The Journey of OHDSI: Where have we been?

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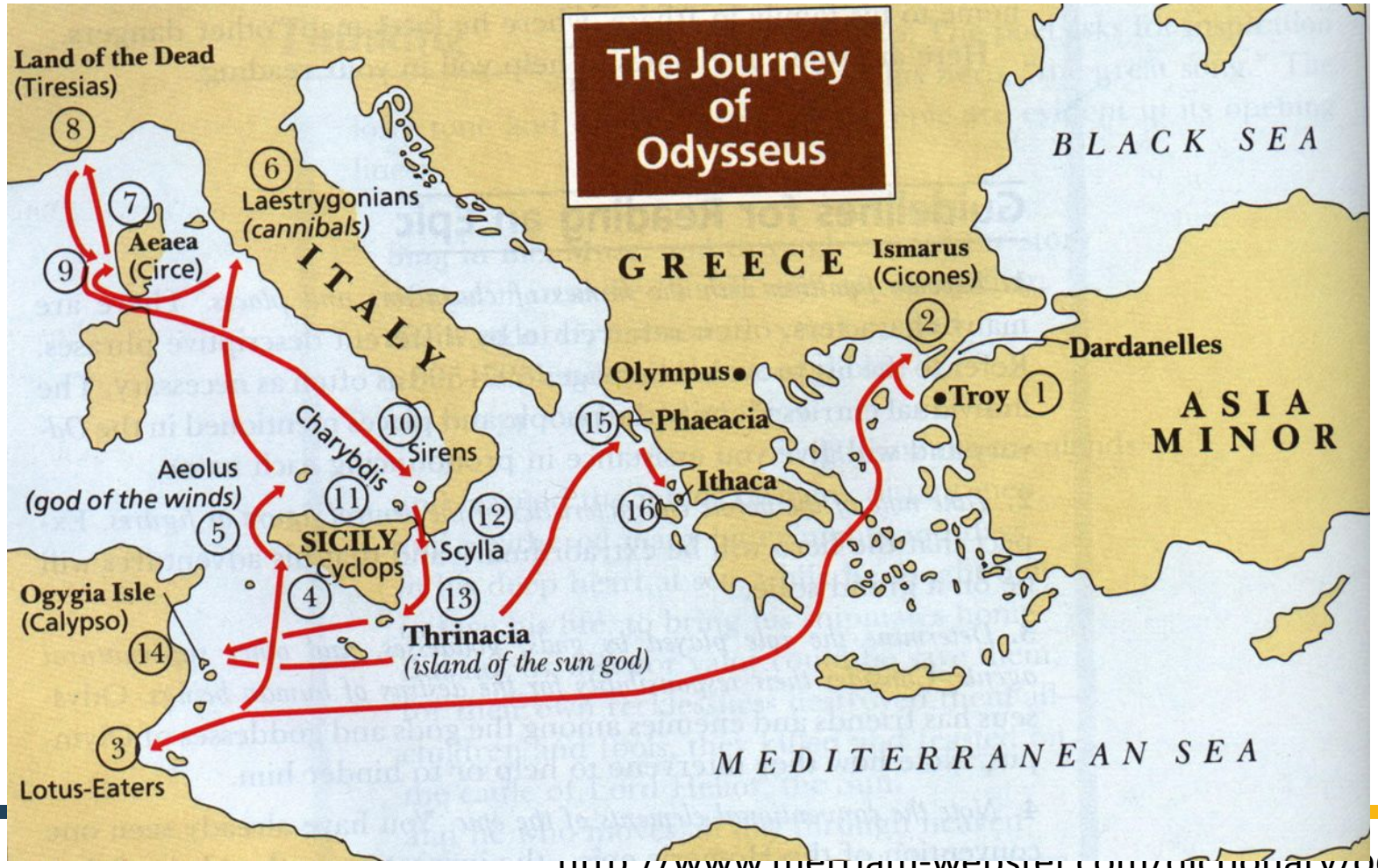
Columbia University, New York, USA

NewYork-Presbyterian Hospital, New York, USA

OHDSI Europe

Odyssey (*noun*): \oh-d-si\

1. A long journey full of adventures



http://www.merriam-webster.com/dictionary/odyssey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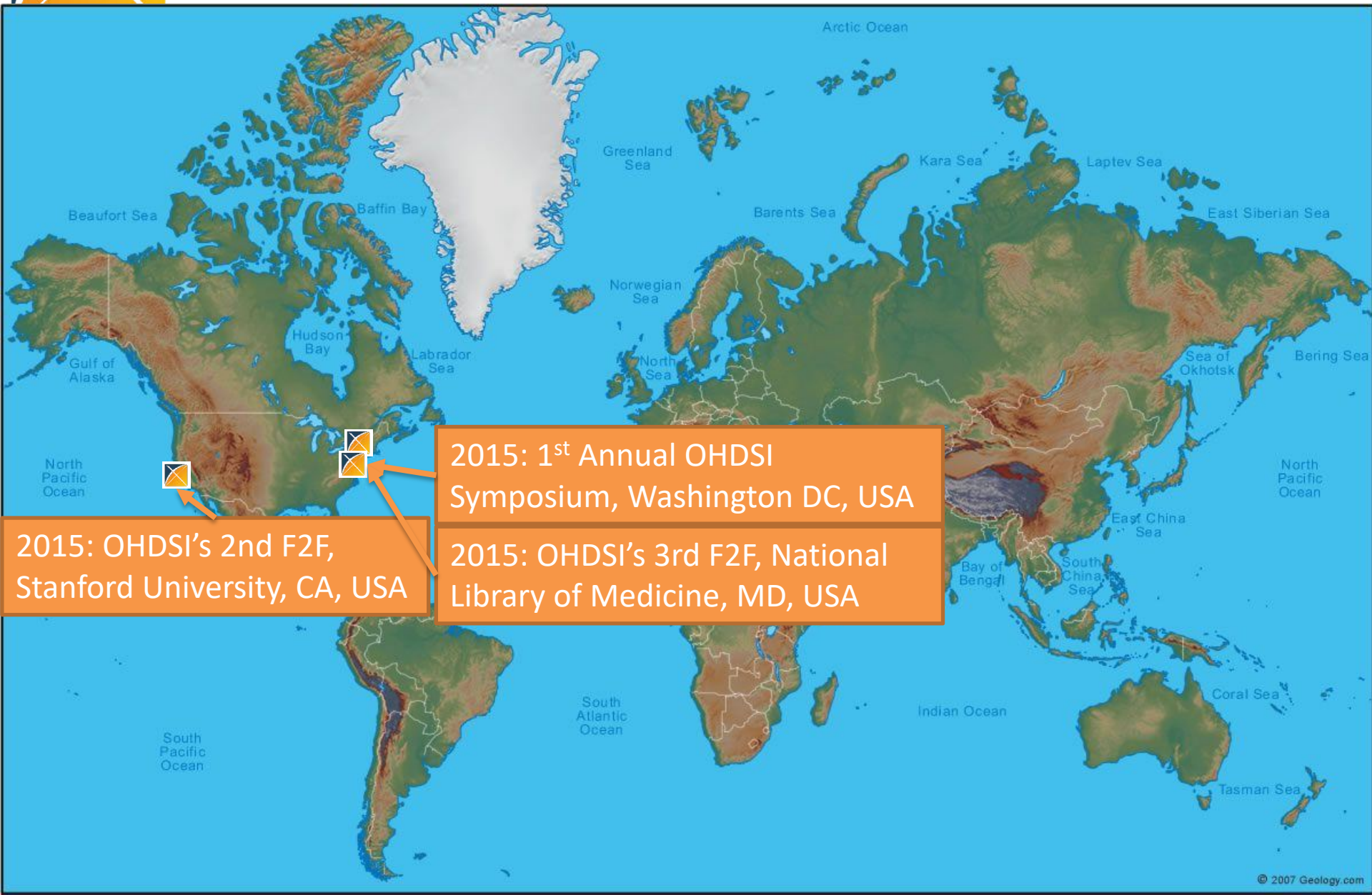
Welcome!
To the OHDSI Community!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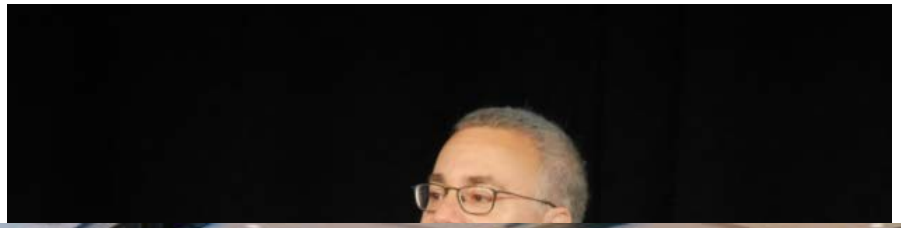


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|일시| 2017년 03월 07일 (화) ~ 03월 09일 (목)
|장소| 아주대학교병원 별관 1층 대강당
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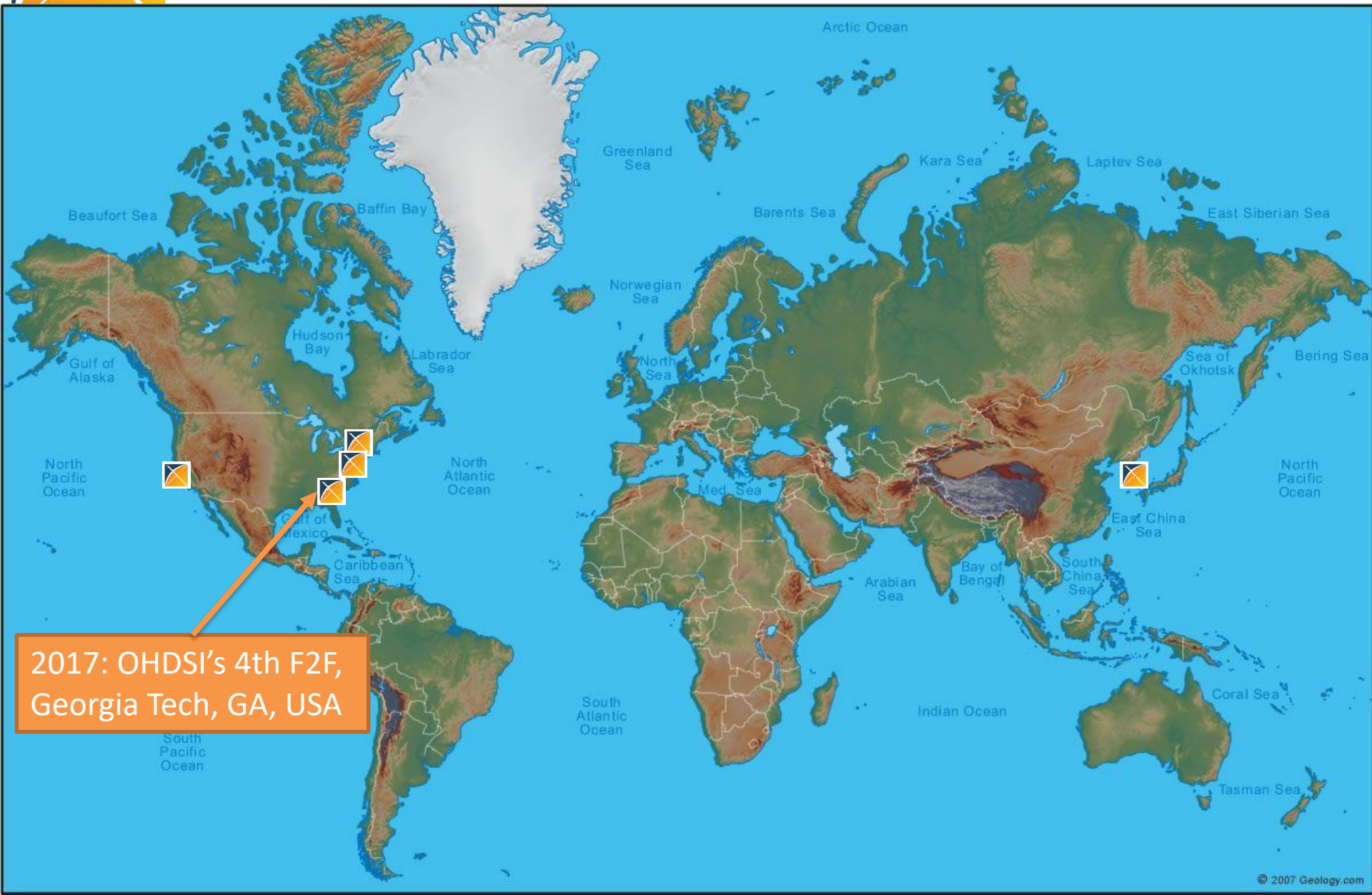
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The OHDSI Evidence Explorer is designed to help you find relevant, high-quality information to support your analytical needs. To begin, tell us more about you.
I RECOMMEND CLINICAL GUIDELINES.
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Problem. Solved.

