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Methods Development: Status Report

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on behalf of OMOP methods team
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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

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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 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

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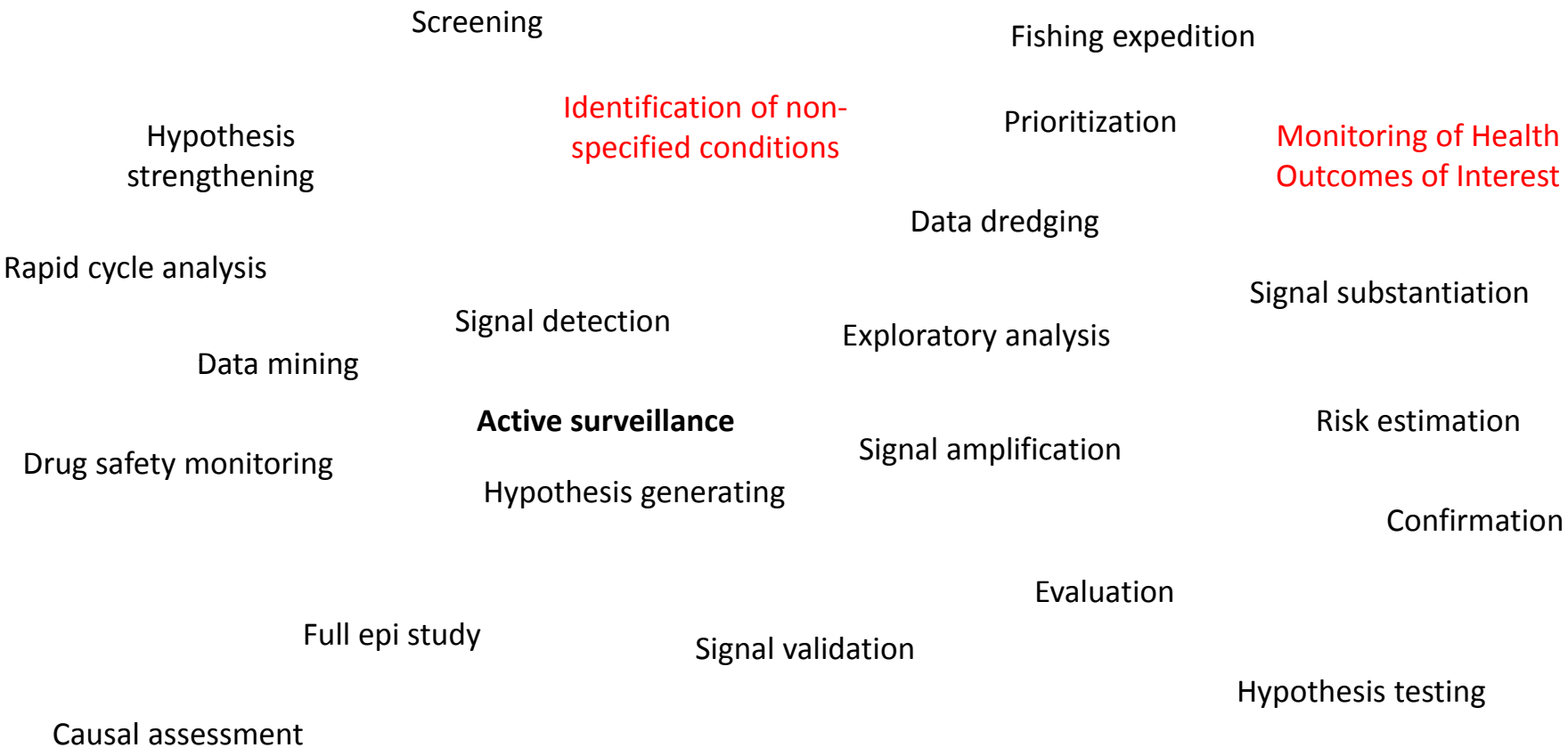
Characterizing Drug-Outcome Associations



