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OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP

Developing Tools for Conducting Observational Database Research Across a Network of Data Sources

Paul Stang, PhD
on behalf of the OMOP team

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A Few Words About Observational Data

- Very **large** datasets: millions of lives
  - **Claims**: represent a financial transaction and include many biases and 'errors'
  - **EHR**: represent a 'clinical' record mostly but are often incomplete; Rx written not filled
- Reflect **underlying health care delivery** system
- **Non-randomized**: measureable and un-measureable confounders and biases
- From Pharma company: 'exploring' database has strong **Regulatory/Criminal repercussions**

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Flag	Site	Provider	ICD		CPT	
	1-OFFICE/CLIN	0106903	7169	ARTHROPATHY NOS	90015	VISIT
	1-OFFICE/CLIN	0106903	5990	URIN TRACT INFECTION NOS	81000	URINALYSIS WITH MICR
	1-OFFICE/CLIN	0106903	5990	URIN TRACT INFECTION NOS	90070	VISIT
	1-OFFICE/CLIN	0106903	9953	ALLERGY, UNSPECIFIED	90060	VISIT
	1-OFFICE/CLIN	0106903	9953	ALLERGY, UNSPECIFIED	J0420	INJECTION
E	1-OFFICE/CLIN	6606905	5751	CHOLECYSTITIS NEC	90070	VISIT
*	1-OFFICE/CLIN	1705175	7890	ABDOMINAL PAIN	90070	VISIT
*	1-OFFICE/CLIN	1705175	7890	ABDOMINAL PAIN	90630	VISIT
*	1-OFFICE/CLIN	2902146	789	OTH ABDOMEN/PELVIS SYMP	90017	VISIT
	3-LAB/RADIOL	3503411	V726	LABORATORY EXAMINATION	80019	19 OR MORE BLOOD/URI
*	3-LAB/RADIOL	3503411	V726	LABORATORY EXAMINATION	82150	ASSAY OF SERUM AMYLA
	3-LAB/RADIOL	3503411	V726	LABORATORY EXAMINATION	83545	AUTO-ASSAY SERUM IRO
	3-LAB/RADIOL	3503411	V726	LABORATORY EXAMINATION	83690	ASSAY BLOOD LIPASE
	3-LAB/RADIOL	3503411	V726	LABORATORY EXAMINATION	83720	BLOOD LIPOPROTEIN AS
	3-LAB/RADIOL	3503411	V726	LABORATORY EXAMINATION	85025	AUTOMATED HEMOGRAM
	3-LAB/RADIOL	3503411	V726	LABORATORY EXAMINATION	85651	RBC SEDIMENTATION RA
*	6-HOSPITAL OP	1606466	7890	ABDOMINAL PAIN	74246	CONTRAST XRAY UPPER
*	6-HOSPITAL OP	1606466	7890	ABDOMINAL PAIN	76700	ECHO EXAM OF ABDOMEN
*	6-HOSPITAL OP	5006031	V726	RADIOLOGICAL EXAM NEC	B0005	X-RAYS
*	1-OFFICE/CLIN	2902146	532	DUODENAL ULCER	90050	VISIT
*	1-OFFICE/CLIN	2902146	789	OTH ABDOMEN/PELVIS SYMP	90050	VISIT
*	3-LAB/RADIOL	1106534	7890	ABDOMINAL PAIN	88305	TISSUE EXAM BY PATHO
*	3-LAB/RADIOL	1106534	7890	ABDOMINAL PAIN	88312	SPECIAL STAINS
*	3-LAB/RADIOL	1106534	7890	ABDOMINAL PAIN	89060	EXAM,SYNOVIAL FLUID
*	6-HOSPITAL OP	2902146	789	OTH ABDOMEN/PELVIS SYMP	43239	UPPER GI ENDOSCOPY,
*	9-IP SURGICTR	6806031	5355	GASTRITIS/DUODENITIS NOS	43234	UPPER GI ENDOSCOPY,
*	1-OFFICE/CLIN	2902146	532	DUODENAL ULCER	90050	VISIT
	1-OFFICE/CLIN	0106903	7865	CHEST PAIN	80019	19 OR MORE BLOOD/URI
	1-OFFICE/CLIN	0106903	7865	CHEST PAIN	83705	ASSAY BLOOD LIPID GR
	1-OFFICE/CLIN	0106903	7865	CHEST PAIN	84478	ASSAY BLOOD TRIGLYCE
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	1-OFFICE/CLIN	0106903	7865	CHEST PAIN	85651	RBC SEDIMENTATION RA
	1-OFFICE/CLIN	0106903	7865	CHEST PAIN	90060	VISIT
	1-OFFICE/CLIN	0106903	7865	CHEST PAIN	93000	ELECTROCARDIOGRAM, C