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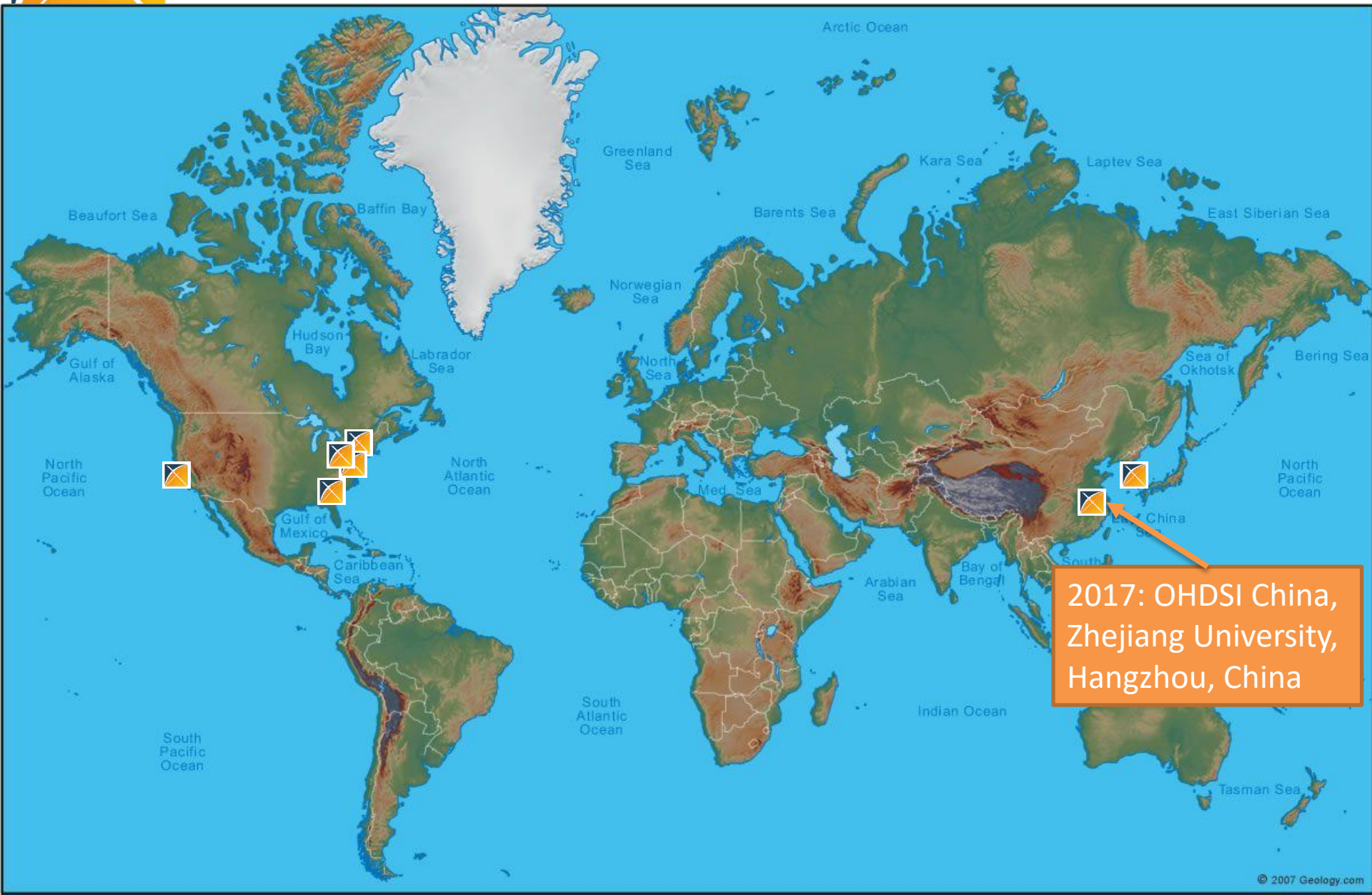
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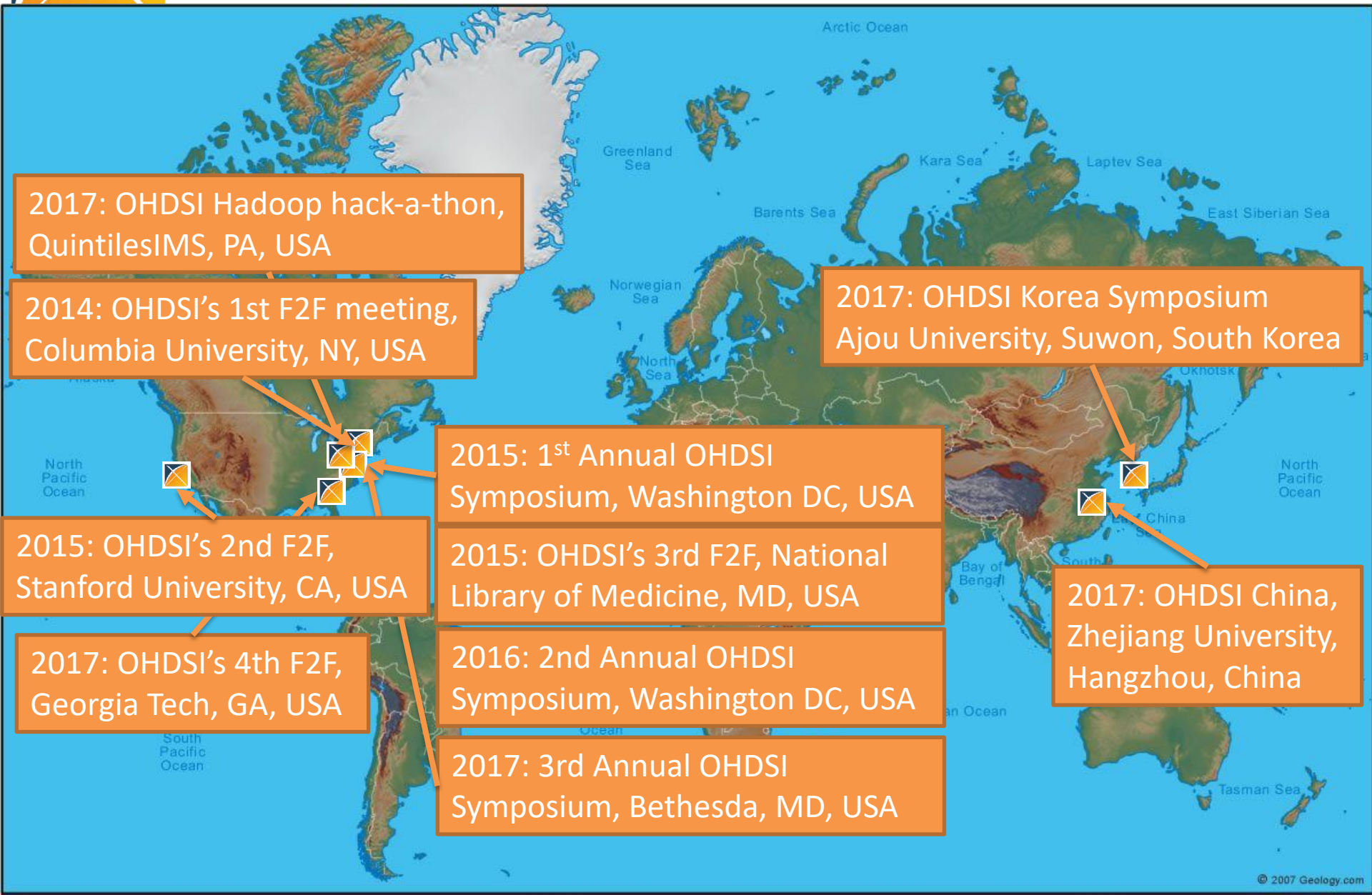
2017 China-US healthcare big data forum / OHDSI China Annual Workshop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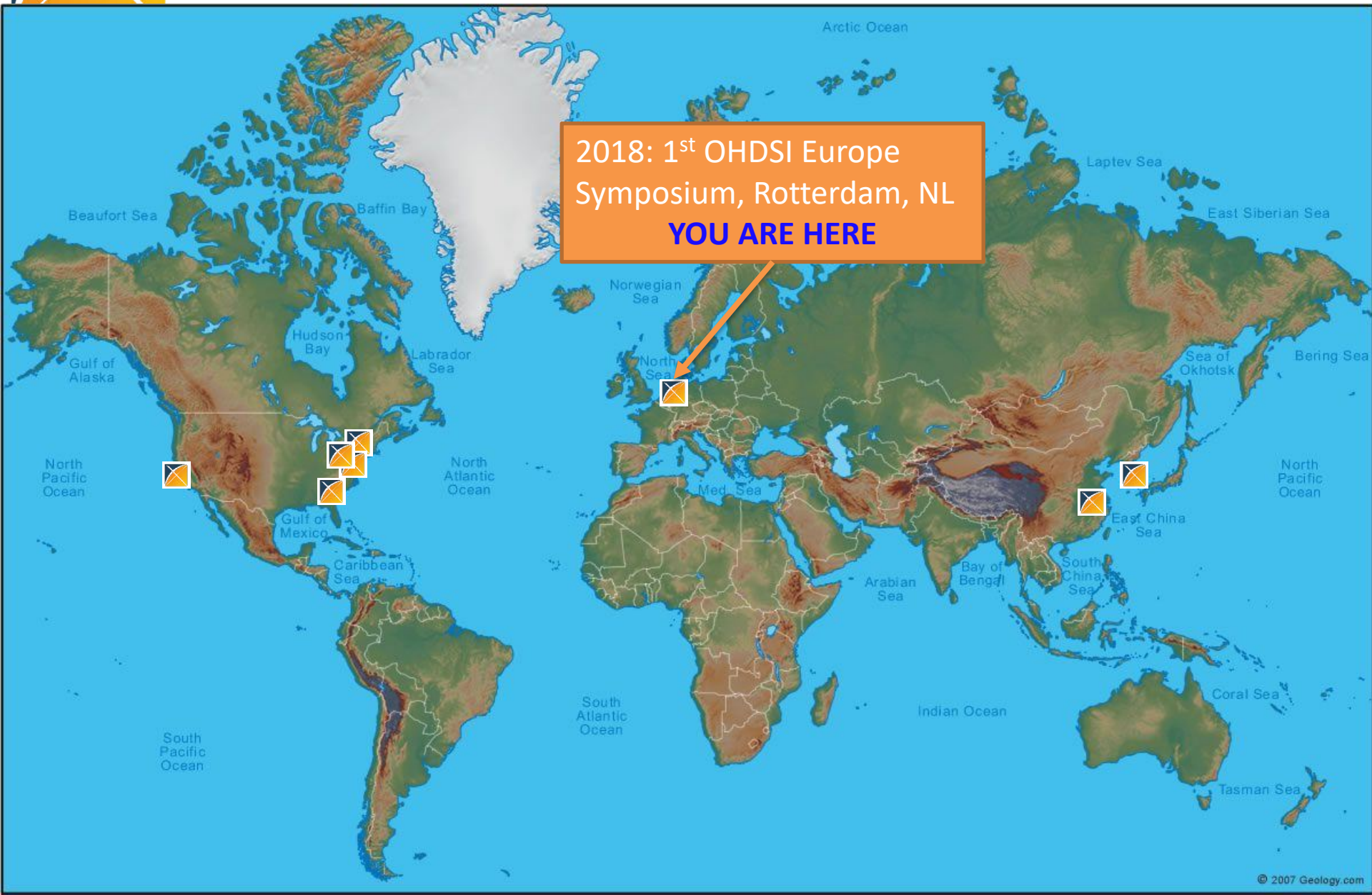
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http://www.ohdsi-europe.org/


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Welcome!

OHDSI is

an open science community

OHDSI's mission

To improve health, by empowering a community to collaboratively generate the evidence that promotes better health decisions and better care

OHDSI's values

- **Innovation**: Observational research is a field which will benefit greatly from disruptive thinking. We actively seek and encourage fresh methodological approaches in our work.
- **Reproducibility**: Accurate, reproducible, and well-calibrated evidence is necessary for health improvement.
- **Community**: Everyone is welcome to actively participate in OHDSI, whether you are a patient, a health professional, a researcher, or someone who simply believes in our cause.
- **Collaboration**: We work collectively to prioritize and address the real world needs of our community's participants.
- **Openness**: We strive to make all our community's proceeds open and publicly accessible, including the methods, tools and the evidence that we generate.
- **Beneficence**: We seek to protect the rights of individuals and organizations within our community at all times.

OHDSI community

We’re all in this journey together…

OHDSI' community engagement

- Weekly community web conferences for all collaborators to share their research ideas and progress
- 15 workgroups for solving shared problems of interest
  - Common Data Model, Population-level Estimation, Patient-level Prediction, Architecture, Phenotype, NLP, GIS, Oncology, …
- Active community online discussion: forums.ohdsi.org
- 594 distinct users have made 8,894 posts on 1,631 topics:
  - Implementers, Developers, Researchers, CDM Builders, Vocabulary users, OHDSI in Korea, OHDSI in China, OHDSI in Europe

OHDSI is

an international data network

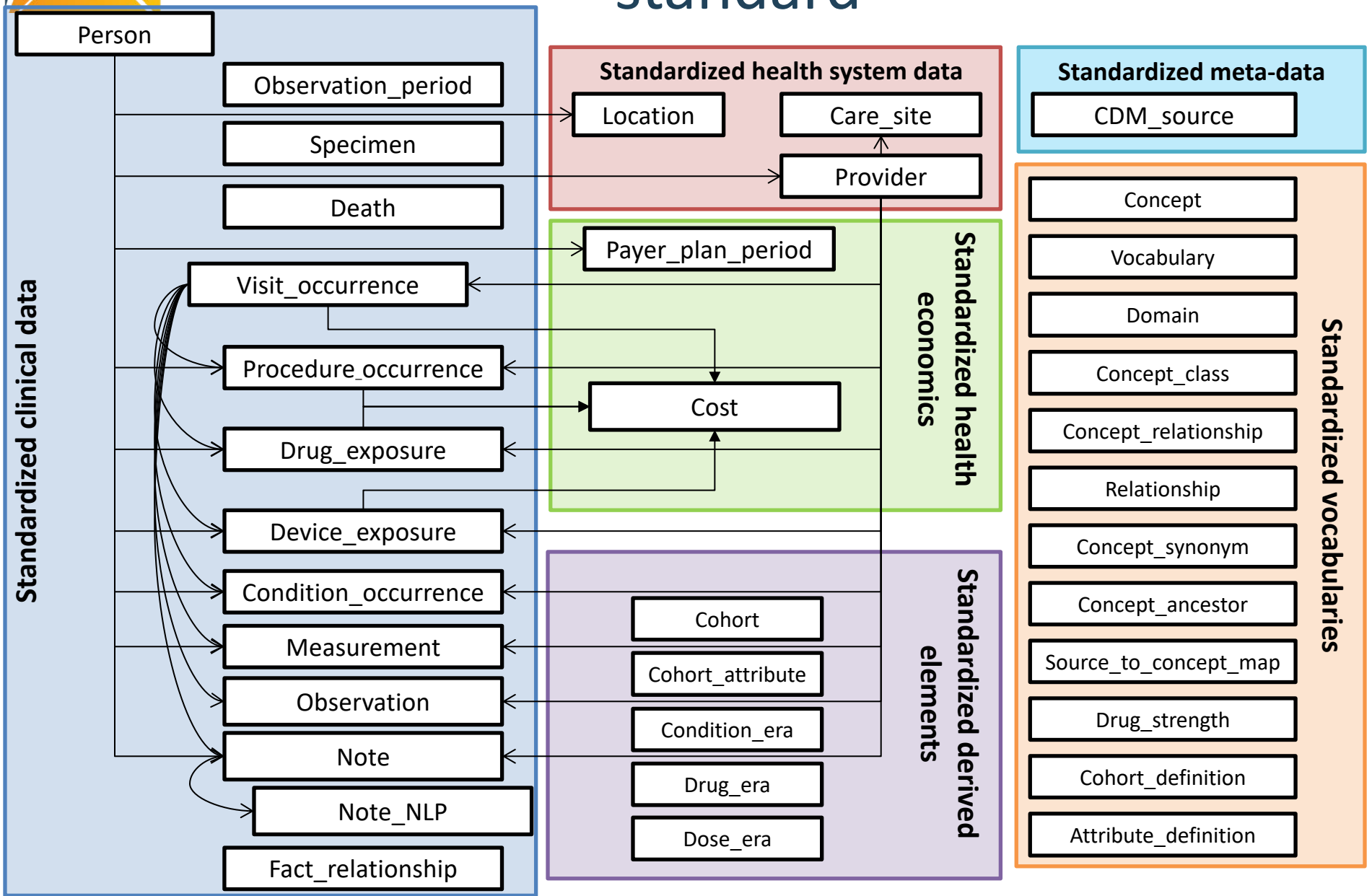
Data across the OHDSI community

- 84 organizations have access to 64 different databases
- Patient-level data from various perspectives:
  - Electronic health records, administrative claims, hospital systems, clinical registries, health surveys, biobanks
- Collectively, totaling 1.26 billion patient records
- Data in 17 different countries, with 115 million patient records from outside US

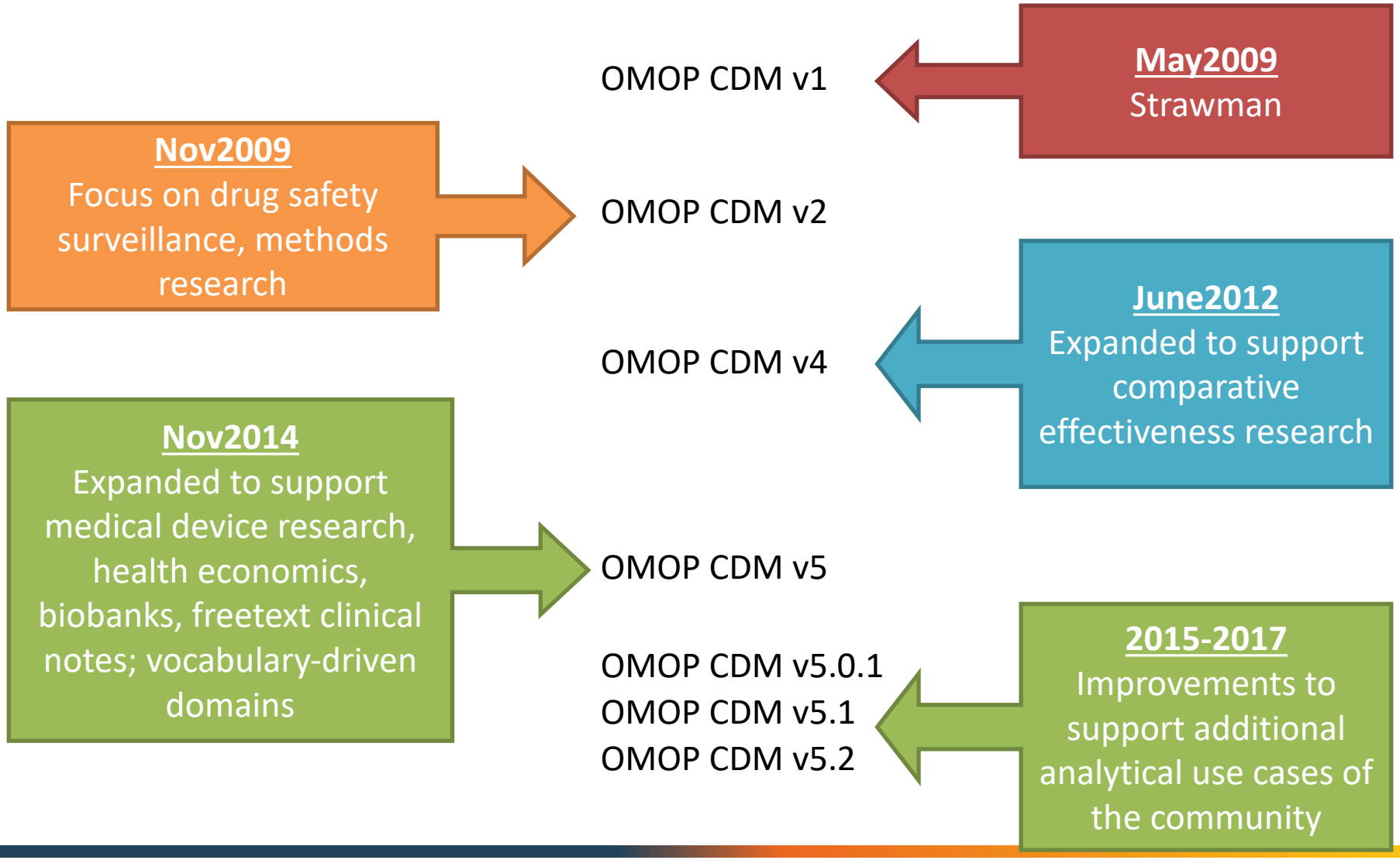
All using one open community data standard:
OMOP Common Data Model

