The OHDSI Collaboration: Mission, Accomplishments, and the Road Ahead

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JAMA

VIEWPOINT

Weighing the Benefits and Risks of Proliferating Observational Treatment Assessments

Observational Cacophony, Randomized Harmony

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Amid the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, substantial effort is being directed toward mining databases and publishing case series and reports that may provide insights into the epidemiology and clinical management of coronavirus disease 2019 (COVID-19). However, there is growing concern about whether attempts to infer causation about the benefits and risks of potential therapeutics from nonrandomized studies are providing insights that improve clinical knowledge and accelerate the search for needed answers, or whether these reports just add noise, confusion, and false confidence. Most of these studies include a caveat indicating that "randomized clinical trials are needed." But disclaimers aside, does this approach help make the case for well-designed randomized clinical trials (RCTs) and accelerate their delivery?[1] Or do observational studies reduce the likelihood of a properly designed trial being performed, thereby delaying the discovery of reliable truth?

The growth of structured registries and organization of claims and electronic health record data have

directly involved in discourse about treatments th
are effective. The natural desire of all elements of society to find effective therapies can obscure the difference between a proven fact and an exaggerated guess. Nefarious motives are not necessary for these problems to occur.

The role of regulators in this context is crucial. In the United States, the 21st Century Cures Act and user fee agreements require industry, academia, and regulators to advance the use of data and evidence f
settings.[3] This legislation directed the US Fo
Administration (FDA) and the National Ir
Health (NIH) to work with the clinical resea
tem to develop robust methods for generati
dence and clear guidance for applying it. Hist
FDA has insisted on high-quality evidence
tion for granting marketing approval for drugs and devices, and for specific marketing claims.

Considerable progress has been made in defining appropriate methods for improving the quality of observational treatment comparisons. Both NIH- and FDA-funded work fosters transparency by publishing study

NIH U.S. National Library of Medicine

ClinicalTrials.gov

as of 2Aug2020

Home > Search Results

Modify Search Start Over

2844 Studies found for: **COVID-19**

1592 are study type = 'Interventional'

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                    Status                          Study.Results
Recruiting             :806   Has Results          :   1
Not yet recruiting     :552   No Results Available:1591
Completed              : 76
Active, not recruiting : 68
Enrolling by invitation: 46
Withdrawn              : 20
(Other)                : 24