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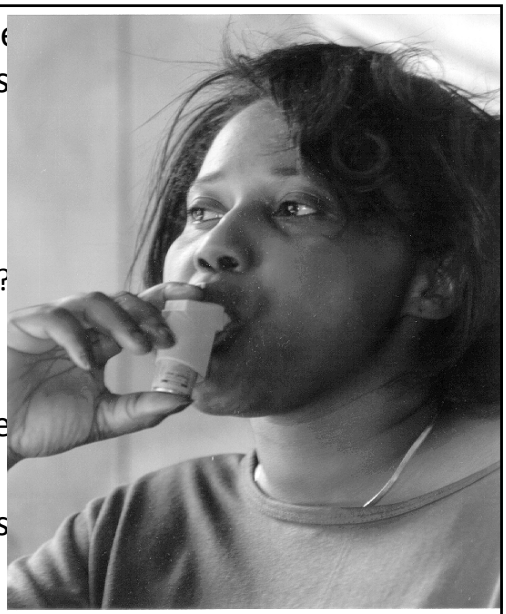
Working with obse
entails

- Exposure
  - Prescriptions written
  - Prescriptions filled
    - How were they taken?
    - What about prn use?
- Outcome
  - Diagnosis codes alone
  - Dx + procedure?
  - Dx, procedure, lab res
  - Site of care?
  - Death?



The News and Observer Sunday, December 8, 1991

"An inhaler prescribed by her doctor helps Gail Pouncy's smoke-scarred lungs- like many survivors, she suffered respiratory injuries in the Imperial fire."

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Observational Data: Information Asymmetry

- Many '**benefits**' (improvement in signs/syptoms, ADL, QoL) are not 'clinical diagnoses' so they are not captured
  - Limited capture of utilization-based measures ("switching drugs", change in ER/hospitalization) or reduction in clinical events
- Most 'risks' ***are*** clinical and would be captured in clinical encounter
  - But we do not know how impactful they are nor what perception is by patients and providers

5

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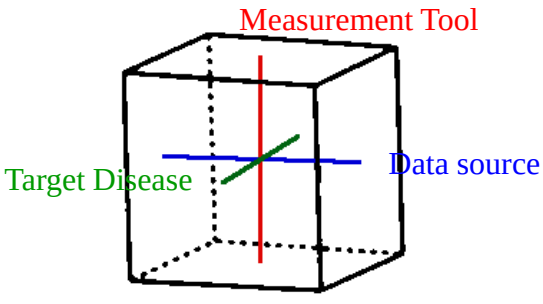
Considerations in Clinical Information

