

**OBSERVATIONAL
MEDICAL
OUTCOMES
PARTNERSHIP**

**Methods Development:
Status Report**

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on behalf of OMOP methods team
April 12, 2010

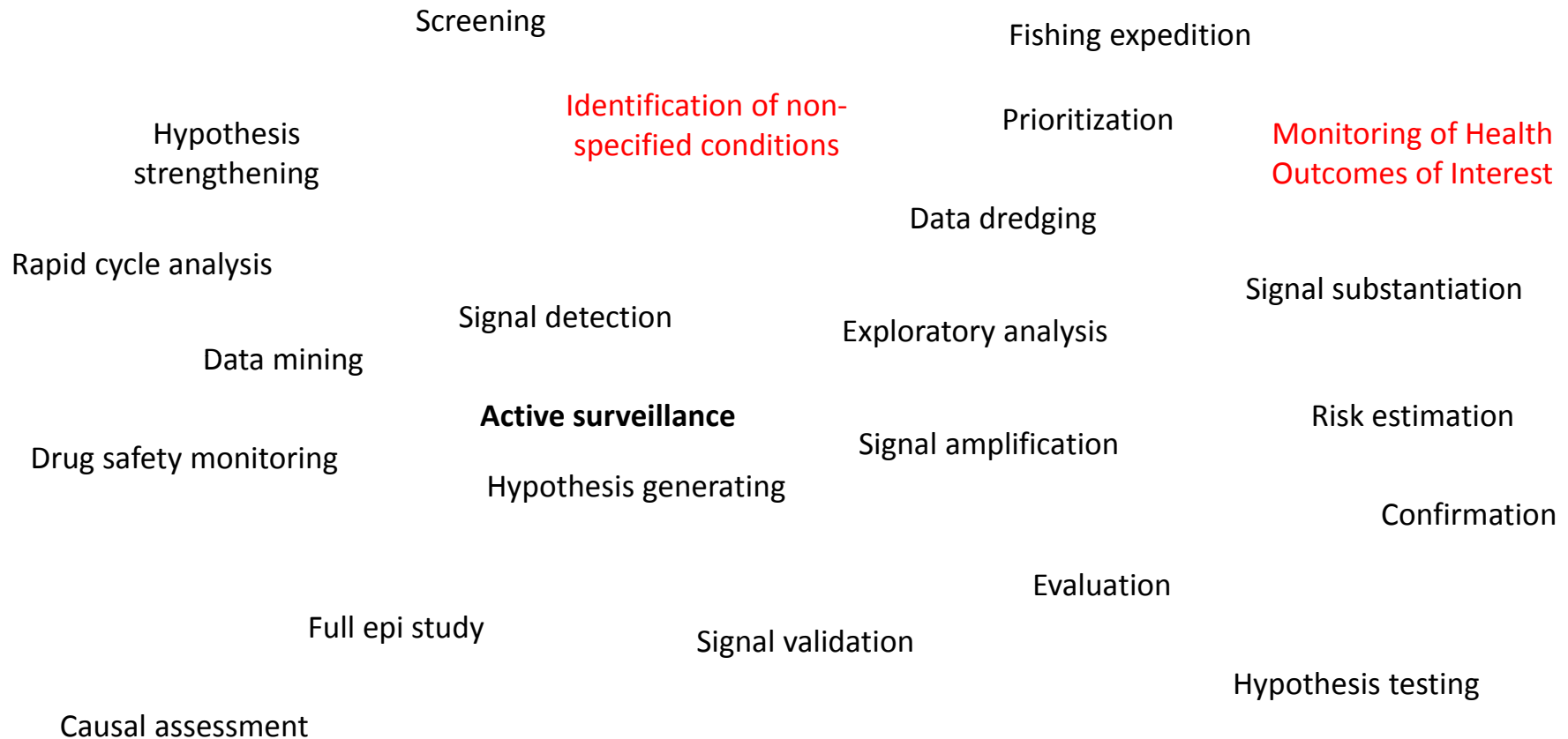
Methods Philosophy

- Many different analysts have considerable experience with different statistical and epidemiological approaches in different observational settings
- Massive claims/EHR databases present challenges where little theory exists to guide methodological choices
- Our approach is empirical
- Implement a broad swathe of methods and evaluate them against “ground truth.” Place code in the public domain
- No magic bullet - but we expect to identify gross differences between different methods in different scenarios

