George Hripcsak, MD, MS
Columbia University Medical Center

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Patient-Centered Outcomes Research Institute (PCORI)

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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.
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

Global stakeholders
- Public
- Academics
- Industry
- Regulator

Evidence
- RCT, Obs

Conduits
- Social media
- Lay press
- Literature
- Guidelines
- Advertising
- Formulary
- Labels

Local stakeholders
- Family
- Patient
- Clinician
- Consultant

Inputs
- Indication
- Feasibility
- Cost
- Preference
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

Type 2 Diabetes Mellitus

Hypertension

Depression

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?

August 2010: “Among patients in the UK General Practice Research Database, the use of oral bisphosphonates was not significantly associated with incident esophageal or gastric cancer.”

Sept 2010: “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

Stat signif > 1

OR

Databases

Methods
Distribution of possible results for one hypothesis

OR

Stat signif > 1

Stat signif < 1

Databases

Methods
Distribution of possible results for one hypothesis

Databases

Methods

Distribution of possible results for one hypothesis

Study #3

JAMA

BMJ

OR

Databases

Methods
Distribution of possible results for one hypothesis
Take a scientific approach to science

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

Breakdown of OHDSI concepts by domain, standard class, and vocabulary
OHDSI ongoing collaborative activities

Methodological research

Open-source analytics development

Clinical applications

Observational data management

Clinical characterization

Population-level estimation

Patient-level prediction
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

Welcome!
To the OHDSI Community!