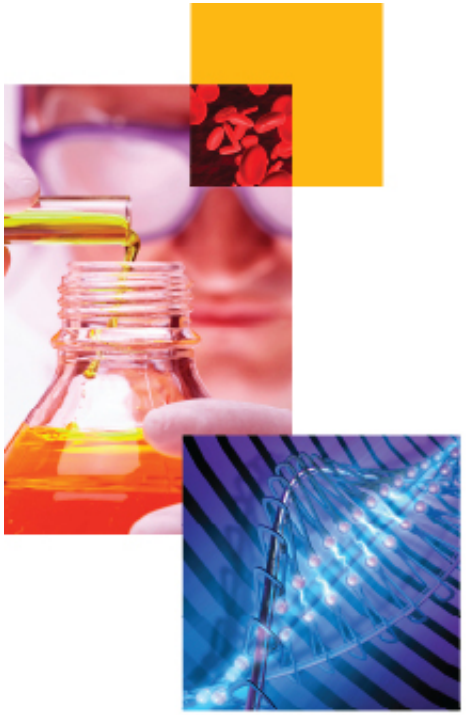


OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP

FOUNDATION FOR THE National Institutes of Health

OMOP Overview and Progress

January 12, 2010

PARTNERS FOR INNOVATION, DISCOVERY, LIFE

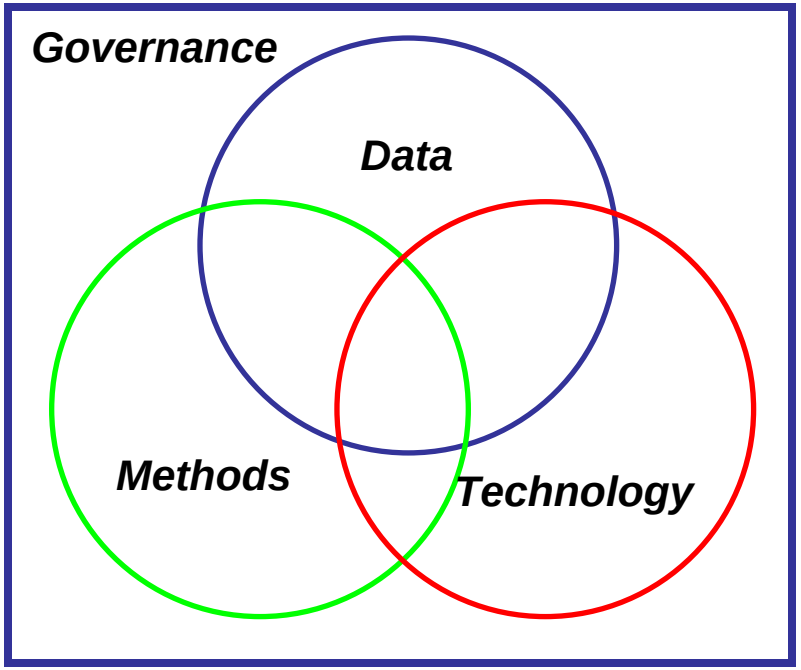
Today's Agenda

- Overview of OMOP
- Research Community
- OMOP Research Plan
- Progress – Phase 1 and Phase 2
- Questions

Observational Medical Outcomes Partnership

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP
FOUNDATION FOR THE National Institutes of Health

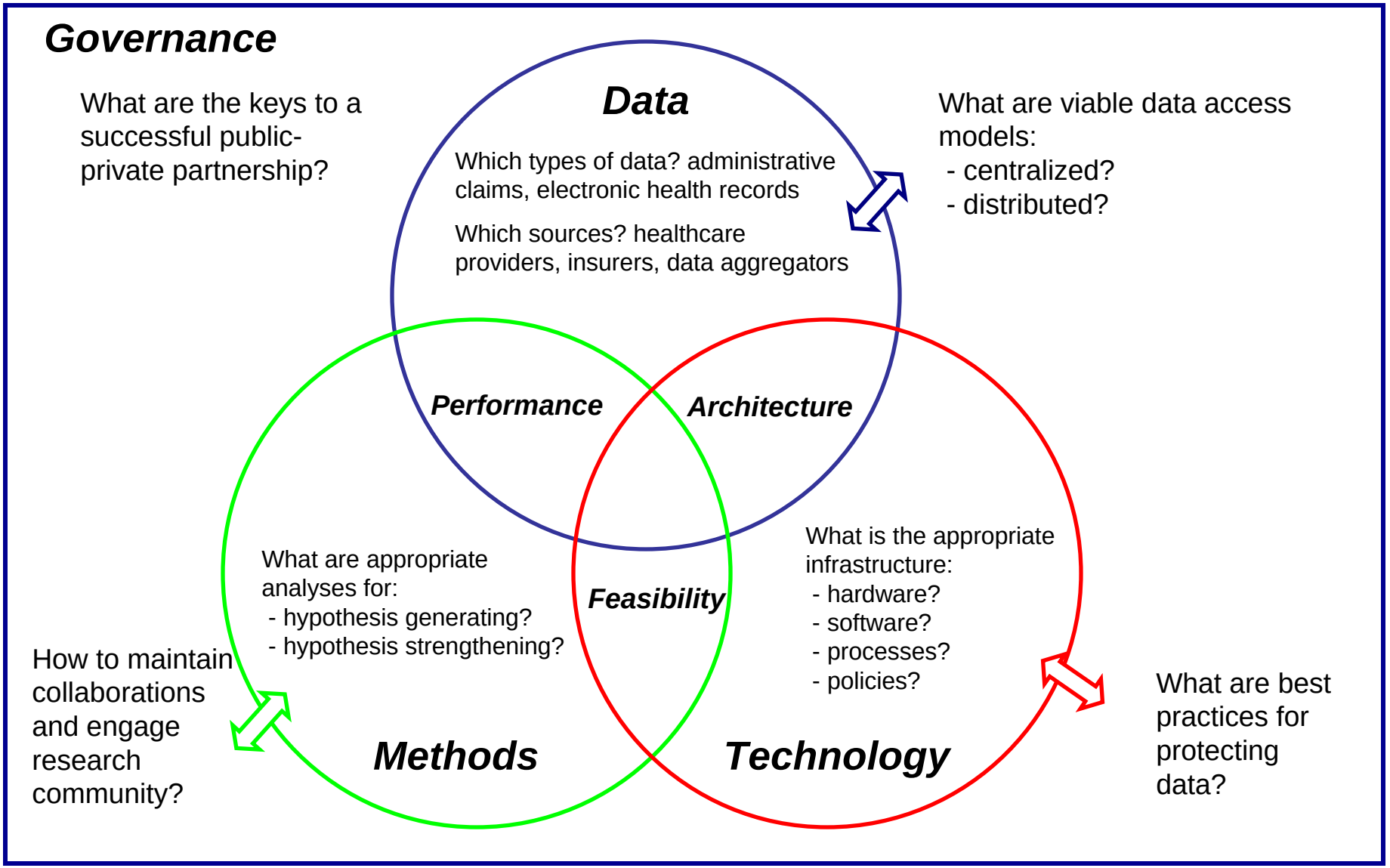
A public-private partnership to serve the public health by testing whether multi-source observational data can improve our ability to assess drug safety and benefits.



