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Reliable Real-World Evidence for Equitable Health Care

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CS531a AI for Health Guest Lecture
Mar 26, 2024

The goal is to integrate causal modeling with machine learning to generate reliable real-world evidence and to build an equitable healthcare system.

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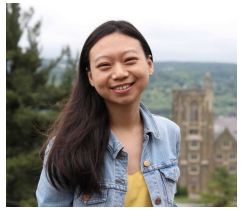
Team

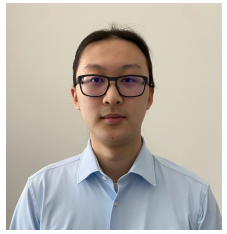
Trainees



Yichen Sun
BIDS PhD student
Washington University



Hsin-Yi “Cindy” Chen
MD/PhD candidate
Columbia University



Ruochong Fan, MS
Senior data analyst



Recruiting

- PhD students
- Post-docs

Mentors and Collaborators



Adam Wilcox



Charles Goss



Thomas Kannampallil



Aditi Gupta



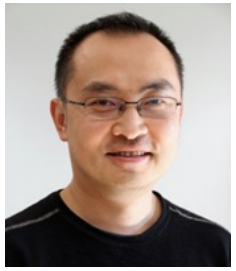
George Hripcsak
Columbia



David Blei
Columbia



Yixin Wang
UMich



Wenyu Song
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OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

UNIVERSITY OF MICHIGAN

HARVARD MEDICAL SCHOOL

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Real-world data (RWD) in health care



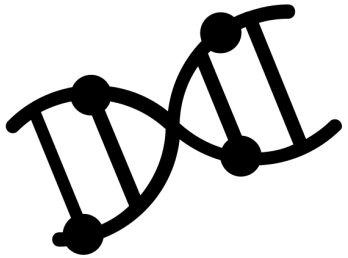
Electronic Health Records (EHRs)



Demographics Diagnoses Drugs Procedures Labs



Medical Images



Genomics



Clinical Notes



Wearables

RWD are data generated from their natural setting (i.e, not strictly controlled clinical trials).

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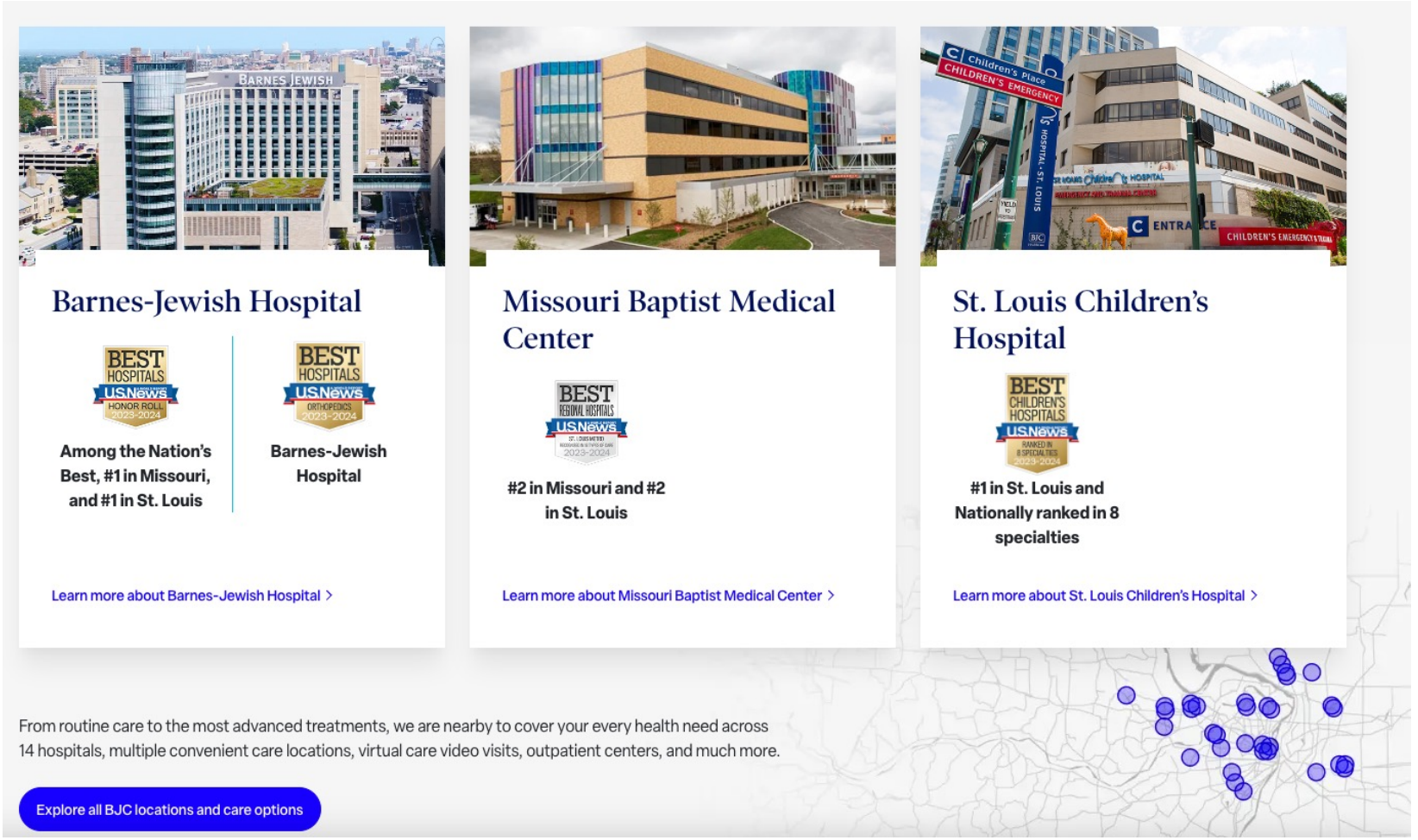
BJC HealthCare/WashU EHRs

- 14 hospitals
- 2M patients



Data -> Evidence -> Practice



TREATMENT EFFECT ESTIMATION

Is a treatment effective?

Is a treatment safe?



HEALTH EQUITY

Is the healthcare system fair?

Is the clinical algorithm fair?



RISK PREDICTION

Can we predict mortality?

What are the risk factors?

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Why real-world evidence is needed in healthcare

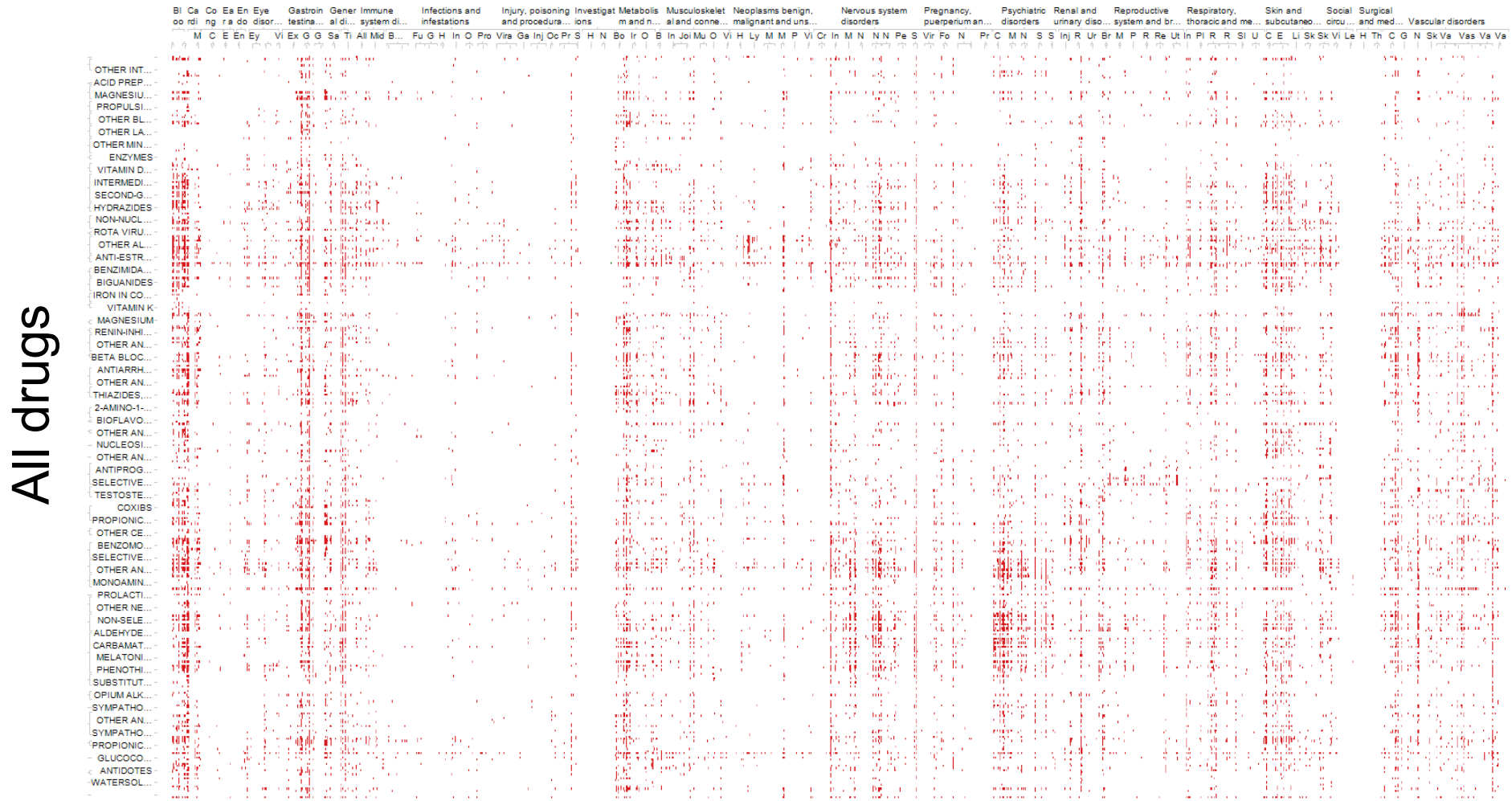

Figure: Patrick Ryan

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Observational Health Data Sciences and Informatics (OHDSI, as “Odyssey”)

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

A multi-stakeholder, interdisciplinary, international collaborative with a coordinating center at Columbia University

http://ohdsi.org



George Hripcsak



Patrick Ryan

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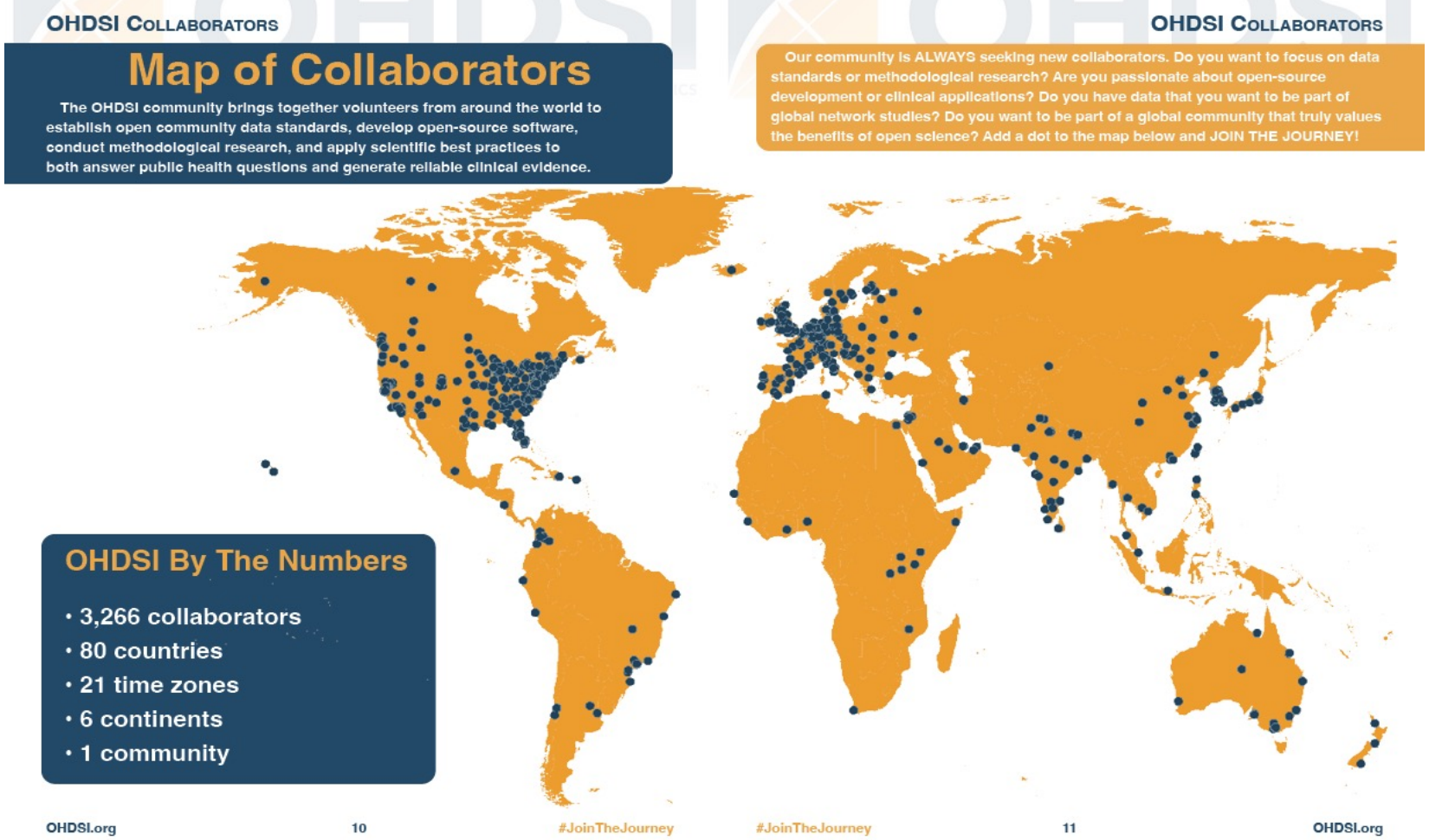

- Experts in informatics, statistics, epidemiology, clinical sciences
- Active participation from academia, government, industry, providers
- Currently records on about **800 million unique patients** in >300 databases
- 344 papers, specific influence on EMA and FDA for COVID-19

