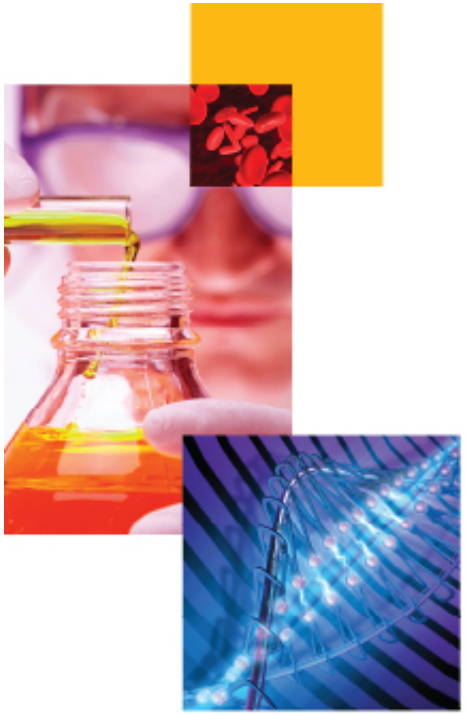

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP

FOUNDATION FOR THE National Institutes of Health

Observational Medical Outcomes Partnership (OMOP)

Patrick Ryan, GlaxoSmithKline
David Madigan, Columbia University

DIA Conference on Signal Detection and Data Mining
17 November 2009

DIA disclaimer

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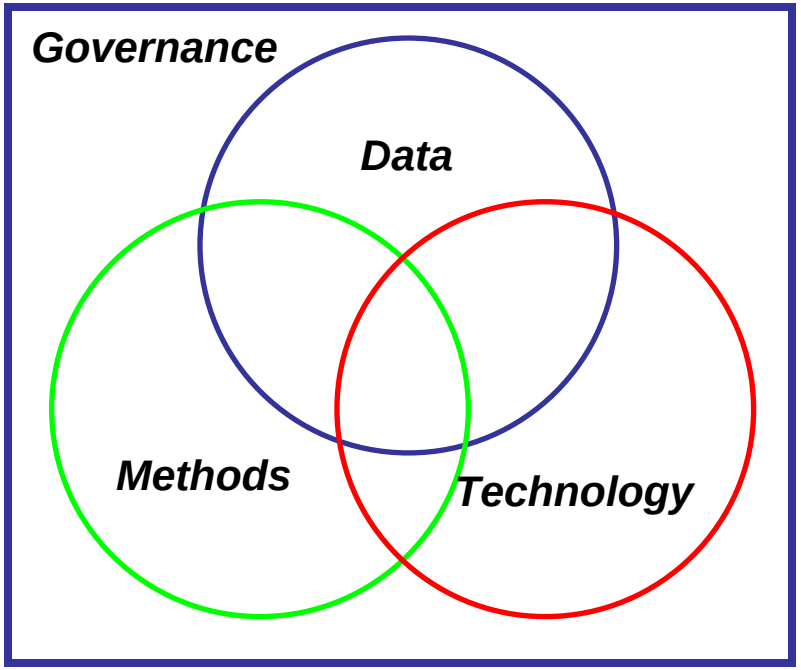
Observational Medical Outcomes Partnership

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

Executive Board

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

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

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

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Senior Program Manager, Research

Christian Reich, MD, PhD
Senior Program Manager, Technology

OMOP Statistics and Programming Team

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Columbia University
OMOP Methods Lead

Ivan Zorych, PhD
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Hayflinger Analytic Services

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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

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
- Rob Thwaites, United BioSource Corporation

Research Collaborators: Data and Infrastructure

as of 11/12/09

Organization	Team Leader	Activity
Computer Sciences Corporation	Dan Foltz	Research Lab
Department of Veterans Affairs Center for Medication Safety	Fran Cunningham, PharmD	Distributed Partner
GE Healthcare	Michael Lieberman, MD	Research Lab
i3 Drug Safety	Arnold Chan, M.D., Sc.D.	Distributed Partner
Indiana University - Regenstrief Institute	J. Marc Overhage, MD, PhD	Distributed Partner
Partners HealthCare System	Shawn Murphy, MD, PhD	Distributed Partner
ProSanos Corporation	Stephanie Reisinger	Simulated Data
SDI Health	Gregory Hess, MD, MBA, MSc	Distributed Partner
Thomson Reuters	Stella Chang, MPH	Research Lab
University of Miami-Humana Health Services Research Center	Vinit Nair, BS Pharm., MS, RPh	Distributed Partner