http://www.ohdsi.org/web/wiki/doku.php?id=resources:2017_data_network

Journey of an open community data standard

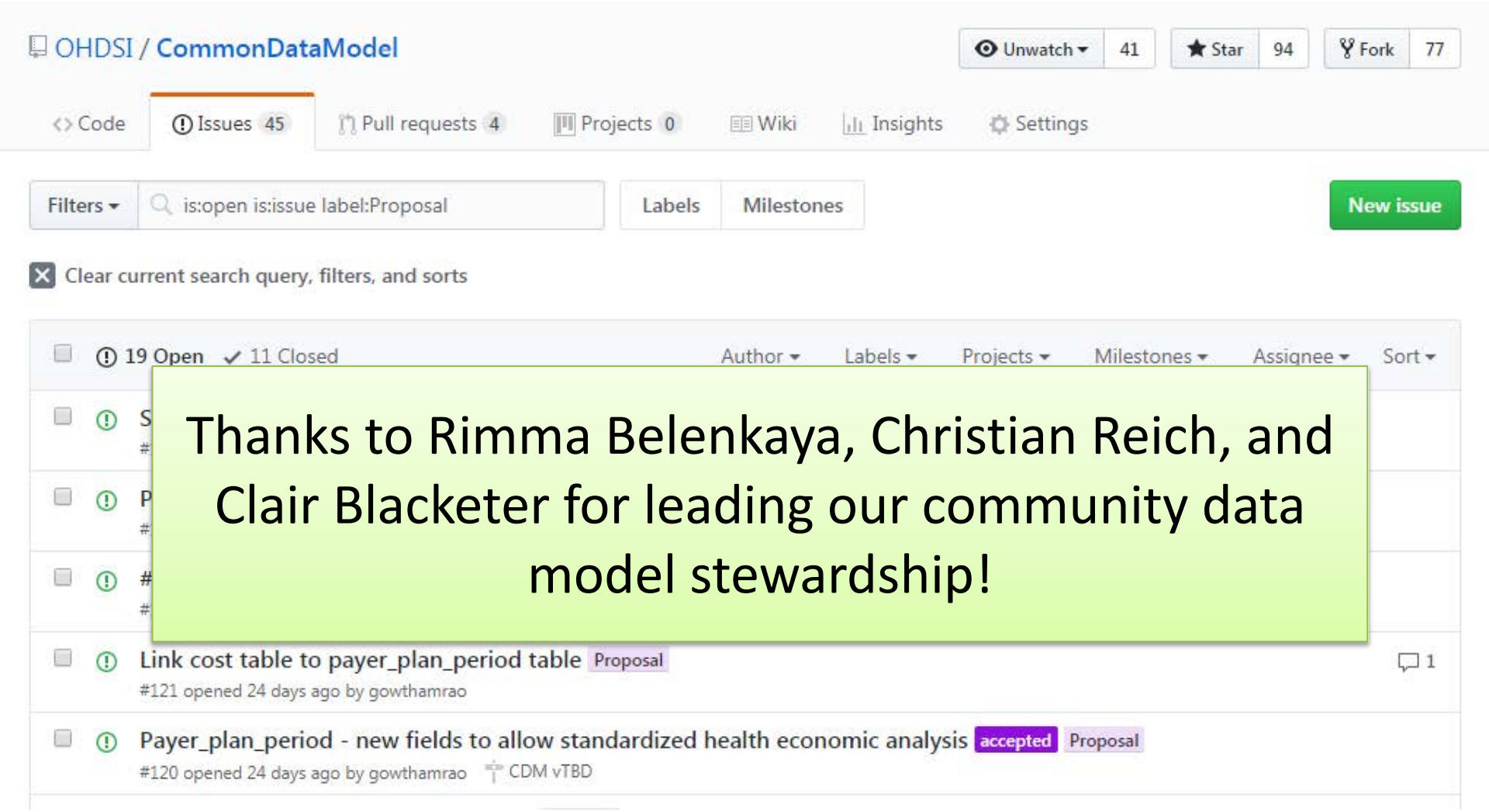


Journey of an open community data standard



https://github.com/OHDSI/CommonDataModel

OMOP CDM v5.3



Thanks to Rimma Belenkaya, Christian Reich, and Clair Blacketer for leading our community data model stewardship!

OHDSI's standardized vocabularies

- 78 Vocabularies across 32 domains
  - MU3 standards: SNOMED, RxNorm, LOINC
  - Disparate sources: ICD9CM, ICD10(CM), Read, NDC, Gemscript, CPT4, HCPCS…
- 5,720,848 concepts

Thank you Christian and the Odysseus team for continue to steward, maintain, and improve this invaluable resource for the entire community!

- 32,612,650 concept relationships

OHDSI is

collaborating to generate reliable evidence

What is OHDSI's strategy to deliver reliable evidence?

- **Methodological research**
  - Develop new approaches to observational data analysis
  - Evaluate the performance of new and existing methods
  - Establish empirically-based scientific best practices
- **Open-source analytics development**
  - Design tools for data transformation and standardization
  - Implement statistical methods for large-scale analytics
  - Build interactive visualization for evidence exploration
- **Clinical evidence generation**
  - Identify clinically-relevant questions that require real-world evidence
  - Execute research studies by applying scientific best practices through open-source tools across the OHDSI international data network
  - Promote open-science strategies for transparent study design and evidence dissemination

Estimation methods

Cohort Method

New-user cohort studies using large-scale regression for propensity and outcome models

Self-Controlled Case Series

Self-Controlled Case Series analysis using few or many predictors, includes splines for age and seasonality.

Self-Controlled Cohort

A self-controlled cohort design, where time preceding exposure is used as control.

IC Temporal Pattern Disc.

A self-controlled design, but using temporal patterns around other exposures and outcomes to correct for time-varying confounding.

Case-control

Case-control studies, matching controls on age, gender, provider, and visit date. Allows nesting of the study in another cohort.

Case-crossover

Case-crossover design including the option to adjust for time-trends in exposures (so-called case-time-control).

Thank you Martijn Schuemie, Marc Suchard, Peter Rijnbeek, and Jenna Reps for leading methods research and development efforts!

Method charac

exposure-outcome pairs to profile and calibrate a particular analysis design.

reference sets as well as simulations injected in real data to evaluate the performance of methods.

Supporting packages

Database Connector

Connect directly to a wide range of database platforms, including SQL Server, Oracle, and PostgreSQL.

Sql Render

Generate SQL on the fly for the various SQL dialects.

Cyclops

Highly efficient implementation of regularized logistic, Poisson and Cox regression.

Ohdsi R Tools

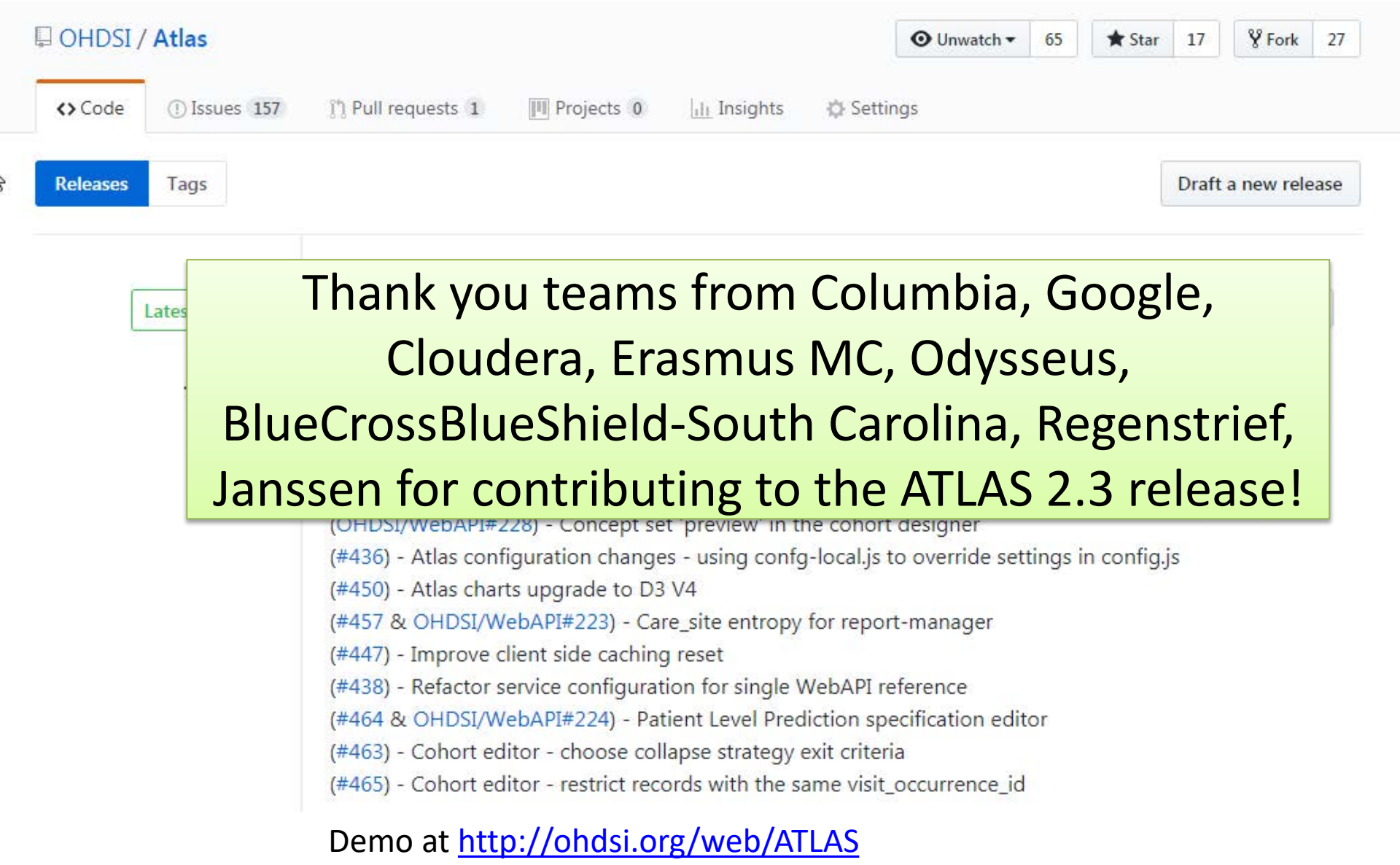
Support tools that didn't fit other categories, including tools for maintaining R libraries.

Under construction

Journey toward open-source analytics development

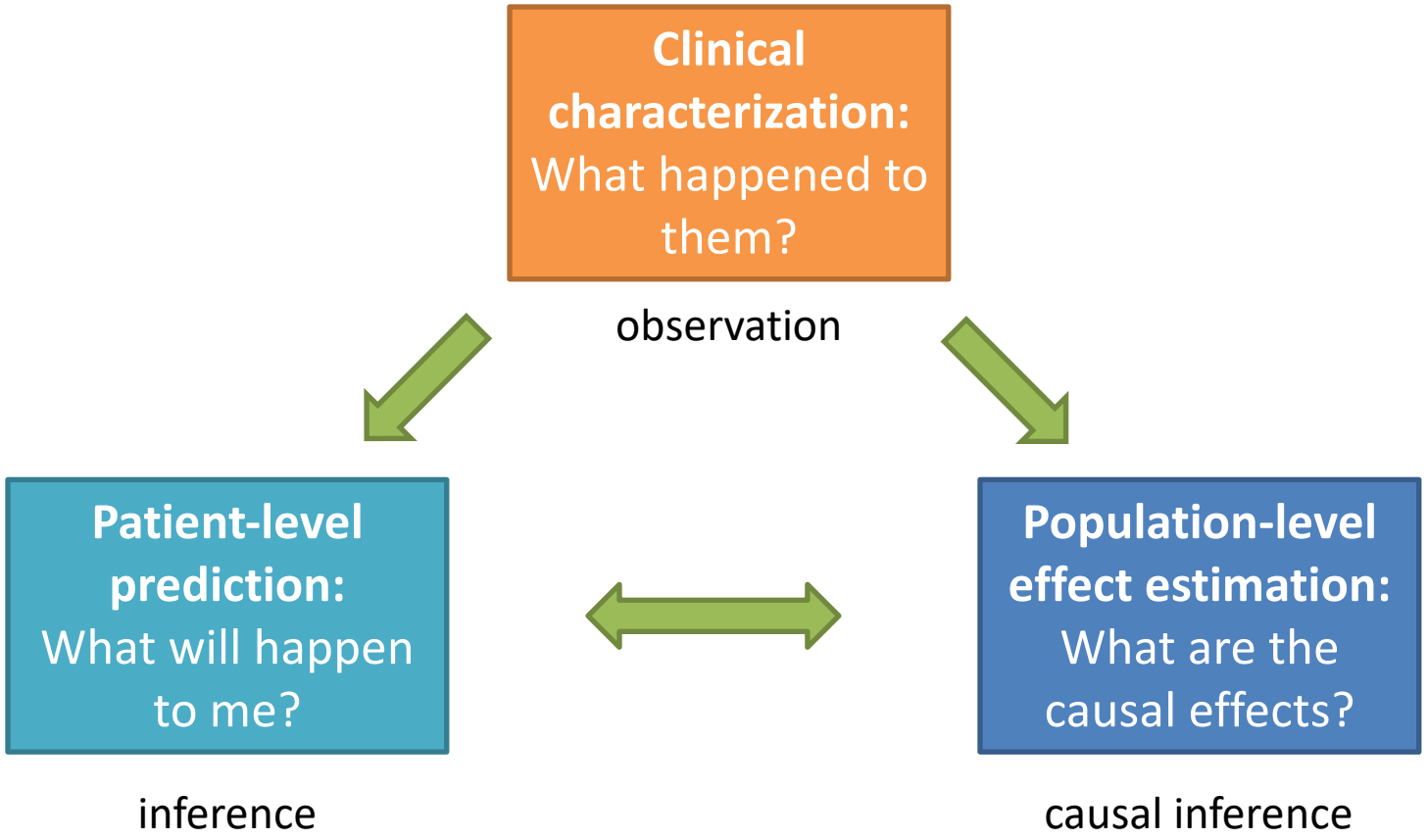
- 88 developers on 101 OHDSI GitHub repositories
- Applications released for:
  - CDM ETL design and implementation
  - Clinical characterization (ACHILLES, ATLAS)
  - Population-level effect estimation
  - Patient-level prediction
  - OHDSI network studies (protocol + source code, ARACHNE)

Journey toward open-source analytics development



Demo at http://ohdsi.org/web/ATLAS

Complementary evidence to inform the patient journey



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G Hripcsak, PB Ryan, JD Duke... - Proceedings of the ..., 2016 - National Acad Sciences
Abstract Observational research promises to complement experimental research by providing large, diverse populations that would be infeasible for an experiment. Observational research can test its own clinical hypotheses, and observational studies also
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F Kury, V Huser - **OHDSI** Symposium, October 2015, 2015 - researchgate.net
Abstract The data made available by the US Centers for Medicare & Medicaid Services (CMS) through the Virtual Research Data Center (VRDC) represent a considerable portion of the total US population and spending on healthcare. The volume of the data, and the
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emerge network
ELECTRONIC MEDICAL RECORDS AND GENOMICS