By Perspective



From Stang et al., Am J Therap, 2008

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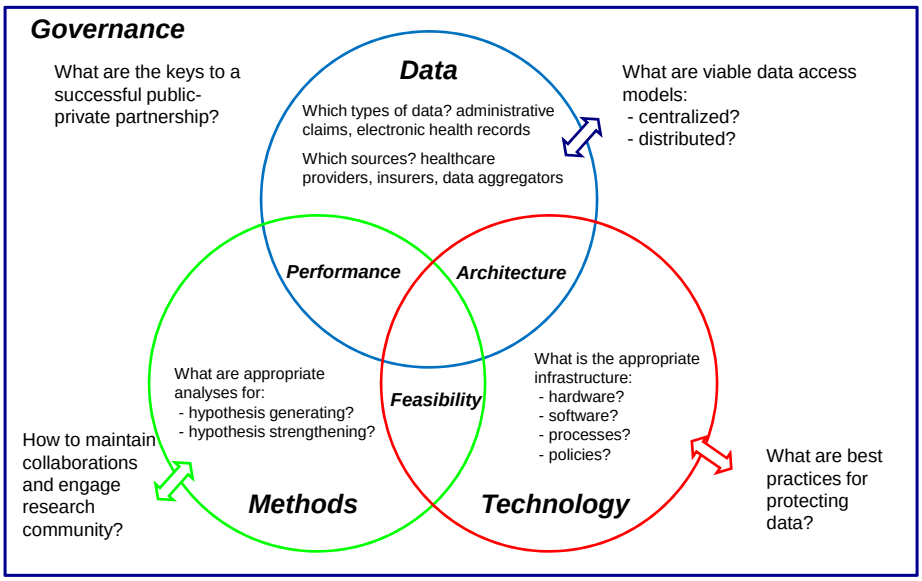
Outstanding questions for active surveillance



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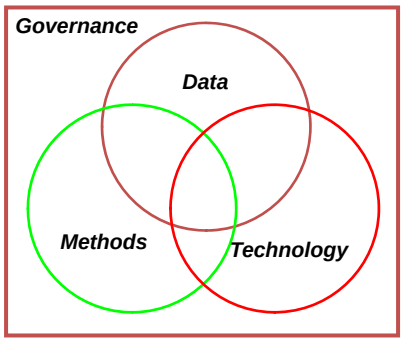
Breadth and diversity of OMOP research community

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 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!

DO NOT DISTRIBUTE

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP

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)

OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP

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: Senior Director, Epidemiology, Johnson & Johnson Pharmaceutical Research and Development

Abraham G. Hartzema PharmD, MSPH, PhD: 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

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OMOP's Methods To Date

- Disproportionality analysis (DP)
- Observational screening (OS)
- Univariate self-controlled case series (USCCS)
- Case-control surveillance (CCS)
- Bayesian logistic regression (BLR)
- Multi-set case control estimation (MSCCE)
- Maximized sequential probability ratio test (MaxSPRT)
- IC Temporal Pattern Discovery (ICTPD)
- High-dimensional propensity score (HDPS)
- Conditional sequential sampling procedure (CSSP)
- Case-crossover (CCO)
- HSIU cohort method (HSIU)
- Statistical relational learning (SRL)
- Incident user design (IUD)

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

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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. HOI
- 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
  - Multivariate modeling
- Output metric/statistic
  - Estimation vs. testing
  - Relative vs. attributable risk
  - Measure of uncertainty

Each method has user input parameters that encode these choices

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Analysis problems under study by OMOP

- **Monitoring of Health Outcomes of Interest (HOIs):**
  - Estimate the strength of the association between drug exposure and specific events (e.g. acute liver failure, bleeding, MI)
  - Modest in number so can customize analytic approach
  - Expert assessment of drug-HOI causal associations based on literature search
- **Identification of non-specified associations:**
  - More exploratory in nature
  - Same goal: estimate the strength of the association between drug exposure and conditions
  - Necessarily more generic analyses (e.g., adjust for age and sex)
  - Causality assessment relies on the product labels
- **Performance against simulated data**
  - Complement 'real world' experiments
  - Ground truth explicitly defined

SAB/HIAB Review Process: *July 2009 Methods strategy / briefing web meeting*

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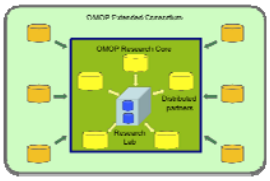
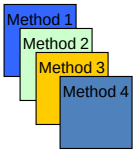
OMOP research experiment workflow