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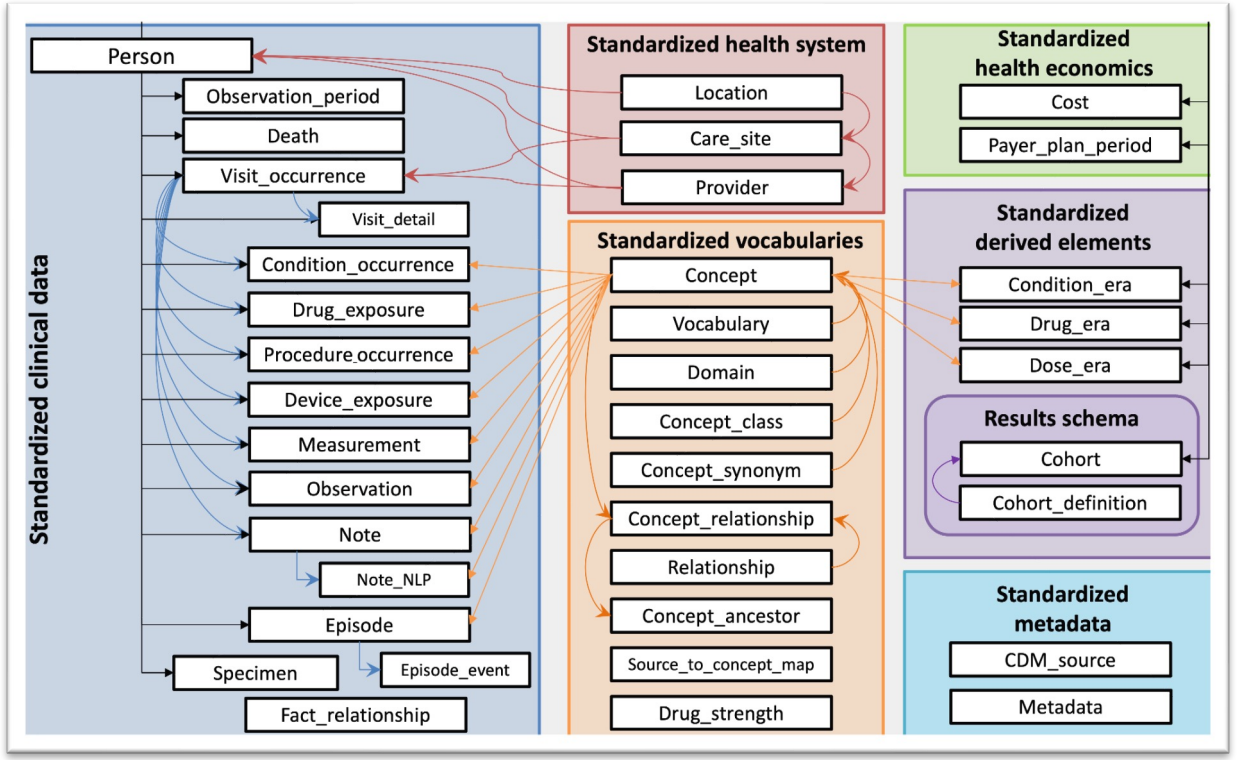
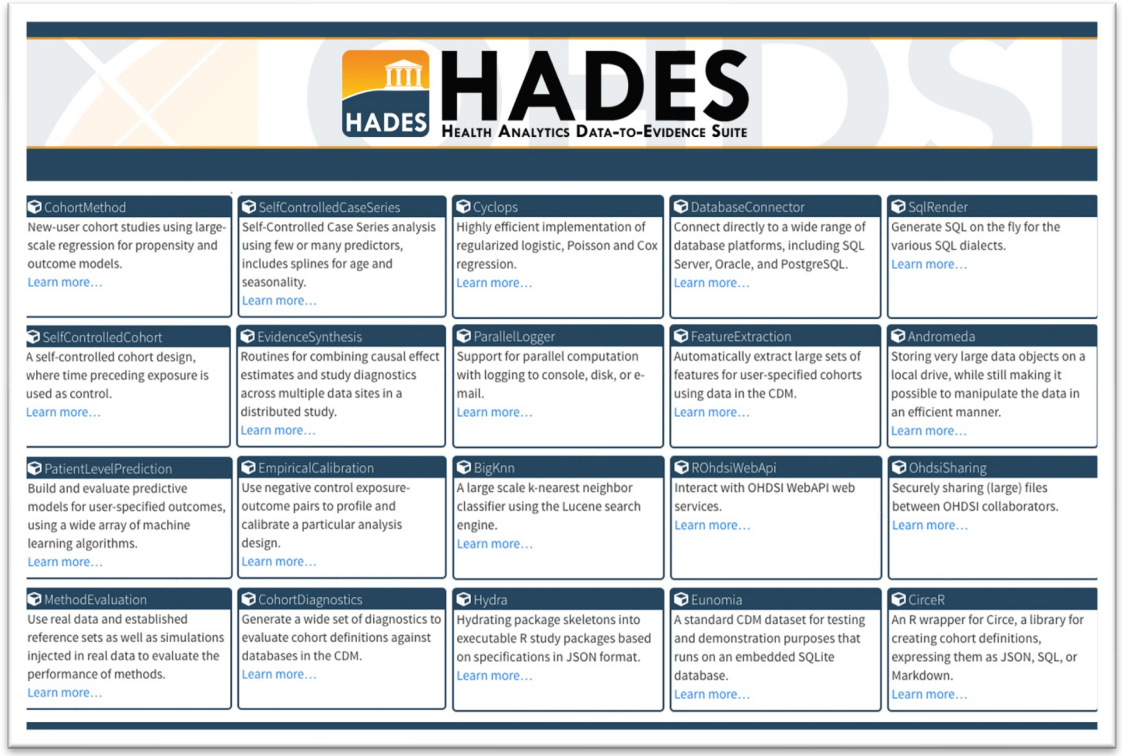
Core foundations for OHDSI



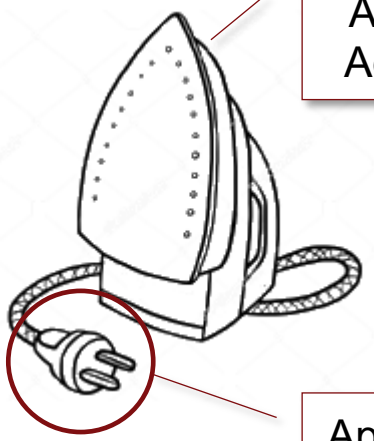
OMOP Common Data Model



Open-Source Analytics

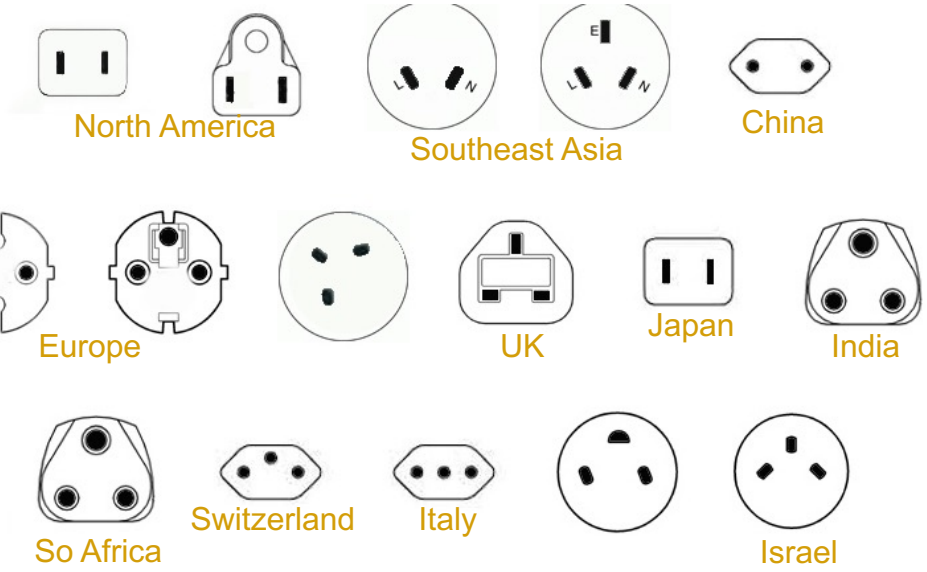
Lack of standards across EHR databases and analytics

"What's the adherence to my drug in the data assets I own?"



Analytical method:
Adherence to Drug

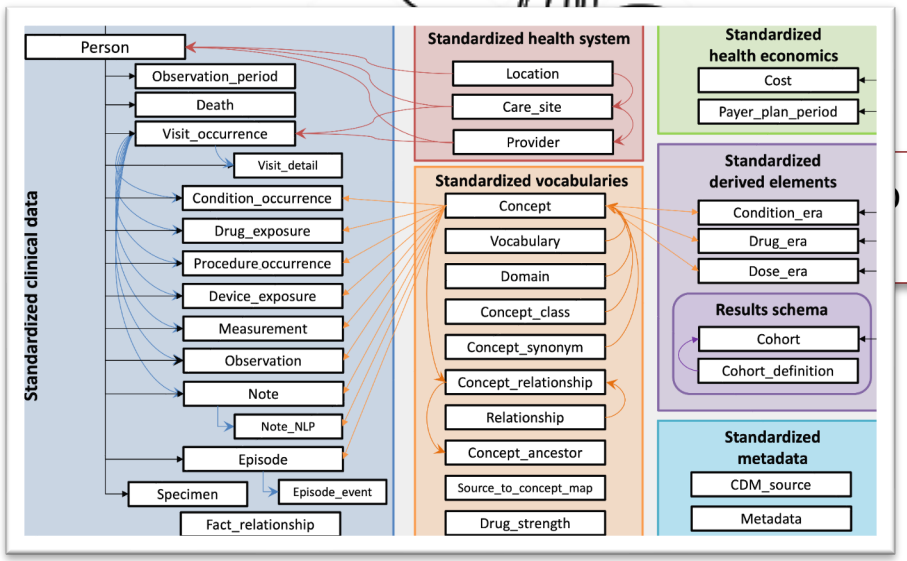
Application to data



Solution 1: OMOP Common Data Model

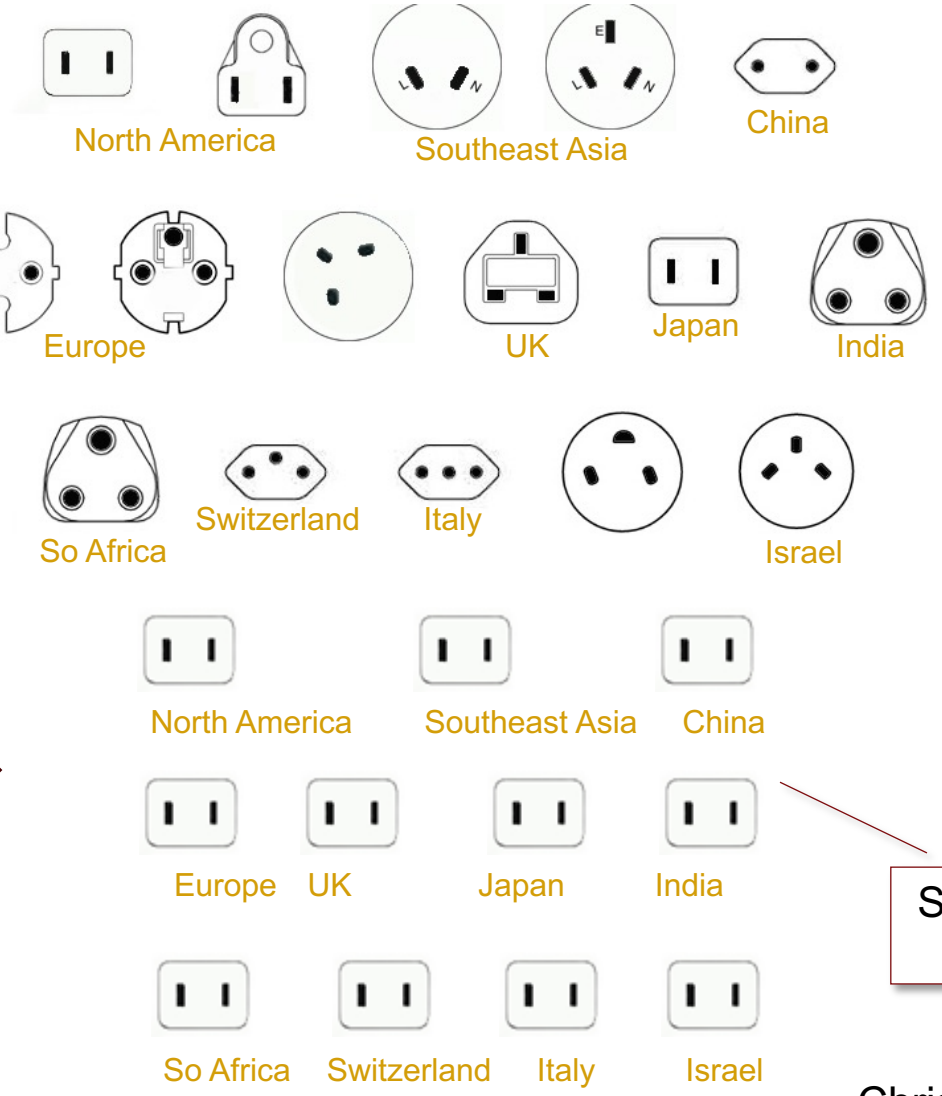
"What's the adherence to my drug in the data assets I own?"