Research Collaborators: Methods

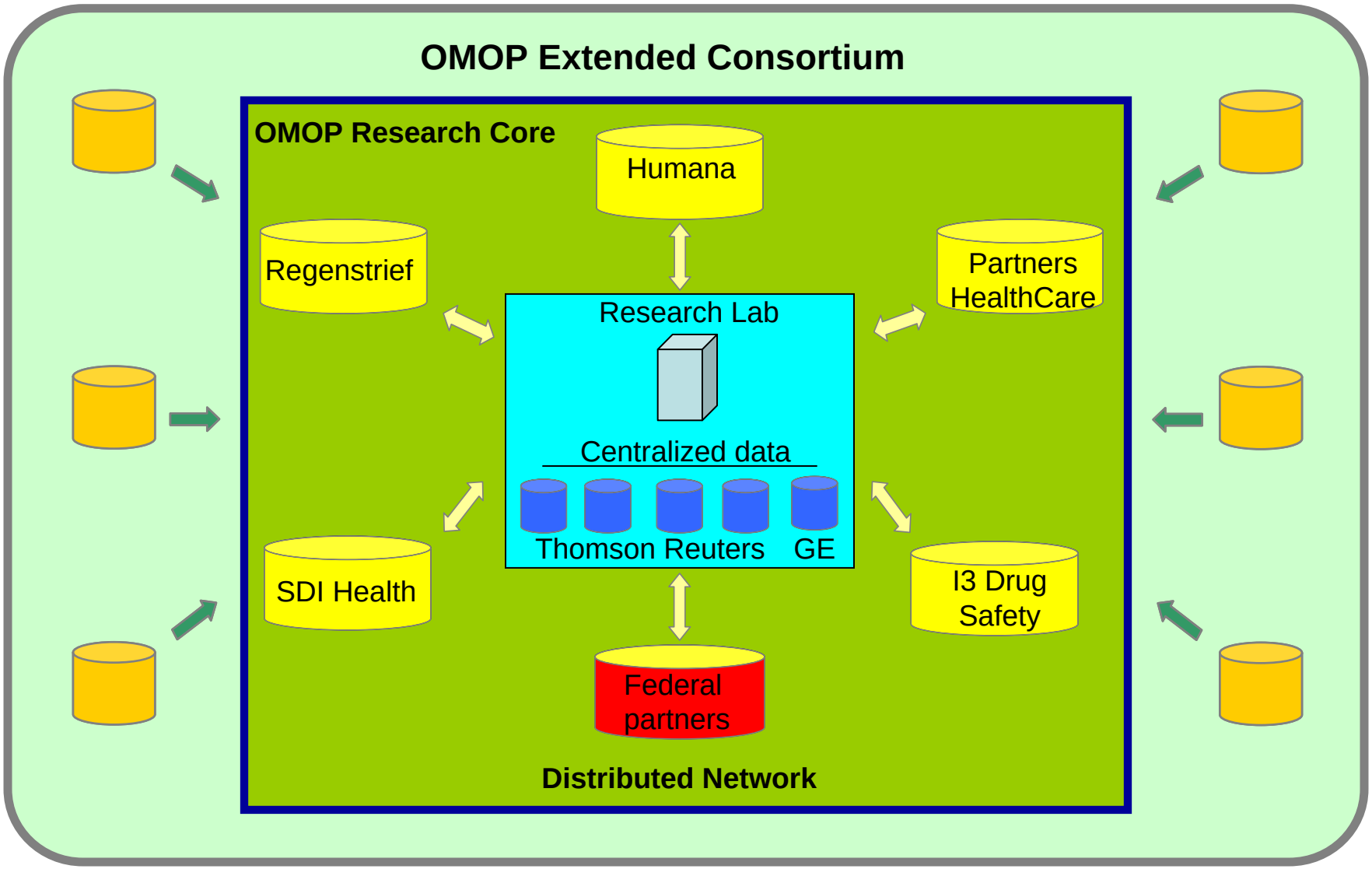
as of 11/12/09

Organization	Team Leader	Activity
Columbia University	David Madigan, PhD	Methods Lead
Eli Lilly and Company	Karin L. Benoit	Methods Partner
GPRD Group of the MHRA	John Parkinson, BSc, PhD	Methods Partner
Harvard Pilgrim Health Care Institute	Lingling Li, PhD	Methods Partner
Indiana University - Regenstrief Institute	Siu L. Hui, PhD	Methods Partner
M Alan Brookhart, PhD and SAS Institute	M. Alan Brookhart, PhD	Methods Partner
Merck Research Laboratories	Dr. A. Lawrence Gould	Methods Partner
ProSanos Corporation	Stephanie Reisinger	Methods Partner
Risk Benefit Statistics LLC	Robert L. (Bob) Obenchain, PhD, FASA	Methods Partner
RTI International	Suzanne L. West, MPH, PhD	HOI Library
Slone Epidemiology Center at Boston University	David Kaufman, ScD	Methods Partner
United BioSource Corporation	Matthew W. Reynolds, PhD	HOI Library
University of North Carolina at Chapel Hill	Stacie Dusetzina	HOI Library
University of Utah	Brian Sauer, PhD	Methods Partner
University of Wisconsin-Madison	David Page, PhD	Methods Partner
Uppsala Monitoring Center	Niklas Norén, PhD	Methods Partner

