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Columbia University Medical Center

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Thank you exhibitors!

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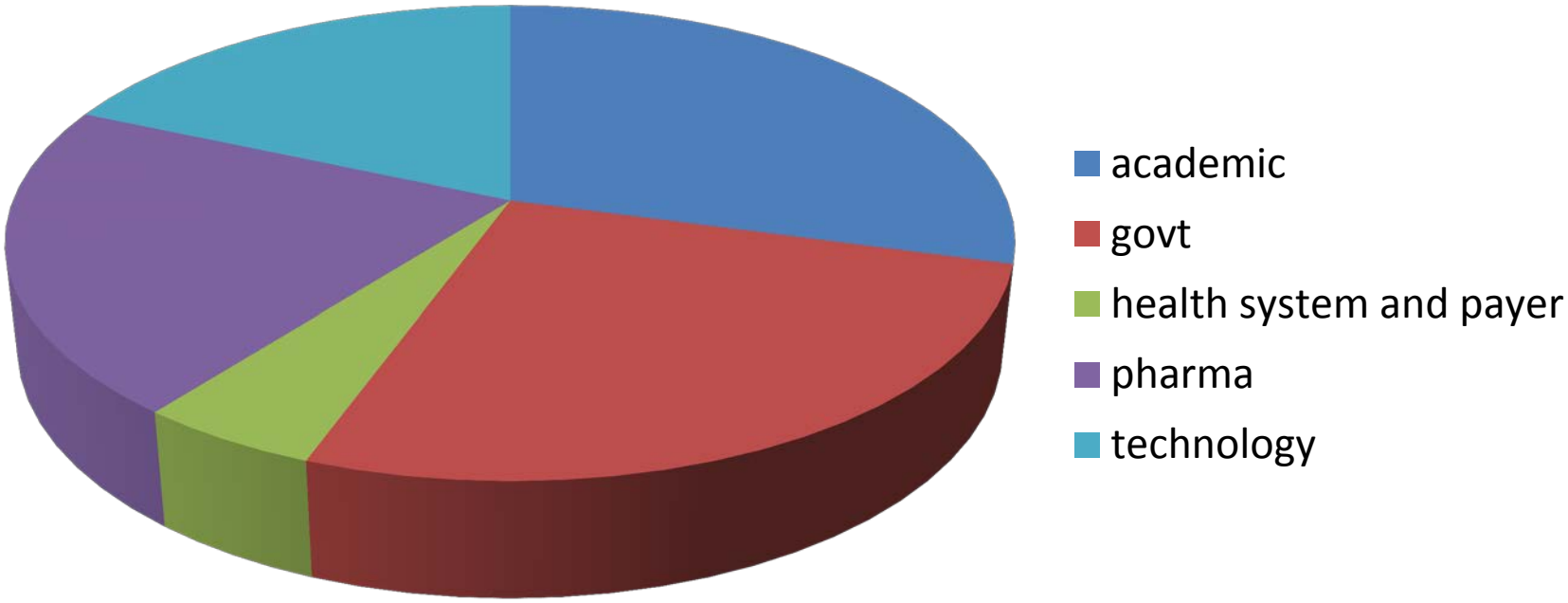
OHDSI Symposium 2016 Breakdown of participants

- 11 countries, 27 US states



Agenda

8:30 Welcome to the journey: OHDSI 2016
- George Hripcsak

9:00 OHDSI's journey toward reliable evidence generation and dissemination
- **The journey toward Clinical Characterization,** Patrick Ryan

9:45 (Break)
- **The journey toward Patient-Level Prediction,** Peter Rijnbeek
- **The journey toward Population-level Effect Estimation,** Martijn Schuemie

12:15 (Lunch)

12:45 OHDSI Collaborator Showcase: Sharing the journey across the community
- Observational data management, Analytics technology and infrastructure, Methodological research, Clinical applications in clinical characterization, population-level effect estimation, and patient-level prediction

2:45 Community Panel: Where are we on the journey right now? How did we get here?
- Kristin Feeney (moderator)
- Stephanie Reisinger, Michael Matheny, Rae Woong Park, Christian Reich, Adler Perotte

3:45 (Break)

4:00 Reaction Panel: What's our journey's destination? How do we get there?
- Jon Duke (moderator)
- Jianying Hu, Kristijan Kahler, Charles Bailey, Nigam Shah, Danica Marinac-Dabic