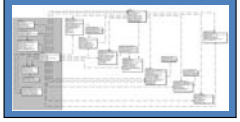


OMOP Methods Library

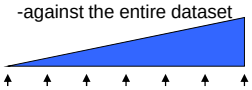


triage

Common Data Model



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



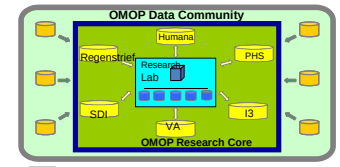
Drugs
- ACE Inhibitors
- Amphotericin B
- Antibiotics
- Antiepileptics
- Benzodiazepines
- Beta blockers
- Bisphosphonates
- Tricyclic antidepressants
- Typical antipsychotics
- Warfarin

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

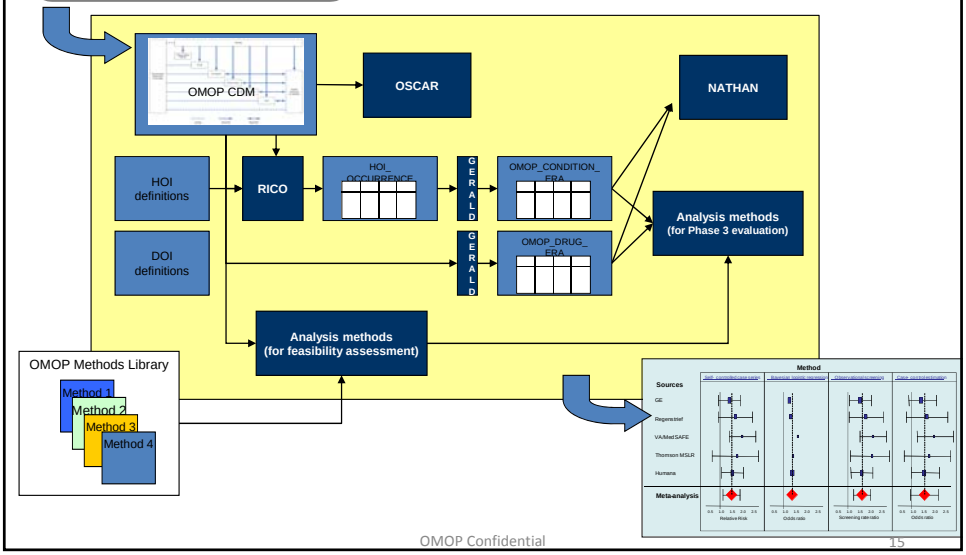
Non-specified conditions

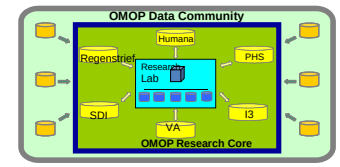
-All outcomes in condition terminology

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

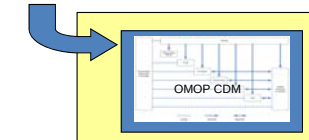


OMOP Project Plan Progression: Tools to support observational database research





Developed OMOP Common Data Model



Each data source has been successfully transformed to the OMOP common data model

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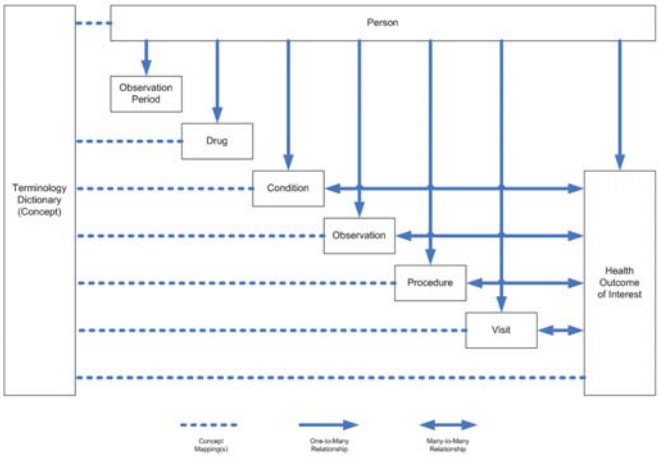
Establishing a Common Data Model