OMOP Research Plan

Overview

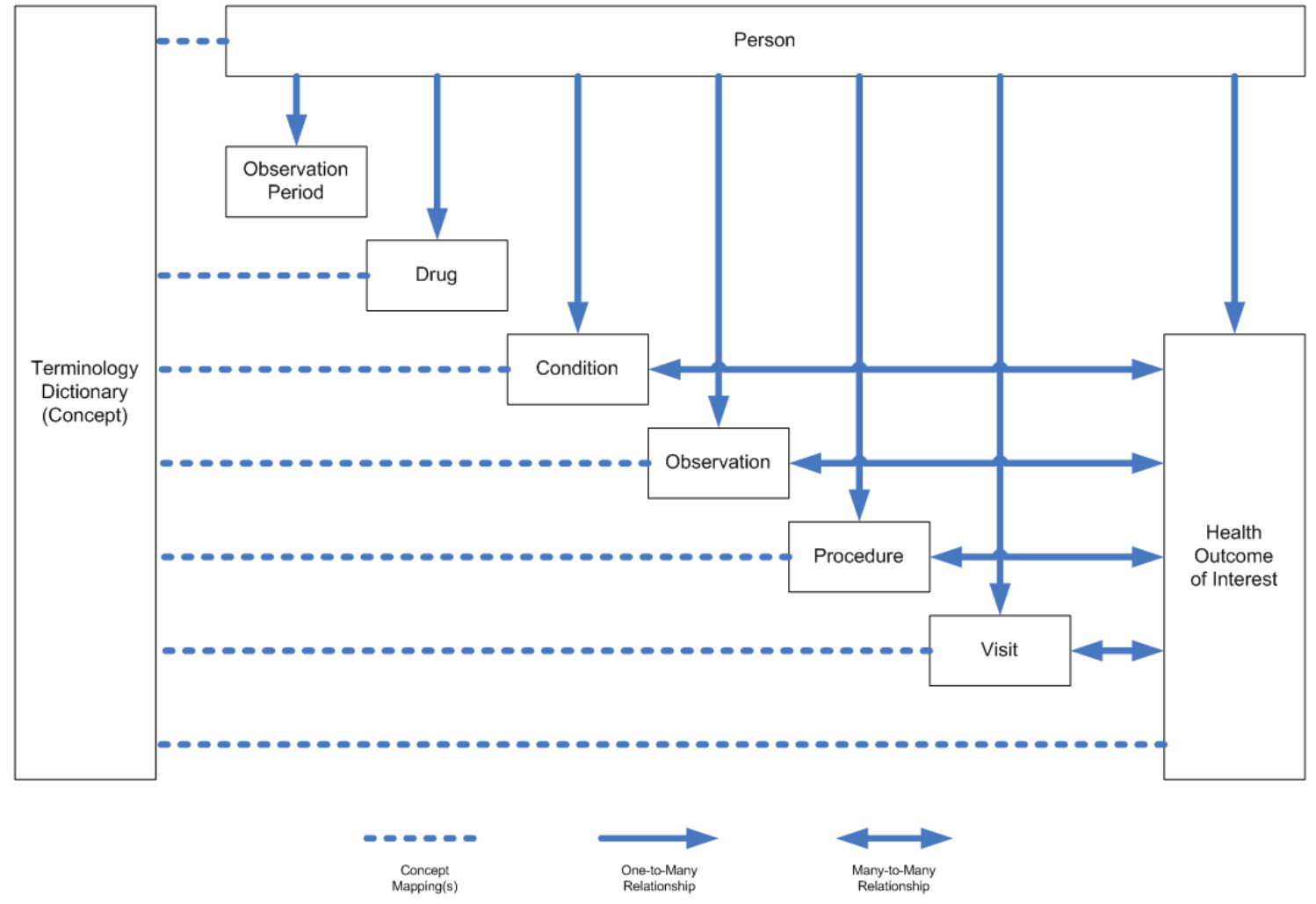
Overview of Partnership Design



OMOP Phases

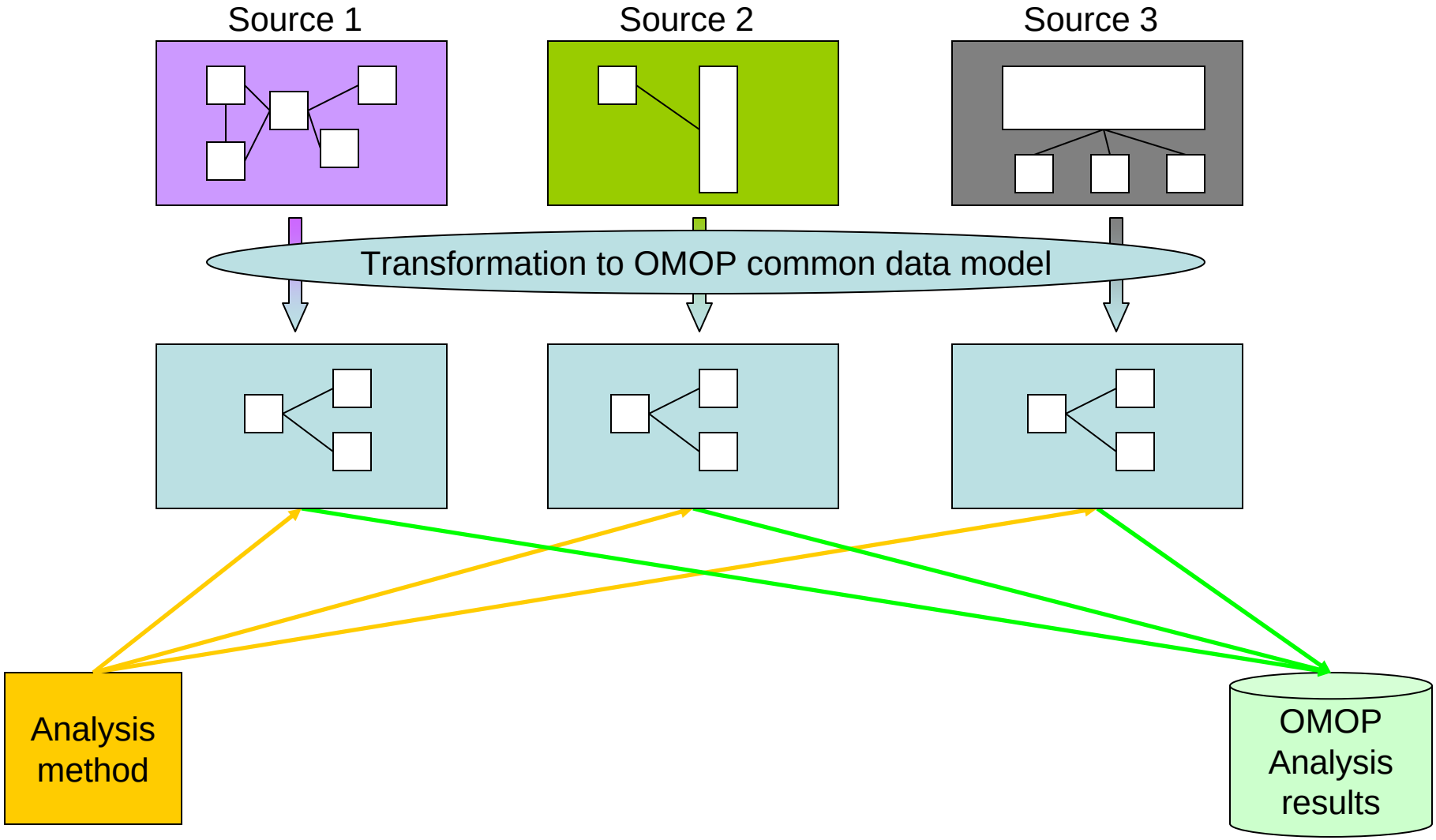
- **Phase 1:** FEASIBILITY OF DATA INFRASTRUCTURE (Feb – July 2009)
  - Establish a consistent framework to use across disparate observational data sources
  - Establish OMOP Research Community
- **Phase 2:** FEASIBILITY OF ANALYSES (Aug – Dec 2009)
  - Develop and test analysis methods within the OMOP 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