- 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

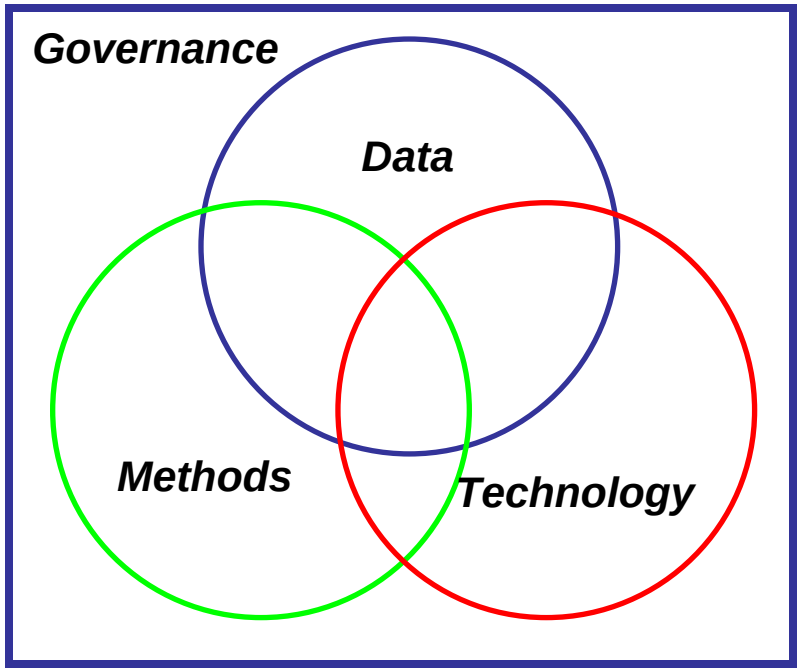
OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP | FOUNDATION FOR THE National Institutes of Health



Breadth and diversity of OMOP research community

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP | FOUNDATION FOR THE National Institutes of Health

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 5 research investigators and PMO

Methods

- 17 methods collaborators

Data

- 6 distributed partners
- 5 central databases included in the OMOP Research Lab

Technology

- 2 data access models, 7 different systems architectures

Over 100 partners collaborating to advance the science of drug safety!

Executive Board

A multi-stakeholder group, the OMOP Executive Board oversees the operation of the Partnership.

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP

FOUNDATION FOR THE National Institutes of Health

Janet Woodcock, MD
Director, Center for Drug Evaluation and Research, Food and Drug Administration
Chair, Observational Medical Outcomes Partnership Executive Board

Rebecca Burkholder
Vice President of Health Policy, The National Consumers League

Sherine Gabriel, MD, MSc
Professor of Medicine and Epidemiology, The Mayo Clinic

Cynthia Gilman, JD
Special Assistant to the President for Advancement of Cancer Research and Collaborative Partnerships, Henry Jackson Foundation

Jesse L. Goodman, MD, MPH
Chief Scientist and Deputy Commissioner for Science and Public Health (acting),
Food and Drug Administration

Ronald L. Krall, MD
Former Senior Vice President and Chief Medical Officer, GlaxoSmithKline

Richard Platt, MD, MSc
Professor and Chair of the Department of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim Health Care

Stephen Spielberg, MD, PhD
Marion Merrell Dow Chair in Pediatric Pharmocogenomics, Children's Mercy Hospital and Dean Emeritus, Dartmouth Medical School

Brian Strom, MD, MPH
George S. Pepper Professor of Public Health and Preventive Medicine; Professor of Biostatistics and Epidemiology, Medicine, and Pharmacology; Chair, Department of Biostatistics and Epidemiology; Director, Center for Clinical Epidemiology and Biostatistics; Vice Dean for Institutional Affairs, University of Pennsylvania School of Medicine
Senior Advisor to the Provost for Global Health Initiatives, University of Pennsylvania

David Wheadon, MD
Senior Vice President, Pharmaceutical Research and Manufacturers of America (PhRMA)

Research Investigators

The Principal Investigators (PIs) are the lead scientists for the OMOP project and guide and participate in the research across all four project phases

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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

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

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

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

Foundation for the NIH Program Staff

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP

FOUNDATION FOR THE National Institutes of Health

Thomas Scarnecchia, MS
Executive Director, OMOP

Emily Welebob, RN, MS
Senior Program Manager, Research

Christian Reich, MD, PhD
Senior Program Manager, Technology

OMOP Statistics and Programming Team

David Madigan, PhD
Columbia University
OMOP Methods Lead

Ivan Zorych, PhD
Columbia University

Cortney Hayflinger
Hayflinger Analytic Services

Mark Khayter
Ephir, Inc.

Ron Mantha
Ephir, Inc.

Carlos Alzola
Data Insights

Emmanuel Angel
Angelic Productions

Reed George
etera solutions

Eric Lantz
University of Wisconsin-Madison

Advisory Boards

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP
FOUNDATION FOR THE National Institutes of Health

A Scientific Advisory Board (SAB) will provide independent review of and expert input into the scientific aspects of OMOP's activities.

