

# OMOP Overview and Insights



46th Annual Meeting  
Washington, DC - 2010

Thomas Scarnecchia  
Executive Director  
Observational Medical Outcomes  
Partnership

**FOUNDATION**  
FOR THE  
National Institutes of Health

**OBSERVATIONAL  
MEDICAL  
OUTCOMES  
PARTNERSHIP**



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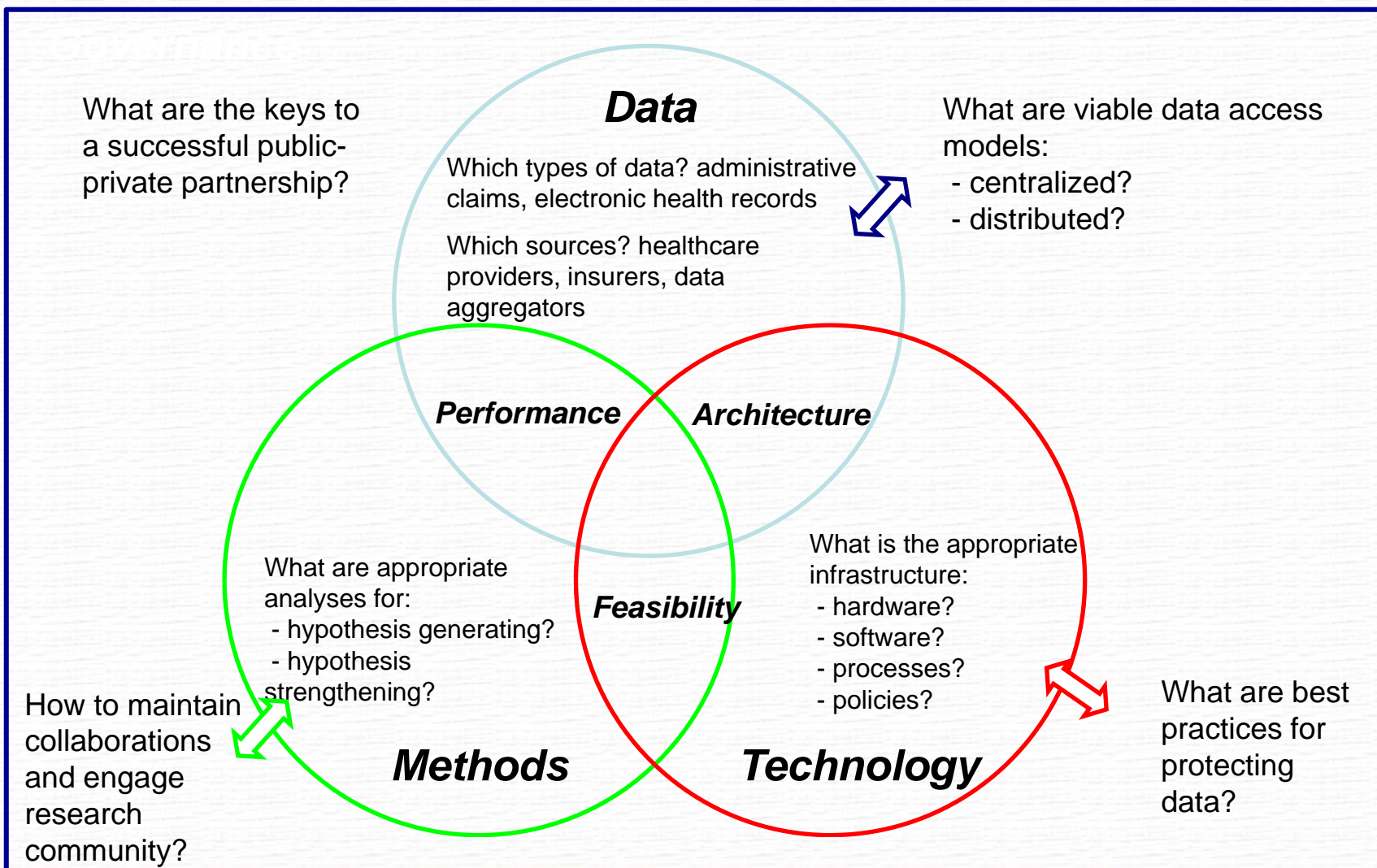
# Observational Medical Outcomes Partnership