Conceptual Schematic of OMOP Common Data Model



http://omop.fnih.org/CDMandTerminologies

Role of common data model in OMOP Analysis process



Opportunities for observational data in active surveillance

- Natural history summary of populations 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)
- Case detection
- Drug-outcome associations

Characterizing Drug-Outcome Associations

Screening

Fishing expedition

Identification of non-specified conditions

Hypothesis strengthening

Prioritization

Monitoring of Health Outcomes of Interest

Data dredging

Signal substantiation

Signal detection

Exploratory analysis

Data mining

Active surveillance

Risk estimation

Signal amplification

Drug safety monitoring

Hypothesis generating

Confirmation

Evaluation

Full epi study

Signal validation

Hypothesis testing

Causal assessment

Fundamental task: *Estimate* the strength of the drug-outcome relationship

Utility and scope of methods within context of active surveillance

- Initial goal: screen to identify and prioritize drug-condition pairs which may require further evaluation

Non-specified vs Health Outcome of Interest

- Ultimate objective: elicit a valid estimate of a temporal relationship between a drug and an outcome

- No conceptual reason why any method cannot be applicable throughout the continuum of association estimation

- Practical tradeoffs: Methodological sophistication vs. scalable execution across large databases
  1. Method designed for specific exposure and outcome
  2. Method generalized for any drug and any outcome
  3. Method scalable to be applied concurrently to multiple drugs and multiple outcomes

OMOP's methods landscape

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

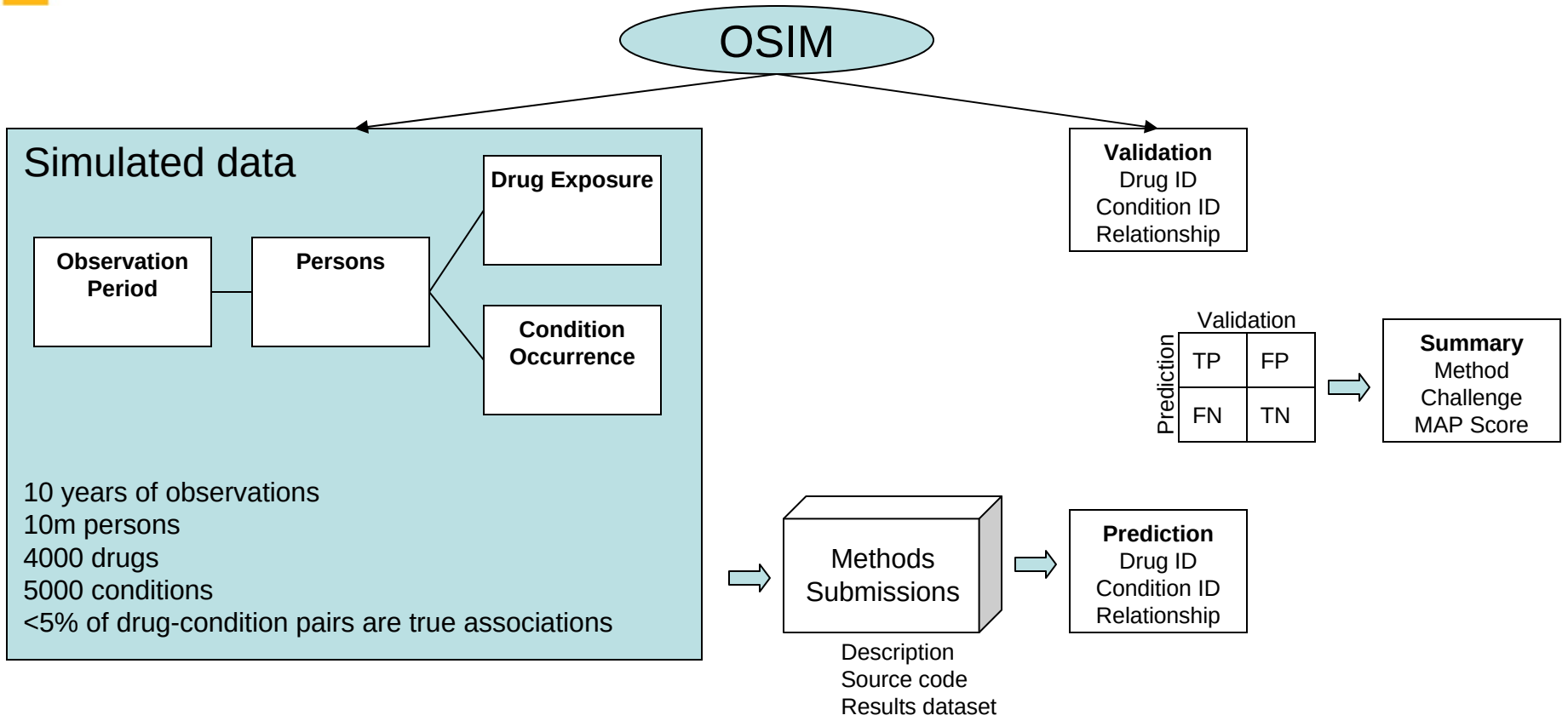
- Bayesian logistic regression
- Statistical relational learning