Analysis problems under study by OMOP

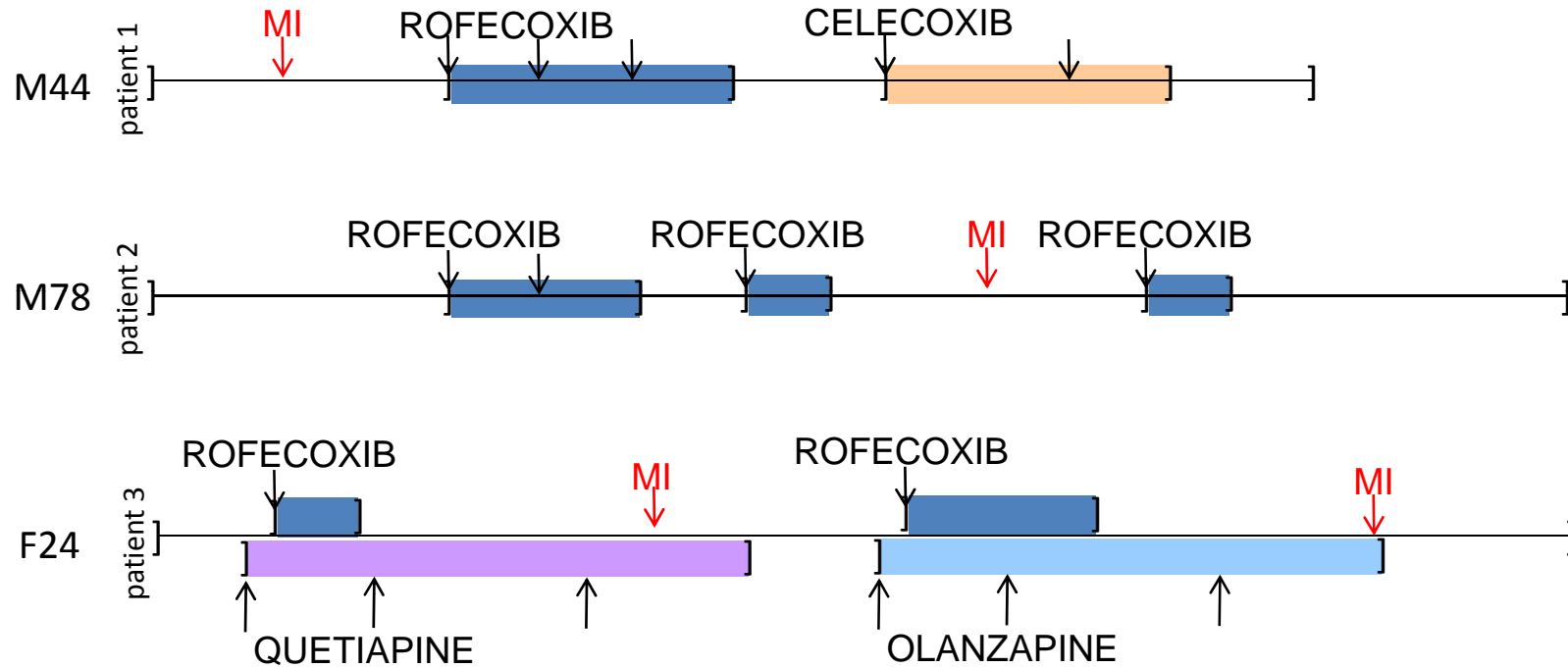
- **Monitoring of Health Outcomes of Interest (HOIs):**
 - Estimate the strength of the association between drug exposure and ten specific events (e.g. acute liver failure, bleeding, MI)
 - Modest in number so can tailor analyses
 - Expert assessment of drug-HOI causal associations
- **Identification 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

Characterizing Drug-Outcome Associations



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

What do the data look like?



- Computational considerations require few passes through the data

OMOP's methods landscape

Disproportionality analysis

QuickTime™ and a decompressor are needed to see this picture.

- Distinct Patients
 - SRS
 - Modified SRS
- X
- MGPS
 - BCPNN
 - PRR
 - Chi
 - etc.
- X
- Stratified
- Temporal Pattern Discovery (WHO)

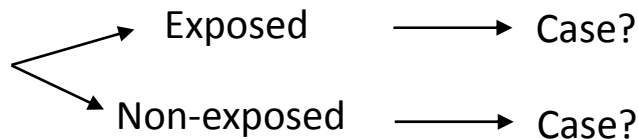
Sequential methods

QuickTime™ and a decompressor are needed to see this picture.