- Elizabeth Andrews, RTI Health Solutions
- Andrew Bate, Pfizer
- Jesse Berlin, Johnson & Johnson
- Robert Davis, Kaiser Permanente
- Steve Findlay, Consumer Union
- Sean Hennessy, University of Pennsylvania
- Mike Katz, FDA patient representative
- Allen Mitchell, Boston University
- David Page, University of Wisconsin
- Ken Rothman, RTI Health Solutions
- Judy Staffa, FDA
- Alec Walker, WHISCON

A Health Informatics Advisory Board (HIAB) will provide independent review and expert input into the OMOP's technology governance and project requirements related to privacy and security, terminology and coding, data and data models.

- Col. Kevin Abbott
- Jeff Brown, Harvard Medical School
- Stan Huff, Intermountain Healthcare
- Diane MacKinnon, IBM (retired)
- Ken Mandl, Harvard University
- Clem McDonald, National Library of Medicine
- David Memel, Klaipeda Consulting
- Joy Pritts, Georgetown University
- Mitra Rocca, FDA
- Rob Thwaites, United BioSource Corporation

OMOP Research Plan

Overview

OMOP Phases

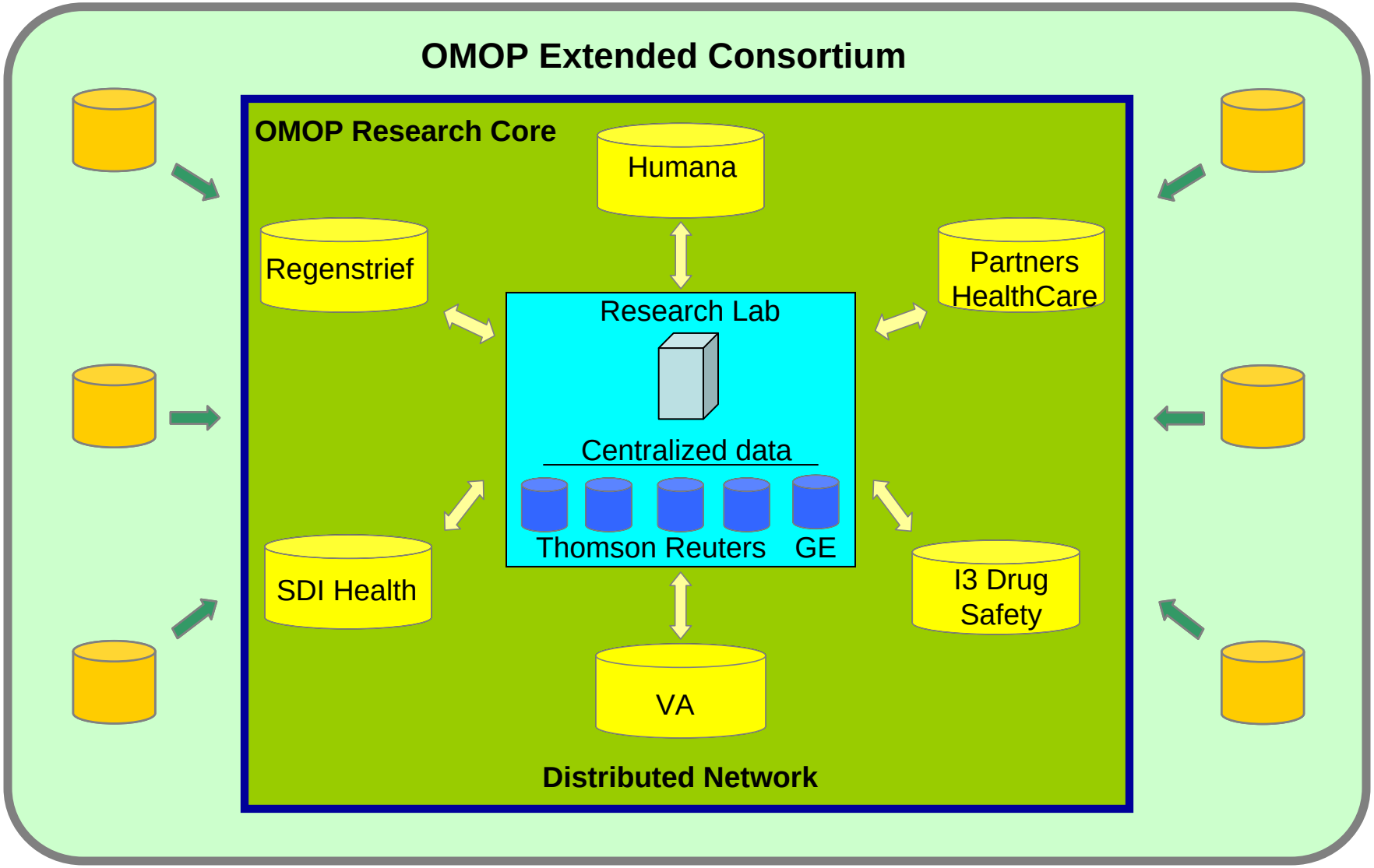
OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP
FOUNDATION FOR THE National Institutes of Health

- **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

http://omop.fnih.org

Overview of Partnership Design

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP
FOUNDATION FOR THE National Institutes of Health



Phase 1 and Phase 2 Progress

Data Source Assessments

Common Data Model

Simulated Dataset

OMOP Research Lab

OMOP Data Community

Health Outcomes of Interest

Data Characteristics Summary

Analysis Methods

Data source assessments

- Data Screening
  - To gather information on available data and potential research partners for further assessment
  - To develop relationships with these potential partners
  - Data Screen responses: 39/70 (56%)

- Data Profile
  - OMOP Distributed Research Partners must have completed the Data Profile
  - 22 Data Profile responses, reflecting diversity in available data
  - OMOP will publish report with de-identified analyses about characteristics of data sources