                 Phases      Enrollment
Phase 2             :11   Min.    :   5.00
Phase 3             : 9   1st Qu.:  29.25
Phase 1             : 3   Median :  68.00
Phase 2|Phase 3:  3   Mean   : 434.77
Phase 4             : 3   3rd Qu.: 246.50
Phase 1|Phase 2:  1   Max.   :4891.00
(Other)             : 0
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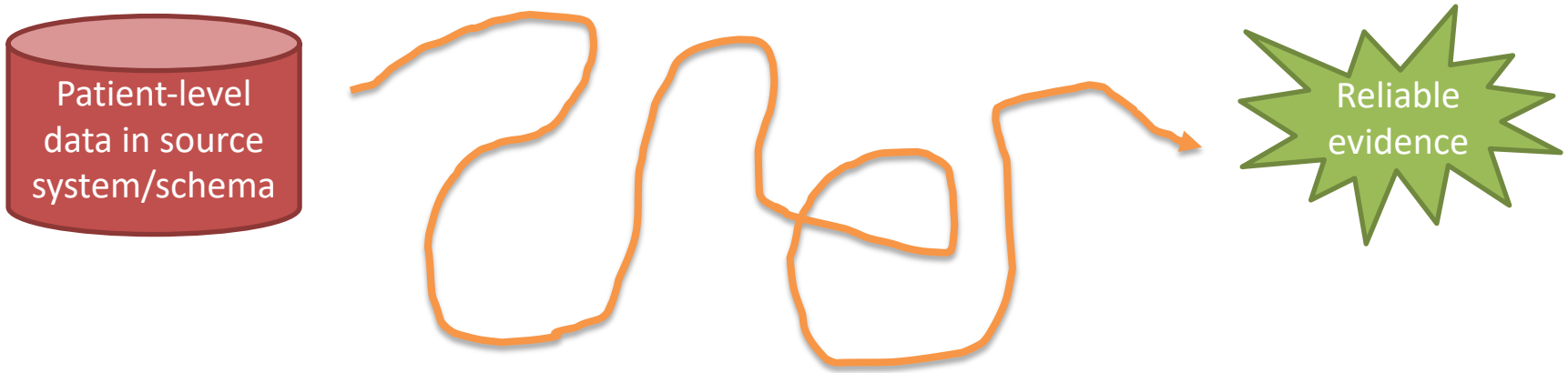
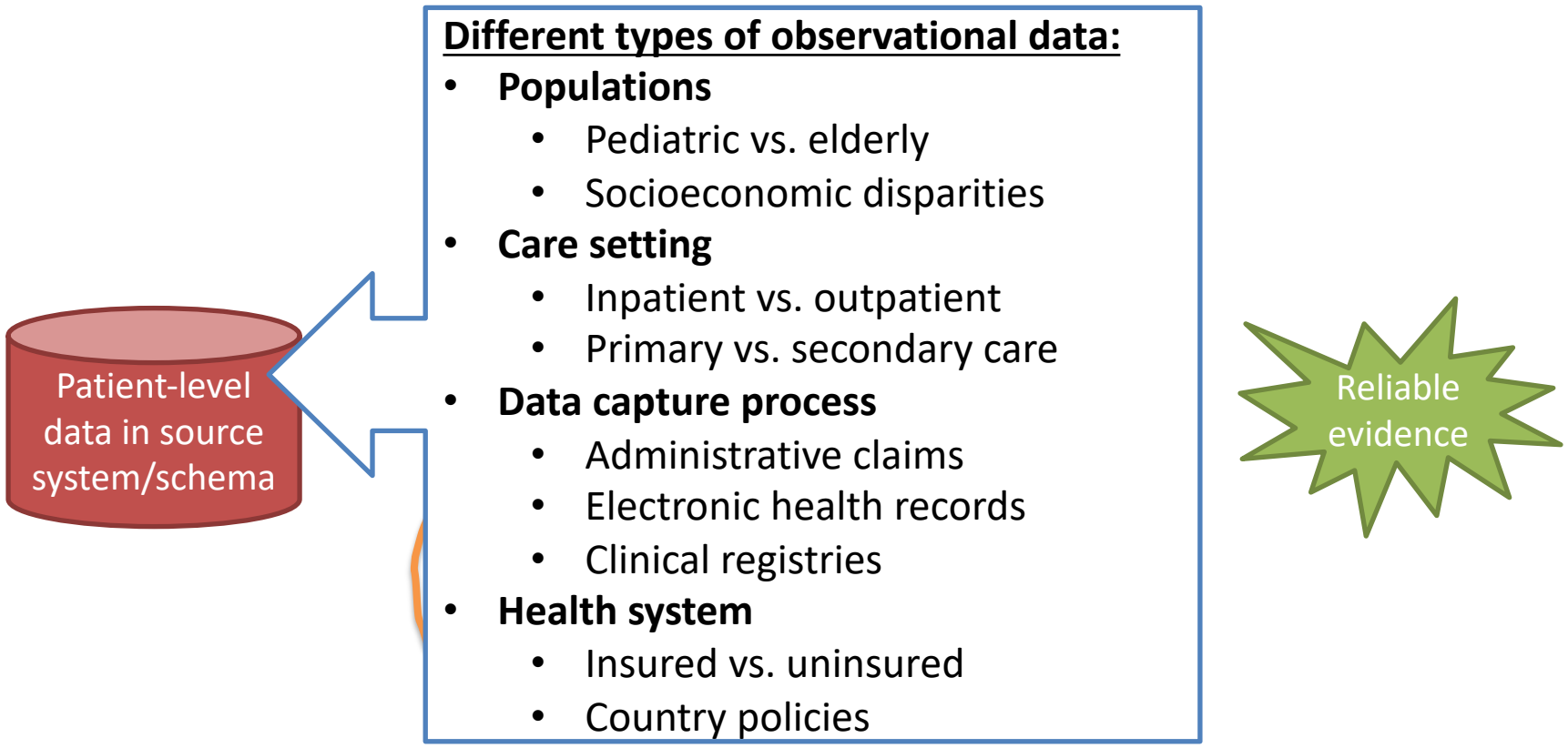
Alternative title (and motivation for OHDSI):
Scientific Cacophony,
Harmony achieved through ***collaboration***, not randomization