*A public-private partnership to serve the public health by testing whether multi-source observational data can improve our ability to assess drug safety and benefits.*

- Assess the appropriate technology and data infrastructure required for systematic monitoring of observational data
- Develop and test the feasibility and performance of the analysis methods
- Evaluate required governance structures



# Outstanding Questions for Active Surveillance



# Research Investigators

*The lead scientists for the OMOP project who guide and participate in the research across all project phases*

**Marc Overhage, MD, PhD:** Director, Medical Informatics and Research Scientist, Regenstrief Institute, Inc.; Regenstrief Professor of Medical Informatics, Indiana University School of Medicine, CEO; President of the Indiana Health Information Exchange

**Judy Racoosin, MD, MPH:** Sentinel Initiative Scientific Lead, US Food and Drug Administration

**Paul Stang, PhD, FISPE:** Senior Director, Epidemiology, Johnson & Johnson Pharmaceutical Research and Development

**Abraham G. Hartzema PharmD, MSPH, PhD, FISPE:** Professor and Eminent Scholar, Pharmaceutical Outcomes & Policy, Perry A. Foote Chair in Health Outcomes Research, University of Florida College of Pharmacy

**Patrick Ryan:** Manager Drug Development Sciences, GlaxoSmithKline R&D  
OMOP Co-Investigator

**David Madigan, PhD:** Professor of Statistics, Columbia University  
OMOP Methods Lead



# OMOP Research Community

*OMOP's research community requires active participation from all key stakeholders, including government, academia, industry, health care organizations, and patient groups.*

## **Governance**

- 10 Executive Board members, chaired by FDA and managed by Foundation for NIH
- 21 Advisory Board members
- Led by 6 research investigators and Program Management Office

## **Methods**

- 17 methods collaborators

## **Data**

- 5 active distributed partners
- 5 central databases included in the OMOP Research Lab
- Simulated, claims and EHR datasets

## **Technology**

- Secure virtual research lab
- 2 data access models
- 6 different systems architectures