5:00 Oh, the places we'll go!
- Patrick Ryan

OHDSI's Mission

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

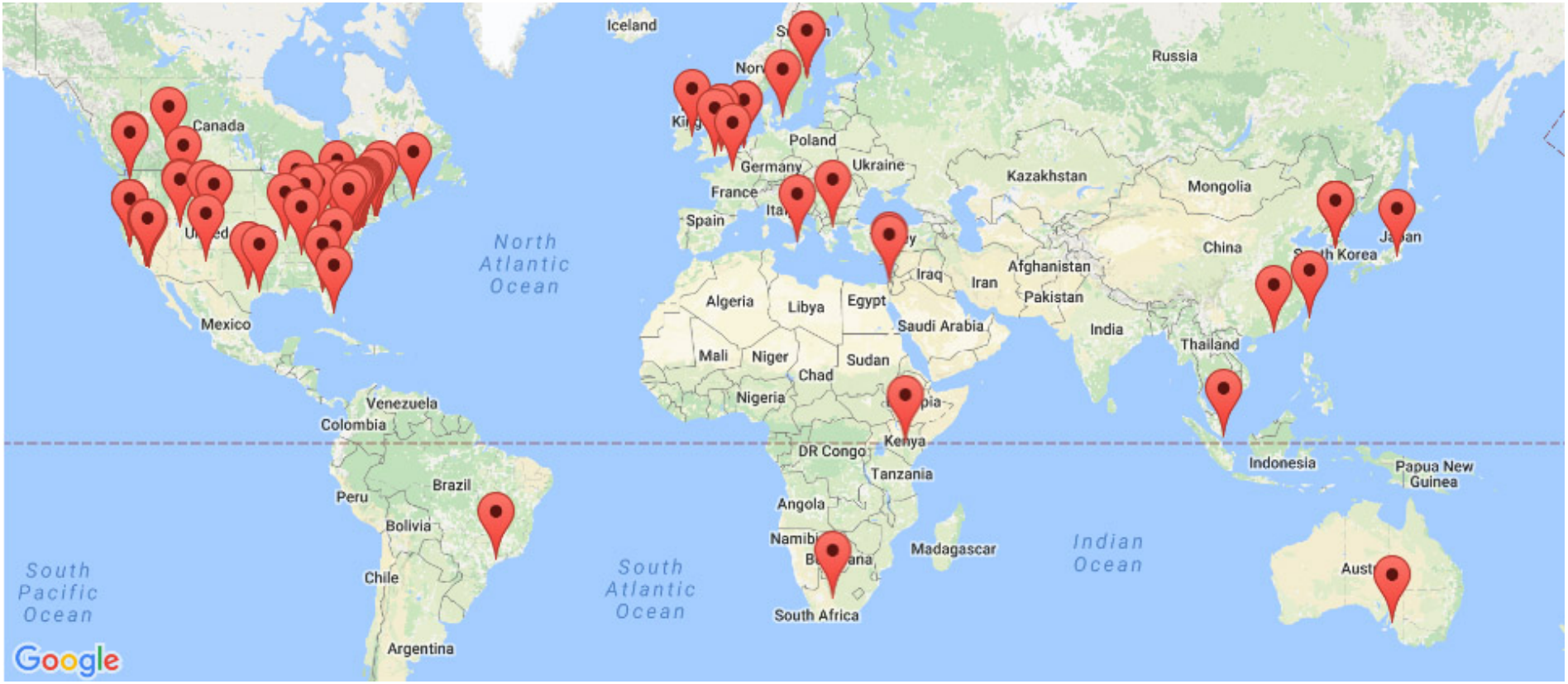
Vision

A world in which observational research produces a comprehensive understanding of health and disease.

Objectives

- **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.

Collaborators



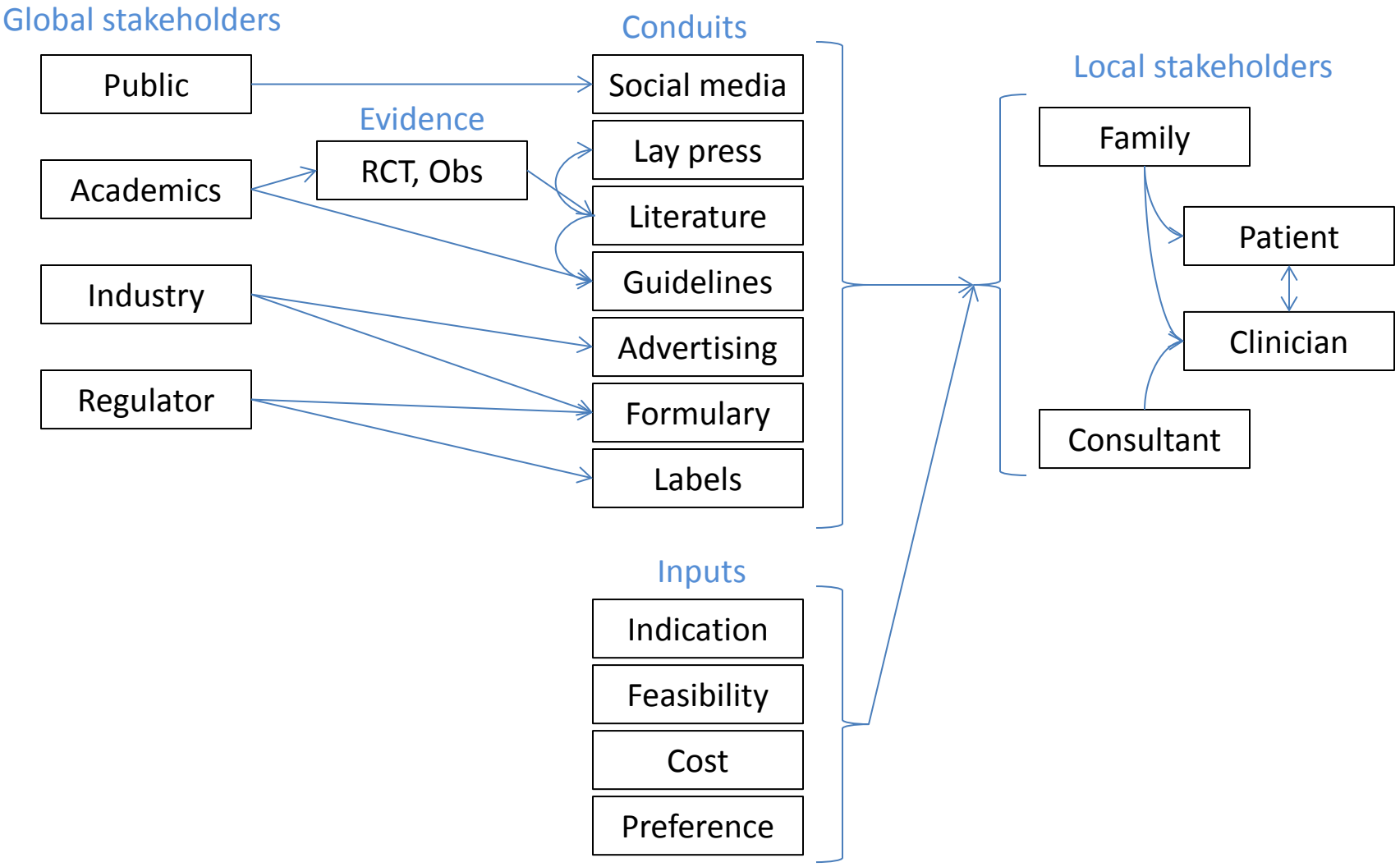
Evidence OHDSI seeks to generate from observational data

- **Clinical characterization**
  - Natural history: Who has diabetes, and who takes metformin?
  - Quality improvement: What proportion of patients with diabetes experience complications?
- **Population-level estimation**
  - Safety surveillance: Does metformin cause lactic acidosis?
  - Comparative effectiveness: Does metformin cause lactic acidosis more than glyburide?
- **Patient-level prediction**
  - Precision medicine: Given everything you know about me, if I take metformin, what is the chance I will get lactic acidosis?
  - Disease interception: Given everything you know about me, what is the chance I will develop diabetes?

Characterization

- Today we carry out RCTs without clear knowledge of actual practice
- There will be no RCTs without an observational precursor
  - It will be required to characterize a population using large-scale observational data before designing an RCT
  - Disease burden
  - Actual treatment practice
  - Time on therapy
  - Course and complication rate
  - Done now somewhat through literature and pilot studies