Analytical method:
Adherence to Drug



Standard vocabulary

Standard data structure



Standardized data

Christian Reich

Solution 2: Open-source Analytics

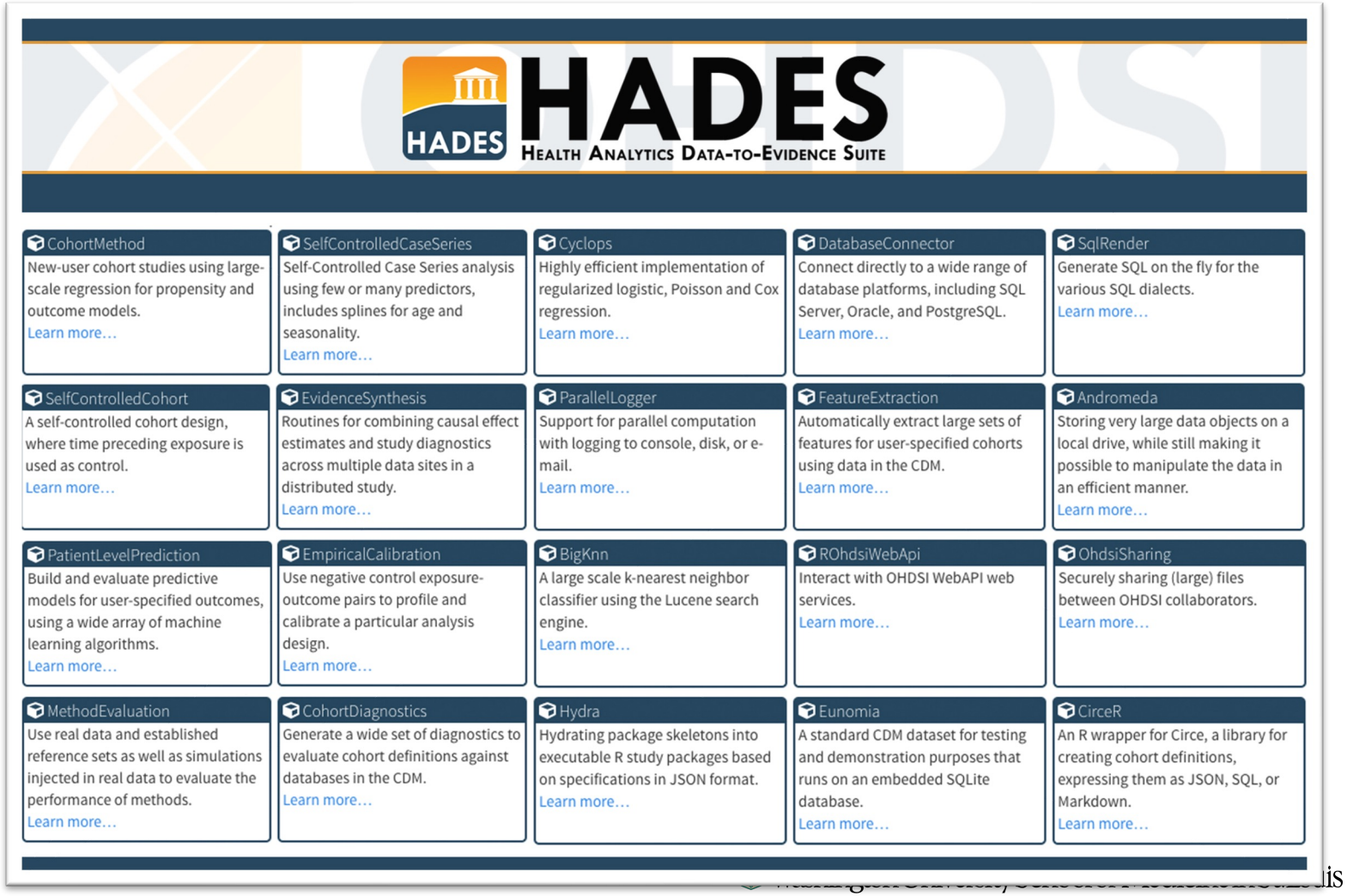
HADES includes over 20 open-source R packages for large scale analytics, including

- population characterization
- population-level effect estimation
- patient-level prediction
- other supporting packages

https://github.com/OHDSI



Martijn Schuemie



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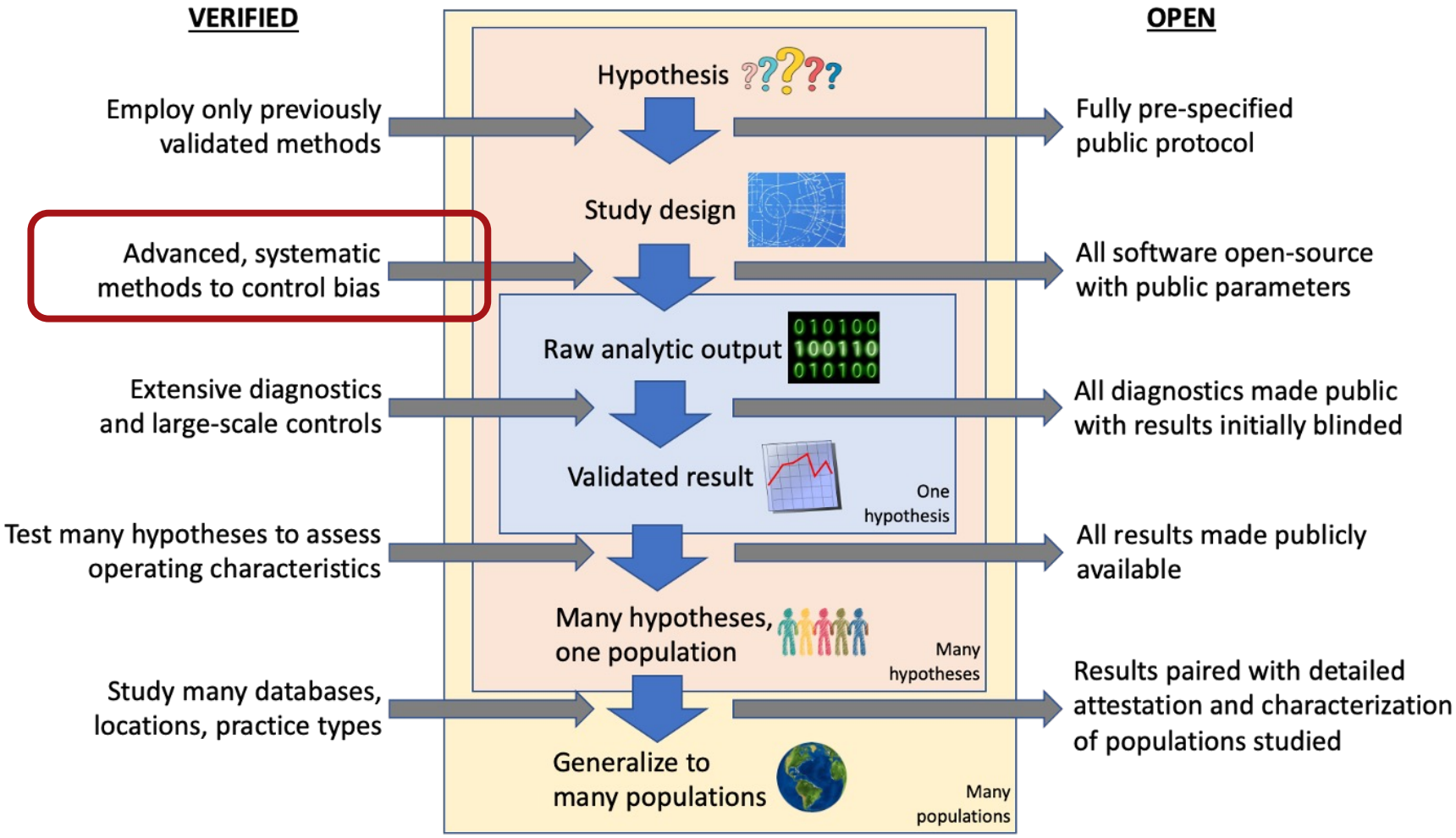
Verified and Open

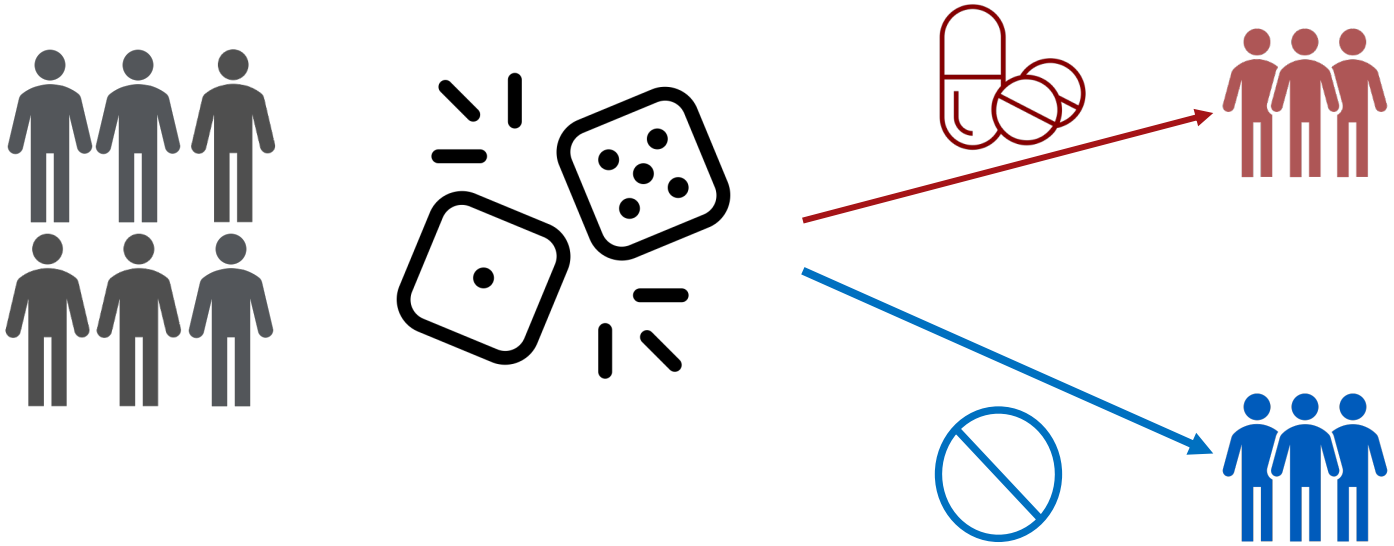


Treatment effect estimation

1. **Method: Large-scale propensity score**
2. Clinical example: Anti-VEGF and kidney failure

Randomized controlled trials: the gold standard

- Randomized controlled trials (RCTs) are prospective studies that measure the efficacy and safety of a treatment.
- RCT is considered as the gold-standard for establishing cause-and-effect relationships.
- Randomization balances participants characteristics and reduces confounding bias.



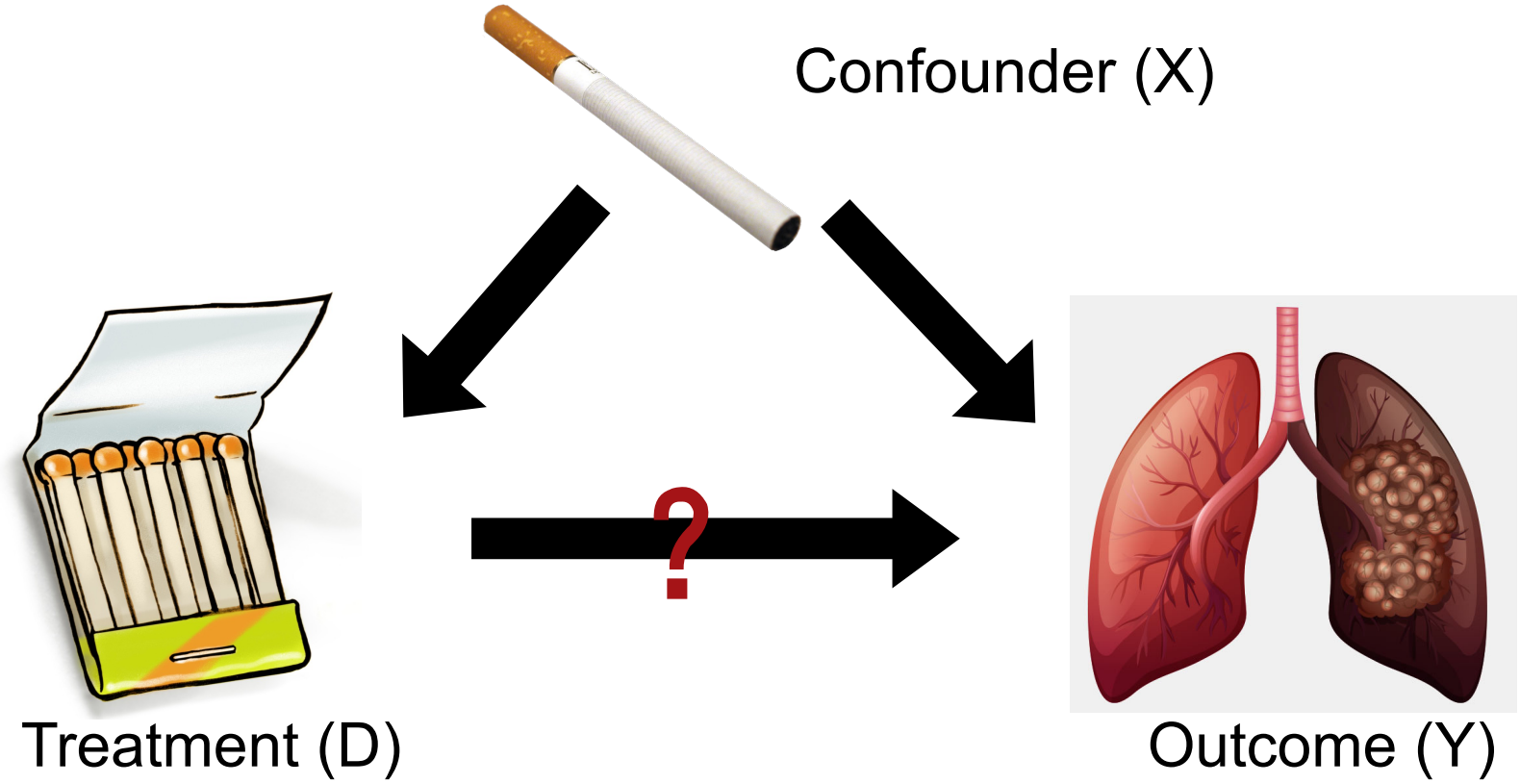
RCT is not always a viable option



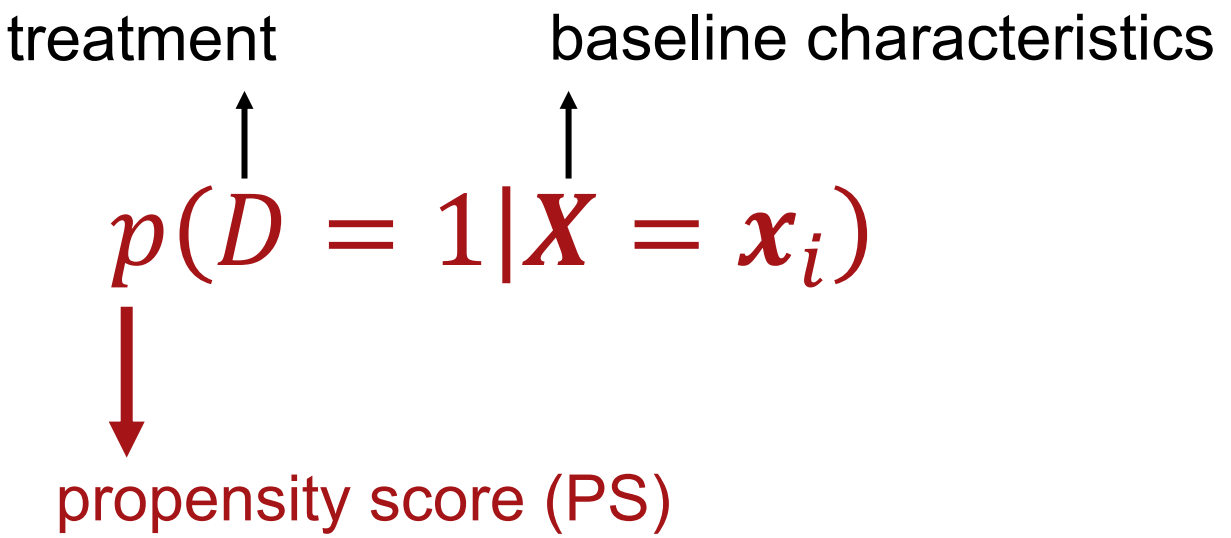
How can we estimate causal effects with observational data?