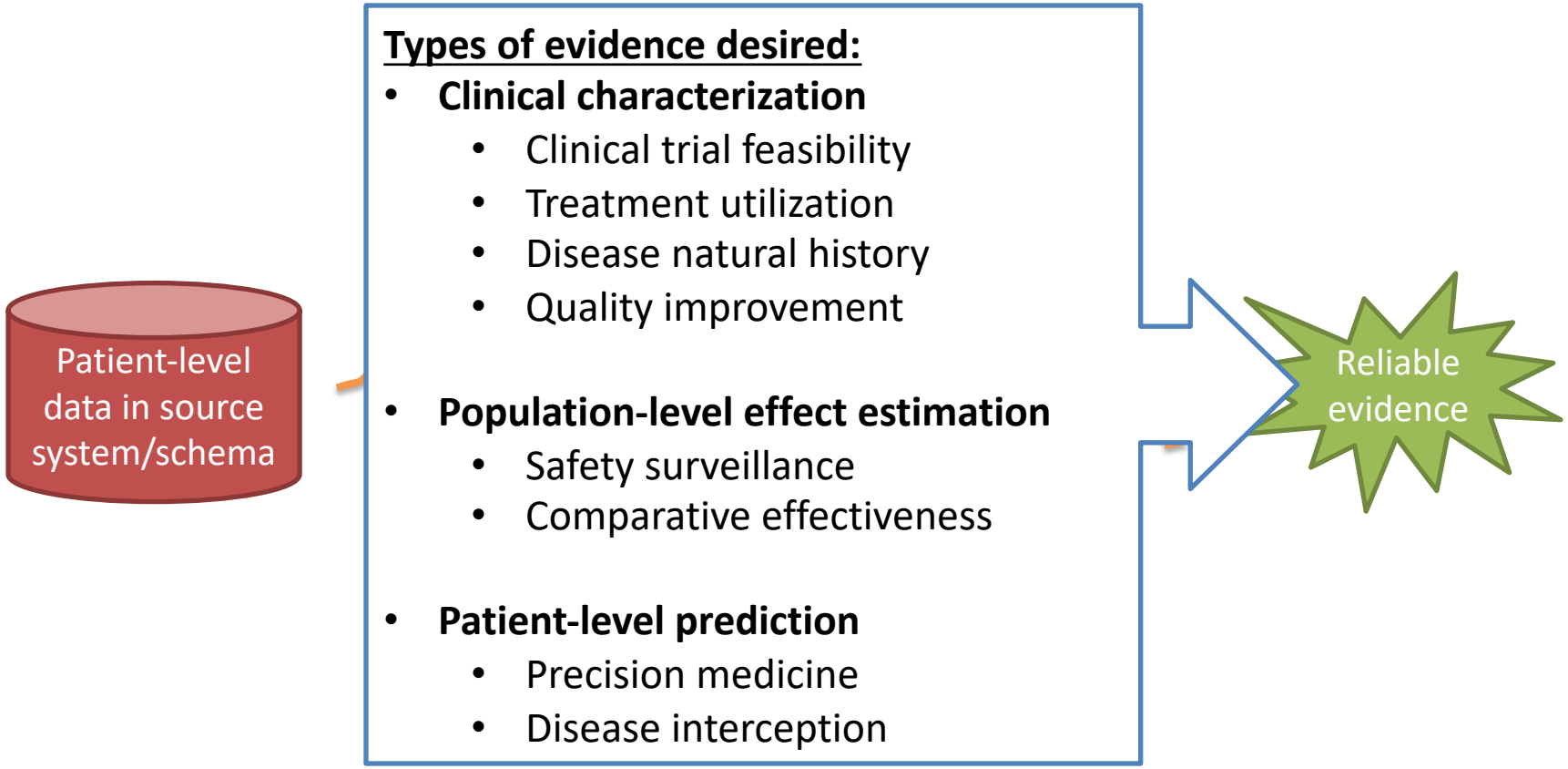
The journey to real-world evidence



The journey to real-world evidence



The journey to real-world evidence



Desired attributes for reliable evidence

Desired attribute	Question	Researcher	Data	Analysis		Result
Repeatable	Identical	Identical	Identical	Identical	=	Identical
Reproducible	Identical	Different	Identical	Identical	=	Identical
Replicable	Identical	Same or different	Similar	Identical	=	Similar