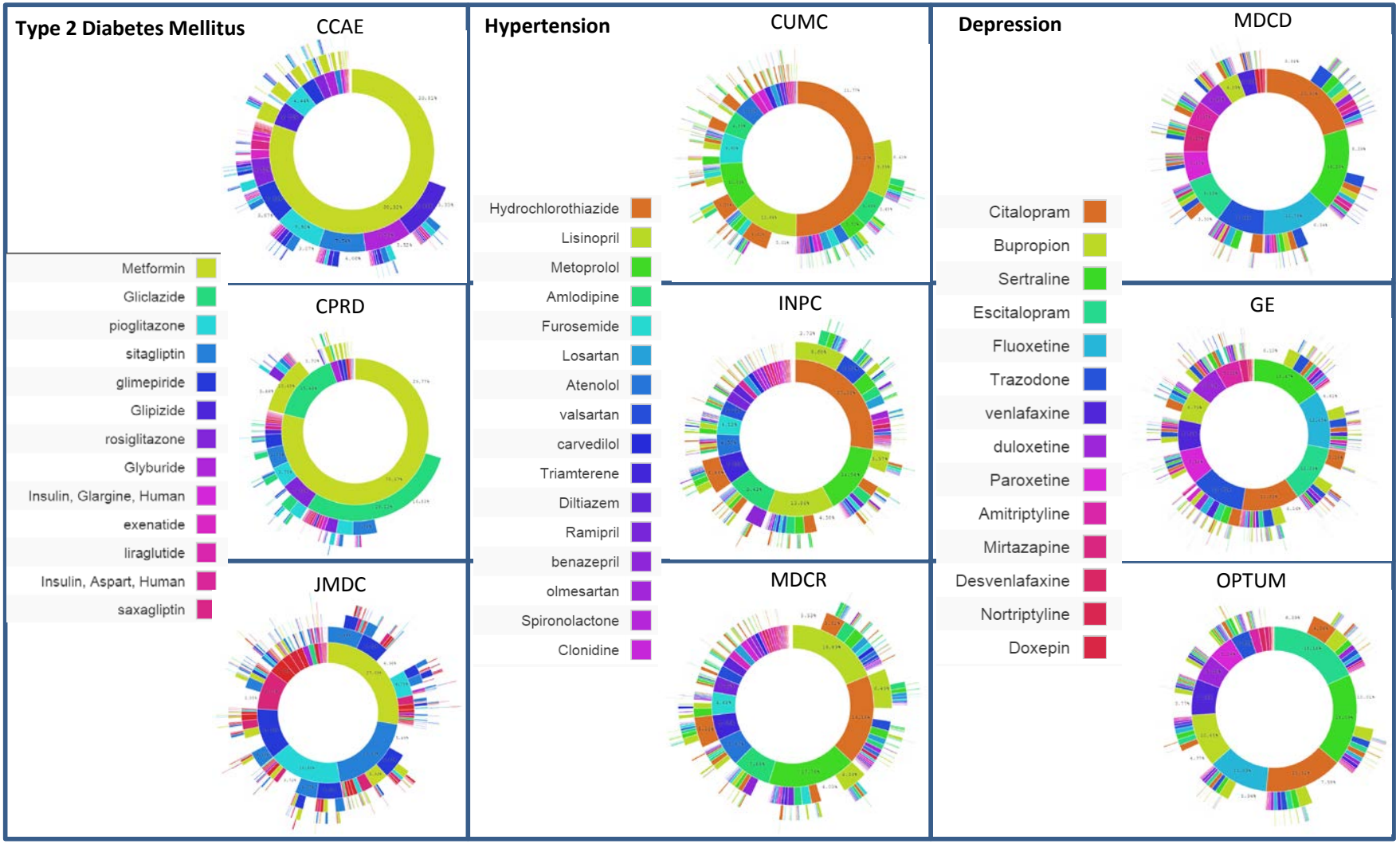
Treatment Pathways



OHDSI in action:
Chronic disease treatment pathways

- Conceived at AMIA 15Nov2014
- Protocol written, code written and tested at 2 sites 30Nov2014
- Analysis submitted to OHDSI network 2Dec2014
- Results submitted for 7 databases 5Dec2014

Population-level heterogeneity



Proceeding of the National Academy of Sciences (PNAS), 2016

Network research

- It is feasible to encode the world population in a single data model
  - Over 600,000,000 records by voluntary effort
- Generating evidence is feasible
- Stakeholders willing to share results
- Able to accommodate vast differences in privacy and research regulation

Pediatric oncology

- 1950
  - Doctors with excellent training, vast experience, and strong motivation tailor treatment to each child, practicing medicine as an **art**
  - 10% childhood cancer cure rate
- 2010
  - 60 years of **scientific** approach to treatment with clinical trials
  - 80% childhood cancer cure rate

What is the quality of the current evidence from observational analyses?

JAMA

Exposure to Oral Bisphosphonates and Risk of Esophageal Cancer

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"

commonly prescribed in elderly women; eg, in 2005, approximately 10% of UK women older than 70 years received a bisphosphonate prescription.[3]

Oral bisphosphonates are known to cause serious esophagitis in some users.[4,5] Crystalline material that resembles ground alendronate tablets has 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-

founders.

Main Outcome Measure Hazard ratio for the risk o
cer in the bisphosphonate users compared with the bis

Results Mean follow-up time was 4.5 and 4.4 yea
control cohorts, respectively. Excluding patients with le
there were 41 826 members in each cohort (81% w
11.4) years). One hundred sixteen esophageal or gas
occurred in the bisphosphonate cohort and 115 (72
cohort. The incidence of esophageal and gastric cancer
person-years of risk in both the bisphosphonate and c
of esophageal cancer alone in the bisphosphonate a
and 0.44 per 1000 person-years of risk, respectively. T
of esophageal and gastric cancer combined between
phonate use (adjusted hazard ratio, 0.96 [95% confic
risk of esophageal cancer only (adjusted hazard ratio,
val, 0.77-1.49]). There also was no difference in risk of
by duration of bisphosphonate intake.

Conclusion Among patients in the UK General Practic

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]