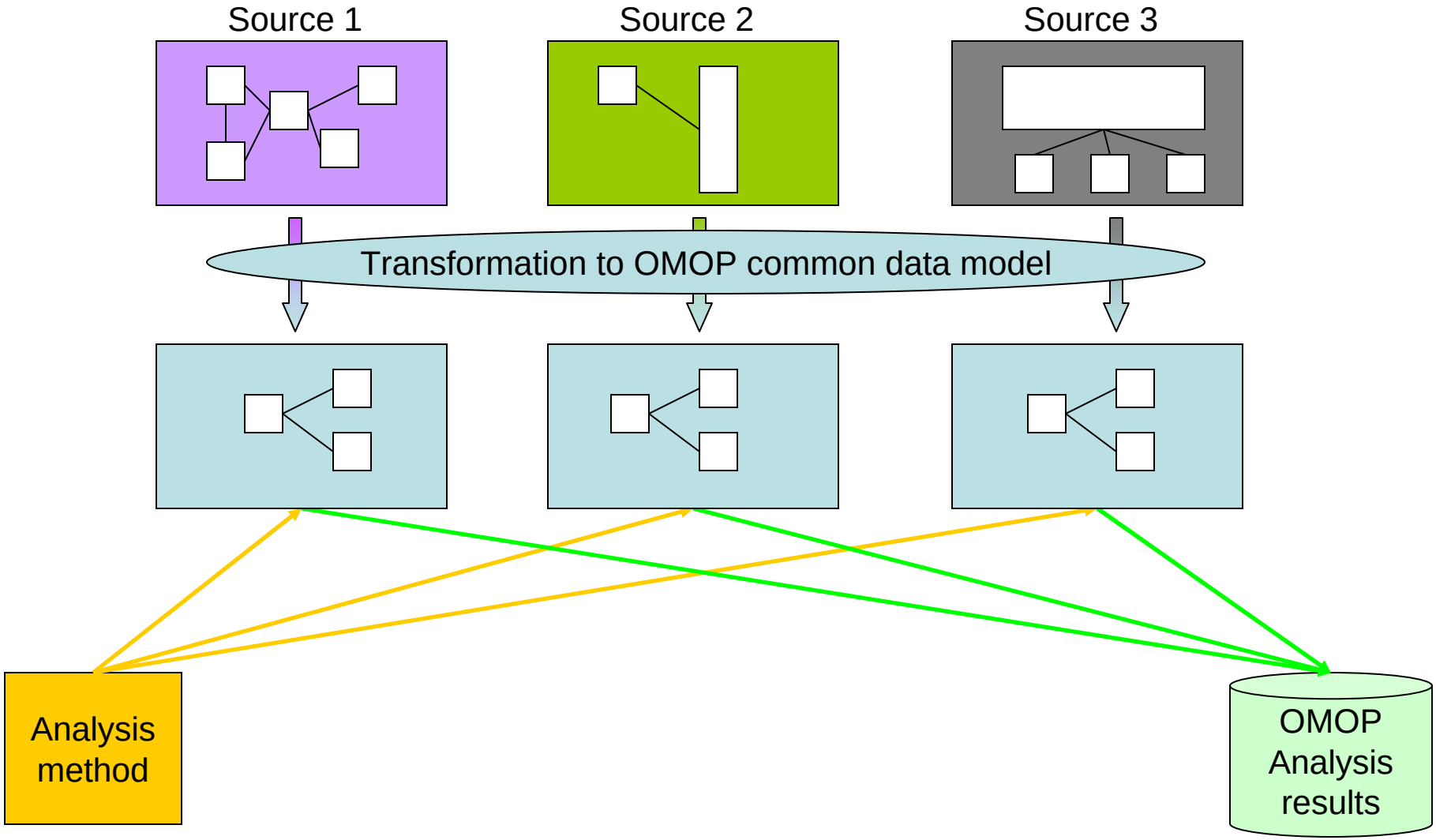
http://omop.fnih.org/DataAssessments

Common Data Model

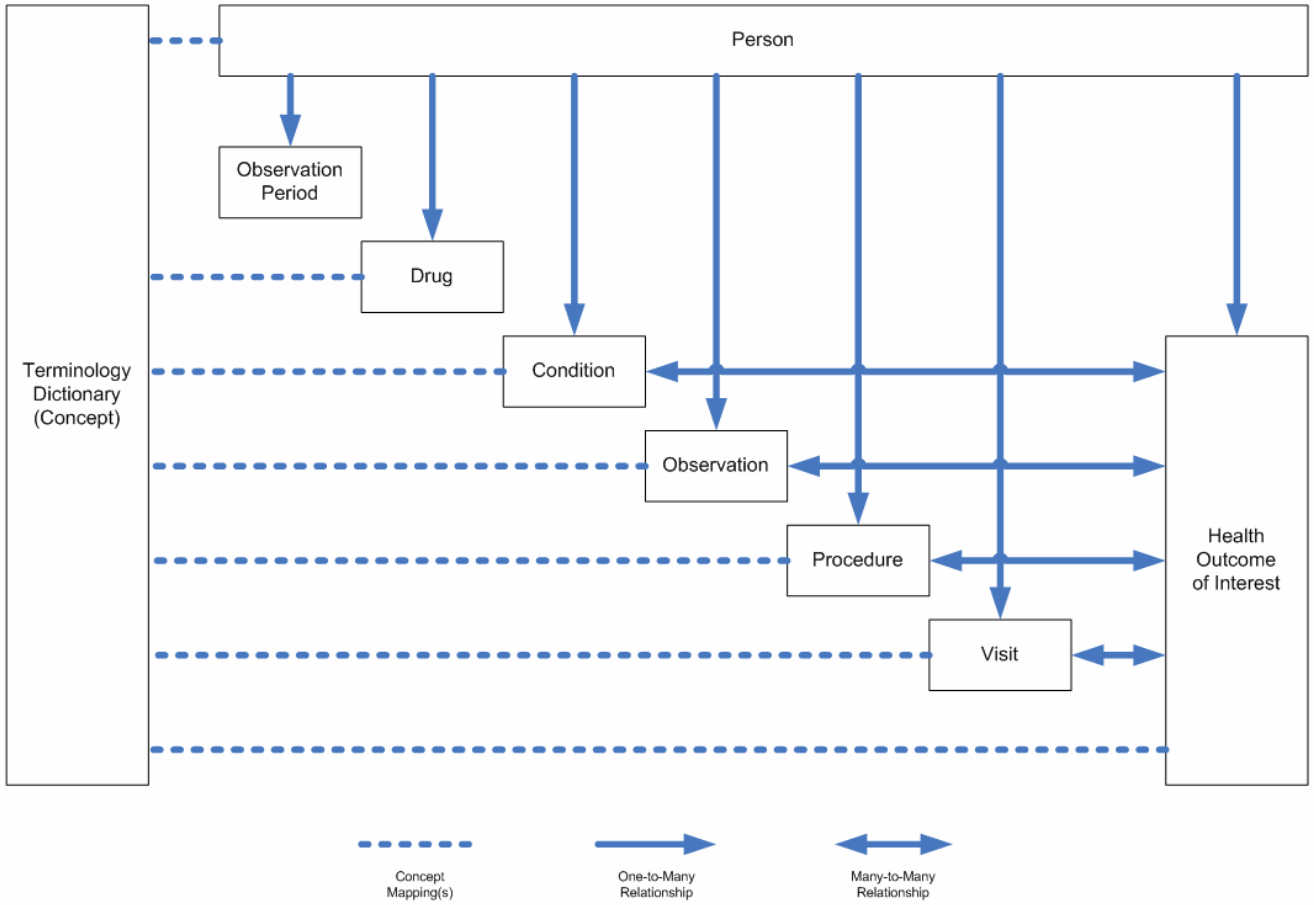
- The common data model includes:
  - A single data schema that can be applied to disparate data types
  - Standardized terminologies
  - Consistent transformation for key data elements
- A common data model can:
  - Enable consistent and systematic application of analysis methods to produce comparable results across sources
  - Create a community to facilitate the sharing of tools and practices
  - Impose data quality standards
  - Create implementation efficiencies