Confounding bias

Confounding remains one of the major challenges to causal inference with observational data.



Propensity score is a popular method to adjust for confounding.



Propensity score is the probability of a patient receiving the treatment given the patient's baseline characteristics.

Propensity scores can be estimated from data

$$\text{logit}(\hat{p}) = \hat{\beta}_0 + \underbrace{\hat{\beta}_1 x_{i1} + \cdots + \hat{\beta}_j x_{ij}}_{\text{“confounders”}}$$

propensity score

- In practice, propensity score is often estimated with a logistic regression.
- Treatment status is regressed on measured covariates that are believed to be confounders.

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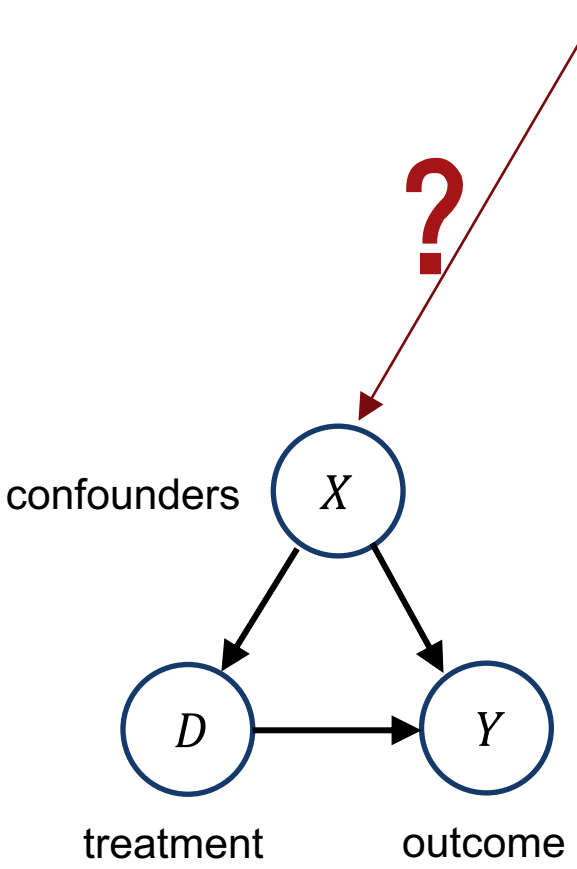
How are confounders selected?

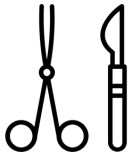


EHR database











Demographics Diagnoses Drugs Procedures Labs



Domain Knowledge

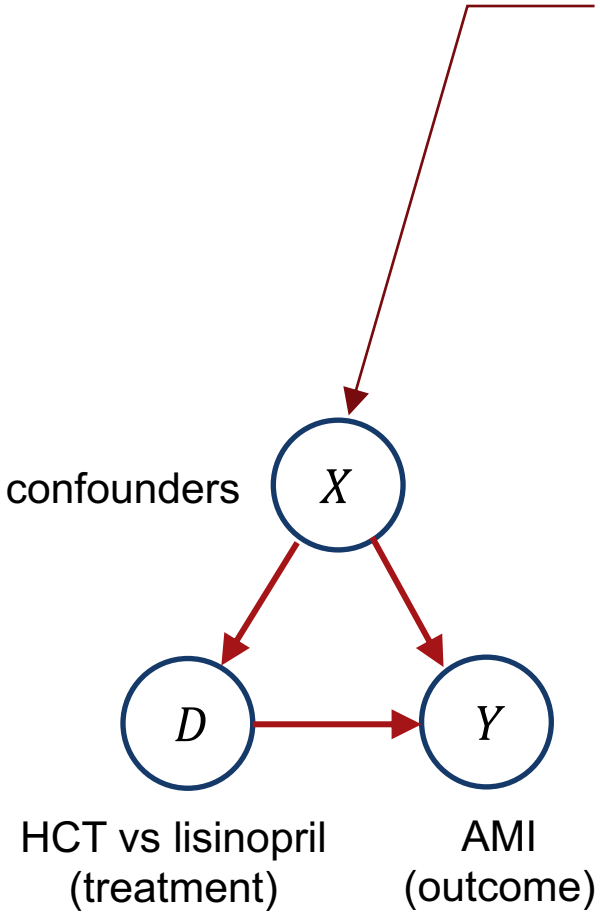


Literature Review



Empirical association

How well do observational studies agree on confounders?



Hicks 2018: age, sex, year of cohort entry, body mass index, smoking status, alcohol related disorders (including alcoholism, alcoholic cirrhosis of the liver, alcoholic hepatitis, and hepatic failure), and history of lung diseases (including pneumonia, tuberculosis, and chronic obstructive pulmonary disease), duration of HTN Rx, statin use, #drugs

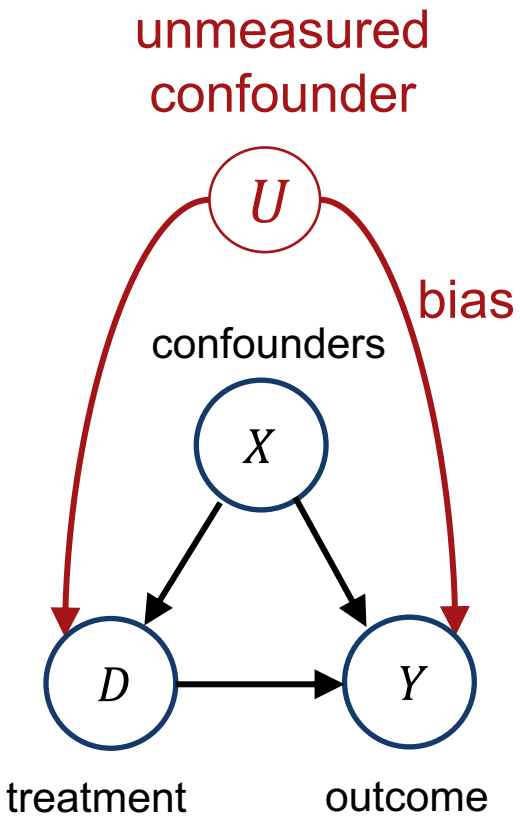
Ku 2018: age, sex, race, income status, baseline HF, baseline myocardial infarction, baseline peripheral artery disease, baseline stroke, baseline eGFR, baseline proteinuria, and time-dependent covariates including diabetes mellitus, obesity, systolic blood pressure, statin use, aspirin use, diuretic use, and concurrent use of other antihypertensive agents for the outcome of HF

Magid 2010: age, gender, days on thiazide prior to 2nd agent start, # of visits prior to thiazide, Mean Systolic BP, Mean Diastolic BP, Chronic Obstructive Pulmonary Disease, Hyperlipidemia, Cancer, Dementia, Chronic liver disease, Depression

Hasvold 2014: age, gender, elevated blood glucose, overweight and low socio-economic status are known risk factors for diabetes, High cholesterol and hypertension are additionally known risk factors for CVD

Blue: good agreement. Green: partial agreement. Red: lack of agreement

Unmeasured confounder leads to biased estimates



- **Poor agreement** among manually selected confounders.
  - Confounding structure is rarely known.
- Missing a confounder will lead to **biased effect estimates**.
- Poor agreement on confounders across studies **weakens the reliability** of evidence from real-world data.

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Large-Scale Propensity Score (LSPS): A systematic approach to adjust for confounding



All (~60,000) covariates

$$p(D = 1|\boldsymbol{X} = \boldsymbol{x}_i)$$

All covariates except

- Mediators (pre-treatment only)
- Simple colliders (pre-treatment only)
- "Instruments" (diagnostics, domain knowledge)
- M-structure collider (no bias if its causes are measured and adjusted)

LSPS includes (nearly) **all covariates** in the propensity model to adjust for confounding.

Tian Y et al. *Int J Epidemiol*. 2018.
Zhang et al. *J of Biomed Inform*. 2022

Study Design: Manual PS vs LSPS

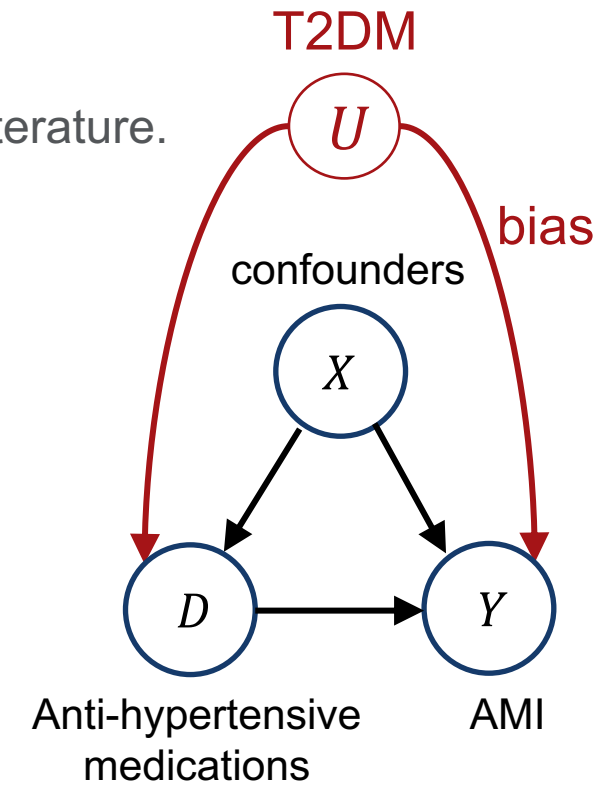
X: Selected covariates (~100s) based on domain knowledge and existing literature.

- Manual (X+U)
- Manual (X)

X: All pre-treatment covariates (~60,000)

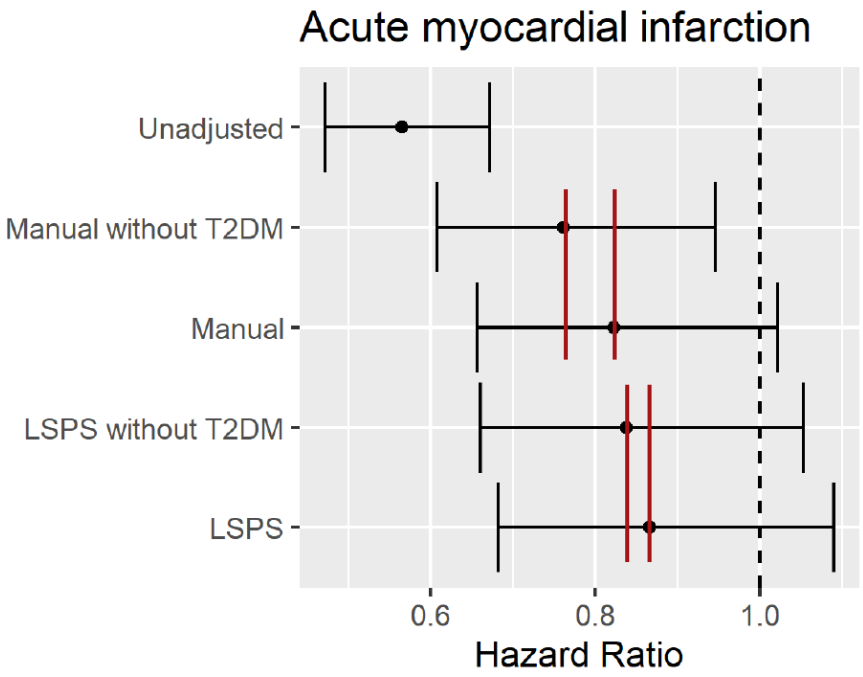
- LSPS (X+U)
- LSPS (X)

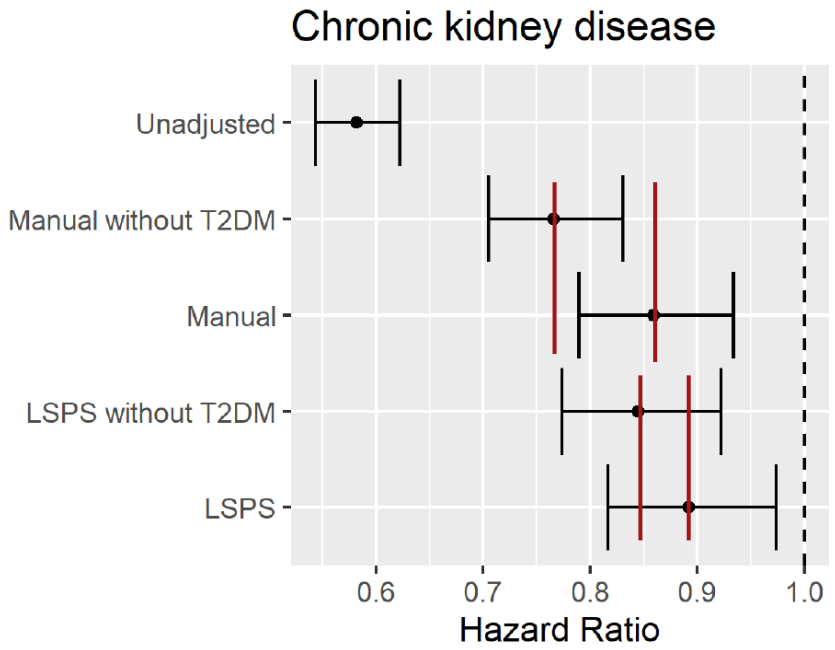
Note: U includes all T2DM diagnoses and anti-glycemic medications (~50).