ABSTRACT

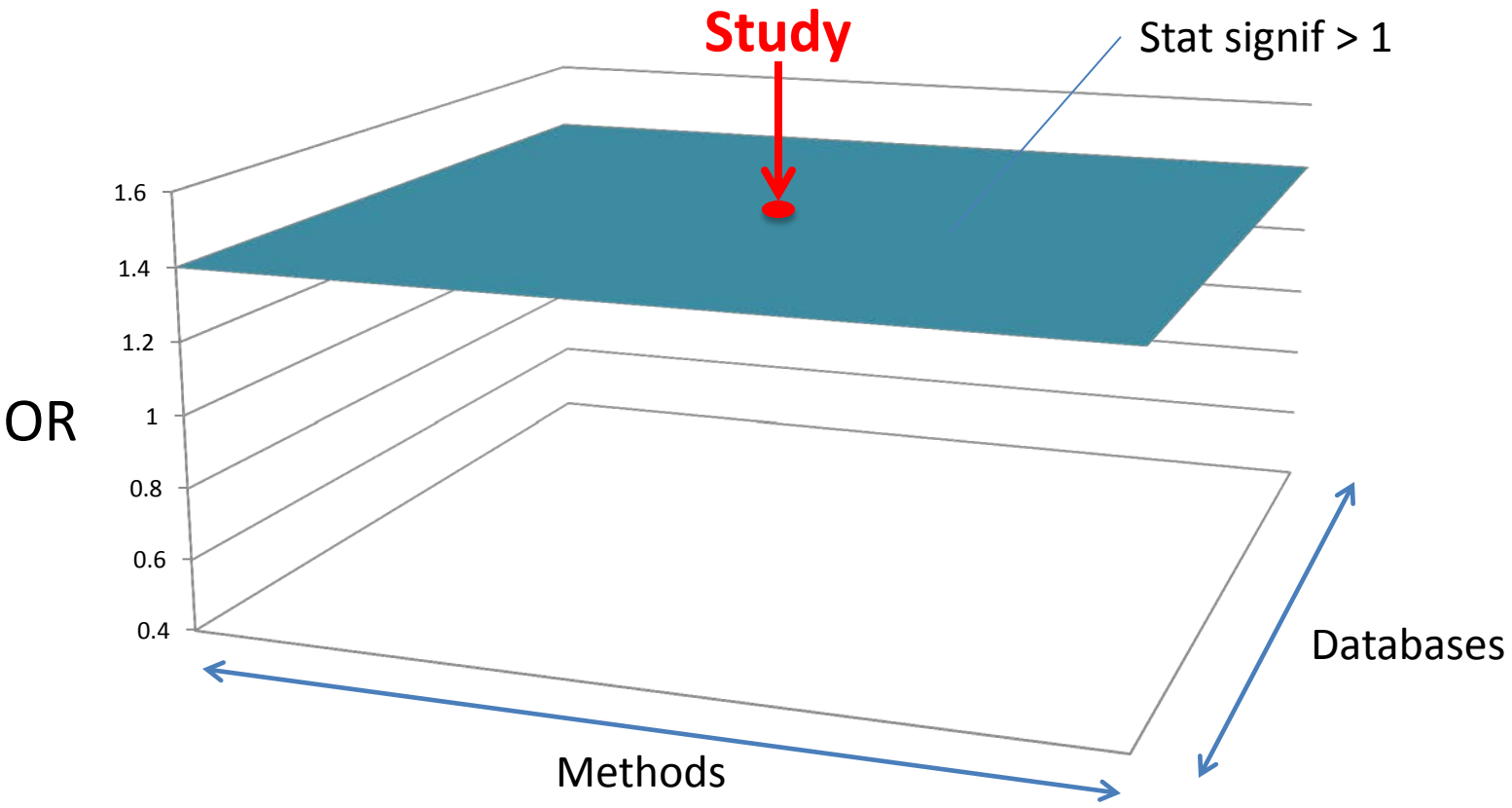
Objective To examine the hypothesis that risk of oesophageal, but not of gastric or colorectal, cancer is increased in users of oral bisphosphonates.

Design Nested case-control analysis within a primary care cohort of about 6 million people in the UK, with

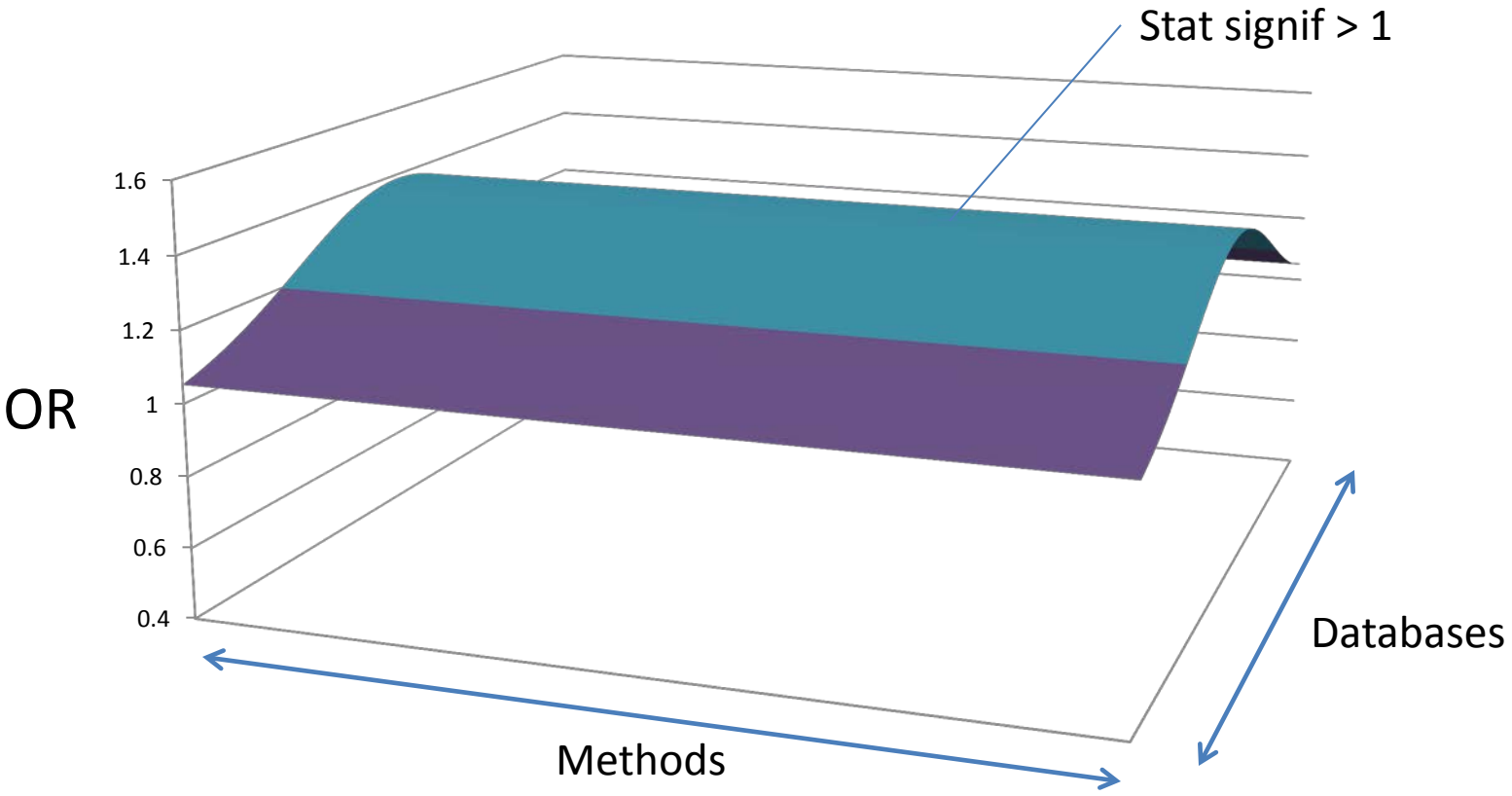
Conclusions The risk of oesophageal cancer increased with 10 or more prescriptions for oral bisphosphonates and with prescriptions over about a five year period. In Europe and North America, the incidence of oesophageal cancer at age 60-79 is typically 1 per 1000 population over five years, and this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

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"