Common Data Model	
What We Are Doing	**What We Are Not Doing**
• Creating one model that could accommodate any relevant type of observational data • Facilitating comparison of analysis results across sources • Providing a conceptual model to allow researchers to develop analysis methods that are be portable across data sources	• Combining multiple datasets into one centralized database • Trying to force claims data into a EHR model or vice versa • Developing a graphical user interface to automatically create structured queries

Role of common data model in OMOP Analysis process



Establishing a common data model

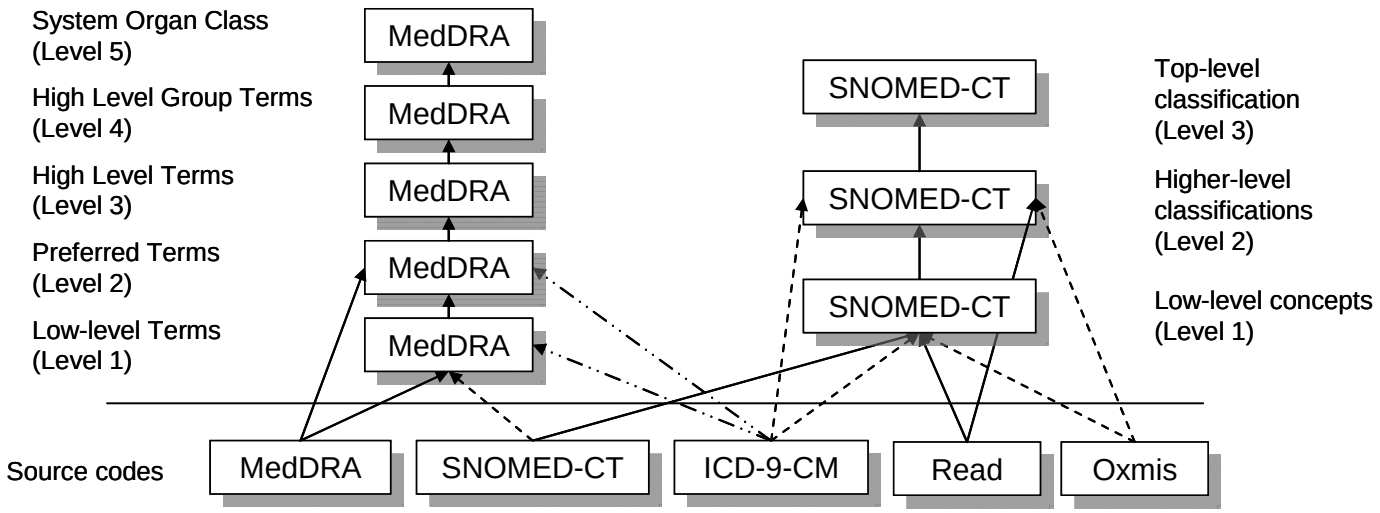


- Developed with broad stakeholder input
- Designed to accommodate disparate types of data (claims and EHRs)
- Applied successfully across OMOP data community

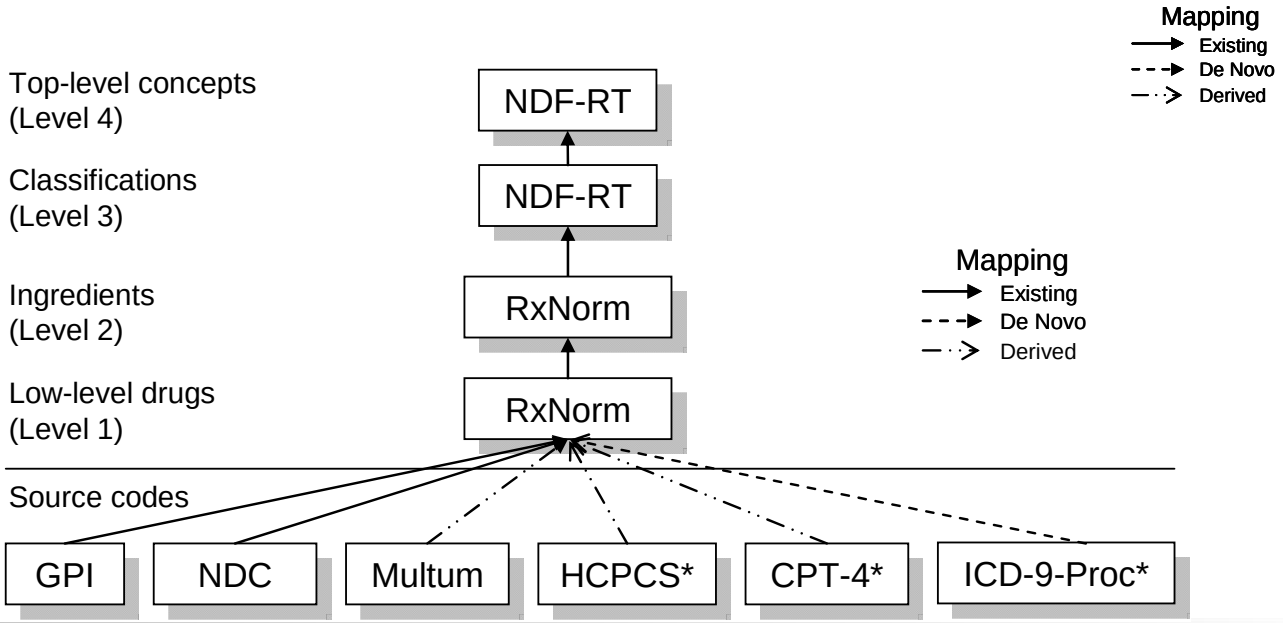
http://omop.fnih.org/CDMandTerminologies