Manual PS vs LSPS

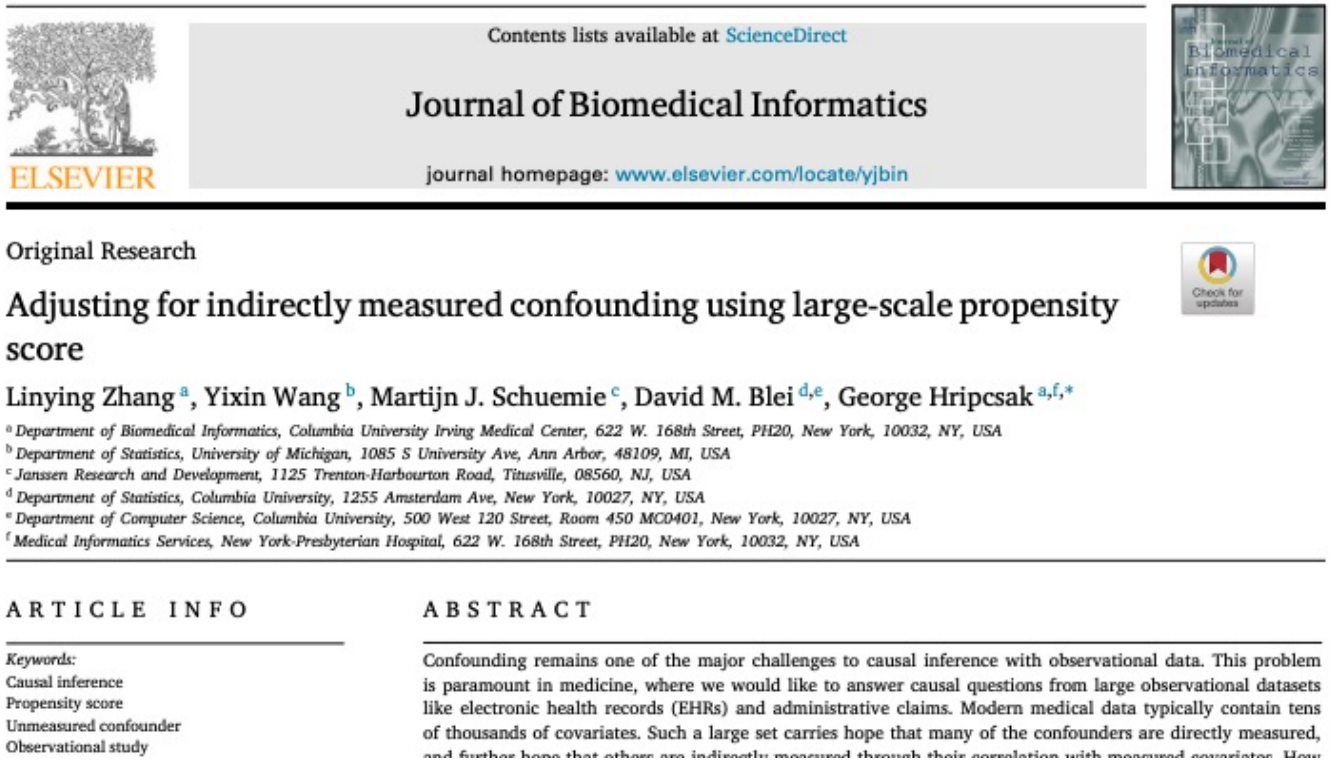
LSPS is more robust to unmeasured confounding than classical PS with manual covariate selection.





Reference

Zhang L., Wang Y., Schuemie M.J., Blei D.M., and Hripcsak G. Adjusting for indirectly measured confounding using large-scale propensity score. *Journal of Biomedical Informatics*, 2022.



Contents lists available at ScienceDirect

Journal of Biomedical Informatics

journal homepage: www.elsevier.com/locate/yjbin

Original Research

Adjusting for indirectly measured confounding using large-scale propensity score

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[d] Department of Statistics, Columbia University, 1255 Amsterdam Ave, New York, 10027, NY, USA
[e] Department of Computer Science, Columbia University, 500 West 120 Street, Room 450 MC0401, New York, 10027, NY, USA
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Propensity score
Unmeasured confounder
Observational study

ABSTRACT

Confounding remains one of the major challenges to causal inference with observational data. This problem is paramount in medicine, where we would like to answer causal questions from large observational datasets like electronic health records (EHRs) and administrative claims. Modern medical data typically contain tens of thousands of covariates. Such a large set carries hope that many of the confounders are directly measured,

Treatment effect estimation

1. Method: Large-scale propensity score
2. **Clinical example: Anti-VEGF and kidney failure**

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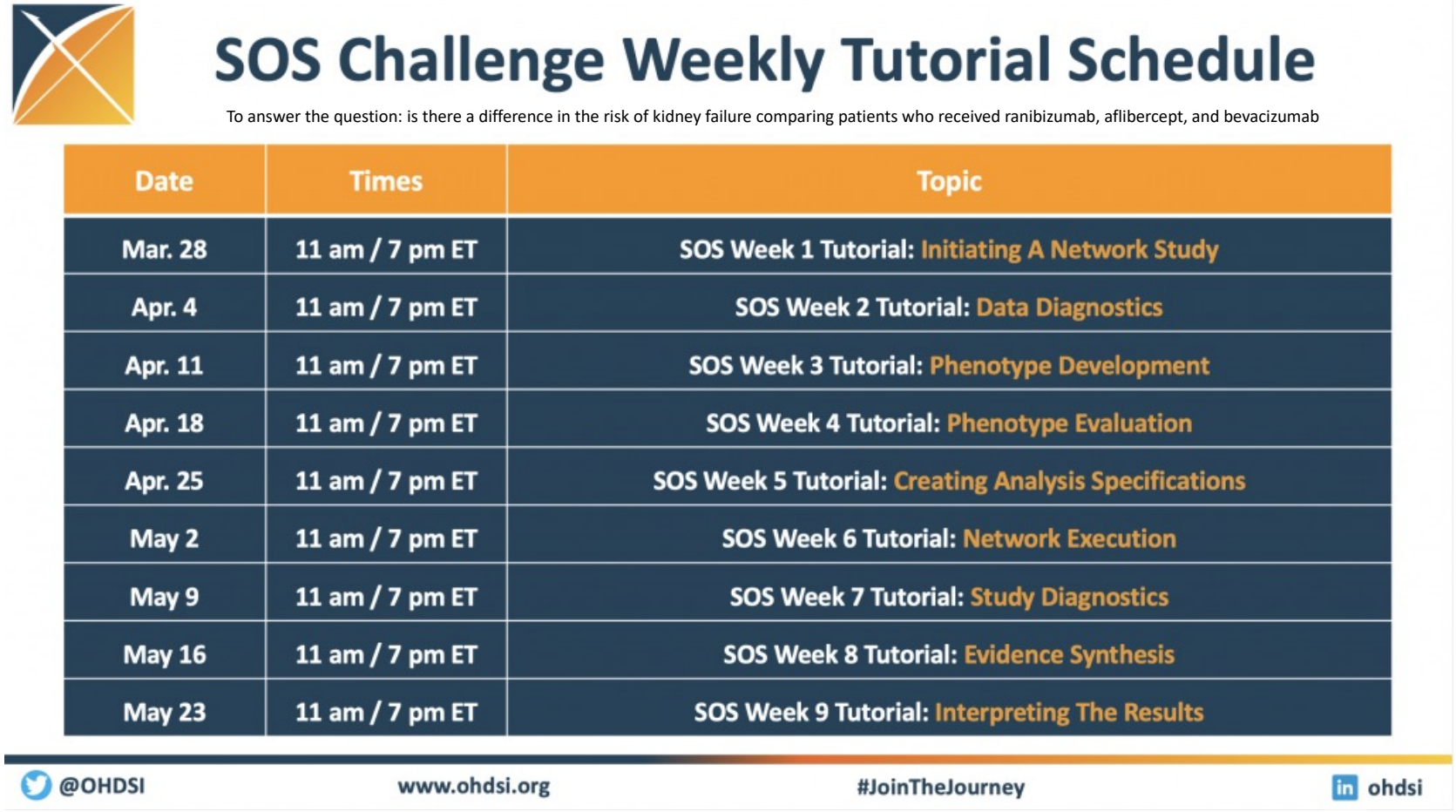

4 network studies in 9 weeks

- Anti-VEGF and kidney failure
- Fluoroquinolone and aortic aneurysms
- Risankizumab and cerebrovascular events
- Multiple Sclerosis biologics and progressive multifocal leukoencephalopathy

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Anti-VEGF and kidney failure

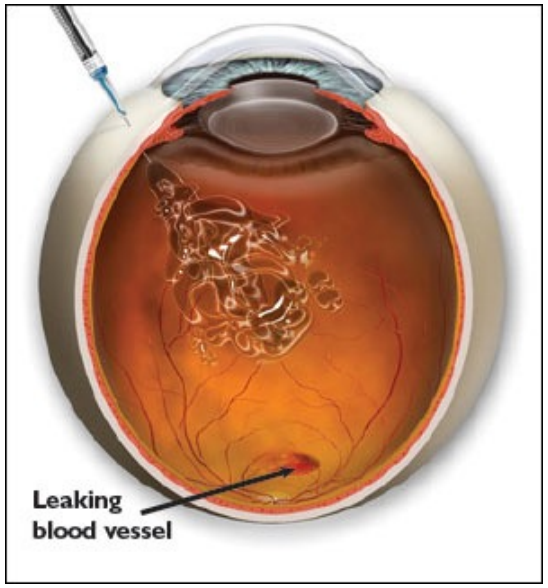
- Anti-vascular endothelial growth factor (anti-VEGF) medications
- Systemic administration of anti-VEGF agents have known adverse kidney side effects
  - Acute kidney injury
  - Proteinuria
  - Hypertension
  - Vascular clotting events
  - Glomerular disease
  - Risk factors for: kidney failure (need for renal replacement therapy with dialysis or kidney transplant, aka end stage kidney disease or end stage renal disease)



Cindy X. Cai

Washington University School of Medicine in St. Louis

Intravitreal Anti-VEGF and Systemic Absorption



Drug	Size	Systemic Elimination (half-life)
Ranibizumab	48 kDa	2 hours
Aflibercept	115 kDa	5-6 days
Bevacizumab	149 kDa	20 days

Detectable/elevated serum drug levels
Decreased plasma concentrations of free-VEGF

Bevacizumab > aflibercept >> ranibizumab

Question: Is there evidence for preferentially choosing ranibizumab to lower the risk of kidney failure?

Hypothesis: in pairwise comparisons, lower risk of kidney failure in patients with blinding diseases who are exposed to ranibizumab

https://www.randeye.com/intravitreal-injection/
Avery RL, Castellarin AA, Steinle NC, et al. SYSTEMIC PHARMACOKINETICS AND PHARMACODYNAMICS OF INTRAVITREAL AFLIBERCEPT, BEVACIZUMAB, AND RANIBIZUMAB. *Retin*. 2017;37(10):1847-1858. doi:10.1097/iae.0000000000001493
https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/125085s0169lbl.pdf

OHDSI Study: Intravitreal anti-VEGF and Kidney Failure

Wilmer Eye Institute
Johns Hopkins Medicine

- Estimating the **comparative risk of kidney failure** associated with intravitreal anti-vascular endothelial growth factor exposure in patients with blinding diseases (DR/DME, AMD, VO)
  - Amongst people with blinding diseases, does exposure to **ranibizumab** increase the risk of kidney failure, relative to **aflibercept**?
  - Amongst people with blinding diseases, does exposure to **bevacizumab** increase the risk of kidney failure, relative to **aflibercept**?
  - Amongst people with blinding diseases, does exposure to **bevacizumab** increase the risk of kidney failure, relative to **ranibizumab**?

Hypothesis: in these pairwise comparisons, lower risk of kidney failure in patients with blinding diseases who are exposed to ranibizumab

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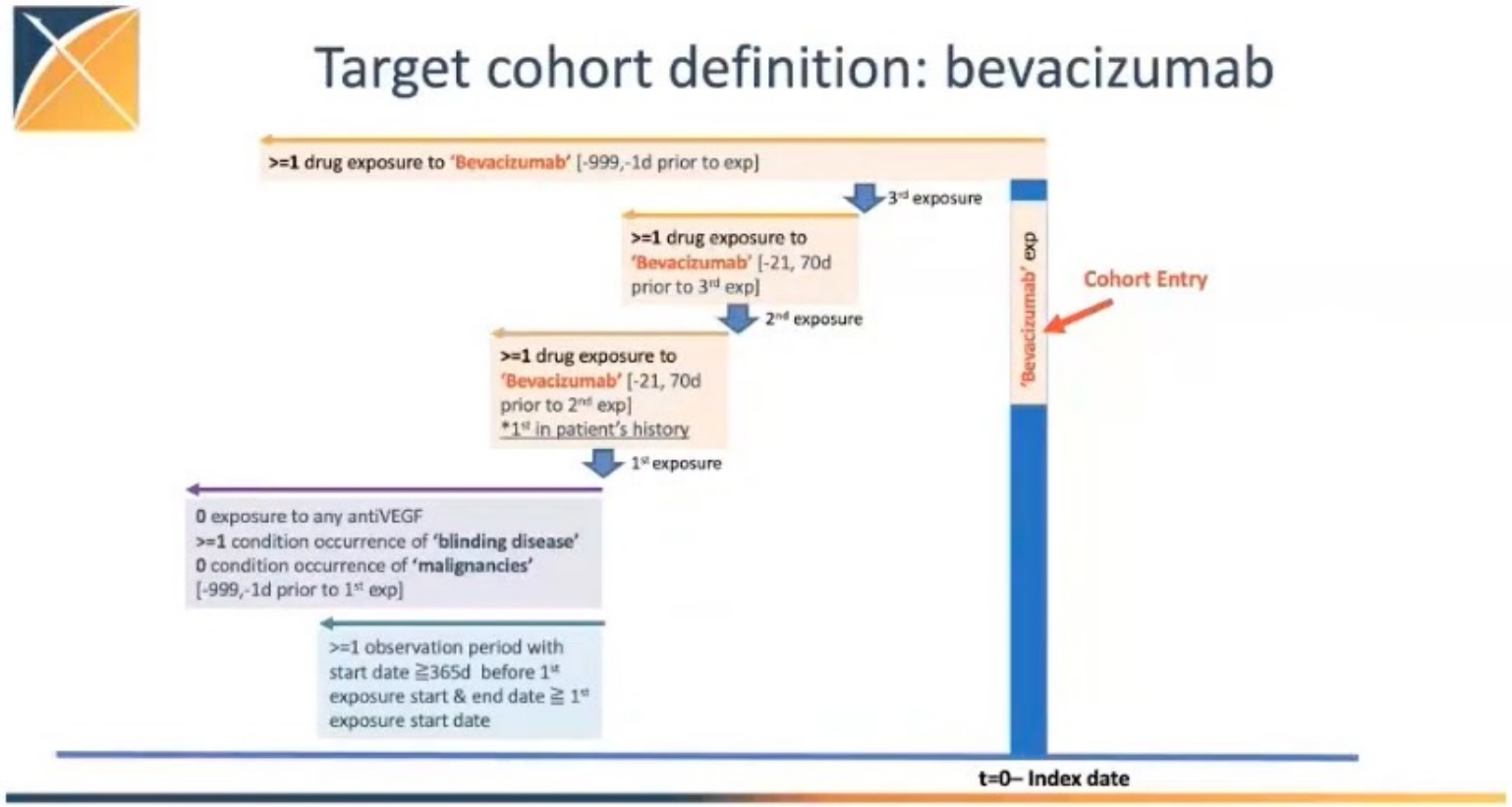
Data databases/partners