***Over 100 researchers involved!***

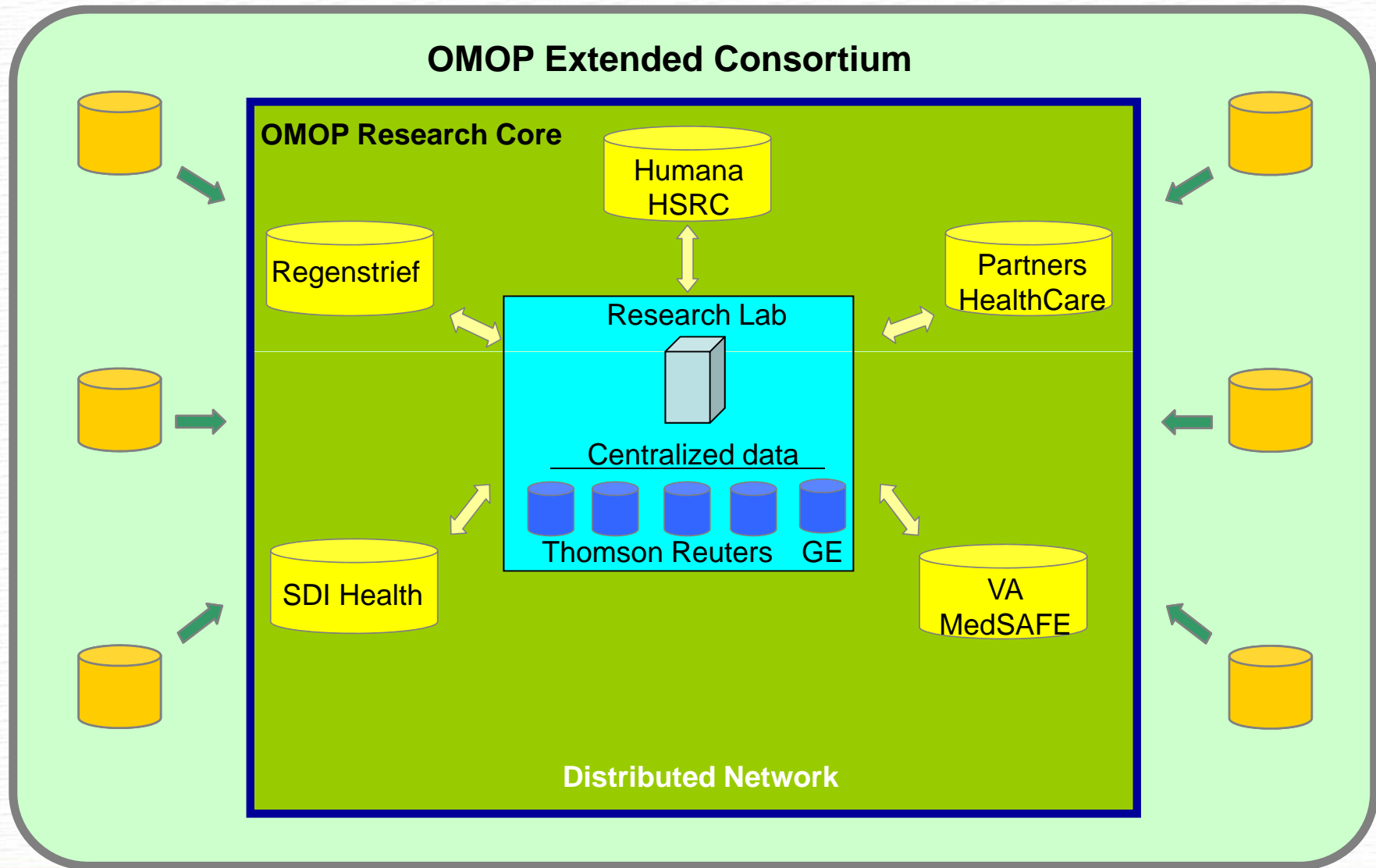


# OMOP Research Phases

- **Phase 1: FEASIBILITY OF DATA INFRASTRUCTURE (Feb – July 2009)**
  - Establish a consistent framework to use across disparate observational data sources
  - Establish OMOP Research Community
- **Phase 2: FEASIBILITY OF ANALYSES (Aug – Dec 2009)**
  - Develop and test analysis methods within the OMOP Research Lab and other data environments
  - Establish standard data characterization procedures
  - Implement health outcomes of interest definitions
  - OMOP to facilitate comparisons across databases
- **Phase 3: PERFORMANCE MEASUREMENTS (Jan – July 2010)**
  - Evaluate performance of methods and data in identifying drug safety issues
  - OMOP to facilitate comparisons across databases
- **Phase 4: UTILITY OF ANALYSES & PROCESS (July – Dec 2010)**
  - Assess the effectiveness and usefulness of how the results and comparisons contribute to decision-making



# OMOP Data Community



# OMOP's Methods Landscape

## Disproportionality Analysis

	<i>AE j = Yes</i>	<i>AE j = No</i>
<b>Drug <i>i</i> = Yes</b>	<i>a=20</i>	<i>b=100</i>
<b>Drug <i>i</i> = No</b>	<i>c=100</i>	<i>d=1080</i>

- Distinct Patients
  - SRS
  - Modified SRS
- X
- MGPS  
BCPNN  
PRR X Stratified  
Chi  
etc.