Standardizing terminologies to accommodate disparate observational data sources

Standardizing conditions:



Standardizing drugs:



Simulated Dataset

- OMOP will test a modest number of real observational data sources
- Observational data is poorly characterized
- Methodological research typically requires some benchmark to measure performance
- Simulated datasets, comprised of hypothetical persons with fictitious drug exposure and condition incidence, can be created with known characteristics that represent the types of scenarios expected in real observational sources

http://omop.fnih.org/osim

Simulated Dataset

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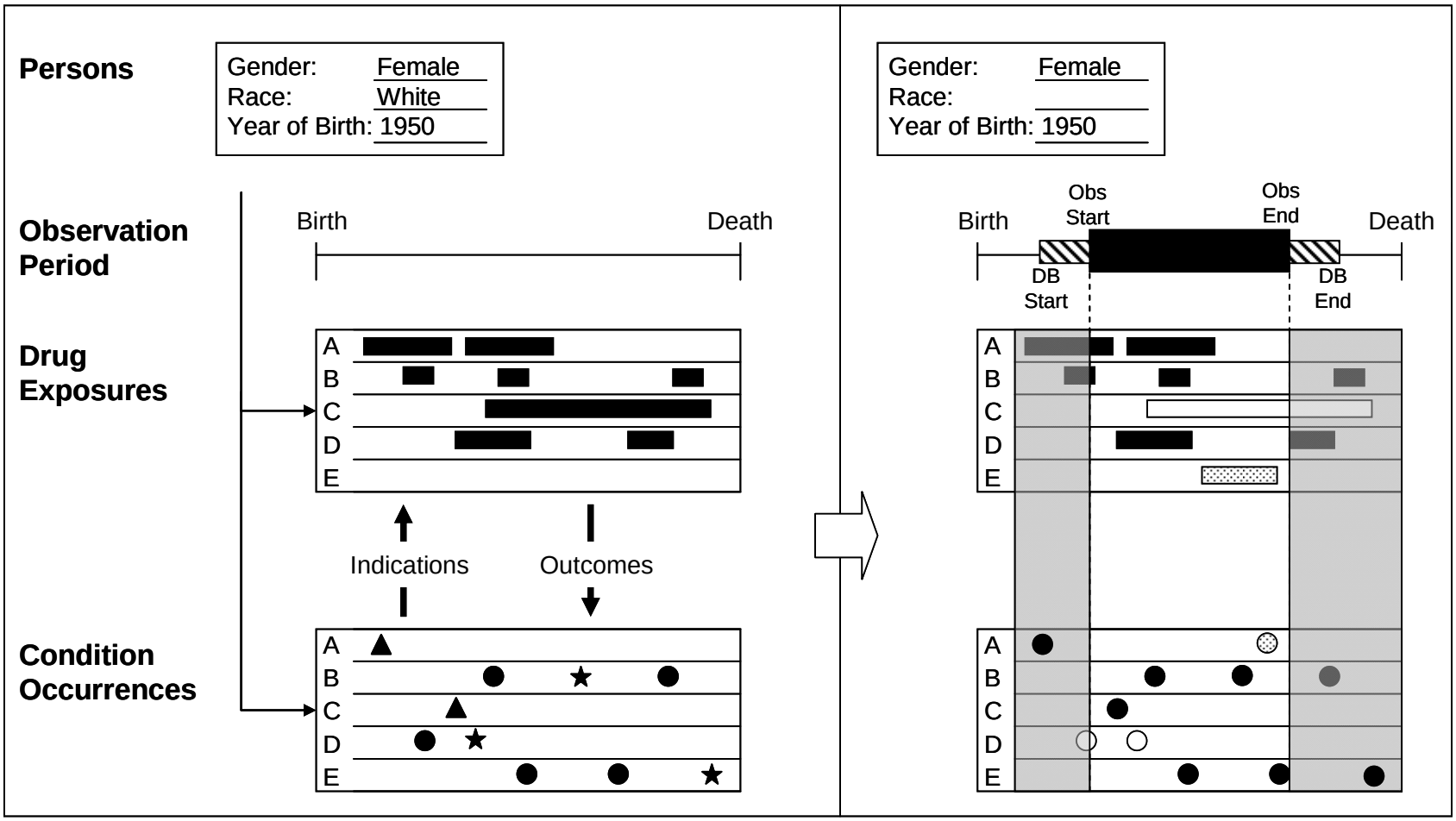