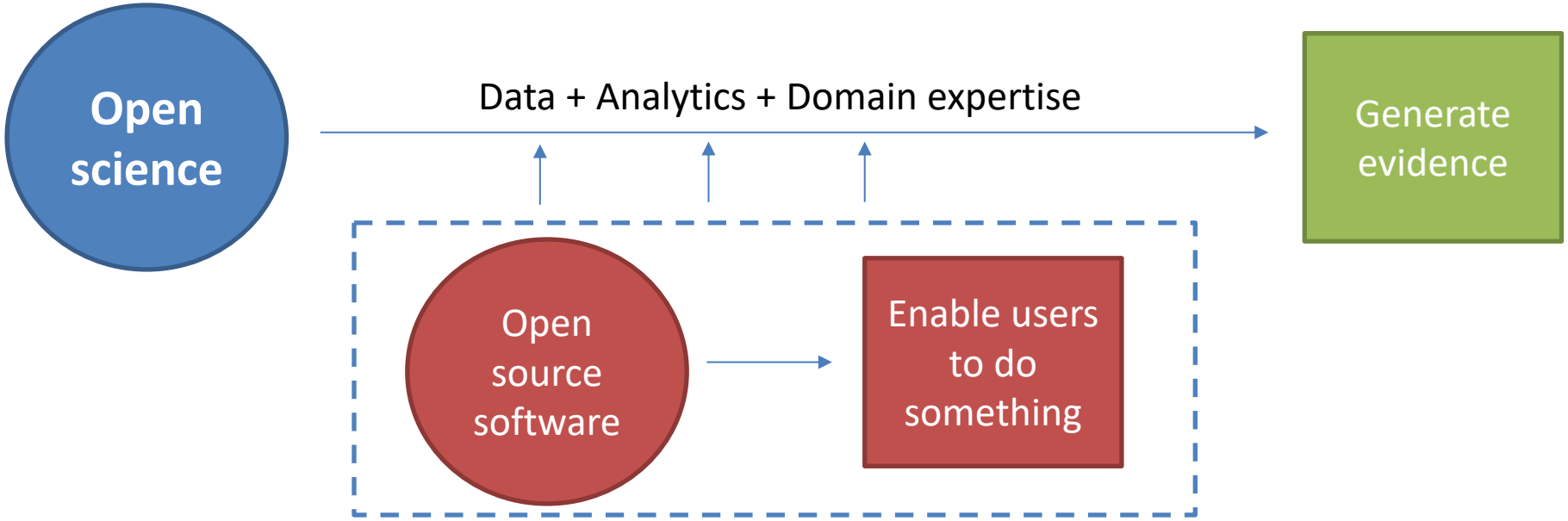
FDA U.S. FOOD & DRUG ADMINISTRATION

NIH National Institutes of Health
All of Us Research Program

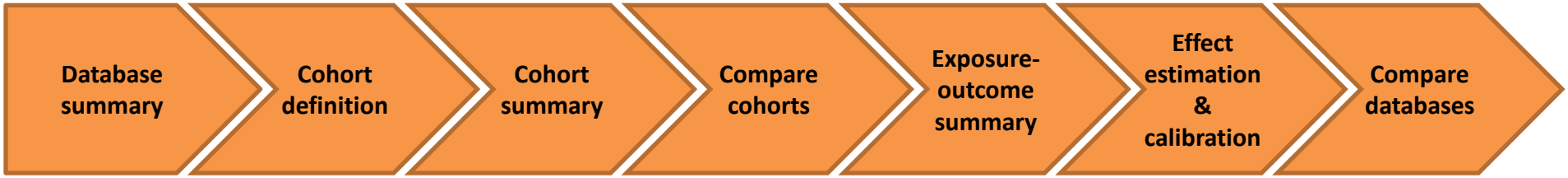
NIH NATIONAL CANCER INSTITUTE

imi innovative medicines initiative

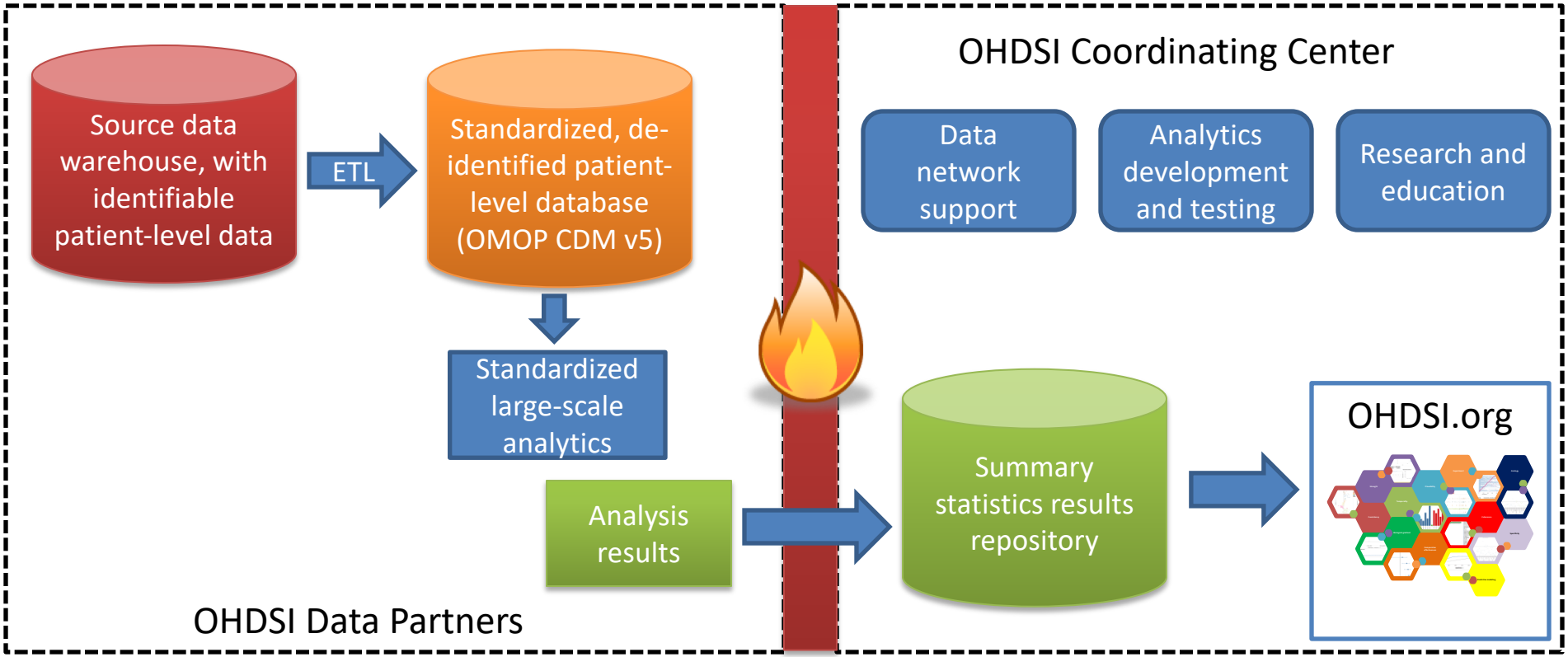
Open Science



Standardized, transparent workflows

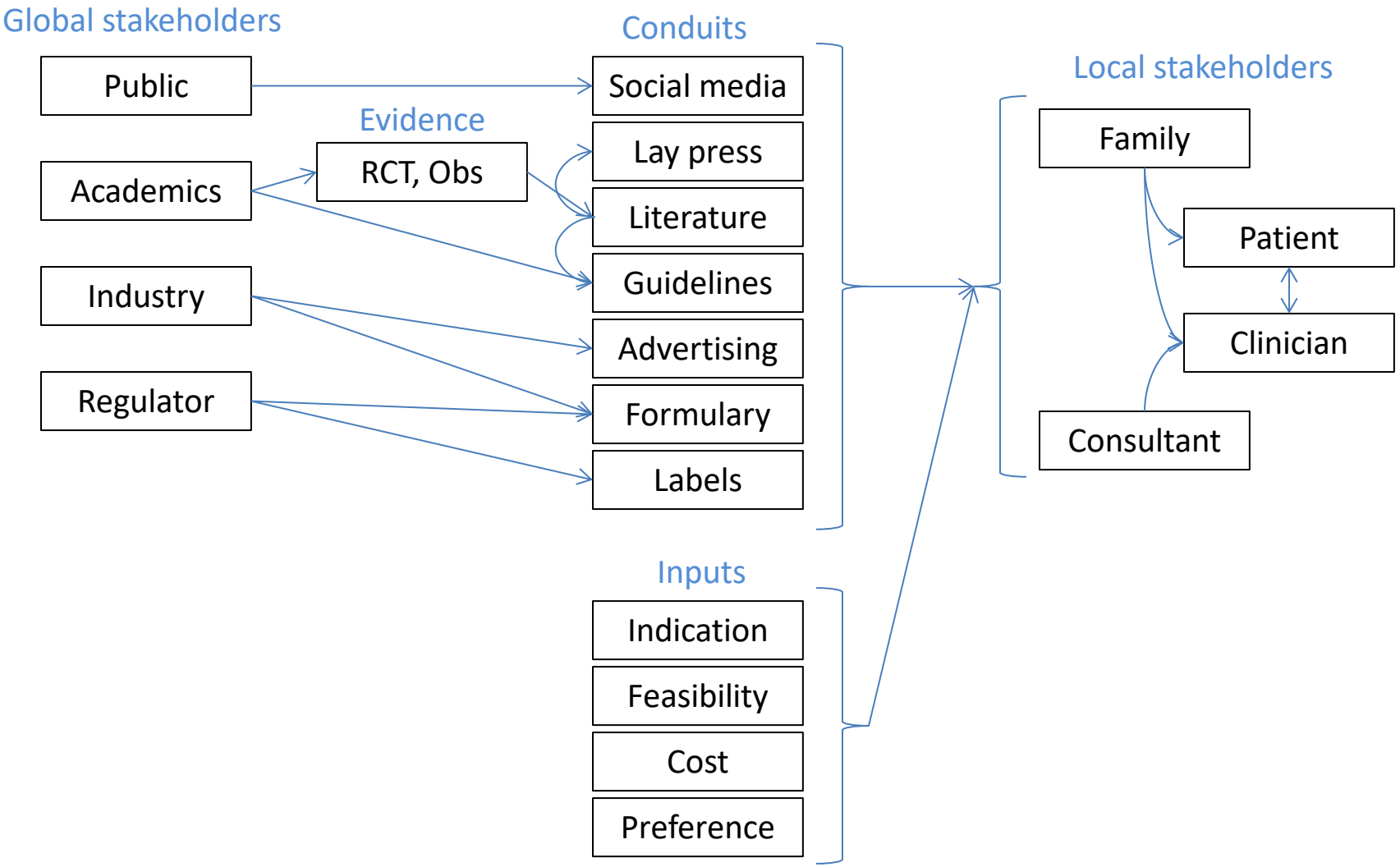


How OHDSI works



OHDSI in Action

Treatment Pathways

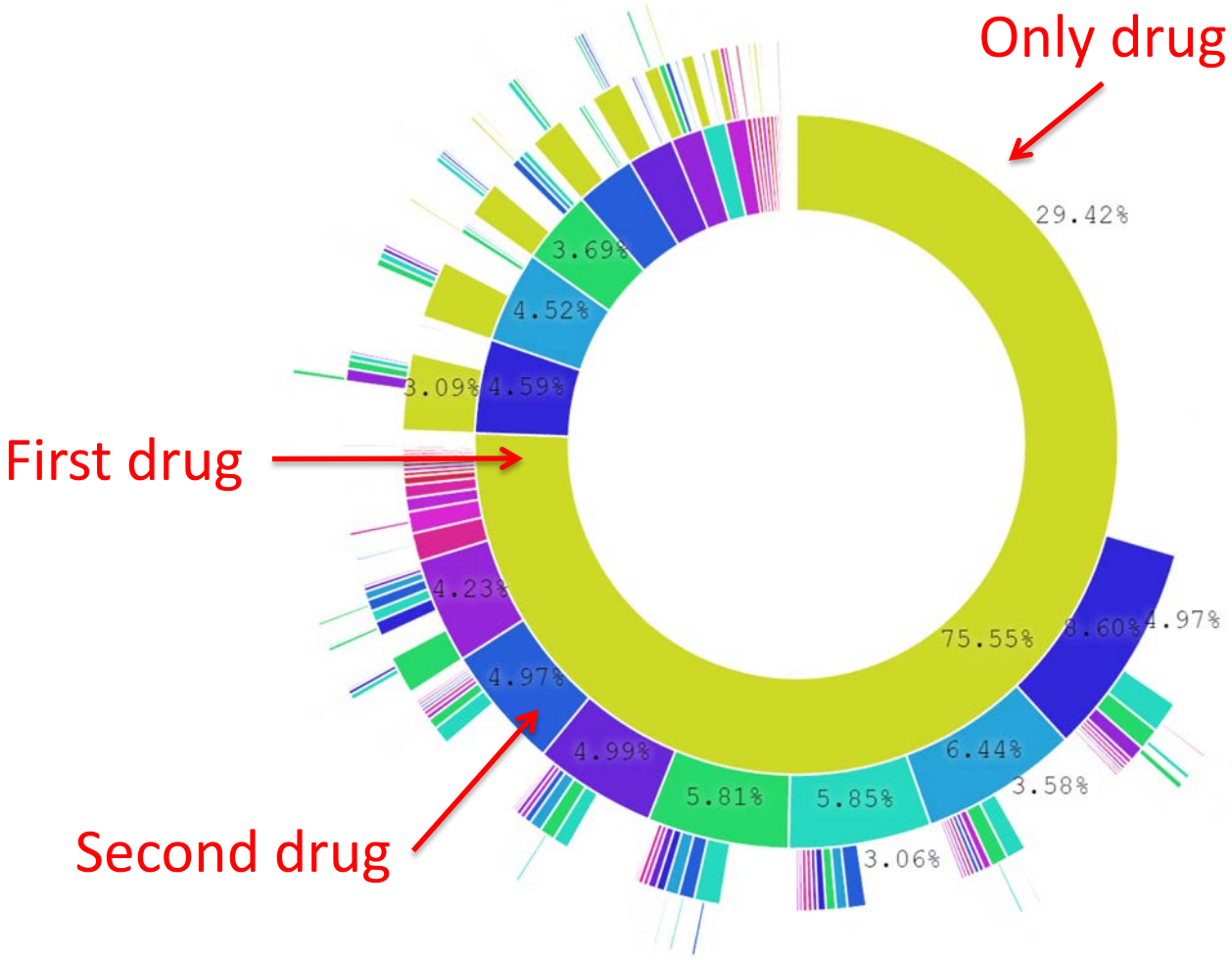


OHDSI partners for this query (250M)

Abbre-viation	Name	Description	Population, millions
AUSOM	Ajou University School of Medicine	South Korea; inpatient hospital EHR	2
CCAE	MarketScan Commercial Claims and Encounters	US private-payer claims	119
CPRD	UK Clinical Practice Research Datalink	UK; EHR from general practice	11
CUMC	Columbia University Medical Center	US; inpatient EHR	4
GE	GE Centricity	US; outpatient EHR	33
INPC	Regenstrief Institute, Indiana Network for Patient Care	US; integrated health exchange	15
JMDC	Japan Medical Data Center	Japan; private-payer claims	3
MDCD	MarketScan Medicaid Multi-State	US; public-payer claims	17
MDCR	MarketScan Medicare Supplemental and Coordination of Benefits	US; private and public-payer claims	9
OPTUM	Optum ClinFormatics	US; private-payer claims	40
STRIDE	Stanford Translational Research Integrated Database Environment	US; inpatient EHR	2
HKU	Hong Kong University	Hong Kong; EHR	1