- Temporal Pattern Discovery (WHO)

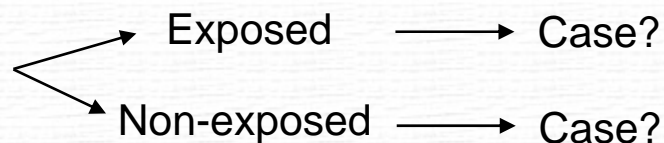
## Sequential Methods

	<i>AE j = Yes</i>	<i>AE j = No</i>
<b>Drug <i>i</i> = Yes</b>	<i>a=20</i>	
<b>Drug <i>i</i> = No</b>		

← Compare to baseline Poisson

- Maximized Sequential Probability Ratio Test (MaxSPRT)
- Conditional Sequential Sampling Procedure (CSSP)

## Exposure Based Methods

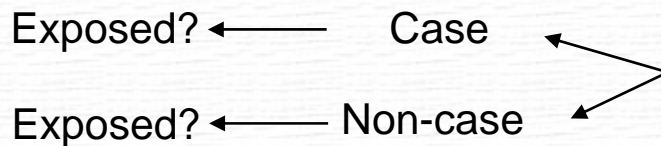


- Observational Screening
- HSIU Cohort Method
- Incident User Designs
- High-Dimensional Propensity Scoring
- Local Control



# OMOP's Methods Landscape

## ***Case Based Methods***



- Case control surveillance
- Multiset case control
- Self-controlled case series
- Case crossover

## ***Other Methods***

- Hi-Dimensional logistic regression
- Statistical relational learning

## ***Future Methods***

- Multivariate self-controlled case series
- Case-time control
- Lasso propensity scoring
- Online algorithms
- OMOP Cup (50+ submissions)



# OMOP Methods Library

<http://omop.fnih.org/MethodsLibrary>

OMOP Methods Library - Download Methods

OMOP is building a library of methods, developed for the OMOP Common Data Model, to solve the problems of Monitoring of Health Outcomes of Interest and Identification of Non-Specific Health Outcomes. These methods are available under the OMOP License.

If you would like to contribute to the methods, please contact OMOP by adding a new method.

**Downloads Available**

**Guidelines**

- **OMOP Methods development guidelines**
- **Disproportionality Analysis Method - OMOP Research Team**
  - **Disproportionality Analysis Method specification** 7Dec 2009
  - **Disproportionality Analysis Method Source Code and Examples** 2Feb 2010
  - **Disproportionality Analysis Feasibility Test #1** 17Jan 2010
  - **Disproportionality Analysis Feasibility Test #2** 17Jan 2010
- **Multi-Set Case-Control Estimation - OMOP Research Team**
  - **Multi-set case-control Method specification** 7Dec 2009
  - **Multi-set case-control Method Source Code and Examples** 2Feb 2010
  - **Multi-set case-control Feasibility Test #1** 17Jan 2010
  - **Multi-set case-control Feasibility Test #2** 17Jan 2010
- **Bayesian Logistic Regression - OMOP Research Team**
  - **Bayesian logistic regression specification** 2Feb 2010
  - **Bayesian logistic regression Source Code and Examples** 16Feb 2010

- Standardized procedures are being developed to analyze *any* drug and *any* condition
- All programs being made publicly available to promote transparency and consistency in research
- Methods will be evaluated in OMOP research against specific test case drugs and Health Outcomes of Interest

# Health Outcomes of Interest Library

- Identified need for open-source library of definitions:
  - more than 1 per Health Outcomes of Interest (HOI)
  - literature review strategies
  - evidence tables
  - Software code to implement definitions
- OMOP is testing a process for defining HOIs
- Welcome contributions to the library

**Observational Medical Outcomes Partnership**

Defining Health Outcomes of Interest

OMOP is establishing an open-source library of ten Health Outcomes of Interest (HOI) definitions for use in observational studies. These ten HOIs are a subset of all conditions that are of importance due to their historical associations with drug toxicities, their medical significance, and/or public health implications. There is little consensus for best practice in defining HOIs in observational databases, as observational studies for the same outcome often use different definitions. In addition, data sources may vary in available data elements that can be used for definition (e.g., labs) and as such. Even in the context of available data elements, the use of many outcomes are based on limited support in validity and reliability information.