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



http://omop.fnih.org/CDMandTerminologies

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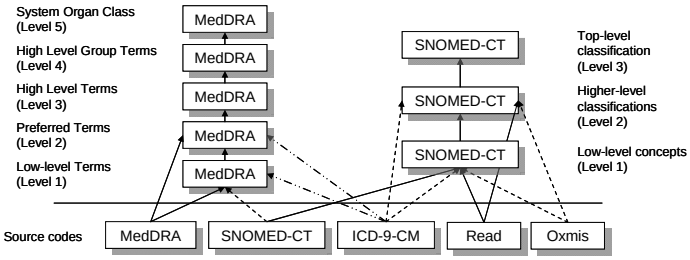
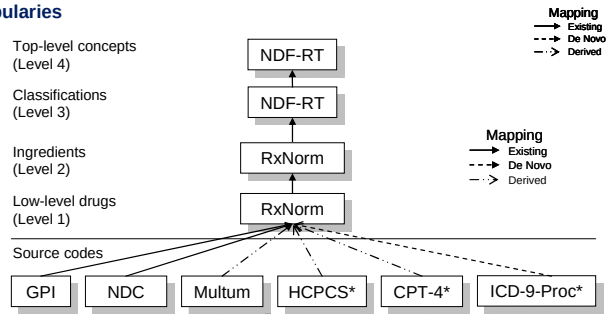
Standardizing terminologies to accommodate disparate observational data sources

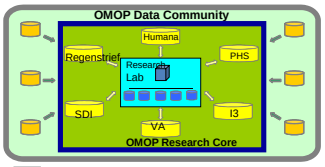
Standardizing conditions:



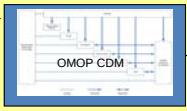
http://omop.fnih.org/Vocabularies

Standardizing drugs:





Executed OSCAR



OSCAR

Observational Source Characteristics Analysis Report (OSCAR) - provides a systematic approach for summarizing all data within the OMOP common data model

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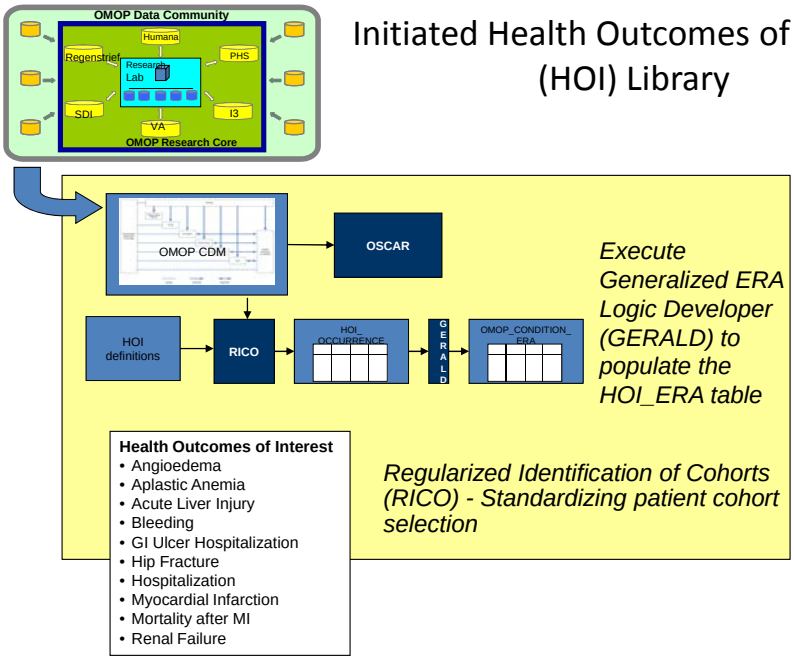
Observational Source Characteristics Analysis Report (OSCAR)

- Provides a systematic approach for summarizing observational healthcare data stored in the OMOP common data model
- Creates a structured output dataset of summary statistics of each table and field in the CDM
  - Categorical variables: one-, two-, and three-way stratified counts (e.g. number of persons with each condition by gender)
  - Continuous variables: distribution characteristics: min, mean, median, stdev, max, 25/75 percentile (e.g. observation period length)
  - OSCAR summaries from each source can be brought together to do comparative analyses
- 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