Distribution of possible results for one hypothesis



Distribution of possible results for one hypothesis



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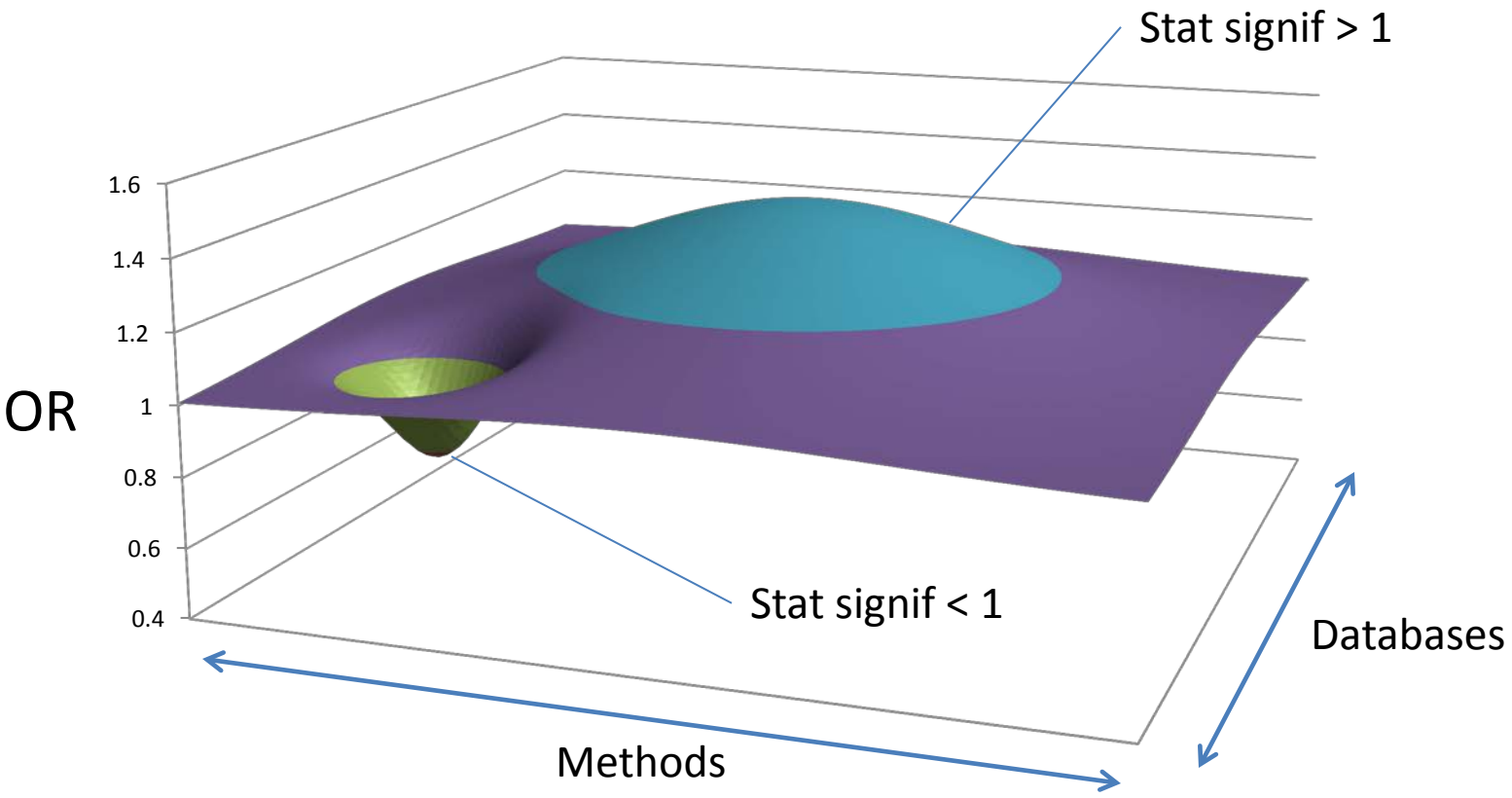
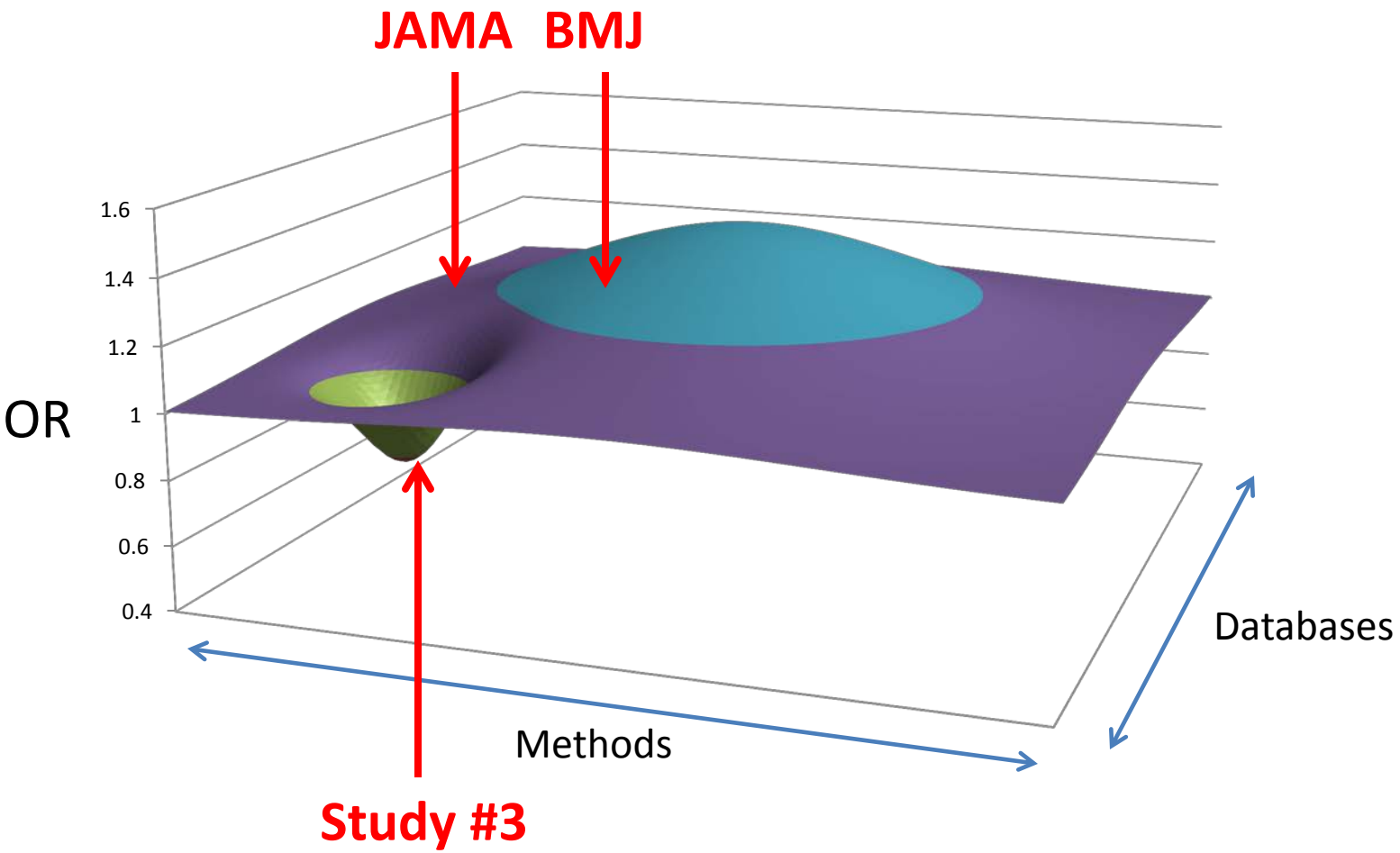
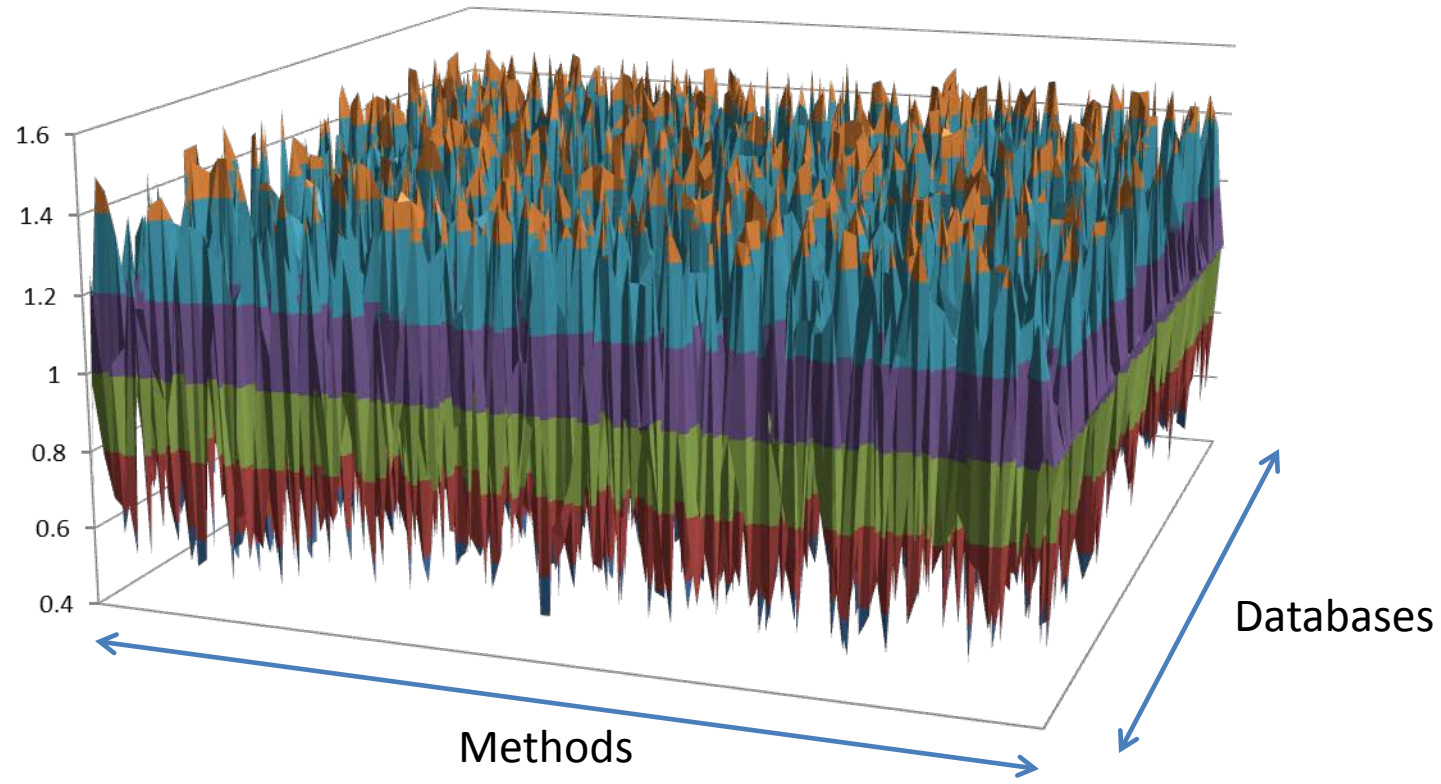