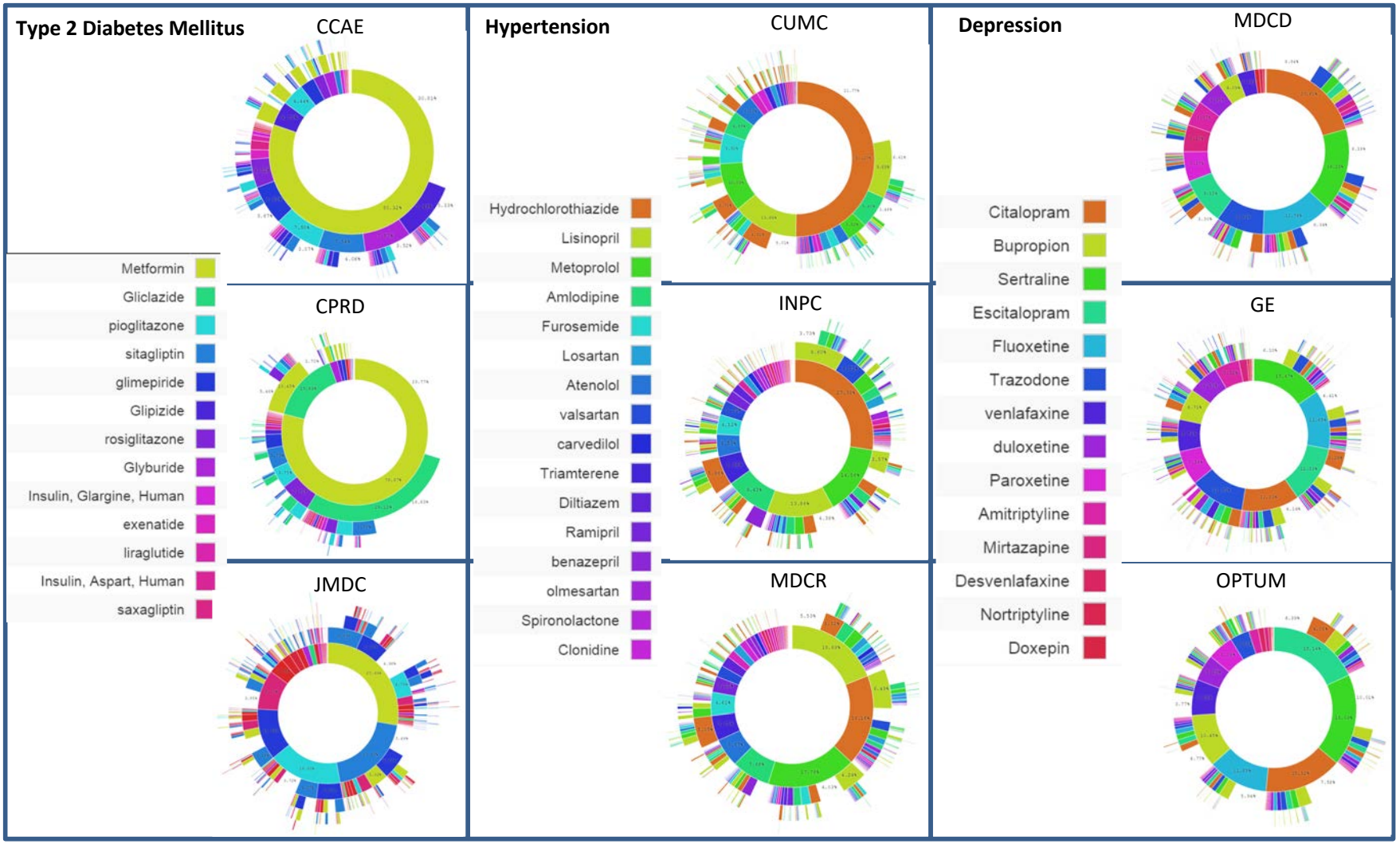
Treatment pathways for diabetes

T2DM : All databases

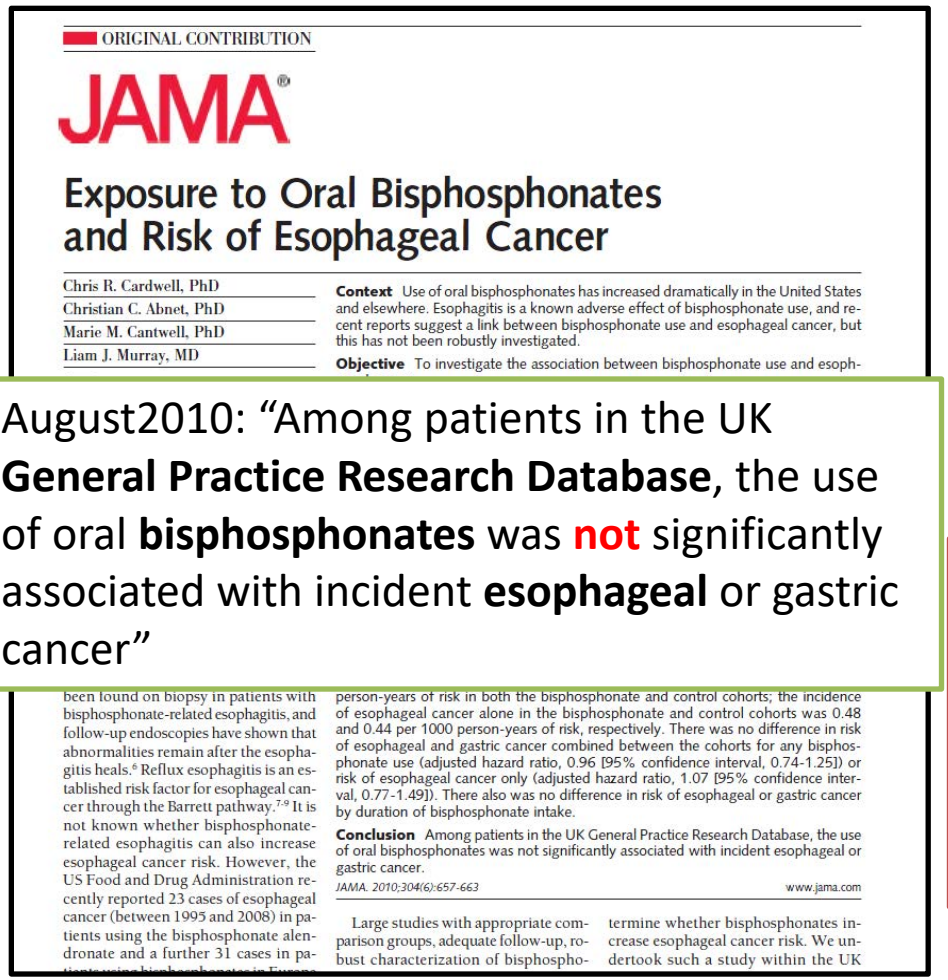


- Metformin
- pioglitazone
- sitagliptin
- Glipizide
- glimepiride
- Gliclazide
- Glyburide
- rosiglitazone
- Insulin, Glargine, Human
- exenatide
- Insulin, Aspart, Human
- liraglutide
- saxagliptin
- Insulin, Lispro, Human
- Glucose
- Insulin, Isophane, Human

OHDSI's first large scale study



Drawing reproducible conclusions



ORIGINAL CONTRIBUTION

JAMA®

Exposure to Oral Bisphosphonates and Risk of Esophageal Cancer

Chris R. Cardwell, PhD
Christian C. Abnet, PhD
Marie M. Cantwell, PhD
Liam J. Murray, MD

Context Use of oral bisphosphonates has increased dramatically in the United States and elsewhere. Esophagitis is a known adverse effect of bisphosphonate use, and recent reports suggest a link between bisphosphonate use and esophageal cancer, but this has not been robustly investigated.

Objective To investigate the association between bisphosphonate use and esoph-

August2010: "Among patients in the UK **General Practice Research Database**, the use of oral **bisphosphonates** was **not** significantly associated with incident **esophageal** or gastric cancer"

been found on biopsy in patients with bisphosphonate-related esophagitis, and follow-up endoscopies have shown that abnormalities remain after the esophagitis heals.[6] Reflux esophagitis is an established risk factor for esophageal cancer through the Barrett pathway.[7-9] It is not known whether bisphosphonate-related esophagitis can also increase esophageal cancer risk. However, the US Food and Drug Administration recently reported 23 cases of esophageal cancer (between 1995 and 2008) in patients using the bisphosphonate alendronate and a further 31 cases in pa-

person-years of risk in both the bisphosphonate and control cohorts; the incidence of esophageal cancer alone in the bisphosphonate and control cohorts was 0.48 and 0.44 per 1000 person-years of risk, respectively. There was no difference in risk of esophageal and gastric cancer combined between the cohorts for any bisphosphonate use (adjusted hazard ratio, 0.96 [95% confidence interval, 0.74-1.25]) or risk of esophageal cancer only (adjusted hazard ratio, 1.07 [95% confidence interval, 0.77-1.49]). There also was no difference in risk of esophageal or gastric cancer by duration of bisphosphonate intake.

Conclusion Among patients in the UK General Practice Research Database, the use of oral bisphosphonates was not significantly associated with incident esophageal or gastric cancer.

JAMA. 2010;304(6):657-663 www.jama.com

Large studies with appropriate comparison groups, adequate follow-up, robust characterization of bisphospho- termine whether bisphosphonates increase esophageal cancer risk. We undertook such a study within the UK

BMJ

RESEARCH

Oral bisphosphonates and risk of cancer of oesophagus, stomach, and colorectum: case-control analysis within a UK primary care cohort

Jane Green, clinical epidemiologist,[1] Gabriela Czanner, statistician,[1] Gillian Reeves, statistical epidemiologist,[1] Joanna Watson, epidemiologist,[1] Lesley Wise, manager, Pharmacoepidemiology Research and Intelligence Unit,[2] Valerie Beral, professor of cancer epidemiology[1]

[1]Cancer Epidemiology Unit, University of Oxford, Oxford OX3 7LF
[2]Medicines and Healthcare products Regulatory Agency, Pharmacoepidemiology Research Unit, London SW8 5NQ
Correspondence to: J Green jane.green@ceu.ox.ac.uk

Cite this as: BMJ 2010;341:c4444
doi:10.1136/bmj.c4444

ABSTRACT

Objective To examine the hypothesis that risk of oesophageal, but not of gastric or colorectal, cancer is increased in users of oral bisphosphonates.

Design Nested case-control analysis within a primary care cohort of about 6 million people in the UK, with prospectively recorded information on prescribing of bisphosphonates.

Setting UK General Practice Research Database cohort.

Participants Men and women aged 40 years or over—

Conclusions The risk of oesophageal cancer increased with 10 or more prescriptions for oral bisphosphonates and with prescriptions over about a five year period. In Europe and North America, the incidence of oesophageal cancer at age 60-79 is typically 1 per 1000 population over five years, and this is estimated to increase to about 2 per 1000 with five years' use of oral bisphosphonates.

INTRODUCTION

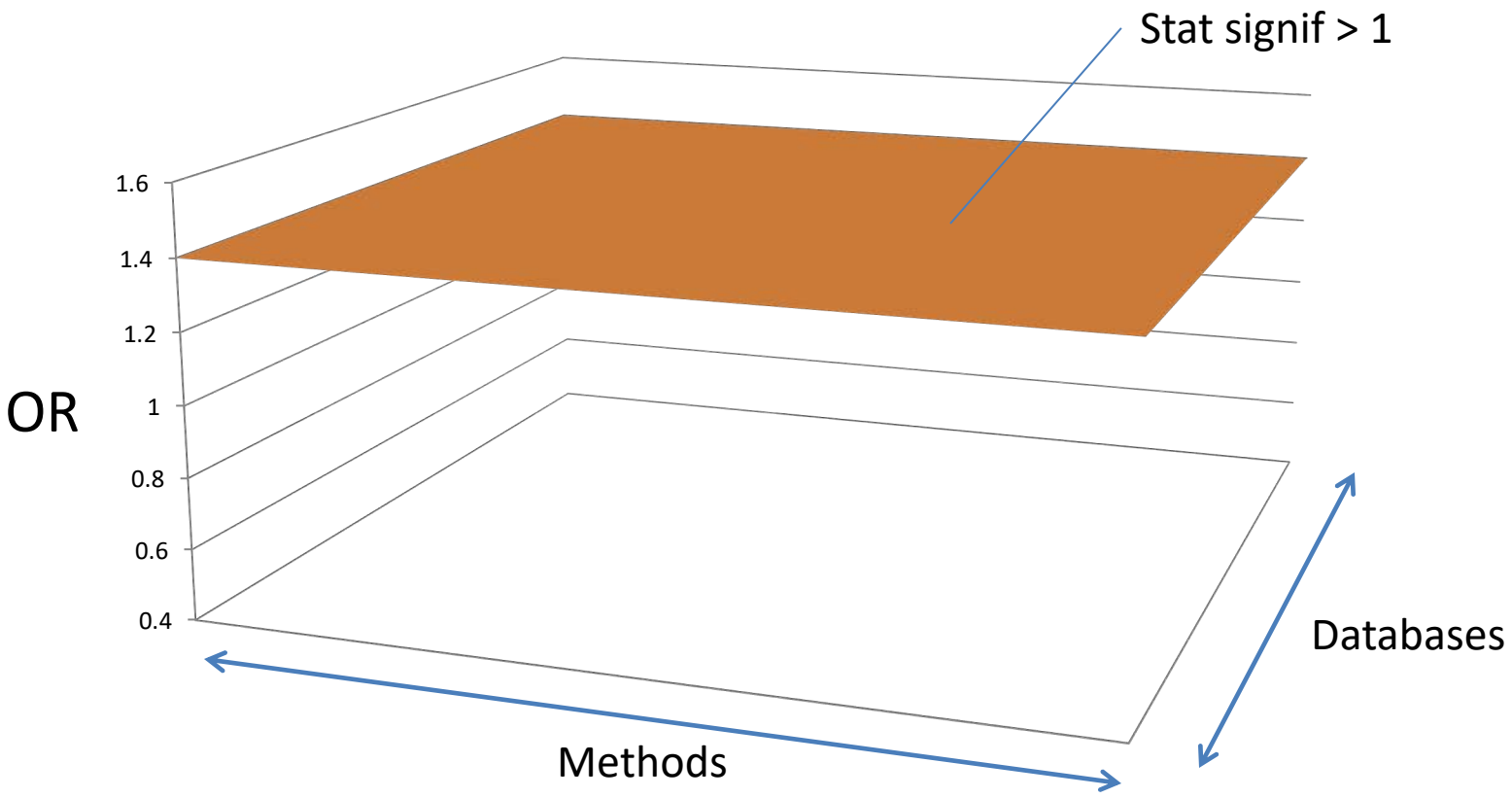
Adverse gastrointestinal effects are common among

Sept2010: "In this large nested case-control study within a UK cohort [**General Practice Research Database**], we found a significantly increased risk of **oesophageal** cancer in people with previous prescriptions for oral **bisphosphonates**"

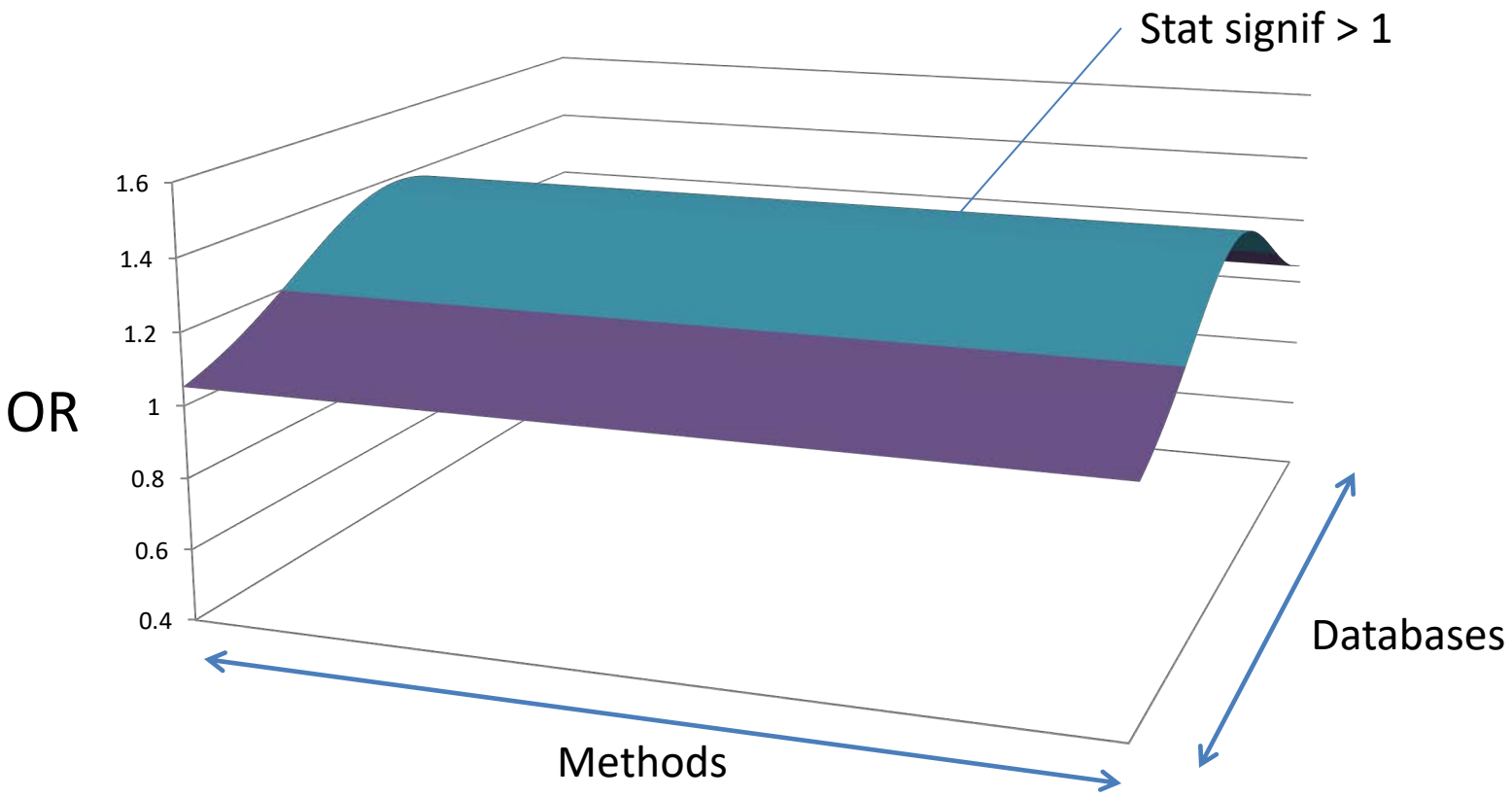
corticosteroids. Cancers of the stomach and colorectum were not associated with prescription of bisphosphonate: relative risks for one or more versus no prescriptions were

style data. General Practice Research Database prescription data have been shown to be virtually complete, and the data on incidence of cancer (based on