Compare to baseline Poisson

- MaxSPRT
- CSSP

Exposure Based Methods

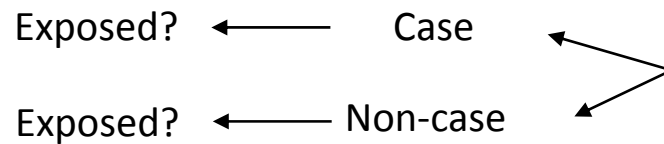


- Observational screening
- HSIU
- Incident User Designs
- High-Dimensional Propensity Scoring
- Local control

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

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 (30+ submissions)

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OMOP Cup

- Spiked simulated data - competitors try to find the signals
- Twofold purpose: build community and generate new ideas
- 50+ competitors with over 600 submissions
- Community-building requires continuity so we need to plan for OMOP Cup II

OMOP Cup Top Performers

- Binary prediction model
- Drug-condition pair is unit of analysis
- Construct a feature vector per pair
- Random forest

- Two stage disproportionality (IC)
- Stage 1: find signals
- Stage 2: remove signals confounded by indication

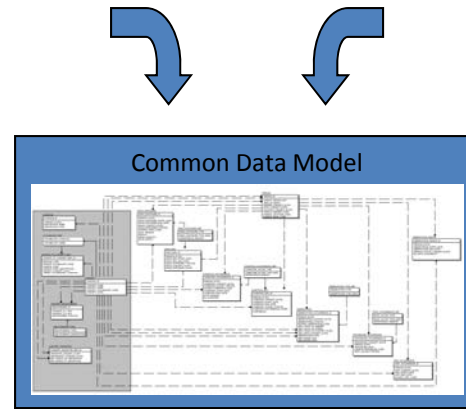
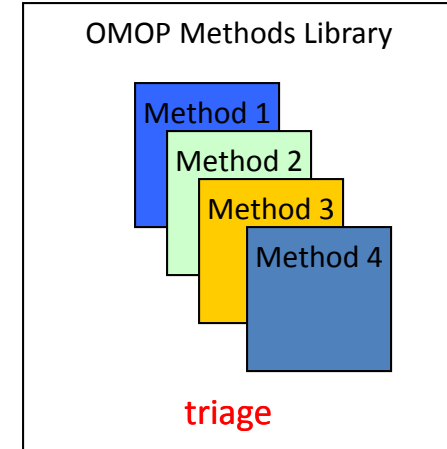
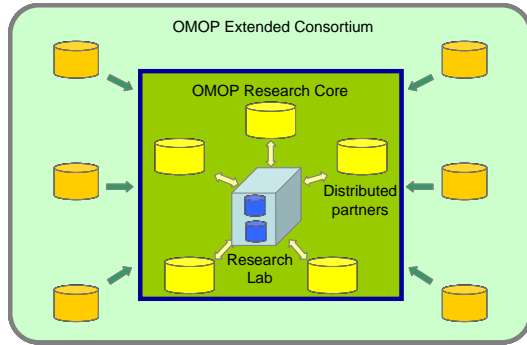
- Ensemble of two disproportionality methods plus Poisson method using exposure times

- Disproportionality
- Ensembling
- Matrix factorization
- Calibration

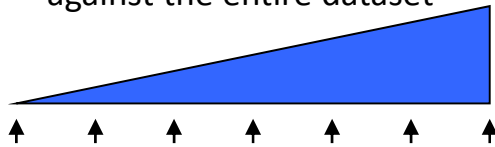
Methodological considerations common across multiple approaches

- 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

OMOP research experiment workflow



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

- Non-specified conditions**
- All outcomes in condition terminology
 - 'Labeled events' as reference
 - Warning
 - Precautions
 - Adverse Reactions
 - Postmarketing Experience

Status

- First round methods implementation and feasibility testing essentially complete
- Mostly standard or modified versions of existing pharmaco/epidemiology methods
- Non-trivial engineering challenges
- Evaluation phase underway

Future

- Computational innovations for compute intensive methods (eg GPU hardware)
- Novel methods (e.g. self-controlled methods with rate depending on prior events)
- Higher fidelity simulation

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Thank you

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