- 12 databases:
  - 6 claims and 6 EHRs
- Total 485 million patients

Data Sources
IBM Health MarketScan Medicare Supplemental and Coordination of Benefits Database (MDCR)
IBM Health MarketScan Commercial Claims and Encounters Database (CCAE)
IBM Health MarketScan Multi-State Medicaid Database (MDCD)
Optum(R) de-identified Electronic Health Record Dataset (OptumEHR)
Optum's Clinformatics Extended Data Mart - Socio-economic Status (SES)
Japan Medical Data Center (JMDC)
Johns Hopkins Medical Enterprise (JHME)
Department of Veterans Affairs (VA)
PharMetrics Plus (NEU)
Columbia University Medical Center (CUMC)
Stanford (STARR)
University of Southern California (USC)

Cohort definition



- New users of 3 monthly anti-VEGF medications with blinding diseases
- Study protocol: https://ohdsi-studies.github.io/AntiVegfKidneyFailure/Protocol.html

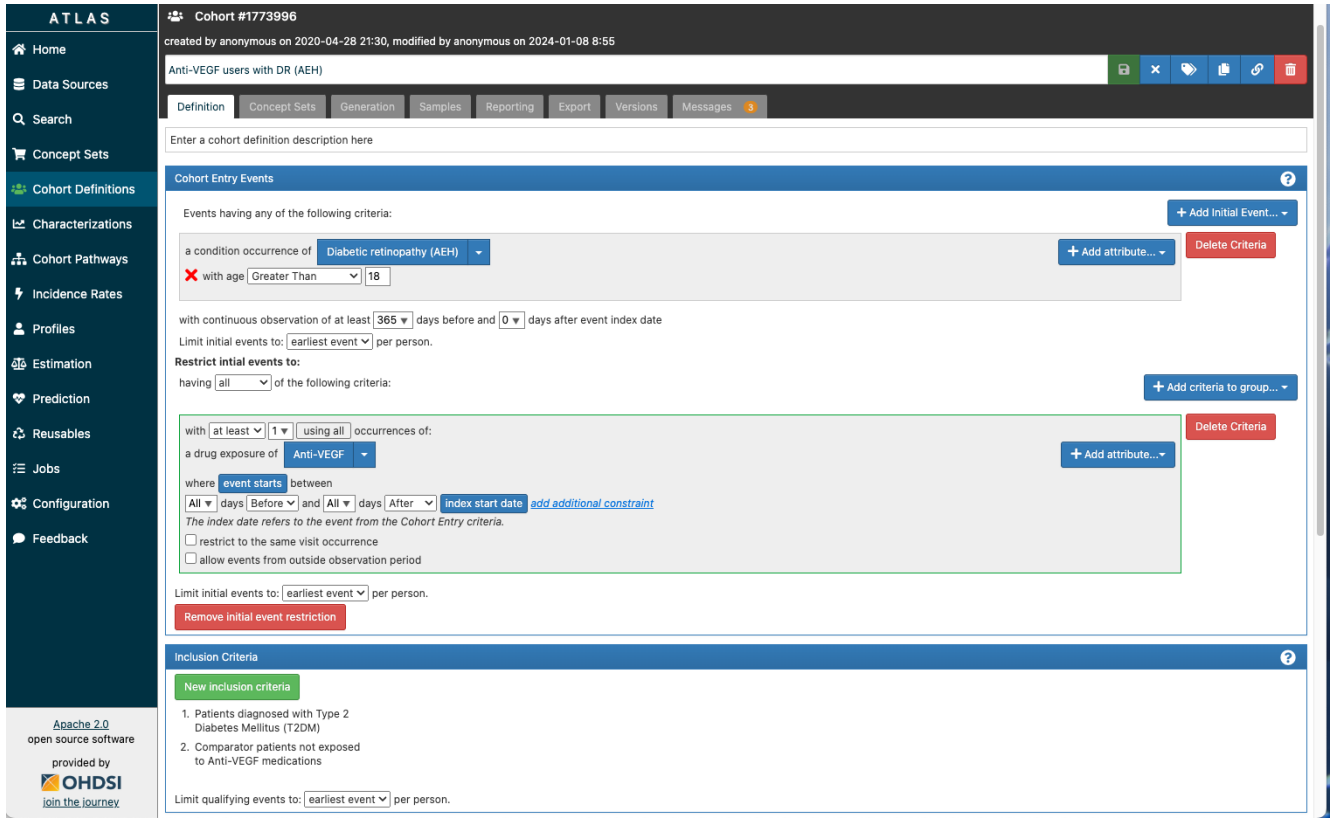
Phenotype Development

- Phenotypes:
  - Binding diseases
  - anti-VEGF medications
  - kidney failure
- Tools:
  - ATLAS WebAPI:

    https://atlas-demo.ohdsi.org/
  - PHOEBE (concept recommender)

    https://data.ohdsi.org/PHOEBE/
  - PheValuator (phenotype diagnostic)

    https://doi.org/10.1016/j.jbi.2019.103258



Population-level effect estimation

- Large-scale propensity score (LSPS) was used to match target/comparator cohorts using 1:1 propensity score matching
- Cox proportional hazards model was used to estimate the risk of kidney failure
- Code repository: https://github.com/ohdsi-studies/AntiVegfKidneyFailure

Study diagnostics

Comparison groups	Database	Maximum standardized mean difference (balance diagnostic)	Equipoise (equipoise diagnostic)	MDRR (MDRR diagnostic)	Attrition Fraction (attrition diagnostic)	EASE (EASE diagnostic)
Aflibercept / Ranibizumab	CCAE	0.065 (pass)	0.607 (pass)	2.049 (pass)	0.536 (pass)	0.054 (pass)
	MDCR	0.056 (pass)	0.729 (pass)	2.736 (pass)	0.498 (pass)	0.050 (pass)
	MDCD§	0.118 (fail)	0.624 (pass)	3.396 (pass)	0.693 (pass)	0.109 (pass)
	OptumEHR§	0.117 (fail)	0.382 (pass)	4.058 (pass)	0.758 (pass)	0.180 (pass)
	SES	0.054 (pass)	0.781 (pass)	1.805 (pass)	0.511 (pass)	0.032 (pass)
	JMDC§	0.260 (fail)	1 (pass)	NA (fail)	0.486 (pass)	0.431 (fail)
	JHME§	0.953 (fail)	0.472 (pass)	NA (fail)	0.981 (pass)	NA (fail)
	NEU	0.084 (pass)	0.900 (pass)	3.217 (pass)	0.583 (pass)	0.085 (pass)
	CUMC§	0.965 (fail)	0.391 (pass)	NA (fail)	0.963 (pass)	NA (fail)
	STARR§	NA (fail)	NA (fail)	NA (fail)	NA (fail)	NA (fail)
	VA	0.080 (pass)	0.357 (pass)	3.746 (pass)	0.847 (pass)	0.092 (pass)
	USC§	NA (fail)	NA (fail)	NA (fail)	NA (fail)	NA (fail)

EASE = Expected Absolute Systematic Error, MDRR = minimum detectable relative risk

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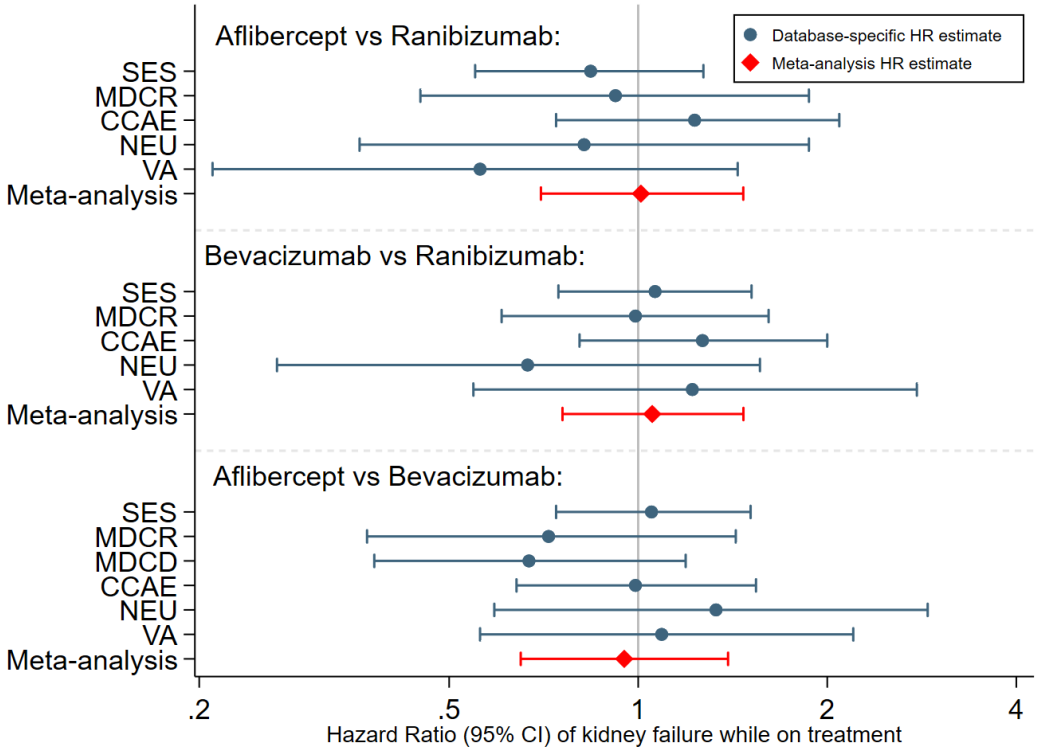
Wilmer Eye Institute
Johns Hopkins Medicine

Anti-VEGF OHDSI Study: Results

- 6.1 million patients with blinding diseases
  - 240,247 anti-VEGF
    - 37,189 received ranibizumab
    - 39,447 aflibercept
    - 163,611 bevacizumab
  - 1209 kidney failure outcomes
- Standardized incidence proportion of kidney failure: 680 per 100,000 persons
- In all pairwise comparison, the hazard ratio was around 1.0



For retina colleagues: can choose between any of these 3 anti-VEGF medications for those at risk for kidney failure

Washington University School of Medicine in St. Louis

Reference

ELSEVIER

Ophthalmology Retina

Available online 20 March 2024

In Press, Journal Pre-proof ⓘ What's this?



Similar risk of kidney failure among patients with blinding diseases who receive ranibizumab, aflibercept, and bevacizumab: an OHDSI Network Study

Cindy X. Cai MD, MS, Akihiko Nishimura PhD, Mary G. Bowring MPH, Erik Westlund PhD, Diep Tran MSc, Jia H. Ng MD, MSCE, Paul Nagy PhD, Michael Cook BS, Jody-Ann McLeggon MPH, Scott L. DuVall PhD, Michael E. Matheny MD, MS, MPH, Asieh Golozar PhD, Anna Ostropolets MD, PhD, Evan Minty MD MSc, Priya Desai MS, Fan Bu PhD, Brian Toy MD, Michelle Hribar PhD, Thomas Falconer MS, Linying Zhang PhD...Patrick B. Ryan PhD

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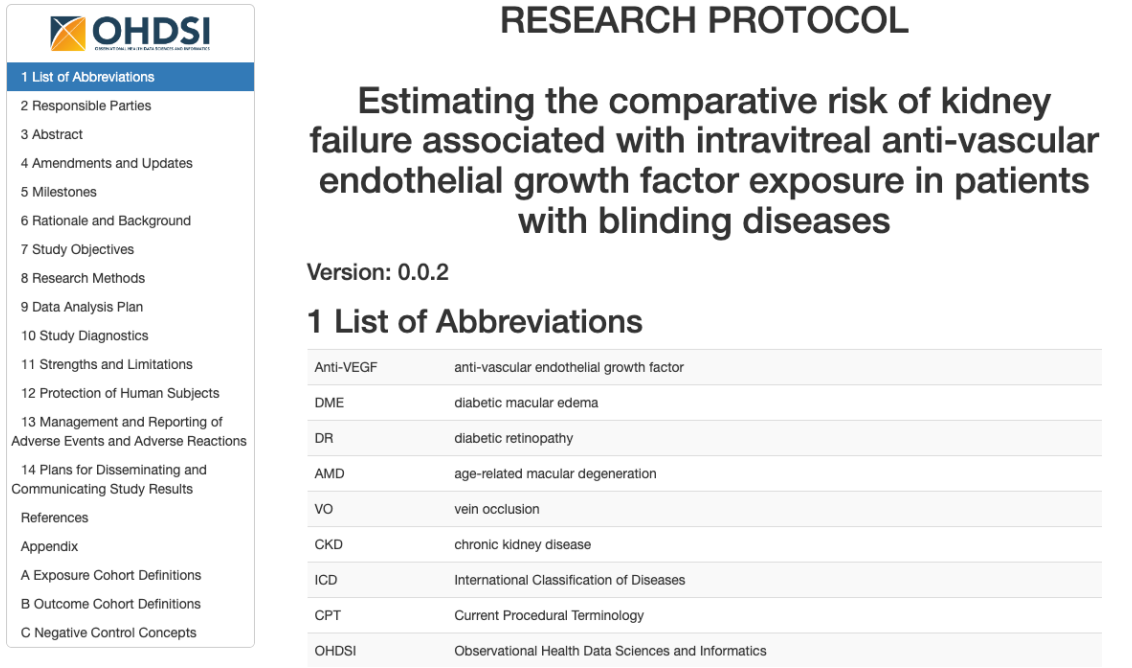
Anti-VEGF and kidney failure