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

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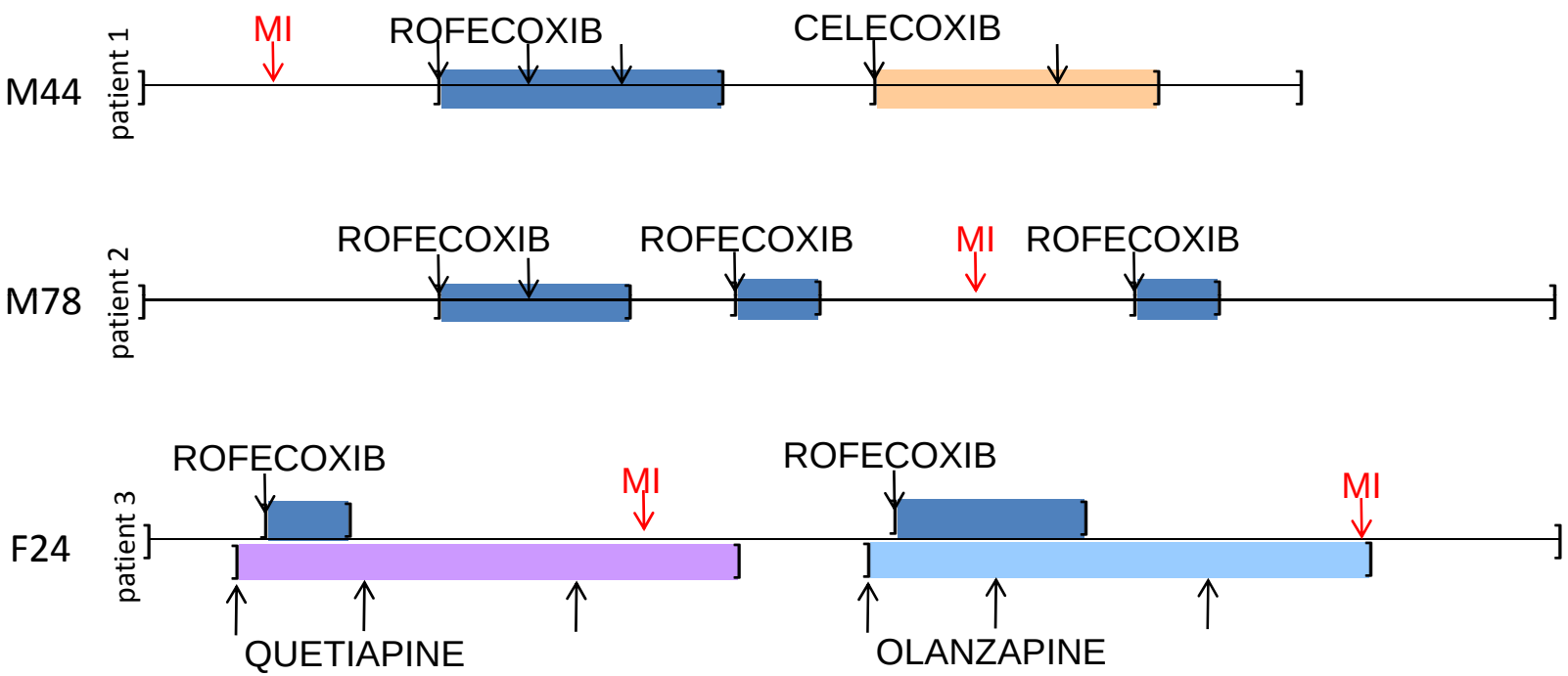
What do the data look like?



- Computational considerations require few passes through the data

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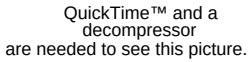
OMOP's methods landscape

Disproportionality analysis



- Distinct Patients
- SRS
- Modified SRS

X

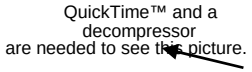
MGPS
BCPNN
PRR
Chi
etc.

X

Stratified

- Temporal Pattern Discovery (WHO)

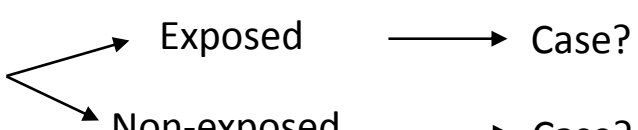
Sequential methods



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

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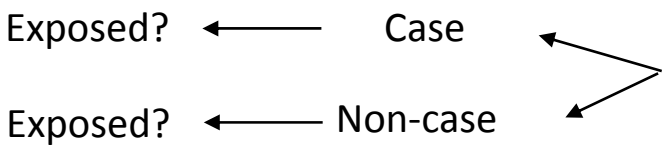
Case Based Methods



- 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

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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

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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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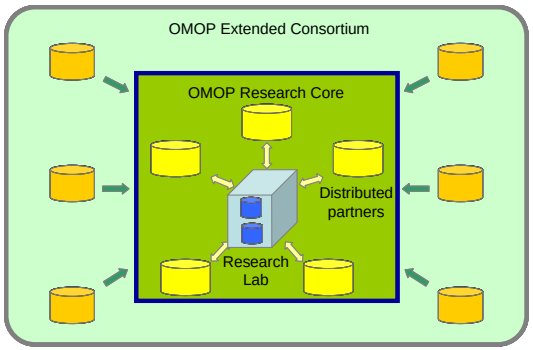
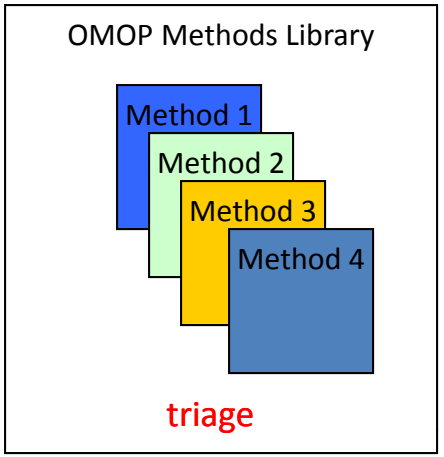
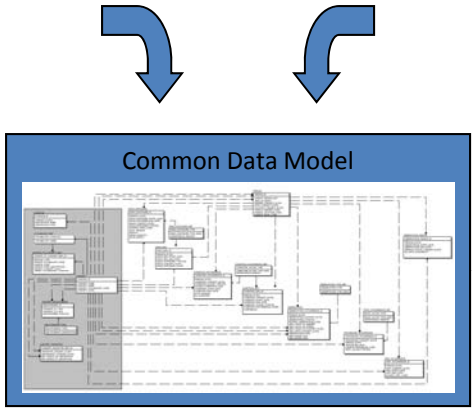
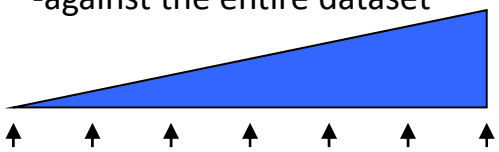
OMOP research experiment workflow







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

http://omop.fnih.org