HOI definitions are the critical focus for the central protocols as they bring to the OMOP investigators an evidence-based summary of prior observational research definitions and clinical guidelines. These definitions will allow OMOP to compare methods across different data sources using defined methods.

**There are 10 HOIs under study in OMOP:**

1. Angioedema
2. Aplastic Anemia
3. Acute Liver Injury
4. Bleeding
5. GI Ulcer Hospitalization
6. Hip Fracture
7. Hospitalization
8. Myocardial Infarction
9. Mortality after Myocardial Infarction
10. Renal Failure

**The Implementation of the HOI Definition Process in OMOP**

A Request for Proposal was disseminated and members of the OMOP research team, Scientific Advisory Board, and Executive Committee selected two independent research organizations after careful evaluation of proposals. Both organizations selected had extensive experience in systematic reviews of the literature to inform meta-analysis, guideline development, and evidence-based medicine reviews.

The OMOP research team defined the following process to be independently followed by the two HOI research organizations:

- 1) Develop optimal search strategy to identify published manuscripts of studies of an HOI in observational datasets
- 2) Identify the relevant literature of studies conducted in observational databases that would inform our definition of an HOI. These were to include any studies reporting definitions, validation studies that measure case ascertainment performance (including sensitivity, specificity, positive predictive value), coding guidelines and clinical diagnostic guidelines
- 3) For each paper, summarize results in an evidence table to help inform the final definition to be implemented in OMOP studies

No communication between the two HOI research organizations was permitted. The research organizations were also asked to identify and abstract clinical guidelines for a given HOI to help further inform the OMOP research team.

The OMOP research team, in collaboration with the two research organizations, developed the evidence table format. The OMOP researchers evaluated actual search strategies and the articles retrieved from each research team as the effort progressed to identify and correct obvious shortcomings in search strategy or results based mainly on relevant citations that were identified by the OMOP researchers but were not captured in the research organization searches. These article citations were provided to the research organization to help them identify gaps in their search strategies.

	Not Required	Download
Clinical Guidelines Search Strategy	Not Required	Download
Bibliography Database	Download	Download
Report of Findings	Download	Download

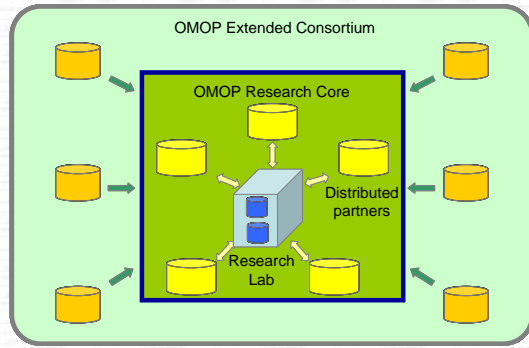
Defining Health Outcomes of Interest      up      HOI Library - Aplastic Anemia