Initiated Health Outcomes of Interest (HOI) Library

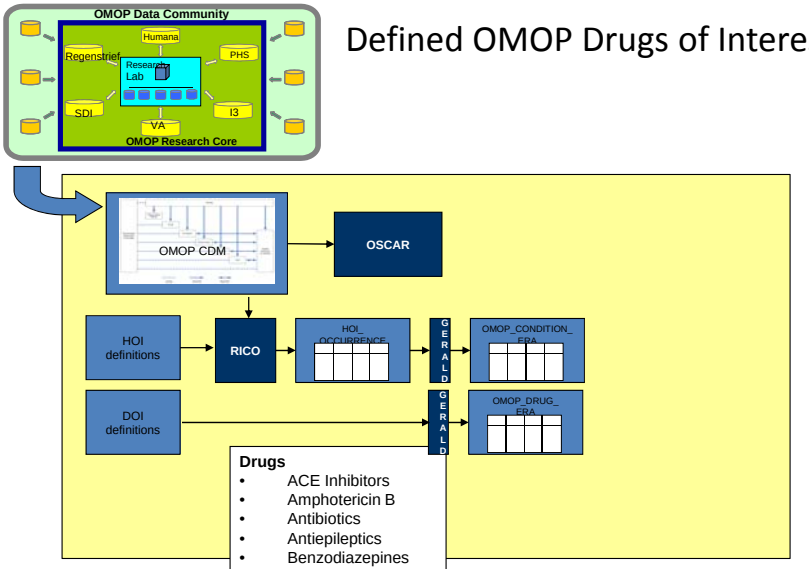


Execute Generalized ERA Logic Developer (GERALD) to populate the HOI_ERA table

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

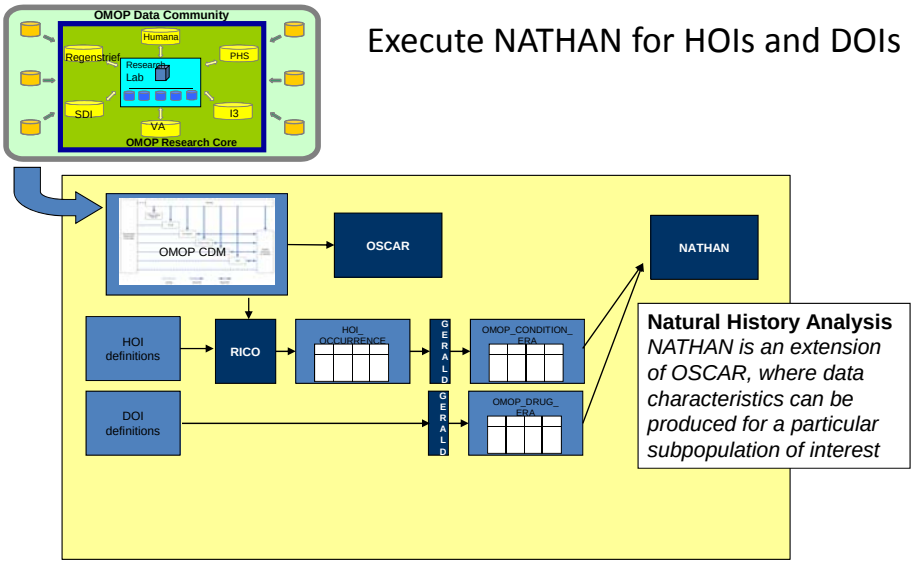
Regularized Identification of Cohorts (RICO) - Standardizing patient cohort selection

Defined OMOP Drugs of Interest (DOI)