Distribution of possible results for one hypothesis



Distribution of possible results for one hypothesis

OR



Take a scientific approach to science

1. Database heterogeneity:
   Holding analysis constant, different data may yield different estimates

Madigan D, Ryan PB, Schuemie MJ et al, American Journal of Epidemiology, 2013
"Evaluating the Impact of Database Heterogeneity on Observational Study Results"

2. Parameter sensitivity:
   Holding data constant, different analytic design choices may yield different estimates

Madigan D, Ryan PB, Schuemie MJ, Therapeutic Advances in Drug Safety, 2013: "Does design matter? Systematic evaluation of the impact of analytical choices on effect estimates in observational studies"

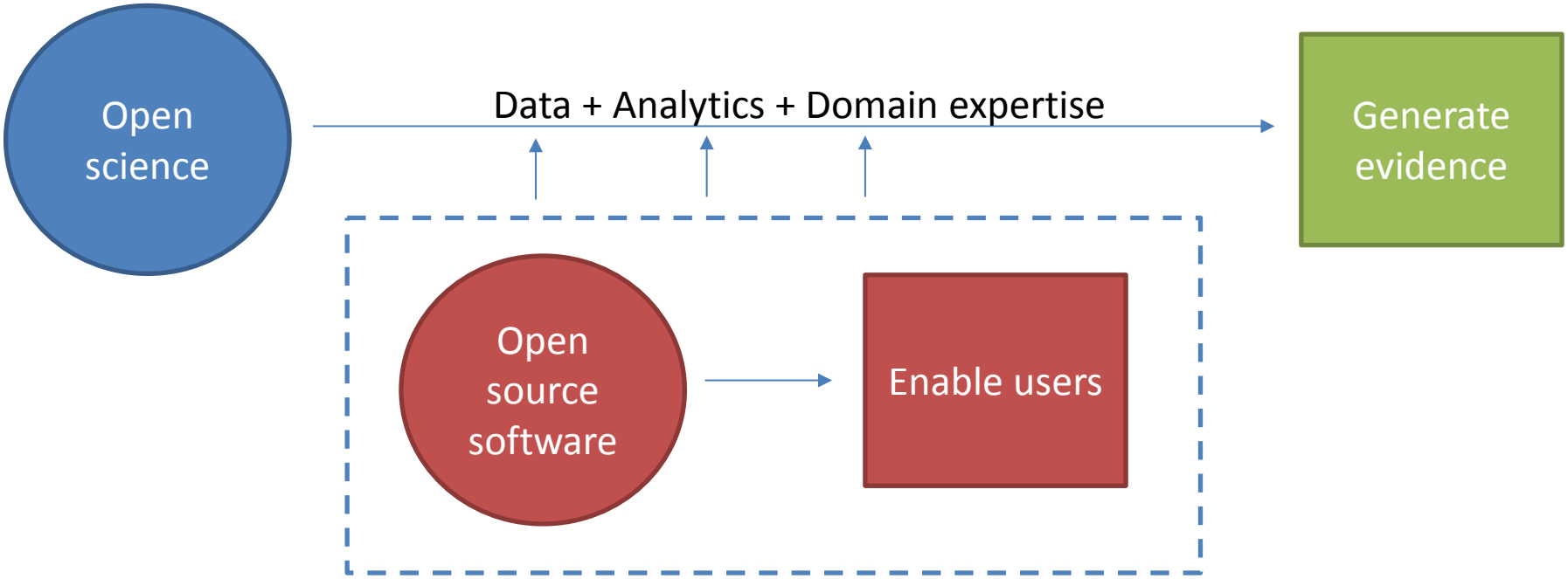
3. Empirical performance:
   Most observational methods do not have nominal statistical operating characteristics