Distribution of possible results for one hypothesis



Distribution of possible results for one hypothesis



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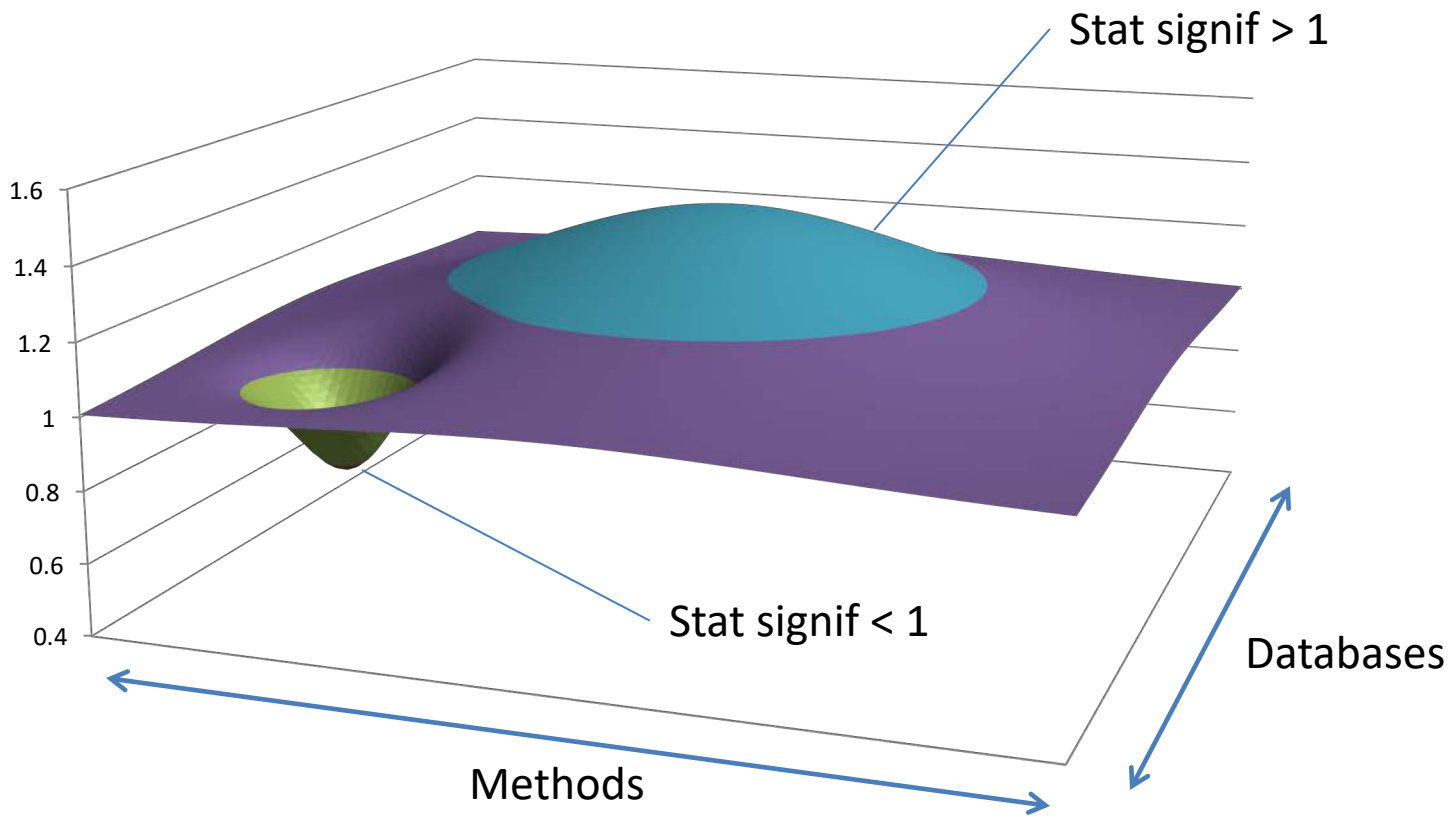

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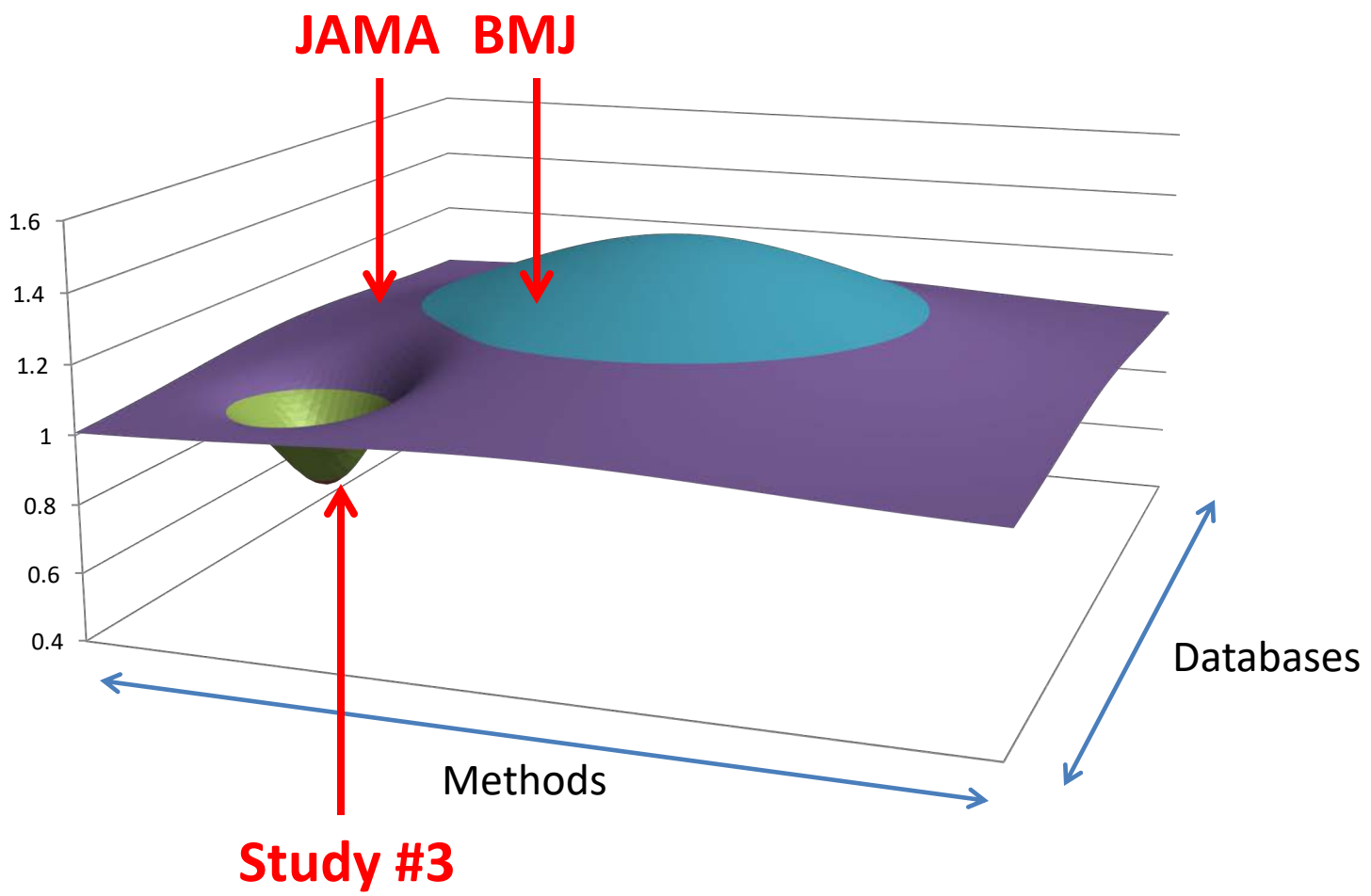
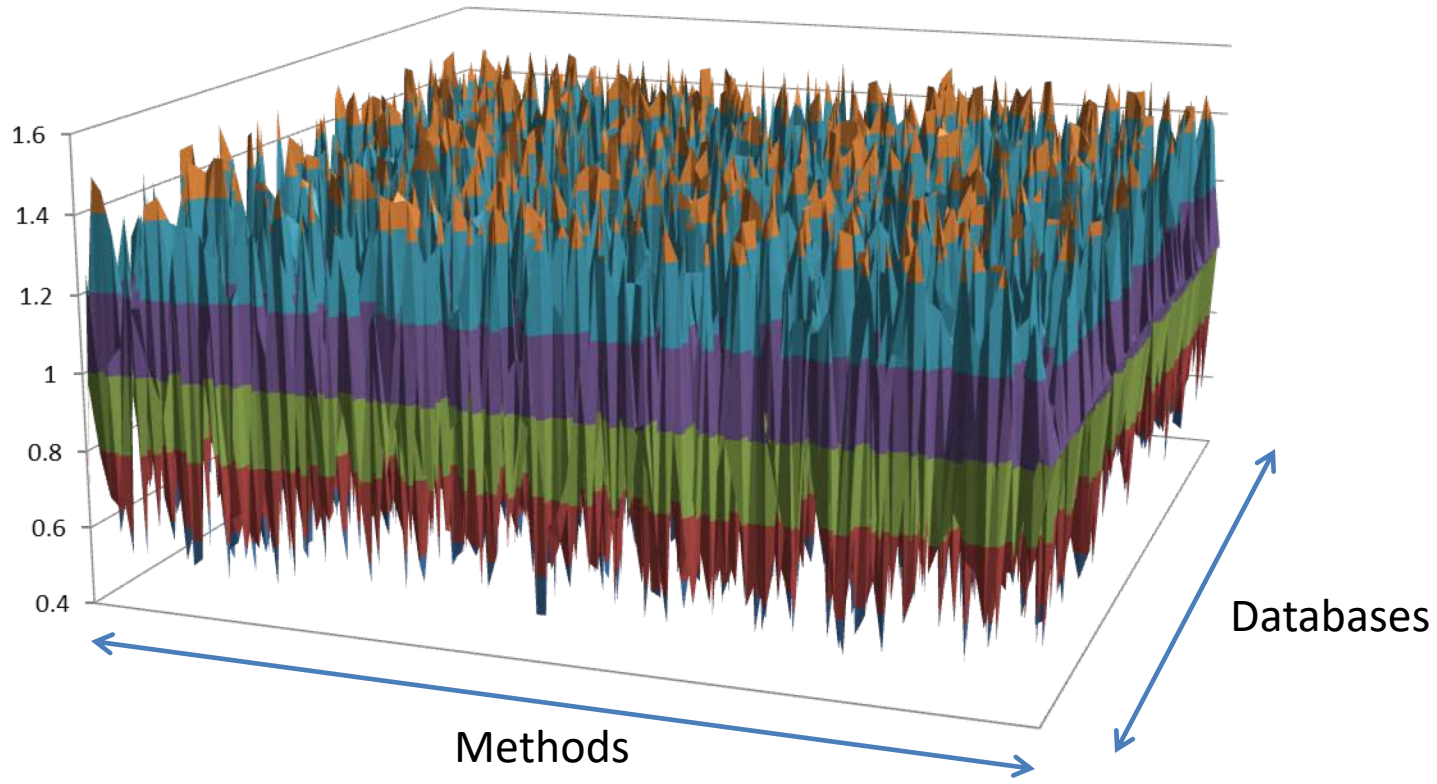


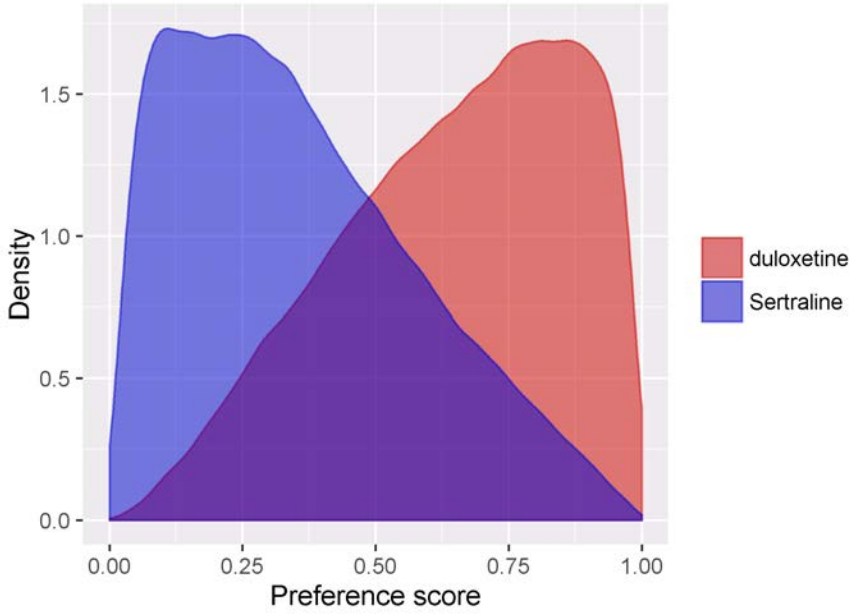
Distribution of possible results for one hypothesis

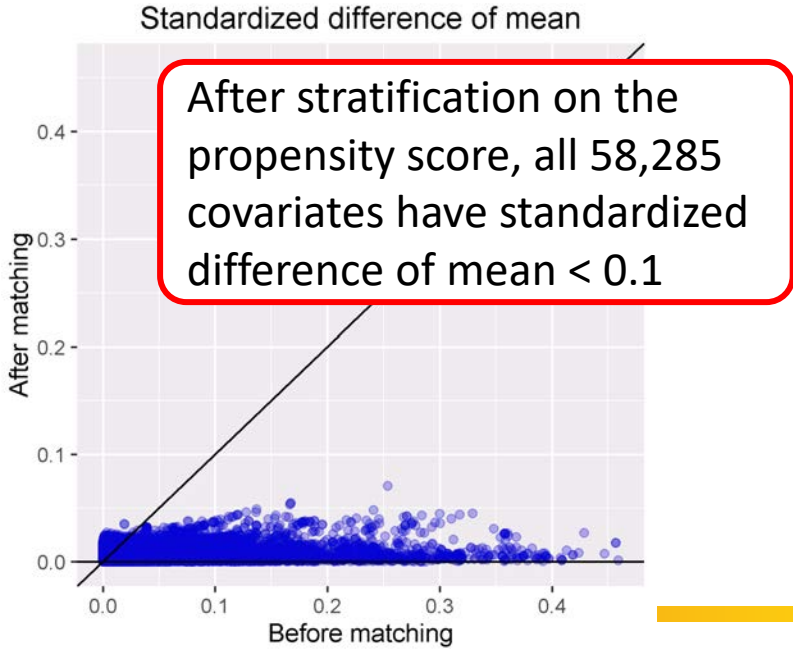
OR



Reproducible research

1. **Address confounding that is measured**
   - **Propensity stratification**
   - ***Systematic* (not manual) variable selection**
     - **Balance 58,285 variables ("Table 1")**