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

Execute NATHAN for HOIs and DOIs



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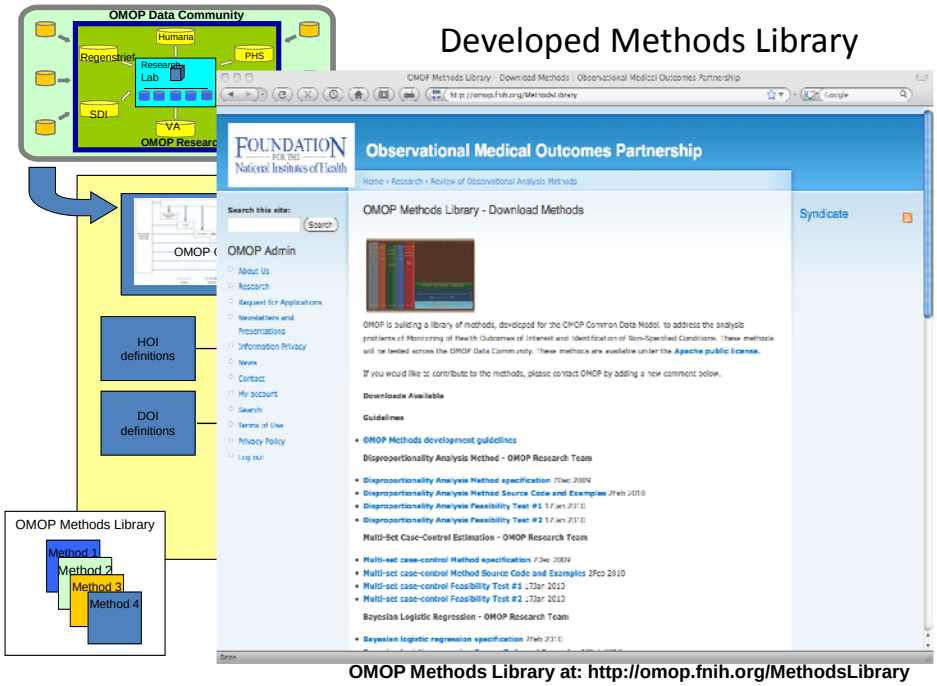
Natural History Analysis (NATHAN)

- 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)
- Additional NATHAN summary statistics provide temporal assessment, relative to index date
  - Ex. conditions 30d prior to drug start
  - Ex. drug exposure any time prior to incident condition
- Uses:
  - Evaluate alternative cohort definitions (HOIs)
  - Comparisons between data sources
  - Providing context for interpreting and analyzing findings of drug safety studies

http://omop.fnih.org/NATHAN

Developed Methods Library



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

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OMOP's Methods Landscape

Disproportionality Analysis

	AE j = Yes	*AE j = No*
Drug *i* = Yes	*a*=20	*b*=100
Drug *i* = No	*c*=100	*d*=1080

- Distinct Patients
- SRS
- Modified SRS

X

MGPS
BCPNN
PRR
Chi
etc.

X Stratified

- Temporal Pattern Discovery (WHO)

Sequential Methods

	AE j = Yes	*AE j = No*
Drug *i* = Yes	*a*=20	
Drug *i* = No		

Compare to baseline Poisson

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

Exposure Based Methods

Exposed → Case?

Non-exposed → Case?

- Observational screening
- HSIU
- Incident User Designs
- High-Dimensional Propensity Scoring
- Local control