Ryan PB, Stang PE, Overhage JM et al, Drug Safety, 2013:
"A Comparison of the Empirical Performance of Methods for a Risk Identification System"

4. Empirical calibration can help restore interpretation of study findings

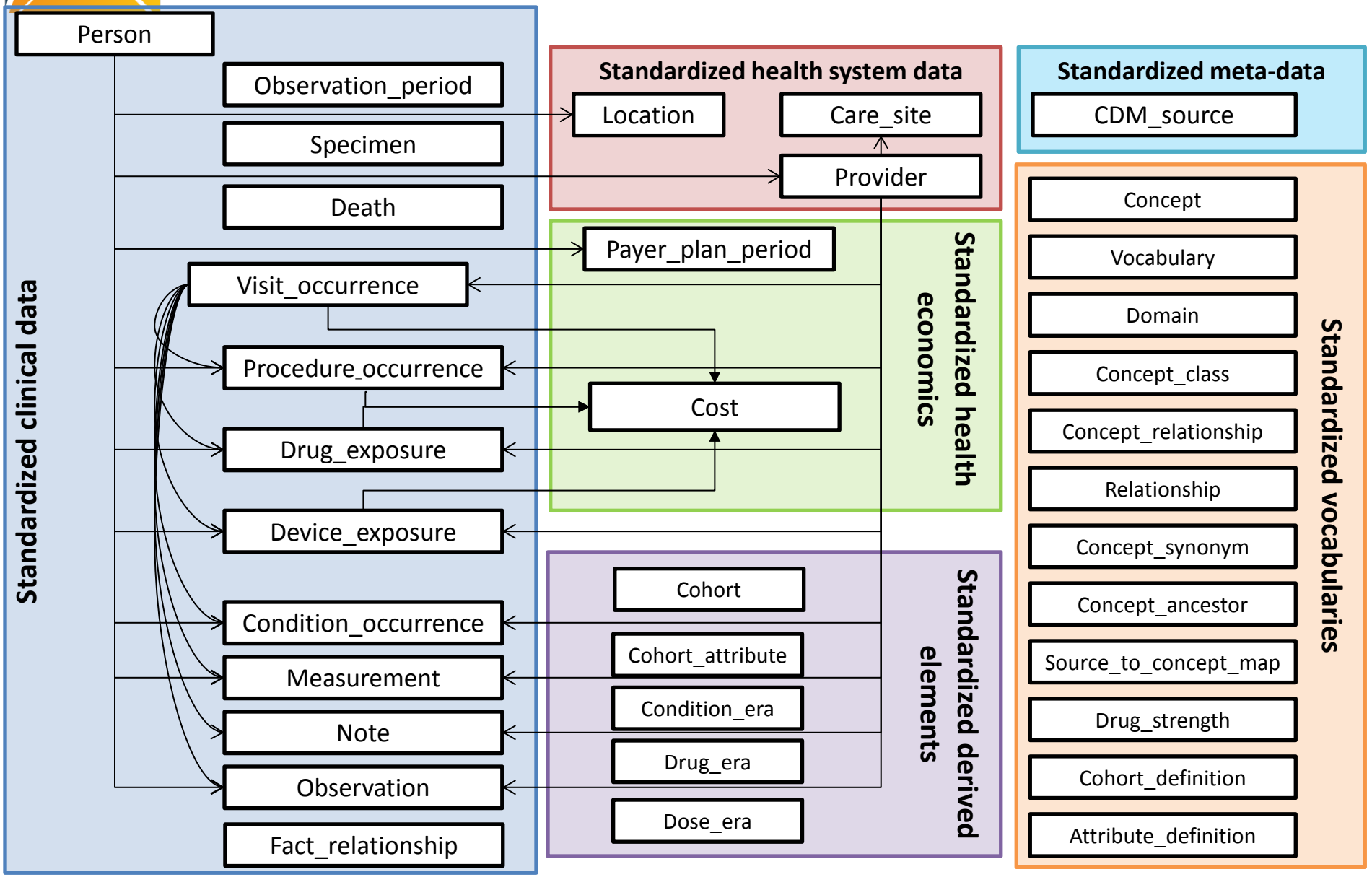
Schuemie MJ, Ryan PB, DuMouchel W, et al, Statistics in Medicine, 2013:
"Interpreting observational studies: why empirical calibration is needed to correct p-values"