Generalizable	Identical	Same or different	Different	Identical	=	Similar
Robust	Identical	Same or different	Same or different	Different	=	Similar
Calibrated	Similar (controls)	Identical	Identical	Identical	=	Statistically consistent

OHDSI is

an open science community

OHDSI's mission

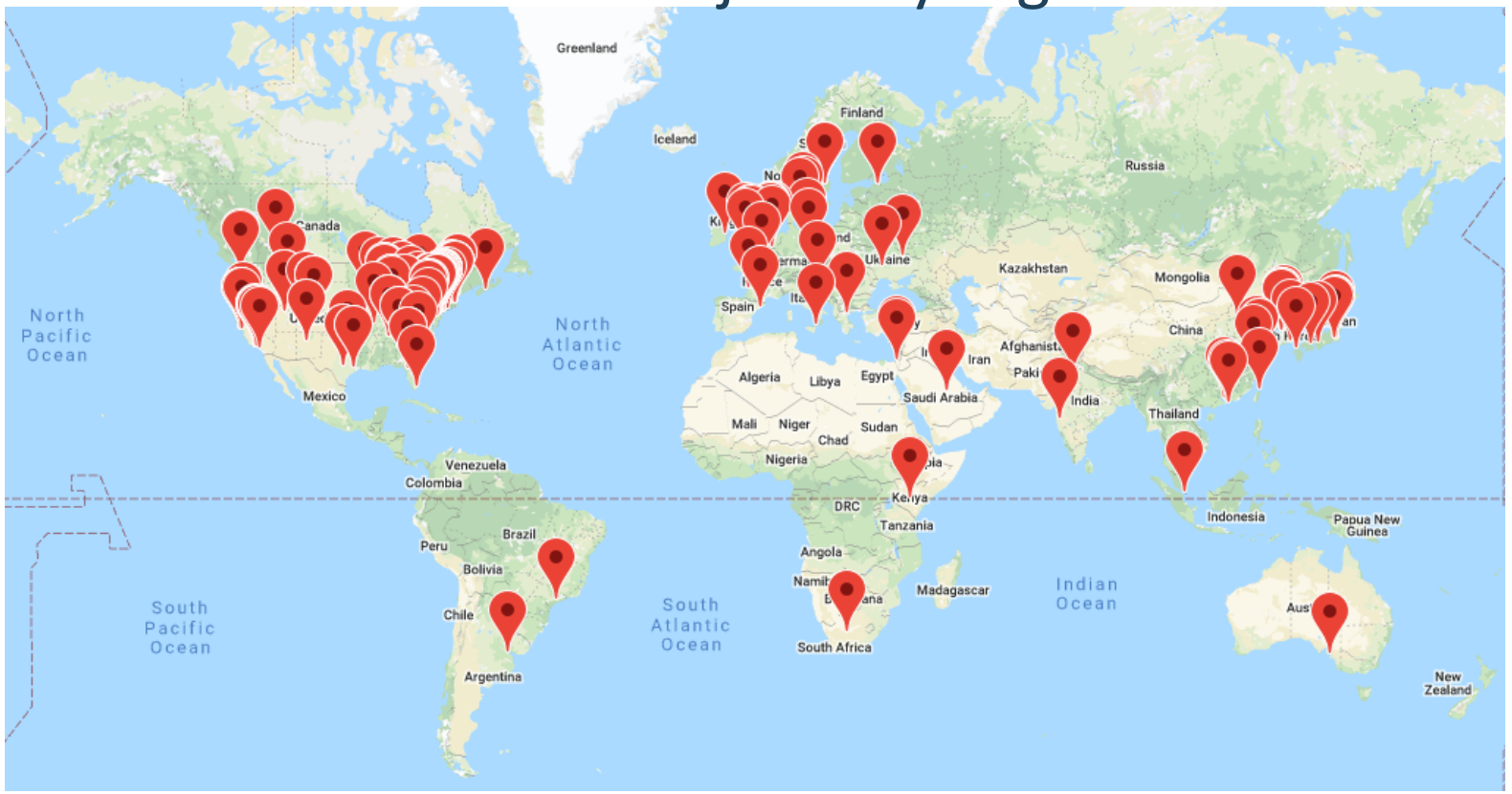
To improve health by empowering a community to collaboratively generate the evidence that promotes better health decisions and better care