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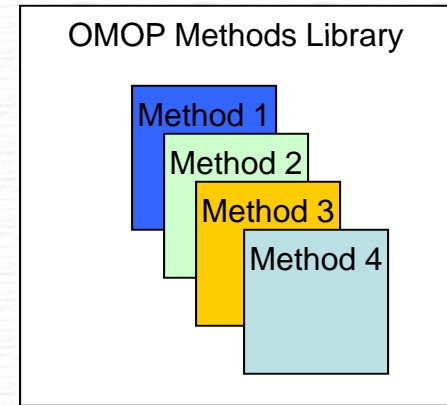
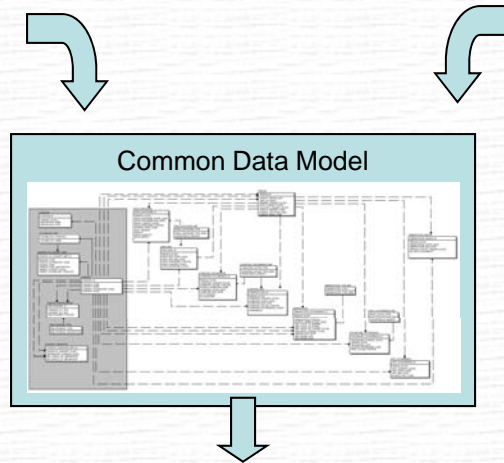
<http://omop.fnih.org/HOIDefinitions>



# OMOP Research Experiment Workflow



Testing in each source:  
 -accumulating over time  
 -against the entire dataset



Testing in each source:  
 -accumulating over time  
 -against the entire dataset

↑ ↑ ↑ ↑ ↑ ↑ ↑

**Monitoring of Health Outcomes of Interest (HOIs)**

- Angioedema
- Aplastic Anemia
- Acute Liver Injury
- Bleeding
- GI Ulcer Hospitalization
- Hip Fracture
- Hospitalization
- Myocardial Infarction
- Mortality after MI
- Renal Failure

**Drugs**

- ACE Inhibitors
- Amphotericin B
- Antibiotics
- Antiepileptics
- Benzodiazepines
- Beta blockers
- Bisphosphonates
- Tricyclic antidepressants
- Typical antipsychotics
- Warfarin

↑ ↑ ↑ ↑ ↑ ↑ ↑

**Identification of non-specified associations**

- All outcomes in condition terminology
- 'Labeled events' as reference
  - Warning
  - Precautions
  - Adverse Reactions
  - Post Marketing Experience

# OMOP Insights

- The establishment of the network of diverse data holding organizations yielded insights into the capabilities needed to be a successful active surveillance site
  - Minimum technology requirements to support analysis of large-scale databases
  - Staff requirements needed to set up and operate an active surveillance site
  - The importance of investigators at each partner site to contribute to the understanding of the variability seen from one data source to another
  - Good governance - the need to balance transparency with participation



# OMOP Insights

- Further research is needed to assess variability across databases and identify the minimum common data requirements for active surveillance
  - We are only beginning to understand the complexity of the interaction of the observational data structure and the research methods for active drug surveillance
  - Statistical and systematic analysis approaches to assess data quality and variability show early potential
  - Visualization and summarization techniques are needed to enhance the use of these analyses to extract as much knowledge as possible
  - Having a lot of data does not make it easier to answer drug safety questions



# OMOP Insights

- Sustainable processes and community support are required to maintain the mappings between the various medical vocabularies encountered across a network of active surveillance databases
  - OMOP has developed specifications for implementation of standard vocabularies for observational data analysis
  - Since vocabularies are ever changing, frequent updates to mappings are required
  - We feel as if we are breaking new ground in using vocabularies in observational analysis
  - Expertise is very hard to find



# OMOP Insights

- Sustainable processes and community support are needed to expand the library of available Health Outcomes of Interest definitions
  - A consensus based approach similar to standards development is the first step
  - Current practice of using literature and manually revisiting source records is not scalable
  - Utilization of automated techniques to create HOI definitions should be explored



# OMOP Insights

- Incontrovertible ground truth is elusive in drug safety
  - OMOP research has benefited greatly from the initial and ongoing development of a high fidelity simulator to know ground truth



# Summary

- OMOP is designed to provide and test:
  - Broad stakeholder participation
  - Transparency in an open innovation model
  - Development of reproducible processes in data and analyses
  - Standards for data models, terminologies, and methods
  - A public-private partnership governance structure with support from advisory boards
  - Empirical evidence that will inform appropriate use and best practices



# Thank you

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