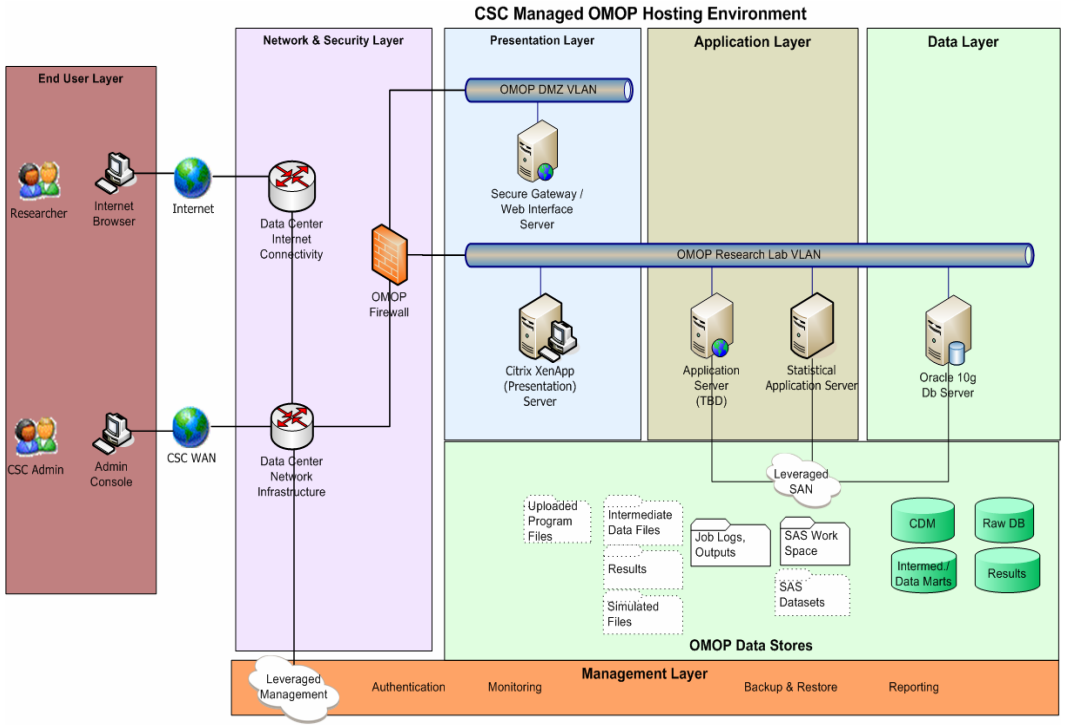
Observational Medical Dataset Simulator: OSIM

- **Capable of generating 1 to 100,000,000+ persons**
- **Two types of output files:**
  - **Simulated Drug & Condition Files:** including attributes used to model confounding (provides "answer key" for analytic research)
  - **Hypothetical Person Files:** longitudinal record of drug exposures and condition occurrences
- **Data characteristics and confounding controlled by input probability distributions**
  - Confounding variables age, gender, race, indication introduced as risk factors for select drugs & conditions
  - Default distributions produced from analysis of real observational data; can be modified by user
- **Format of Hypothetical Person Files conforms to OMOP Common Data Model**

Implementation by ProSanos Corporation

OMOP Research Lab

- Data Management environment up and running
  - Simulated Data in CDM format
  - Oracle database server
  - GE Healthcare, Thomson Reuters (Commercial, Medicare, Medicaid, Lab) loaded and transformed into the OMOP CDM format
  - Licenses for vocabulary use and distribution obtained
- Analysis environment up and running
  - SAS, R, SQL, C++ and Perl
  - Methods Collaborators are driving need for additional tools



In use by OMOP Statistics Team and on-boarded methods collaborators

http://omop.fnih.org/ResearchLab

OMOP Data Community

- Distributed Partners
  - Humana (PI: Vinit Nair)
  - i3 Drug Safety (PI: Arnold Chan)
  - Partners Healthcare System (PI: Shawn Murphy)
  - Regenstrief Institute (PI: J. Marc Overhage)
  - SDI Health (PI: Greg Hess)
  - Veterans Affairs Center for Medication Safety/Outcomes Research (PI: Fran Cunningham)

Health Outcomes of Interest

- Goals
  - To identify and organize definitions used to date for Health Outcomes of Interest (HOIs) as reflected in literature (from observational studies)
  - To test the process for identifying and organizing this information
  - To identify clinical criteria for the HOI
- Consistent with these goals, we are testing the process as well as assure quality of final deliverable
  - Engaged two groups to perform systematic literature reviews for 10 HOIs to ensure at least one report for each HOI is completed and provide independent replication of review process
- Outcomes
  - Standard evidence table and HOI reporting structure
  - HOI Library, with 10 HOI reports
  - 35 definitions for 10 HOIs, with implementations for OMOP common data model

http://omop.fnih.org/HOI

Drug-HOI Pairs

Drug/class	Health Outcome of Interest
ACE inhibitors	Angioedema
ACE inhibitors	Hospitalization (including readmission and mortality)
Amphotericin B	Renal failure
Antibiotics: erythromycins, sulfonamides, and tetracyclines	Acute liver injury (symptomatic hepatitis)
Antiepileptics: carbamazepine and phenytoin	Aplastic anemia
Benzodiazepines	Hip fracture
Beta blockers	Mortality after MI
Bisphosphonates: alendronate	GI ulcer hospitalizations
Tricyclic antidepressants	Myocardial infarction
Typical antipsychotics	Myocardial infarction
Warfarin	Bleeding

Observational Source Characteristics Analysis Report (OSCAR)

- Provides a systematic approach for summarizing observational healthcare data stored in the OMOP common data model.
- Uses
  - Validation of transformation from raw data to OMOP common data model
  - Comparisons between data sources
  - Comparison of overall database to specific subpopulations of interest (such as people exposed to a particular drug or people with a specific condition)
  - Providing context for interpreting and analyzing findings of drug safety studies

http://omop.fnih.org/OSCAR

Natural History Analysis (NATHAN)

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- OSCAR provides a systematic approach for summarizing all data within the OMOP common data model.
- Natural History Analysis (NATHAN) is an extension of OSCAR, where data characteristics can be produced for a particular subpopulation of interest
  - Exposed population (e.g. patients taking antibiotics)
  - Cases (e.g. patients with acute liver injury)
  - Exposed cases (e.g. patients taking antibiotics with acute liver injury)
- Uses:
  - Evaluate alternative cohort definitions (HOIs)
  - Comparisons between data sources
  - Providing context for interpreting and analyzing findings of drug safety studies