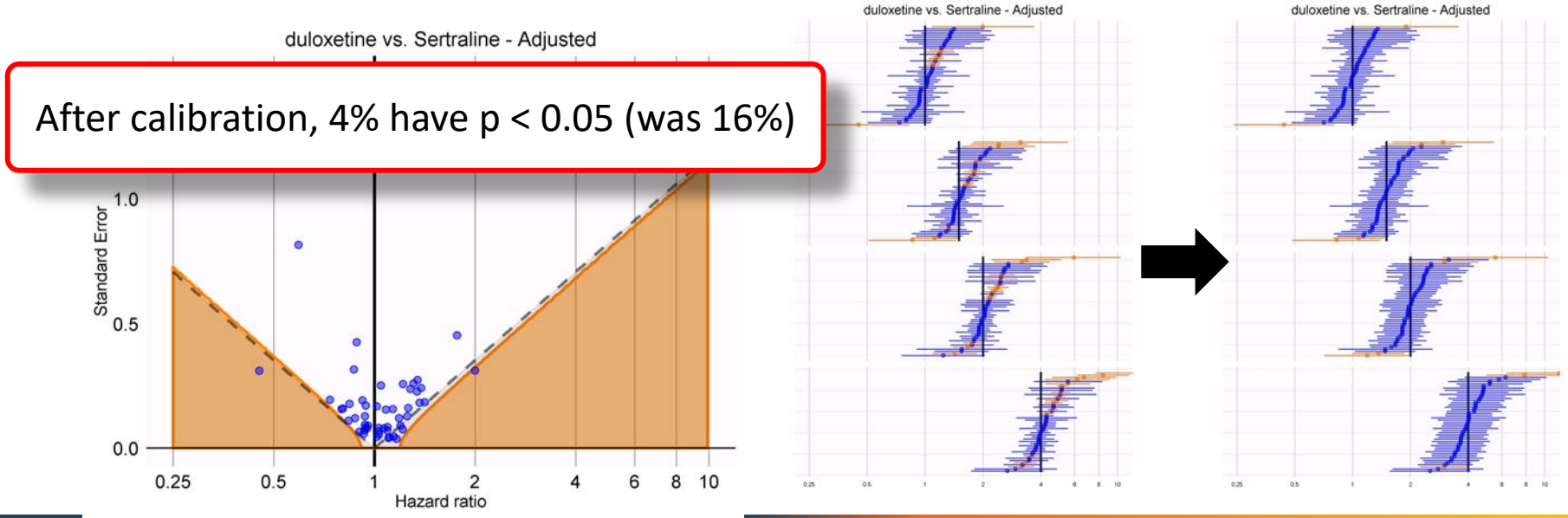


After stratification on the propensity score, all 58,285 covariates have standardized difference of mean < 0.1

Reproducible research

2. Unmeasured (residual) **confounding**

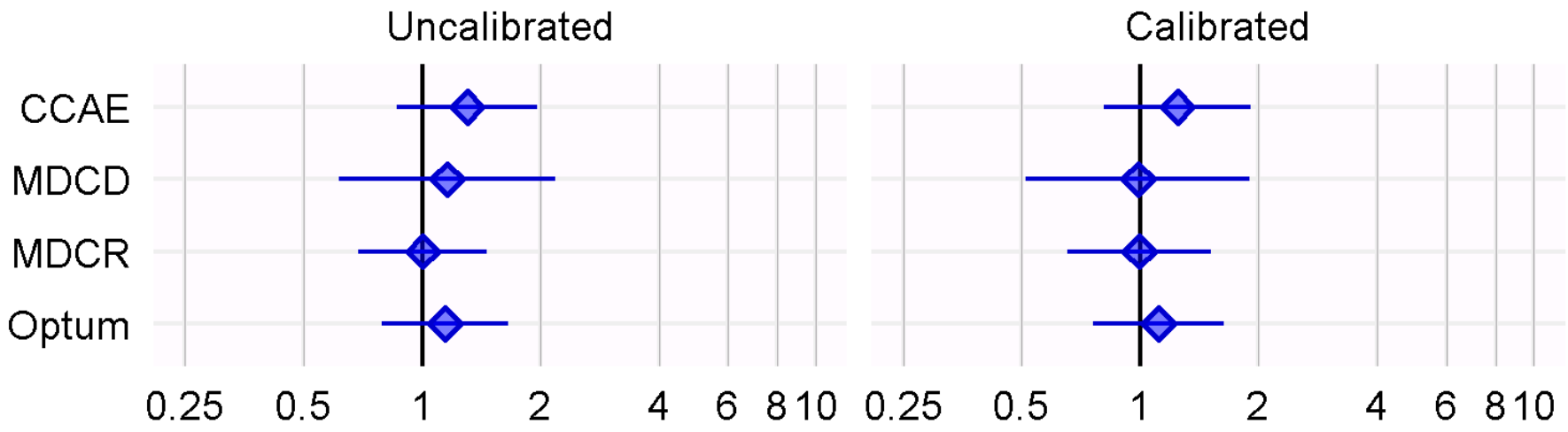
- **Confidence interval calibration**
  - **Adjust for all uncertainty, not just sampling**
- **Many negative controls**
  - **Unique to OHDSI** (PNAS in press)



Reproducible research

3. Multiple databases, locations, practice types

- **Exploit international OHDSI network**



Reproducible research

4. Open: publish all

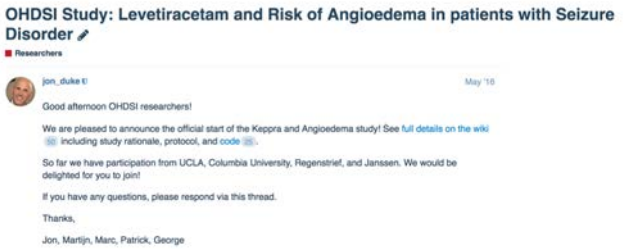
- **Hypotheses**
- **Code**
- **Parameters**
- **Runs**

Drawing reproducible conclusions

Potential Signals of Serious Risks/New Safety Information Identified by the FDA Adverse Event Reporting System (FAERS) between October - December 2015

Keppra (levetiracetam) tablet, oral solution, injection	Angioedema	FDA is evaluating the need for regulatory action.

- Protocol completed, code tested, study announced



OHDSI Study: Levetiracetam and Risk of Angioedema in patients with Seizure Disorder

Researchers

jon_duke t! May '16

Good afternoon OHDSI researchers!

We are pleased to announce the official start of the Keppra and Angioedema study! See full details on the wiki including study rationale, protocol, and code.

So far we have participation from UCLA, Columbia University, Regenstrief, and Janssen. We would be delighted for you to join!

If you have any questions, please respond via this thread.

Thanks,

Jon, Martijn, Marc, Patrick, George

- 50 viewed protocol, 25 viewed the code, and 7 sites ran the code on 10 databases (5 claims / 5 EHR), 59,367 levetiracetam patients matched with 74,550 phenytoin patients

Drawing reproducible conclusions

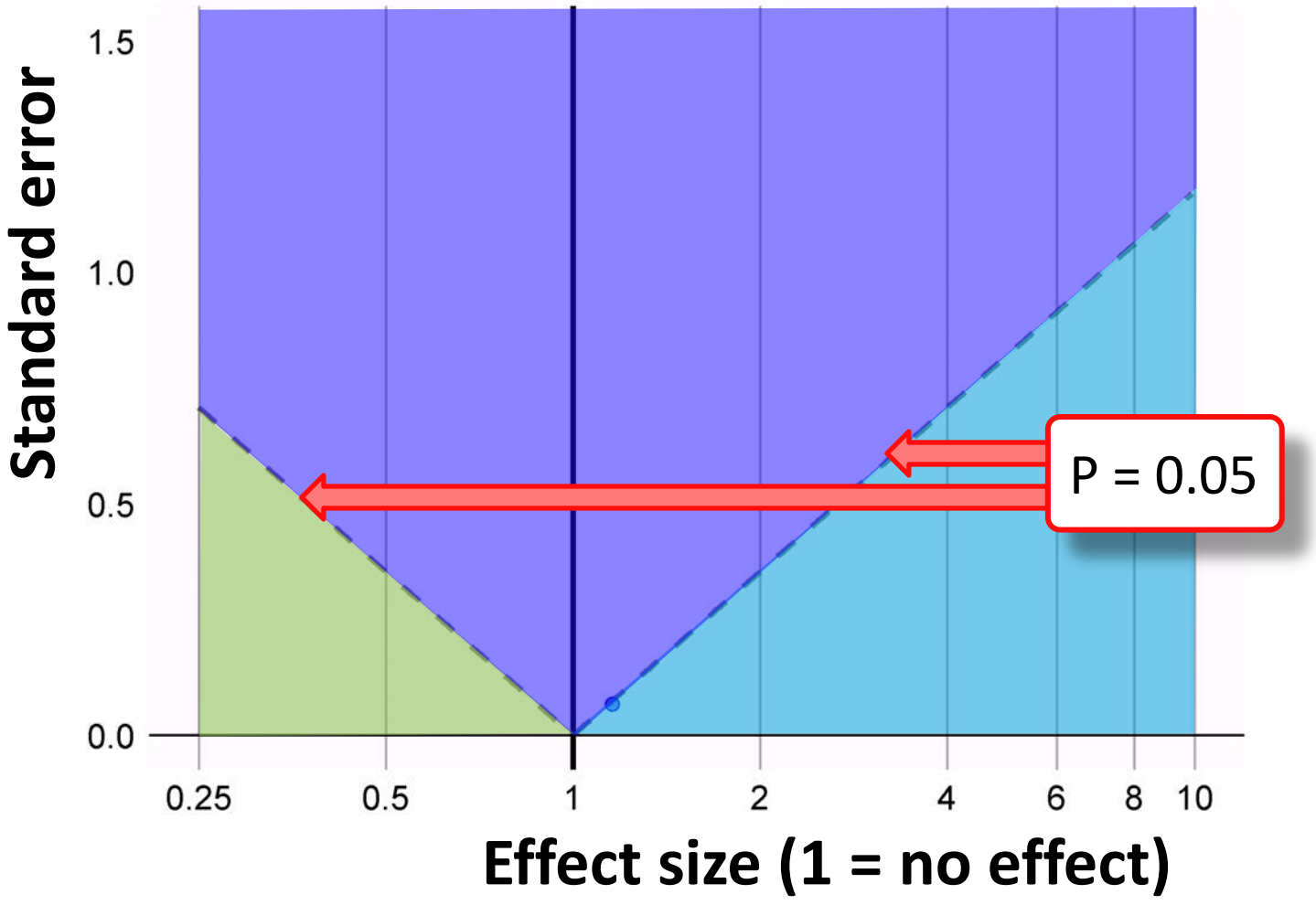
No evidence of increased angioedema risk with levetiracetam use compared with phenytoin use

"The study is focused, appears well designed, and provides new insight that should be of interest to clinicians and regulators... This is an important contribution to improved pharmacovigilance."

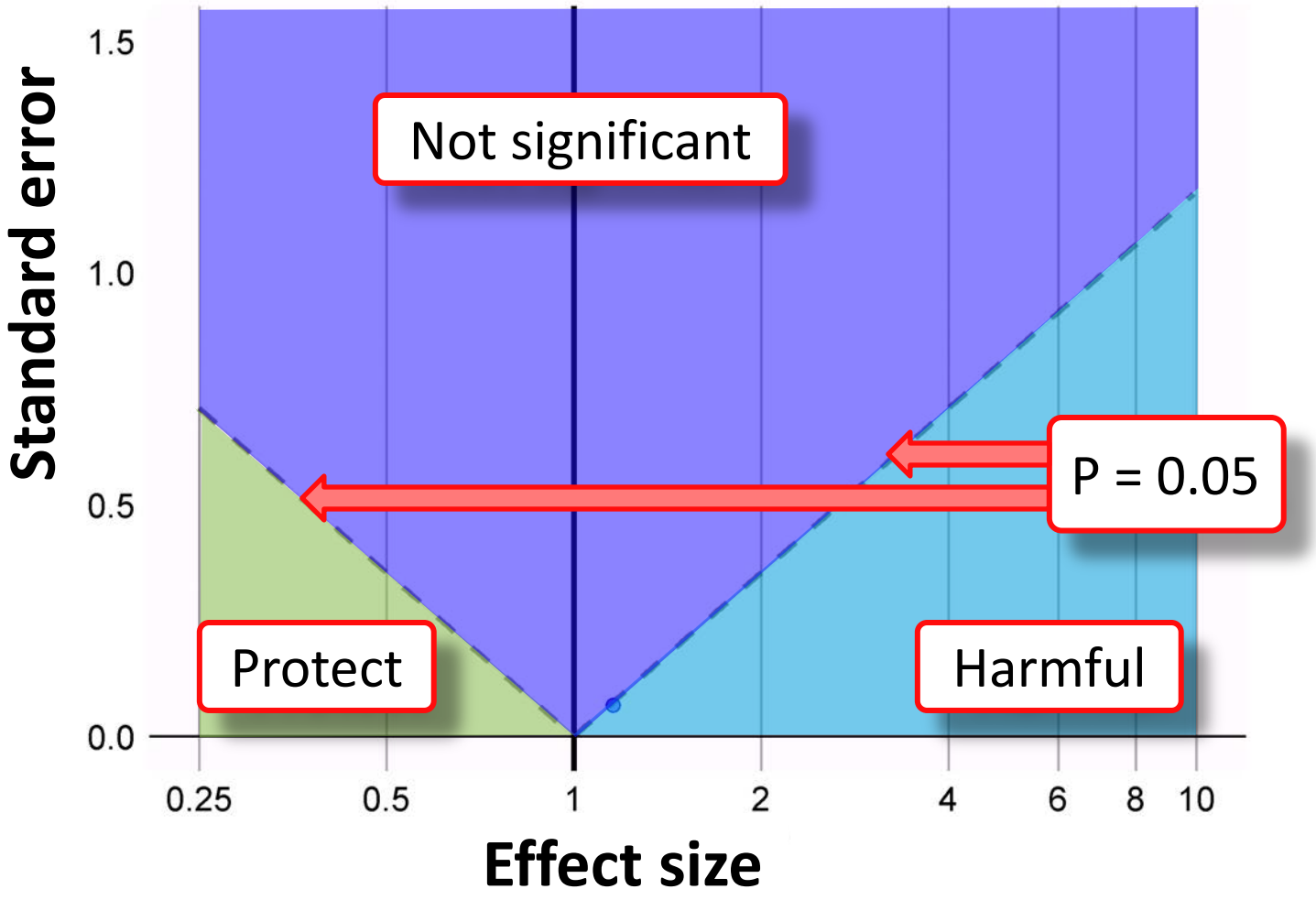
Add word to title, move diagram from supplement to body

