Session III: Can the analytic methods faithfully identify a "rate"?**
- **Transparency**

Issues and Challenges

- **1) Disease-Specific Incidence of "Co-morbidities," "Outcomes," and "Disease Sequellae"**
  - The kinds of outcomes captured in observational data and where Sentinel will be most useful
  - Explicitly needs to be created for commonly treated diseases with temporal adjustments and relationships
    - Ex: Diabetes + MI, CHF, CVA, arrhythmia, hypertension, PVD, retinopathy, CKD and ESRD, fractures, falls, anemia, depression, asthma…
  - Consider AHRQ or other partnership for automated systematic survey and disease assessment
  - Can not easily ignore some handling of drug class exposure in disease analysis
    - Slippery slope from "Refinement" to "Evaluation"?

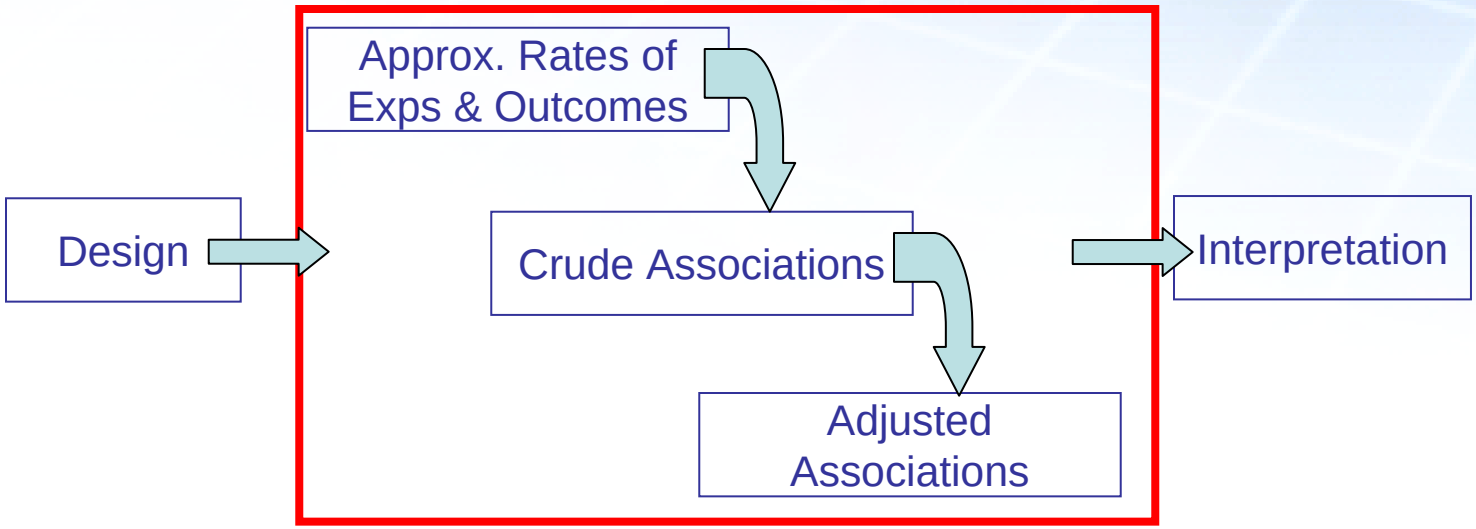
Issues and Challenges (cont'd)

- **2) Incidence & sequellae when conditions/events are data elements not routinely captured in EMR/administrative claims**
  - OTC products, alternative medicine products
  - Medical devices
  - Diagnostic test results (genetic or other)
  - May be role for use of registries & existing trials
- **3) Should you control for *some* confounding in Signal Refinement?**

Standardized Steps – Systematic Implementation

- **The only way to make Sentinel and Signal Refinement scalable and sustainable**
  - Allow multiple Signal Refinement workflows specific to the type of Product-Outcome pair being evaluated
  - Database Normalization (into analysis common analysis format)
  - Concept Mapping and Coding
  - Definition of Cohort
  - Definition of Outcome(s)
  - Range of Analytic Methods
  - Rapid Performance
- **Same steps also applicable to the foundation for "Disease Sequellae" process**

The Impact of Standardization



Cognitive Evaluation

10 minutes – few hours

Cognitive Evaluation

DISCUSSION

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