OHDSI's vision

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

OHDSI community

We're all in this journey together…



Different stakeholders: academia, medical product industry, regulators, government, payers, technology providers, health systems, clinicians, patients

Different disciplines: computer science, epidemiology, statistics, biomedical informatics, health policy, clinical sciences

OHDSI's community engagement

- Active community online discussion: forums.ohdsi.org
  - **>3,800** distinct users have made **>24,400** posts on **>4,200** topics
  - Implementers, Developers, Researchers, CDM Builders, Vocabulary users, OHDSI in Korea, OHDSI in China, OHDSI in Europe
- Weekly community web conferences for all collaborators to share their research ideas and progress
- >25 workgroups for solving shared problems of interest
  - ex: Common Data Model, Population-level Estimation, Patient-level Prediction, Phenotype, NLP, GIS, Oncology, Women of OHDSI
- Quarterly tutorials in OHDSI tools and best practices, taught by OHDSI collaborators for OHDSI collaborators
- OHDSI Symposiums held annually in North America, Europe and Asia to provide the community opportunities to showcase research collaborations (2020 Symposium virtual Oct 18-22)
- Follow us on Twitter @OHDSI and LinkedIn

OHDSI is

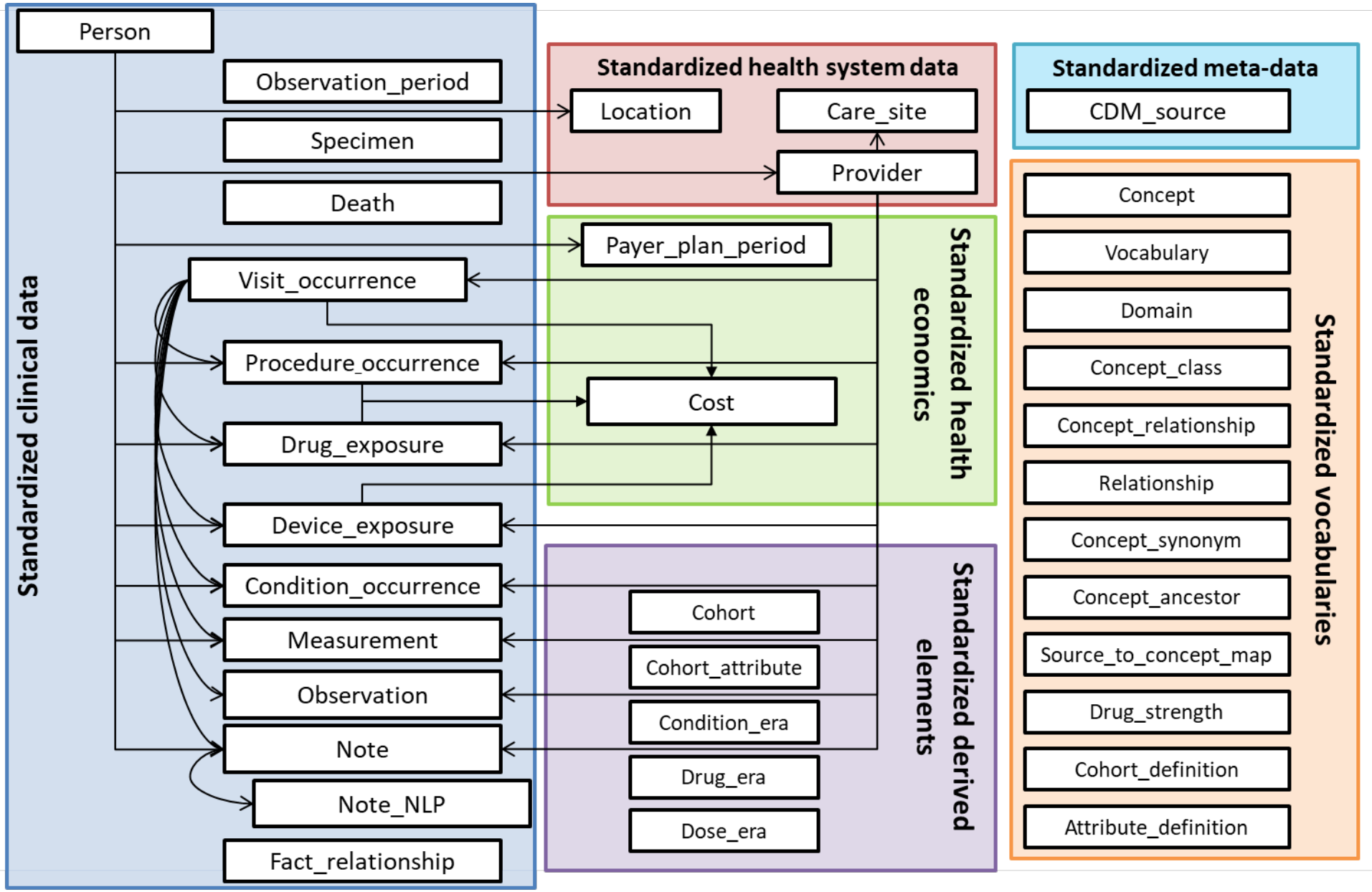
an international data network

Data across the OHDSI community

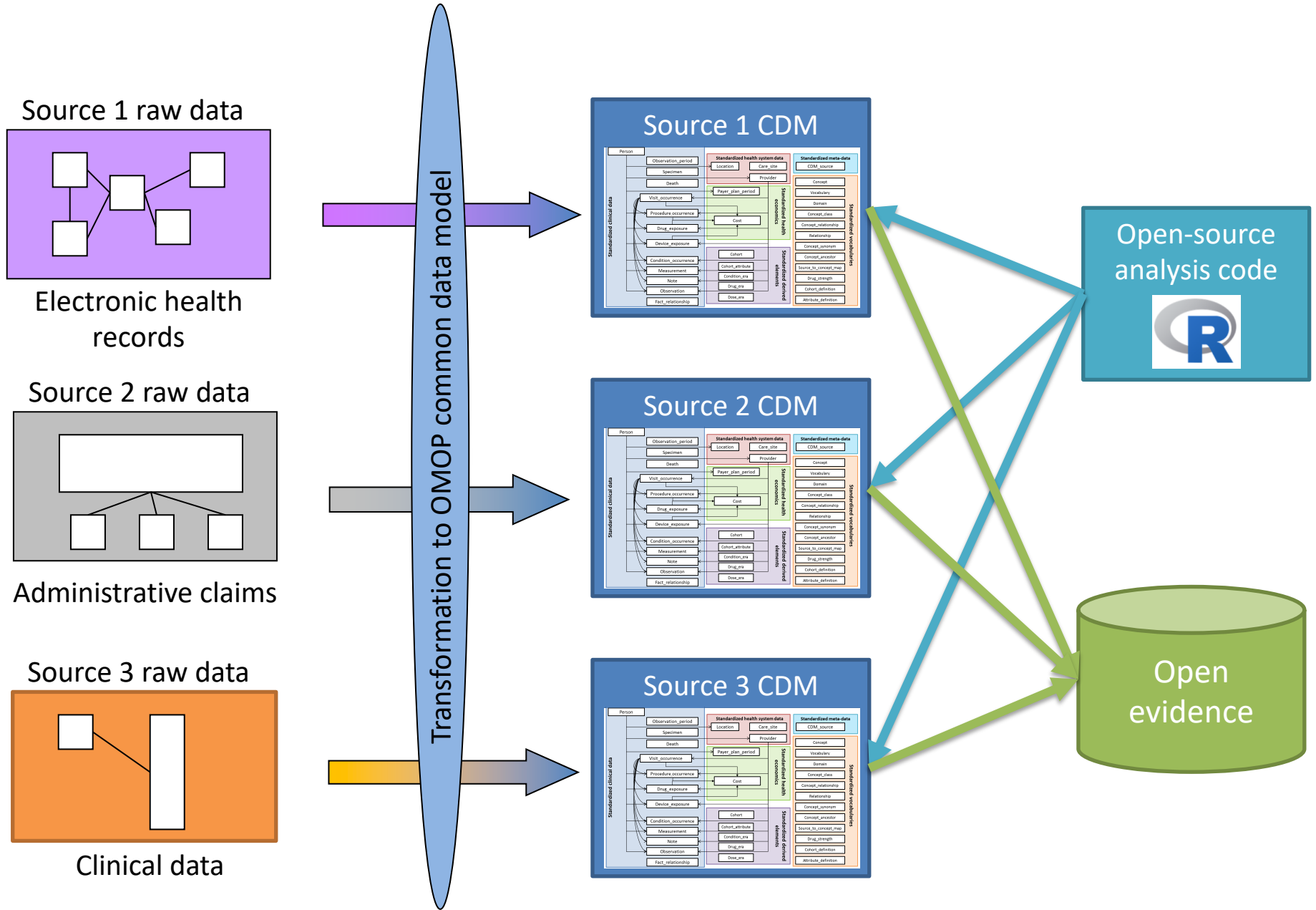
- 152 entries on 2019 OHDSI data network inventory
- 133 different databases with patient-level data from various perspectives:
  - Electronic health records, administrative claims, hospital systems, clinical registries, health surveys, biobanks
- Data in 18 different countries, with >369 million patient records from outside US