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

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OMOP's Methods Landscape

Case Based Methods

Exposed? ← Case

Exposed? ← Non-case

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

Other Methods

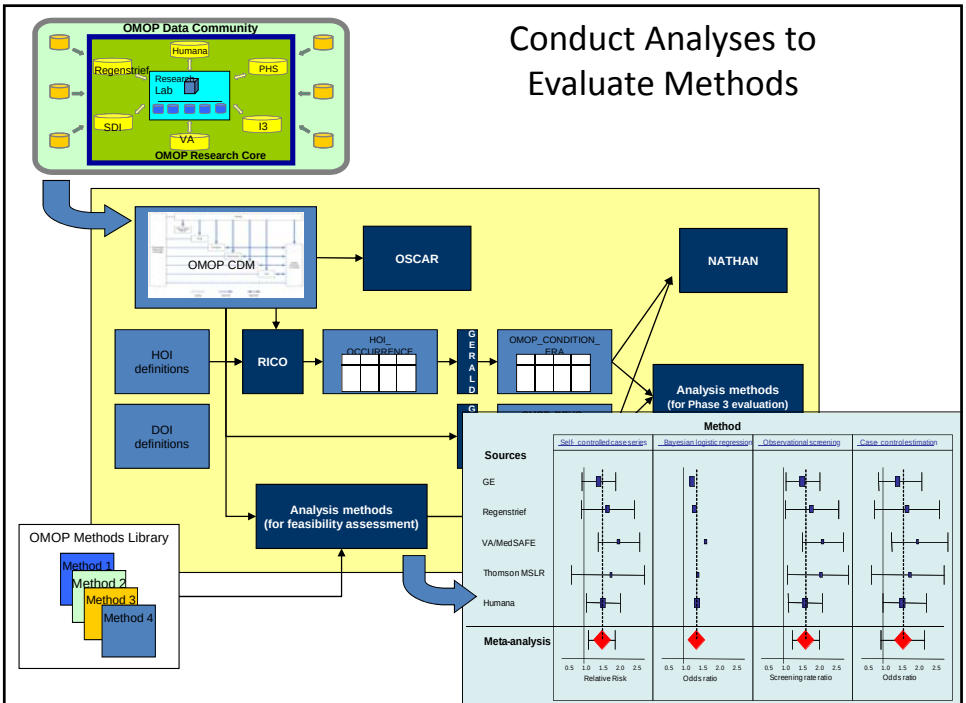
- Hi-Dimensional logistic regression
- Statistical relational learning

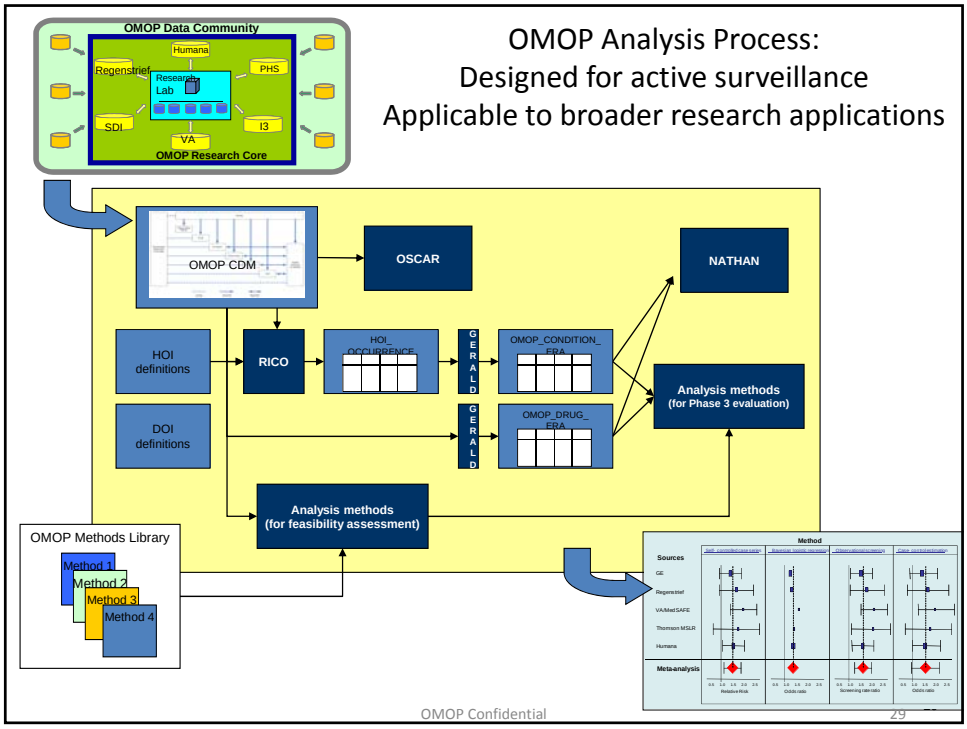
Future Methods

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

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

Conduct Analyses to Evaluate Methods





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Derivative Products and Impacts

- Validation tools
- Standards: Connected to Office of the National Coordinator
- Feedback loop to data capture in EHRs
- Decision-making tools
- Visualizations
- ‘Natural Experiments’

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For further information

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