Method strategy update

- "Review of observational analysis methods" posted on website
- Research Core statistics and programming team formed
- Call for Participation: Implementing Observational Analysis Methods issued May 28, 2009
  - 23 submissions received from industry and academia, both domestic and internationally
- Methods are developed and tested in Research Lab, and are being made publicly available
- OMOP Cup Methods Competition : http://omopcup.orwik.com
  - Initiated September 2009
  - Announced Progress winners in December 2009
  - Concludes in March 2010

Methods testing strategy: non-specified conditions

- Each method will be implemented in the OMOP Research Lab against the central databases, and tested against simulated data and across the OMOP data community
- Methods performance tested within an entire observational dataset and as data accumulates over time
- Studies across OMOP data community will explore all outcomes for 10 drugs and compare to 'labeled events'
  - 'Labeled event' extracted from structured product labels through natural language processing program developed by Regenstrief
  - 'Labeled events' characterized by where they are listed on label
    - Warning
    - Precautions
    - Adverse Reactions
    - Postmarketing Experience
  - For purposes of methodological research, all 'labeled events' will be classified as 'true' associations and all other codes in the reference condition ontology will be classified as 'false' associations. Any association identified by the method that is not a 'true' association is to be considered a 'false positive' and will not be further reviewed.

Heart of OMOP's methodological research: Assessing the diversity in analysis methods

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Disproportionality analysis

- Proportional reporting ratio
- Multi-item Gamma Poisson Shrinker
- Bayesian confidence propagation neural network
- Temporal pattern discovery

Other novel approaches? OMOP Cup

Exposure-based approaches

- Cohort Screening
- Incident user designs
- High dimensional propensity scoring
- Local control

Sequential methods

- Maximized sequential probability ratio test
- Conditional sequential sampling procedure

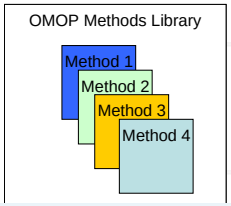
Case-based approaches

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

- Bayesian logistic regression
- Statistical relational learning

OMOP Methods Library at: http://omop.fnih.org/MethodsLibrary

OMOP Methods Library



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OMOP Methods Library - Download Methods

View | Edit | Outline | Track

OMOP is building a library of methods, developed for the OMOP Common Data Model, to address the analysis problems of Monitoring of Health Outcomes of Interest and Identification of Non-Specified Conditions. These methods will be tested across the OMOP Data Community. These methods available under the **Apache public license.**

Downloads Available

Guidelines

- **OMOP Methods development guidelines**

Disproportionality Analysis Method - OMOP Research Team

- **Disproportionality Analysis Method specification**
- **Disproportionality Analysis Method Source Code and Examples**

Multi-Set Case-Control Estimation - OMOP Research Team

- **Multi-set case-control Method specification**
- **Multi-set case-control Method Source Code and Examples**

Bayesian Logistic Regression - OMOP Research Team NEW

- **Bayesian logistic regression specification**
- **Bayesian logistic regression Source Code and Examples**

IC Temporal Pattern Discovery - the Uppsala Monitoring Centre NEW

- **IC Temporal Pattern Discovery Specification**
- **IC Temporal Pattern Discovery Source Code**

Regularized Identification of Cohorts (RICO) - ProSanos Corporation NEW

- **RICO Oracle**
- **RICO SAS**

High-dimensional propensity score adjusted cohort design - OMOP Research Team NEW

- 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

OMOP Methods Library at: http://omop.fnih.org/MethodsLibrary

OMOP research experiment workflow

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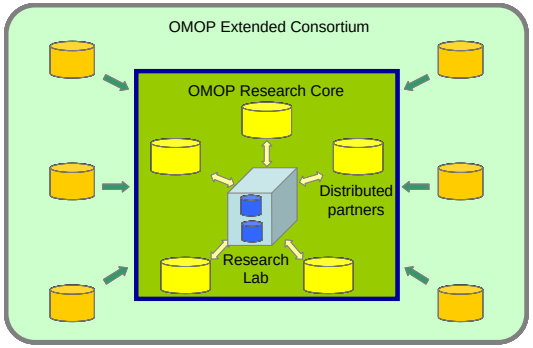
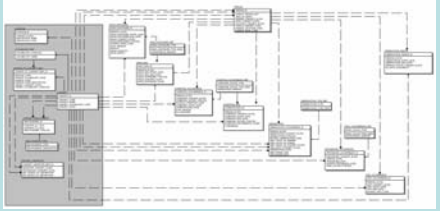


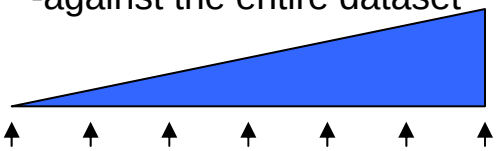
OMOP Methods Library

Method 1
Method 2
Method 3
Method 4

Common Data Model



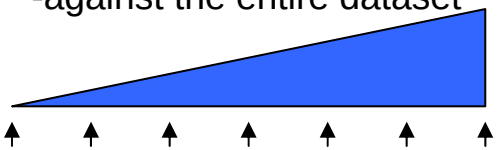
Testing in each source:
-accumulating over time
-against the entire dataset



Health Outcomes of Interest
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 MI
10. Renal Failure

Drugs
1. ACE Inhibitors
2. Amphotericin B
3. Antibiotics
4. Antiepileptics
5. Benzodiazapines
6. Beta blockers
7. Bisphosphonates
8. Tricyclic antidepressants
9. Typical antipsychotics
10. Warfarin

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



Non-specified conditions

-All outcomes in condition terminology

-'Labeled events' as reference
-Warning
-Precautions
-Adverse Reactions
-Postmarketing Experience

Questions

Contact information:

Thomas Scarnecchia, MS
Executive Director, OMOP
tscarnecchia@fnih.org

Emily Welebob, RN, MS
Senior Program Manager, Research
ewelebob@fnih.org

Christian Reich, MD, PhD
Senior Program Manager, Technology
christian@reich.net

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OMOP Cup website: http://omopcup.orwik.com