How can we improve the literature

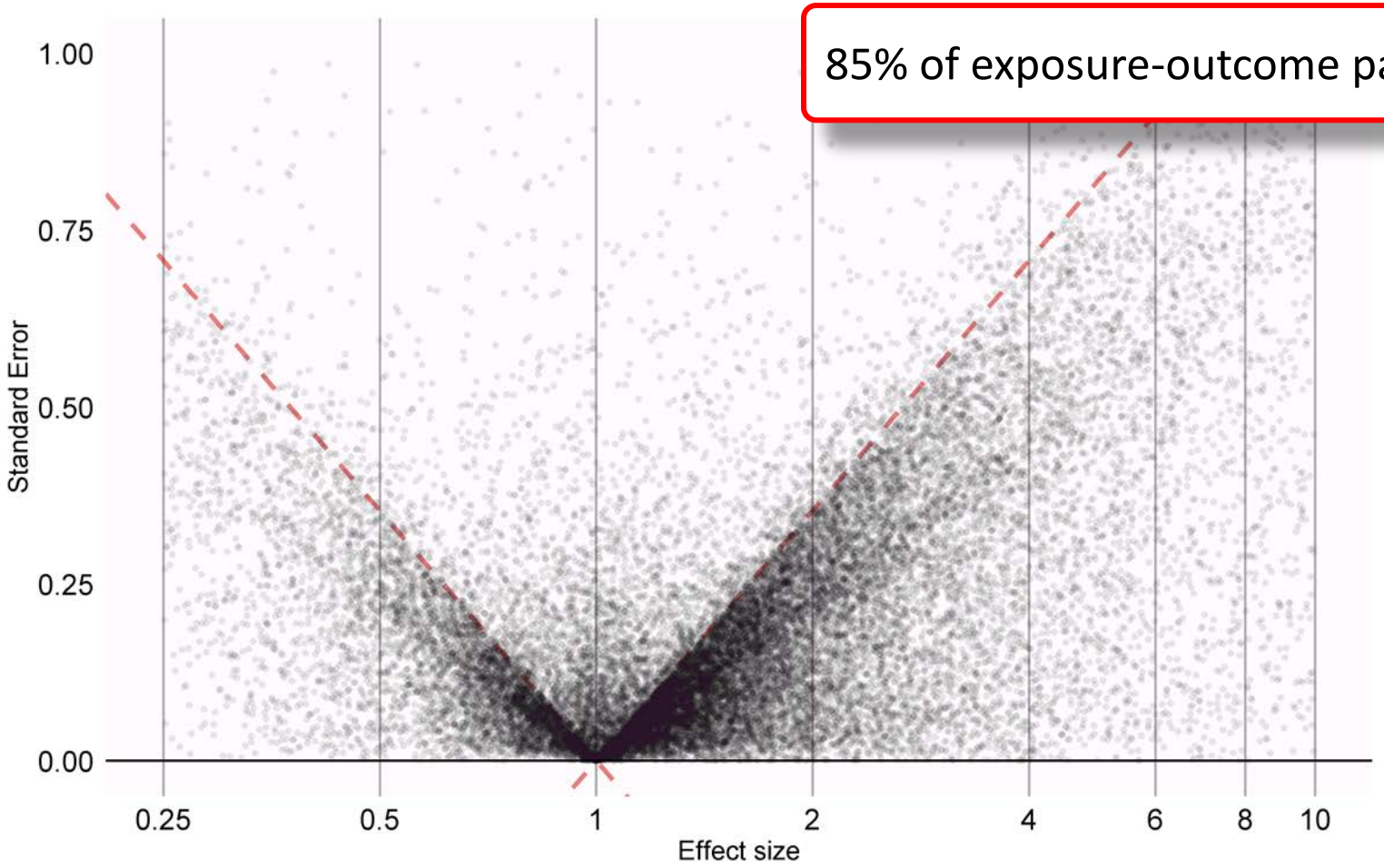
Drawing reproducible conclusions



Drawing reproducible conclusions



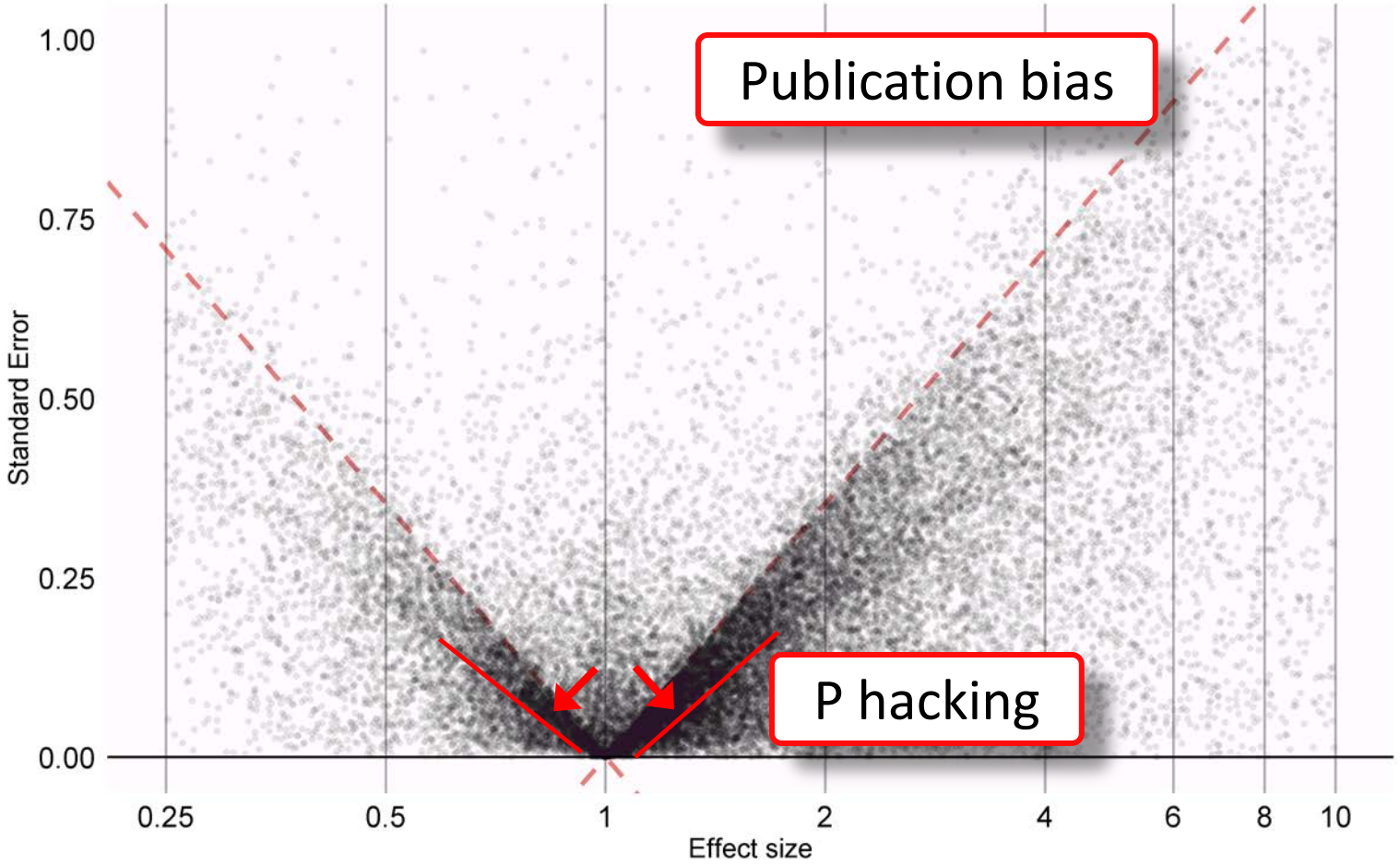
Drawing reproducible conclusions



85% of exposure-outcome pairs significant

29,982 estimates
11,758 papers

Drawing reproducible conclusions



29,982 estimates
11,758 papers

5. Carry out on aligned hypotheses at scale

Duloxetine vs. Sertraline for these 22 outcomes:

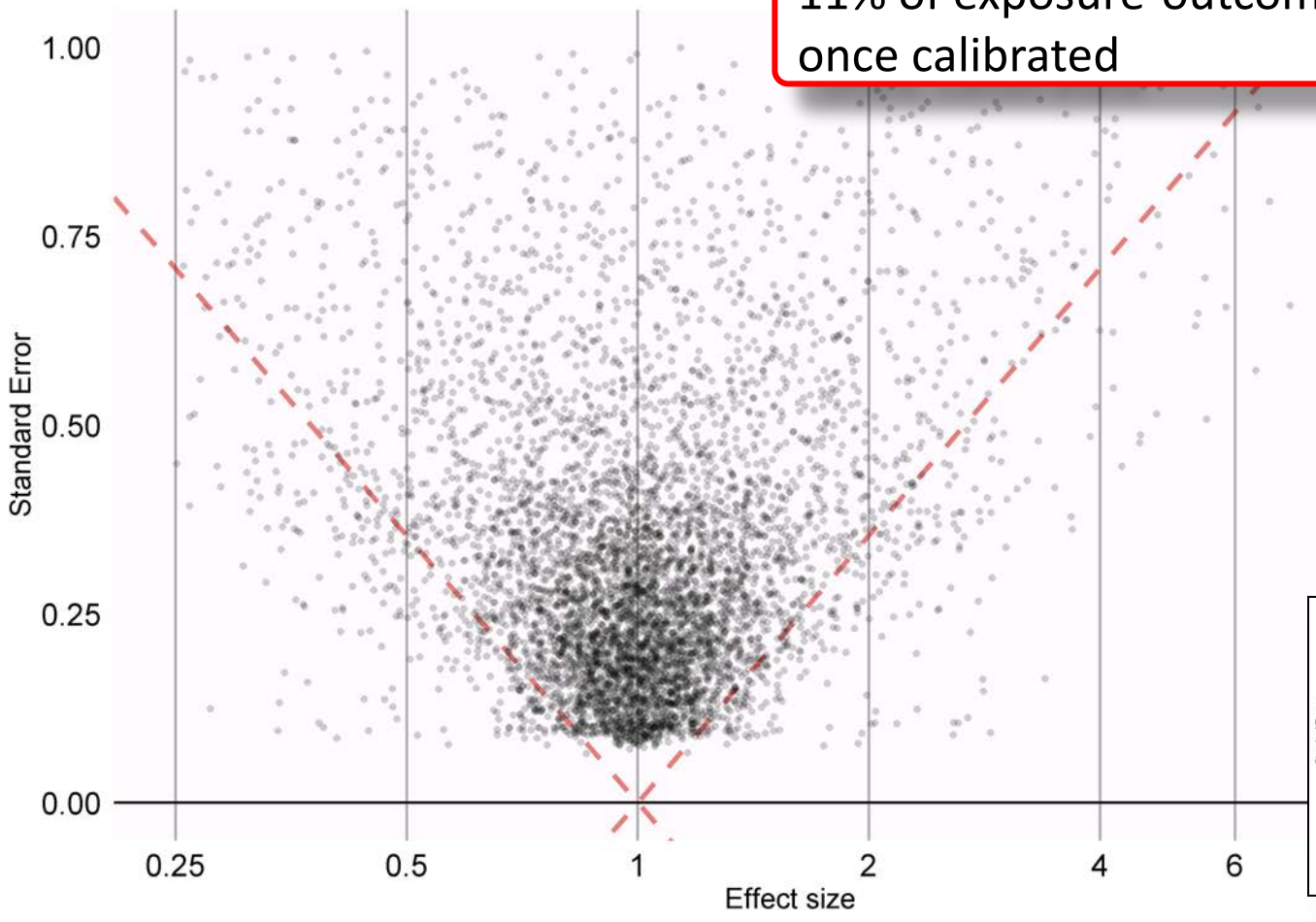
Acute liver injury	Hypotension
Acute myocardial infarction	Hypothyroidism
Alopecia	Insomnia
Constipation	Nausea
Decreased libido	Open-angle glaucoma
Delirium	Seizure
Diarrhea	Stroke
Fracture	Suicide and suicidal ideation
Gastrointestinal hemorrhage	Tinnitus
Hyperprolactinemia	Ventricular arrhythmia and sudden cardiac death
Hyponatremia	Vertigo

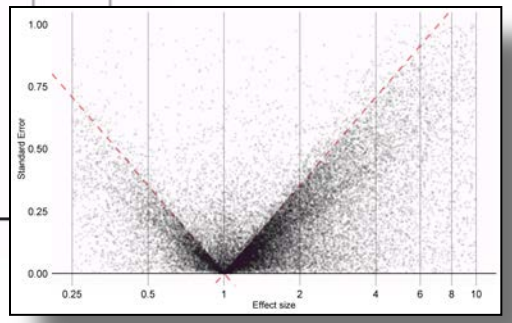
Many treatments at once

Type	Class	Treatment
Drug	Atypical	Bupropion
Drug	Atypical	Mirtazapine
Procedure	ECT	Electroconvulsive therapy
Procedure	Psychotherapy	Psychotherapy
Drug	SARI	Trazodone
Drug	SNRI	Desvenlafaxine
Drug	SNRI	duloxetine
Drug	SNRI	venlafaxine
Drug	SSRI	Citalopram
Drug	SSRI	Escitalopram
Drug	SSRI	Fluoxetine
Drug	SSRI	Paroxetine
Drug	SSRI	Sertraline
Drug	SSRI	vilazodone
Drug	TCA	Amitriptyline
Drug	TCA	Doxepin
Drug	TCA	Nortriptyline

Drawing reproducible conclusions

11% of exposure-outcome pairs are significant once calibrated





Large-scale estimation for depression

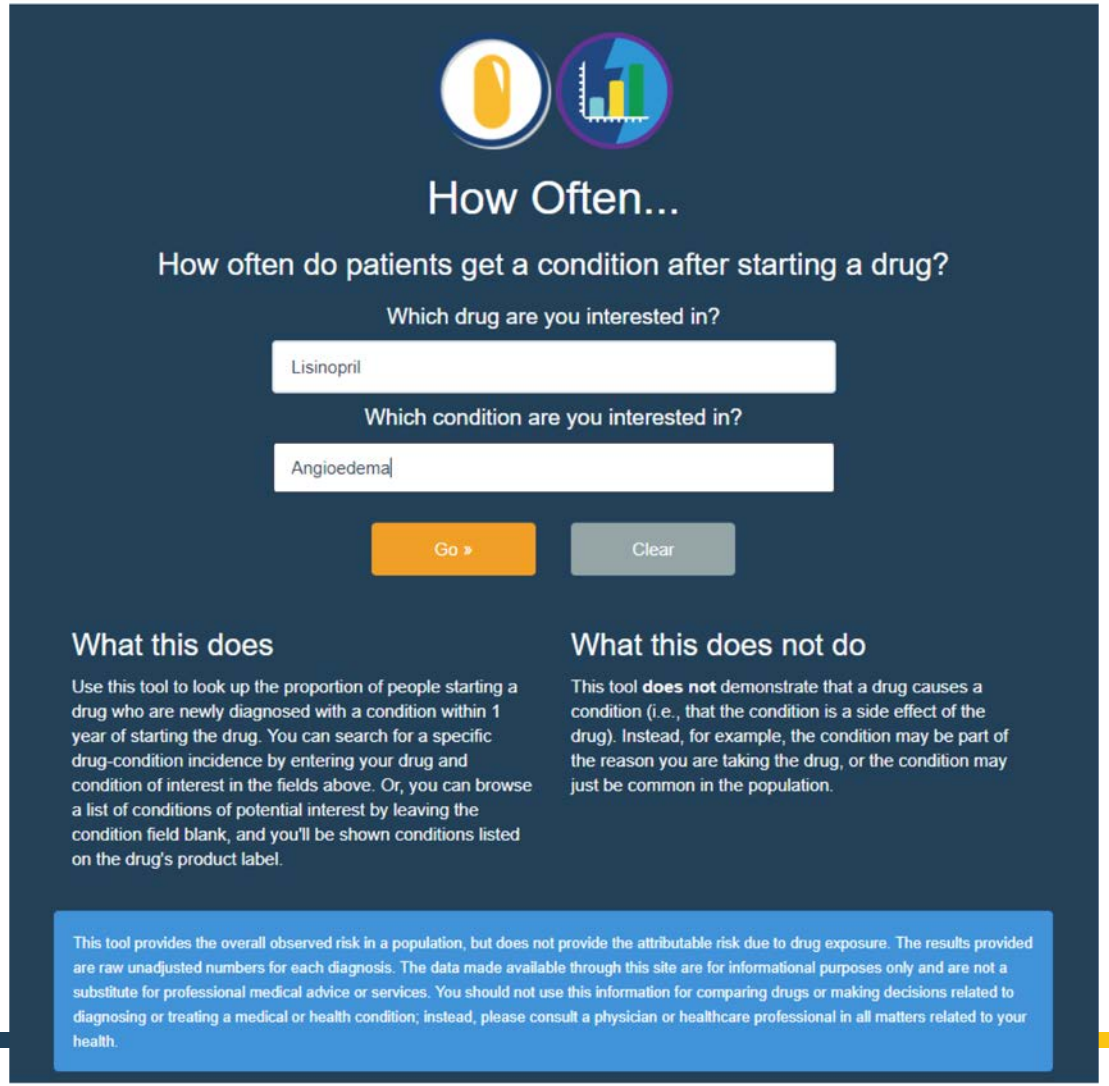
- How do we use it? Troll for effects?
- Professor what should I study this year?
  - Simple, go to Pubmed and find the smallest p-values in the literature; surely those must be the most significant things to study
- Which is safer?
  - Seizure in 0.0000000001 to 0.0000000002 (p=0.00001)
  - Seizure in 0 to 0.2 (p=.45)
- Large-scale studies become the literature
  - Come with hypothesis and ask a question

Drawing reproducible conclusions

- Current literature is a data dredging machine
  - Dredging is not about how many things you test; it is about what you secretly throw away
- Open science approach effectively replaces the observational literature
- Collaborative open effort

howoften.org

- Incidence of side effects
  - Develop condition for first time after get drug
  - Within time at risk
- Any drug on the world market
- Any condition
- Absolute risk
  - Not causal (Characterization)
- On the Internet



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