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

OMOP Common Data Model v5.3



Common data model to enable standardized analytics



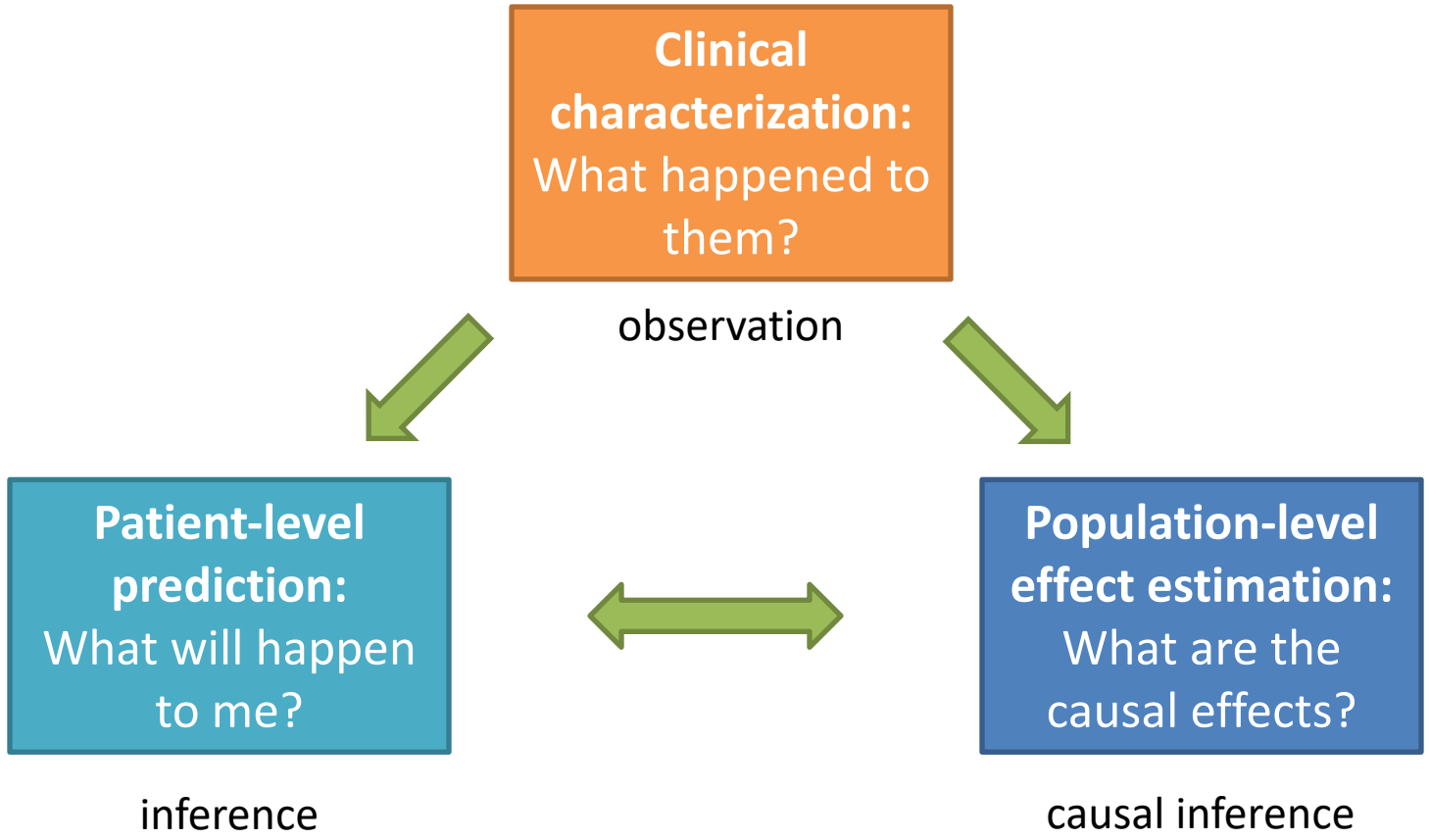
OHDSI is

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

Complementary evidence to inform the patient journey



Harmony through collaboration: Case study in COVID-19 pandemic

- Real-world data for COVID-19 standardized to OMOP CDM in OHDSI network (16 databases in US, Europe, Asia)
  - 4.5 million patients tested for SAR-COV-2
  - 1.2 million patients diagnosed or tested positive
  - 380k patients with a confirmed positive laboratory test
  - 249k patients hospitalized with a COVID diagnosis or positive test
- Real-world evidence generated by OHDSI community
  - COVID disease natural history: Patients hospitalized with COVID are systematically different from those hospitalized with flu (link to paper)
  - Comparative safety of hydroxychloroquine: In history use in RA population, HCQ alone is generally safe but combination of HCQ+azithromycin shows doubling of risk of 30-day cardiovascular mortality (link to paper)
  - Psychiatric safety of hydroxychloroquine: EMA was concerned about risk of neuropsychiatric events associated with HCQ based on spontaneous reports, but we showed no difference between HCQ and sulfasalazine (link to paper)
  - ACE inhibitors and susceptibility to COVID: There is no difference in risk of developing COVID between prevalent users of ACE inhibitors, ARBs, or other antihypertensive medications. (link to paper)
  - COVID risk prediction: developed and externally validated a model that can predict hospitalization, intensive service use, and death amongst symptomatic patients (link to paper)
- Regulatory impact:
  - 3 invited presentations to FDA/Reagan-Udall Evidence Accelerator sessions to guide RWE best practices in COVID research
  - EMA risk communication on HCQ cites OHDSI study (link)
  - EMA requests OHDSI to study neuropsychiatric events on HCQ after spontaneous reports emerge; results delivered to EMA in weeks
  - EMA/ENCEPP guidelines on pharmacoepidemiology cite OHDSI studies as illustrative best practices (link to guidance)