- Study protocol: https://ohdsi-studies.github.io/AntiVegfKidneyFailure/Protocol.html
- Code: https://github.com/ohdsi-studies/AntiVegfKidneyFailure
- Results explorer:
  - https://data.ohdsi.org/AntiVegfKidneyFailure/ (main results);
  - https://data.ohdsi.org/AntiVegfKidneyFailure2/ (sensitivity analysis)



OHDSI

1 List of Abbreviations
2 Responsible Parties
3 Abstract
4 Amendments and Updates
5 Milestones
6 Rationale and Background
7 Study Objectives
8 Research Methods
9 Data Analysis Plan
10 Study Diagnostics
11 Strengths and Limitations
12 Protection of Human Subjects
13 Management and Reporting of Adverse Events and Adverse Reactions
14 Plans for Disseminating and Communicating Study Results
References
Appendix
A Exposure Cohort Definitions
B Outcome Cohort Definitions
C Negative Control Concepts

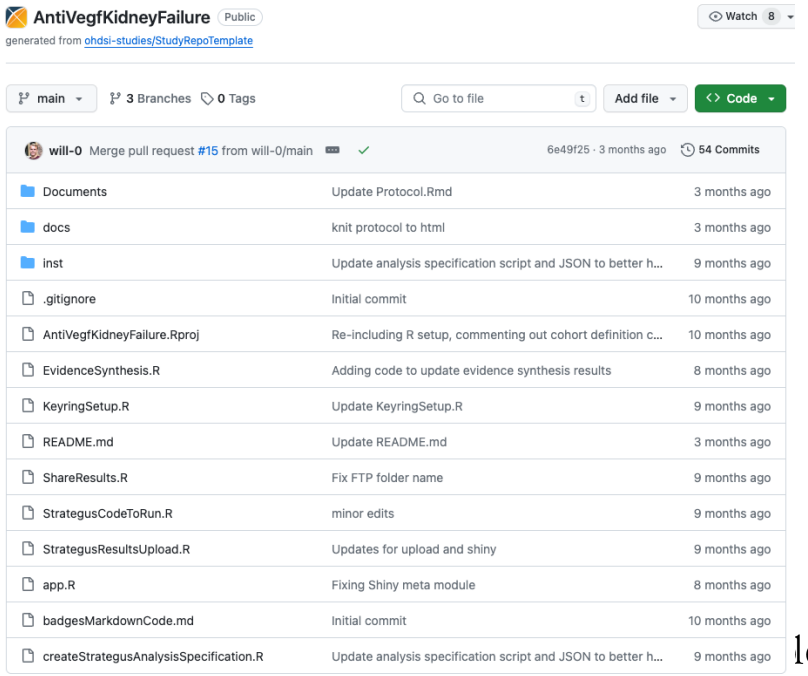
RESEARCH PROTOCOL

Estimating the comparative risk of kidney failure associated with intravitreal anti-vascular endothelial growth factor exposure in patients with blinding diseases

Version: 0.0.2

1 List of Abbreviations

Anti-VEGF	anti-vascular endothelial growth factor
DME	diabetic macular edema
DR	diabetic retinopathy
AMD	age-related macular degeneration
VO	vein occlusion
CKD	chronic kidney disease
ICD	International Classification of Diseases
CPT	Current Procedural Terminology
OHDSI	Observational Health Data Sciences and Informatics



AntiVegfKidneyFailure Public

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will-0 Merge pull request #15 from will-0/main 6e49f25 · 3 months ago · 54 Commits

Documents	Update Protocol.Rmd	3 months ago
docs	knit protocol to html	3 months ago
inst	Update analysis specification script and JSON to better h...	9 months ago
.gitignore	Initial commit	10 months ago
AntiVegfKidneyFailure.Rproj	Re-including R setup, commenting out cohort definition c...	10 months ago
EvidenceSynthesis.R	Adding code to update evidence synthesis results	8 months ago
KeyringSetup.R	Update KeyringSetup.R	9 months ago
README.md	Update README.md	3 months ago
ShareResults.R	Fix FTP folder name	9 months ago
StrategusCodeToRun.R	minor edits	9 months ago
StrategusResultsUpload.R	Updates for upload and shiny	9 months ago
app.R	Fixing Shiny meta module	8 months ago
badgesMarkdownCode.md	Initial commit	10 months ago
createStrategusAnalysisSpecification.R	Update analysis specification script and JSON to better h...	9 months ago

OHDSI

- Website: https://ohdsi.org/
- Weekly community call: Tuesday 10 am Central Time
  - Recordings: https://ohdsi.org/community-calls/
- Annual Global Symposium: https://www.ohdsi.org/ohdsi2023/
- 32 Workgroups: https://www.ohdsi.org/workgroups/

#JoinTheJourney



Data -> Evidence -> Practice



TREATMENT EFFECT ESTIMATION

Is a treatment effective?

Is a treatment safe?



HEALTH EQUITY

Is the healthcare system fair?

Is the clinical algorithm fair?



RISK PREDICTION

Can we predict mortality?

What are the risk factors?

Explaining Treatment Disparities with Causal Modeling

1. **Method: Causal fairness model**
2. Application: Revascularization in cardiology

Advancing Health Equity

"***Health equity*** is attainment of the highest level of health for all people."

-- Healthy People 2030





Clinical process



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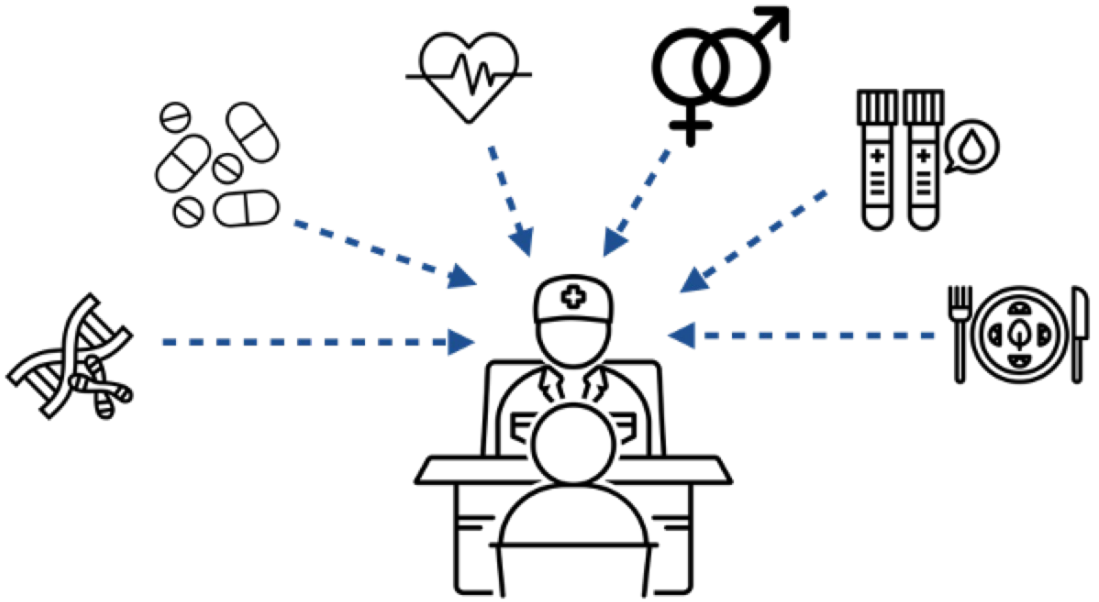
Understanding Treatment Disparities

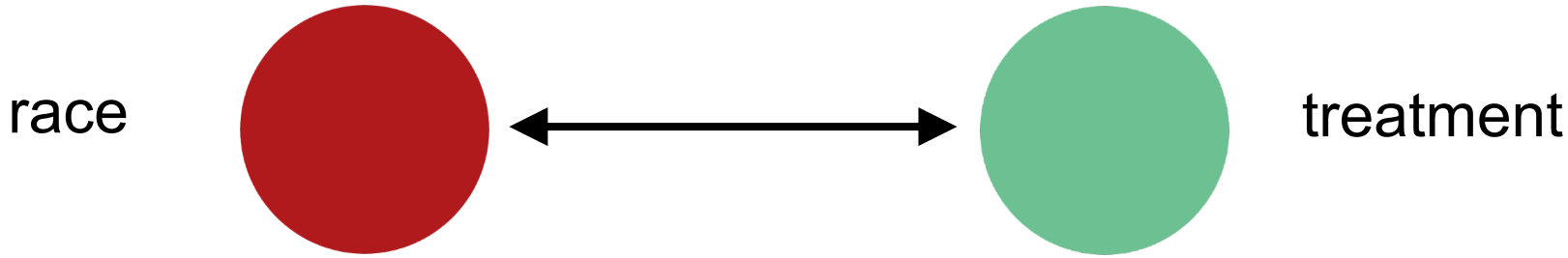
Care Access → Testing → Diagnosis → **Treatment** → Outcome Follow-up



From Quantifying to Explaining Disparities

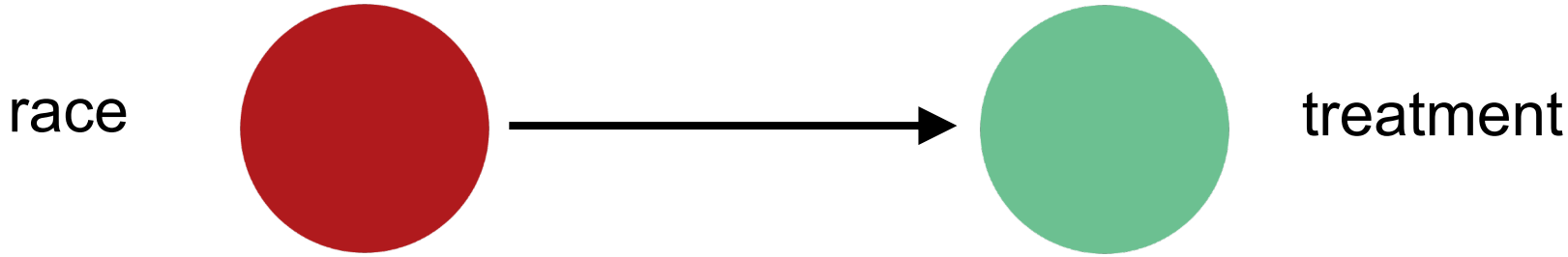
- In health disparities research, women and racial and ethnic minorities are often found to receive less treatment in various clinical domains.
- However, research on health disparities often relies on correlational analysis, which may not reveal the underlying causal mechanisms behind disparities.
- Question: How can we explain observed disparities in the data in terms of the unobservable causal mechanisms?

Causal Mechanisms



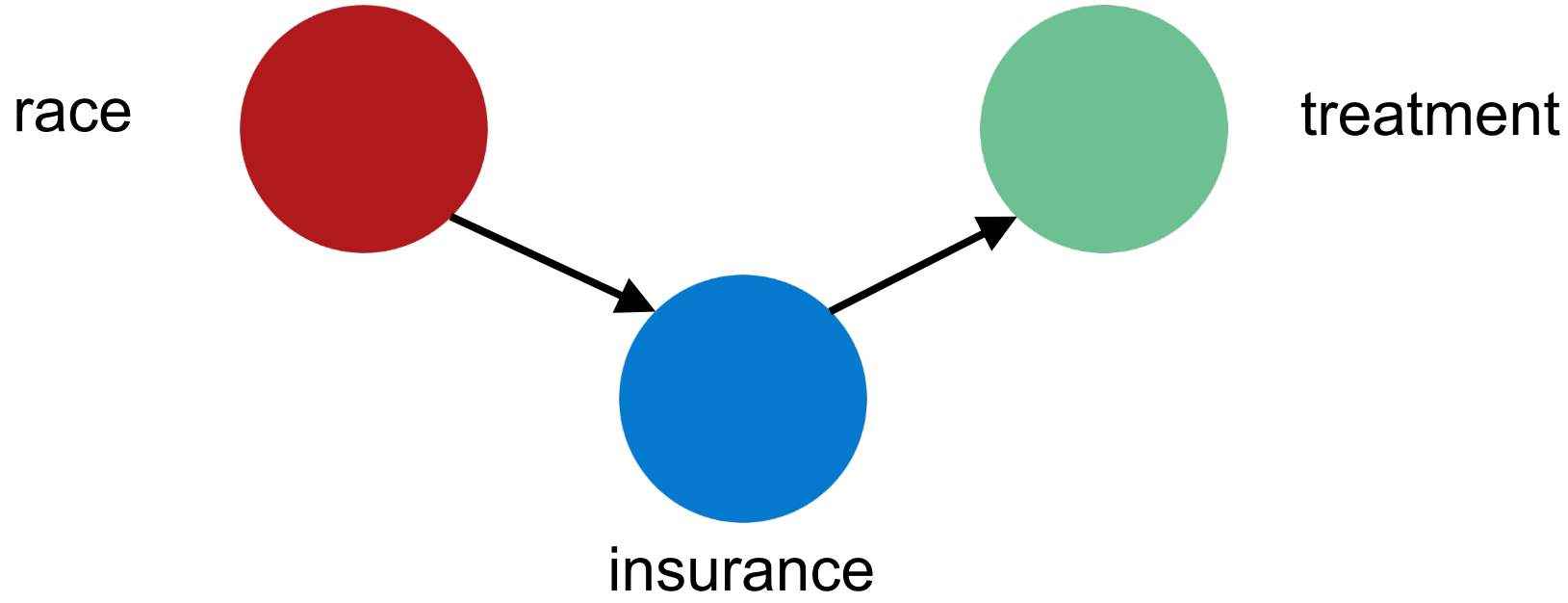
- There is racial difference in treatment pattern.