OHDSI's approach to **open science**



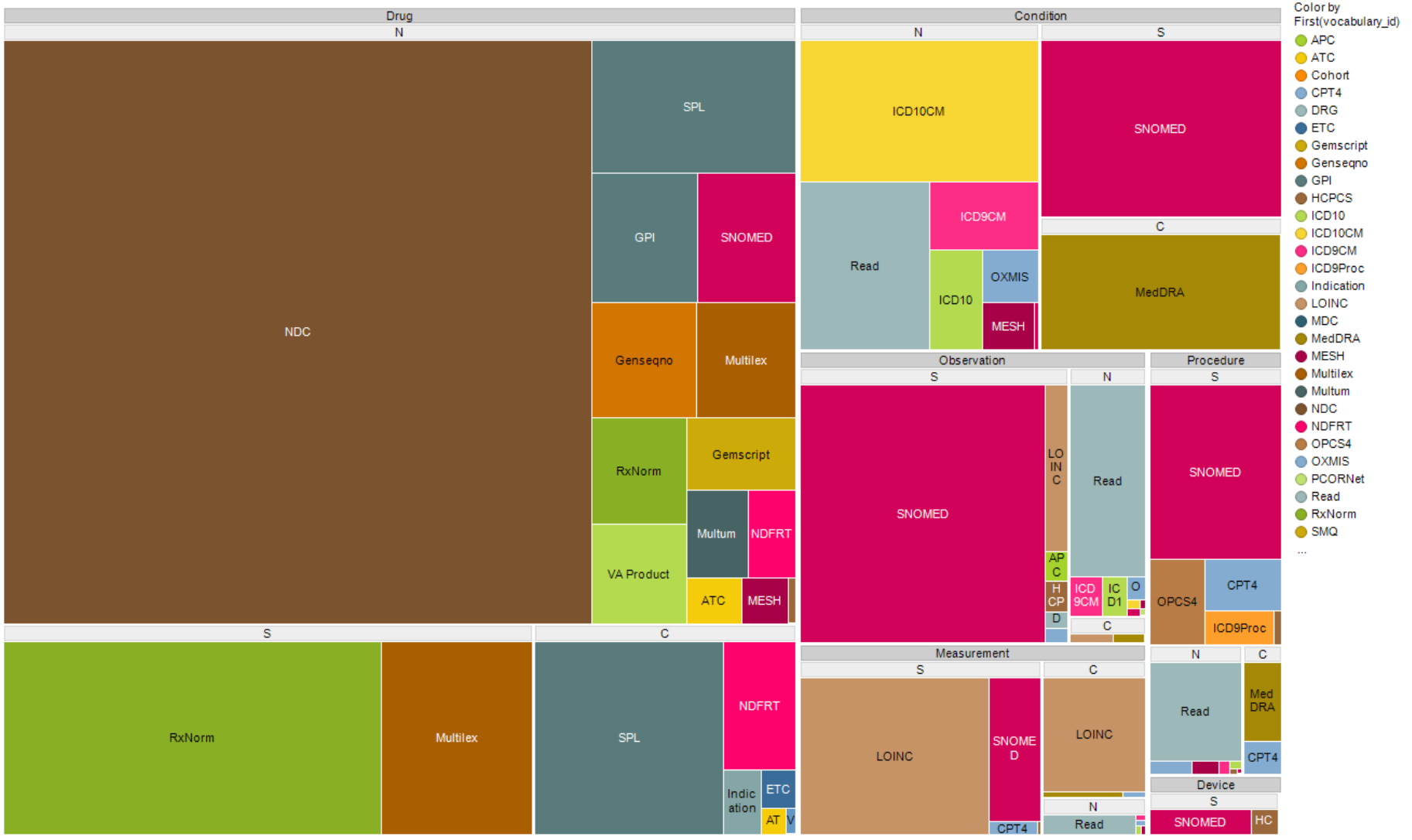
- Open science is about sharing the journey to evidence generation
- Open-source software can be part of the journey, but it's not a final destination
- Open processes can enhance the journey through improved reproducibility of research and expanded adoption of scientific best practices

Deep information model
OMOP CDM v5.0.1

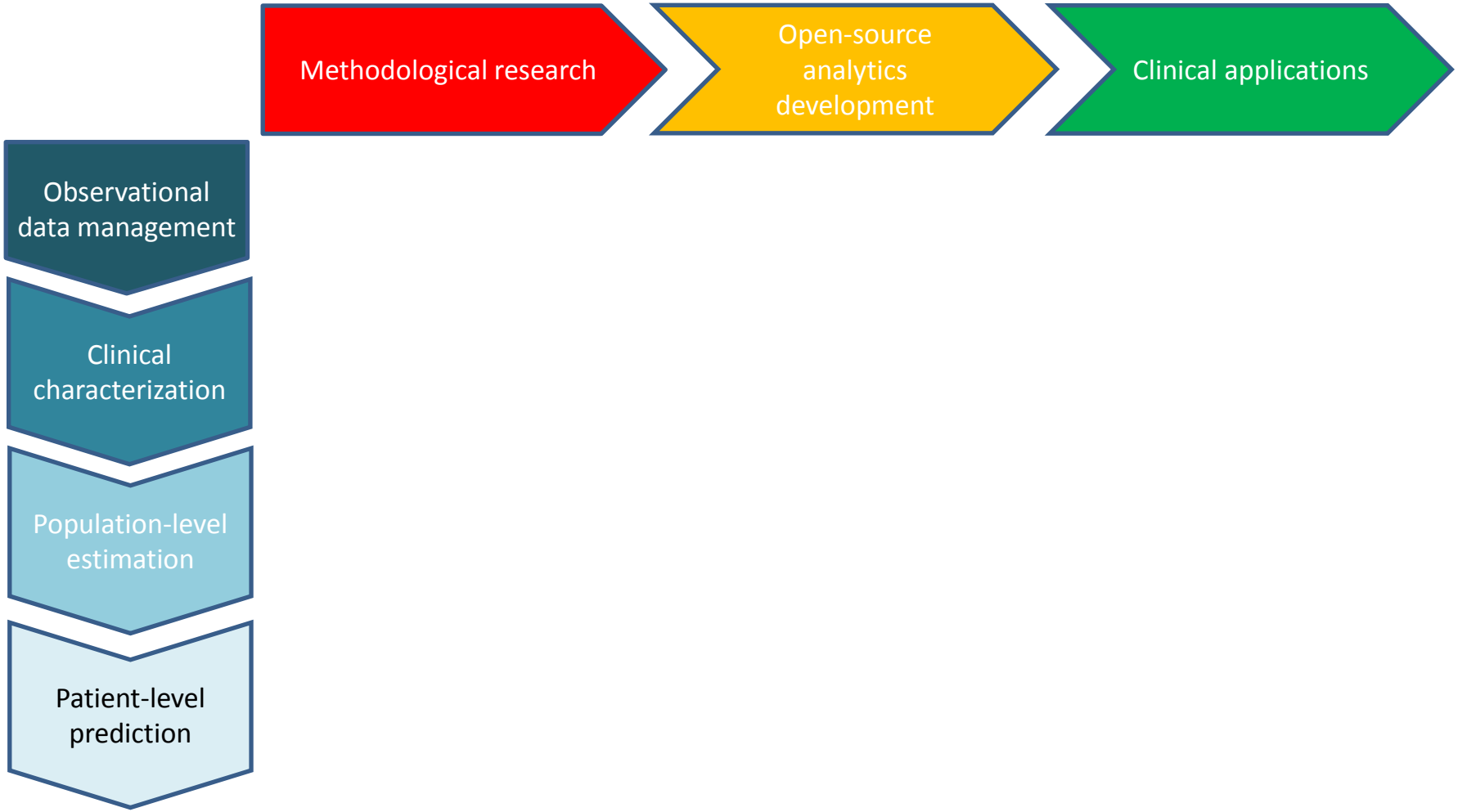


Extensive vocabularies

Breakdown of OHDSI concepts by domain, standard class, and vocabulary



OHDSI ongoing collaborative activities



Open science

- Admit that there is a problem
- Study it scientifically
  - Define that surface and differentiate true variation from confounding …
- Total description of every study
- Research into new methods

Thanks!

Join the journey
www.OHDSI.org