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

Methodological considerations common across multiple approaches

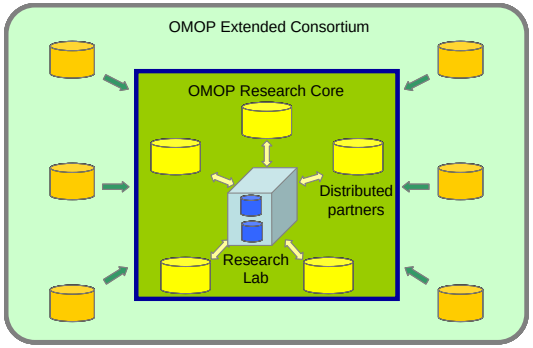
- Exposure definition
  - Incident vs. prevalent exposure
  - Source of data capture
- Outcome definition
  - Incident vs. prevalent events
  - Diagnosis codes vs. rules across data elements
- Defining temporal relationship
  - Time from exposure start
  - Time after exposure end
- Comparator selection
- Inclusion/exclusion criteria
  - Baseline history
  - Follow-up time
- Covariate selection and adjustment
  - Matching
  - Stratification
  - Clustering
  - Multivariate modeling
- Output metric/statistic
  - Test threshold vs. effect estimate
  - Relative vs. attributable risk
  - Measure of uncertainty

OMOP Cup: Methods Competition



- Two competitions: http://omopcup.orwik.com
  - Challenge 1: Identifying drug-condition associations within an entire observational dataset
  - Challenge 2: Identifying drug-condition associations as data accumulates over time
- Evaluation criteria: Weighted Mean Average Precision
- Winning entries will be given cash prize and methods will be further tested against OMOP data community

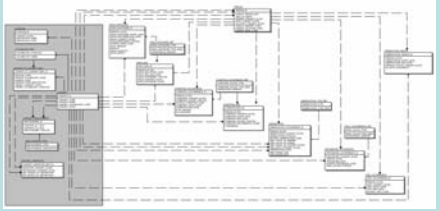
Methods experiment workflow



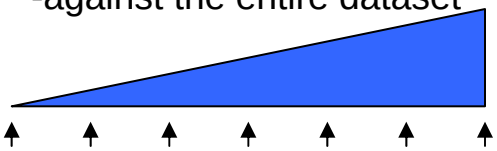
OMOP Methods Library

Method 1
Method 2
Method 3
Method 4

Common Data Model



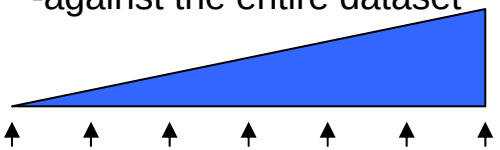
Testing in each source:
-accumulating over time
-against the entire dataset



Health Outcomes of Interest
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
Benzodiazapines
Beta blockers
Bisphosphonates
Tricyclic antidepressants
Typical antipsychotics
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

Contact information

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OMOP website: http://omop.fnih.org
OMOP Cup website: http://omopcup.orwik.com