Causal Mechanisms



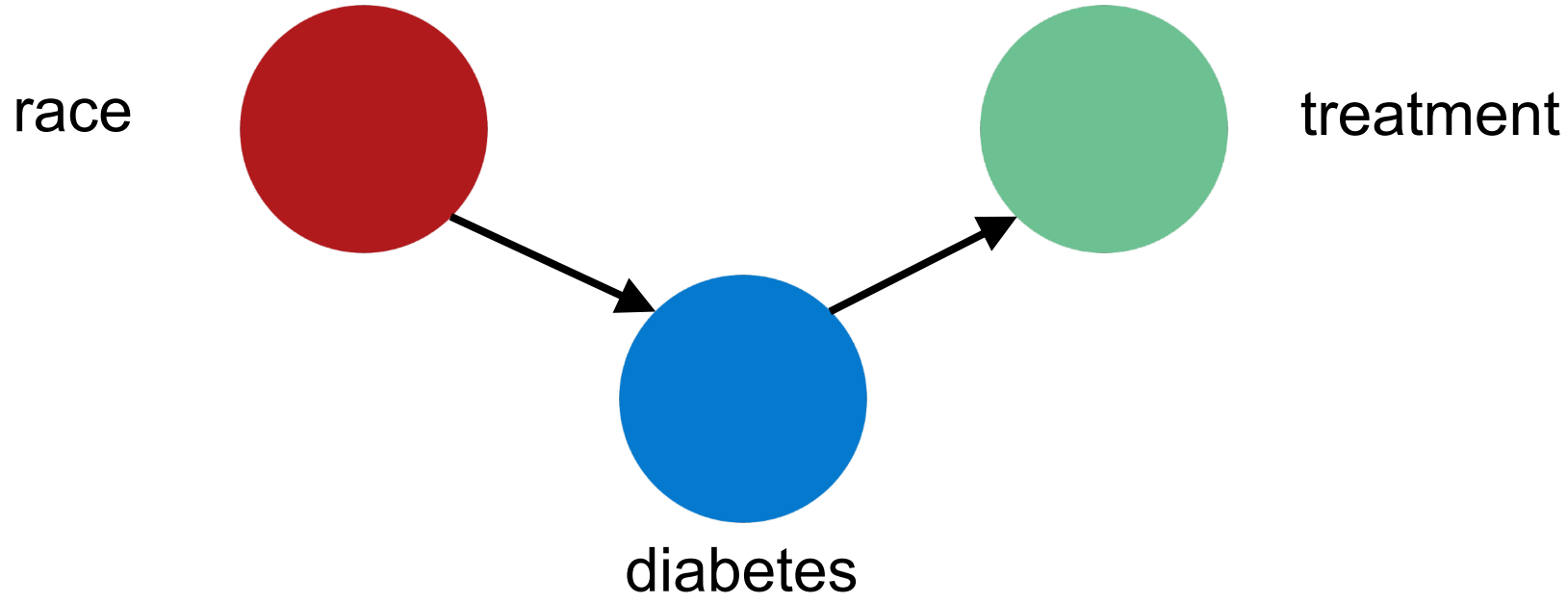
- Possible scenario 1:
  - Race is used *directly* in treatment decision-making.

Causal Mechanisms



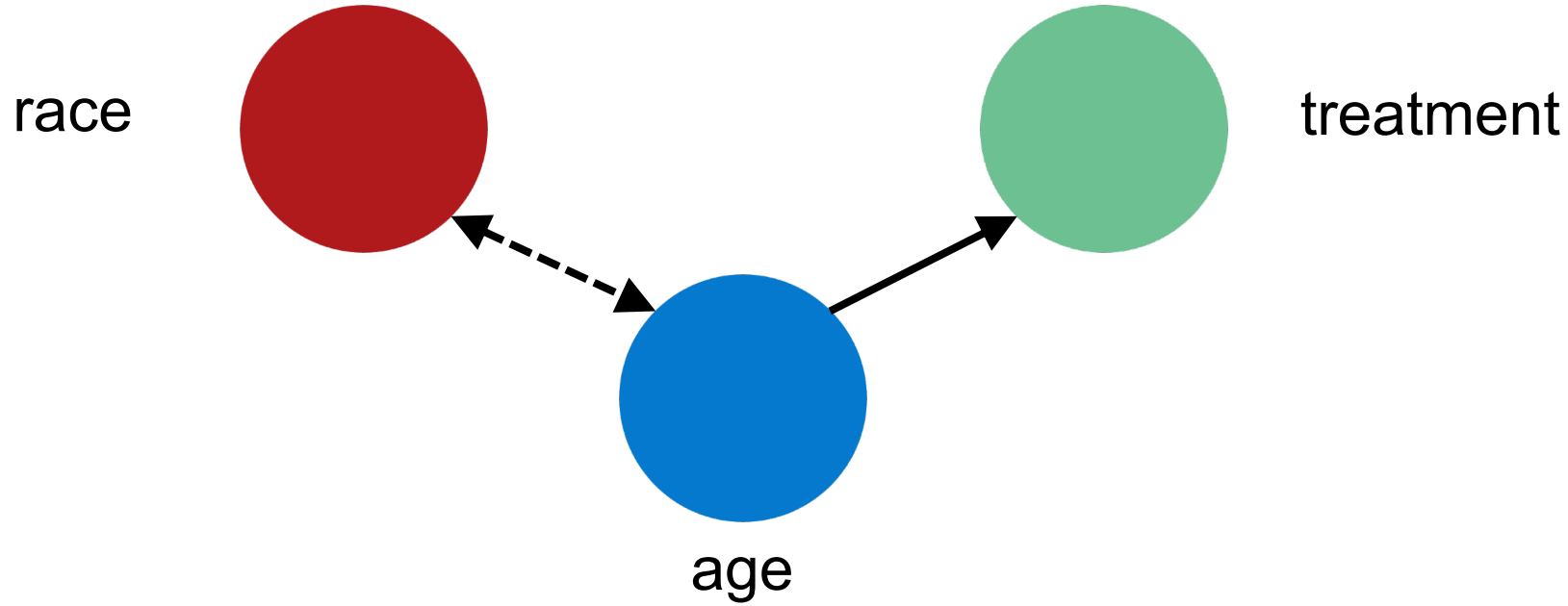
- Possible scenario 2.1:
  - Race *indirectly* causes difference in treatment patterns (via social factors)

Causal Mechanisms



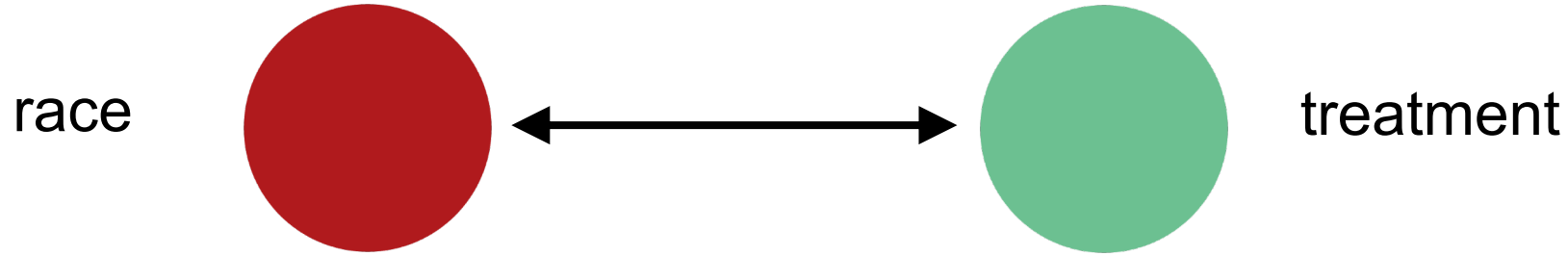
- Possible scenario 2.2:
  - Race *indirectly* causes difference in treatment patterns (via clinical factors).

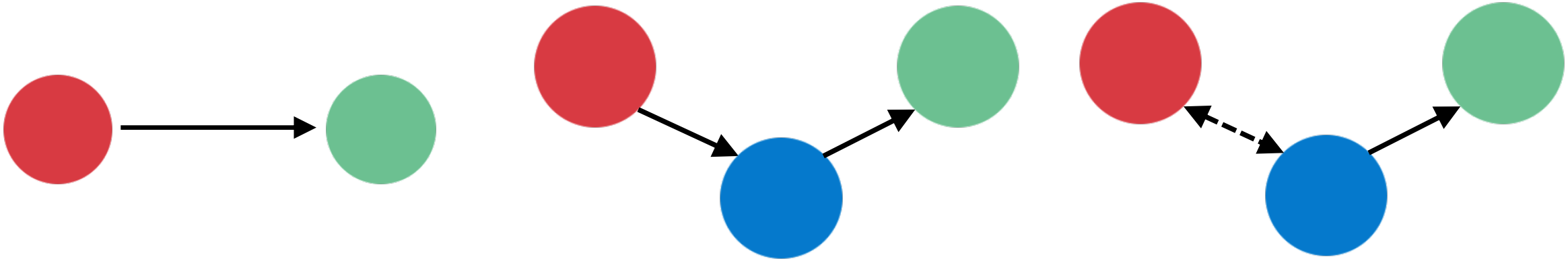
Causal Mechanisms



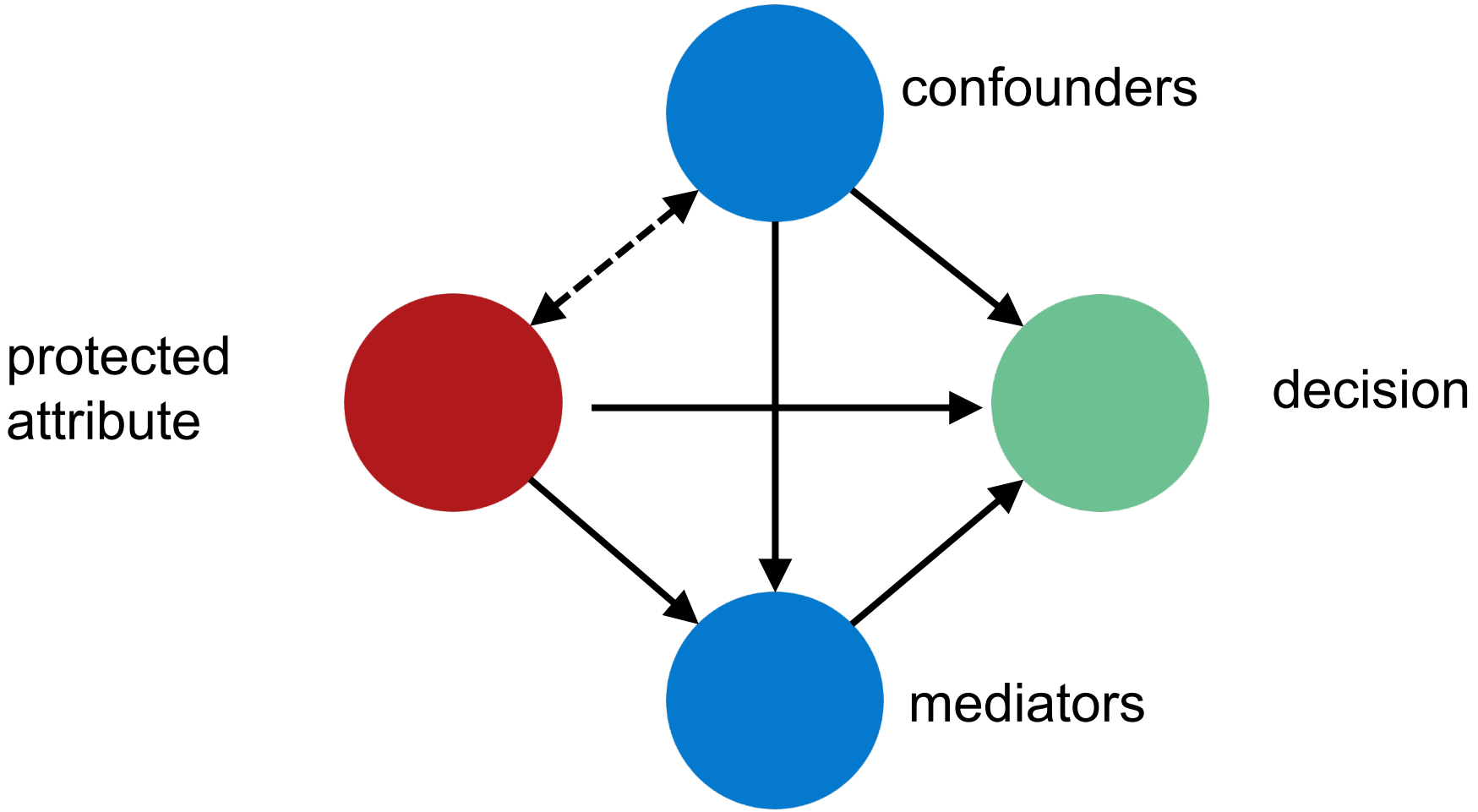
- Possible scenario 3:
  - Race *is associated with other demographics* (via complex societal processes).

Causal Mechanisms





Standard Fairness Model



Plečko D and Bareinboim E, Causal Fairness Analysis. *Foundations and Trends® in Machine Learning*. 2024.

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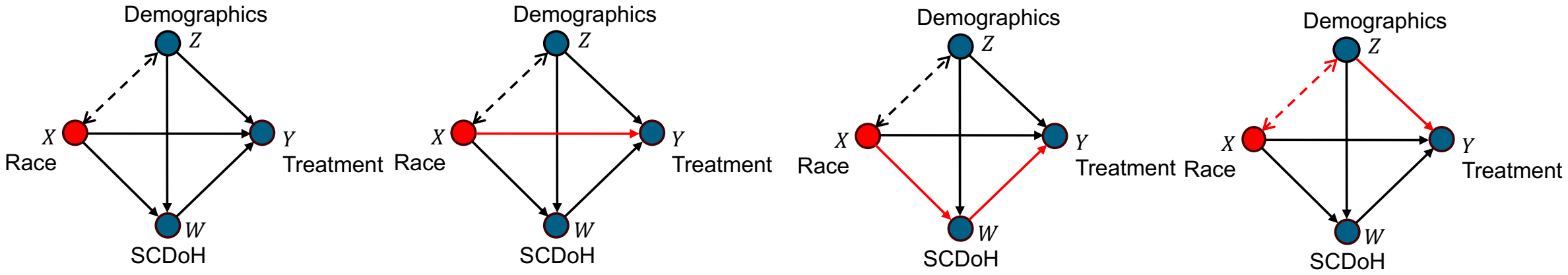
Standard Fairness Model



(a) Causal fairness model (b) Direct effect (c) Indirect effect via SCDoH (d) Confounded effect

Health disparity decomposition formula:

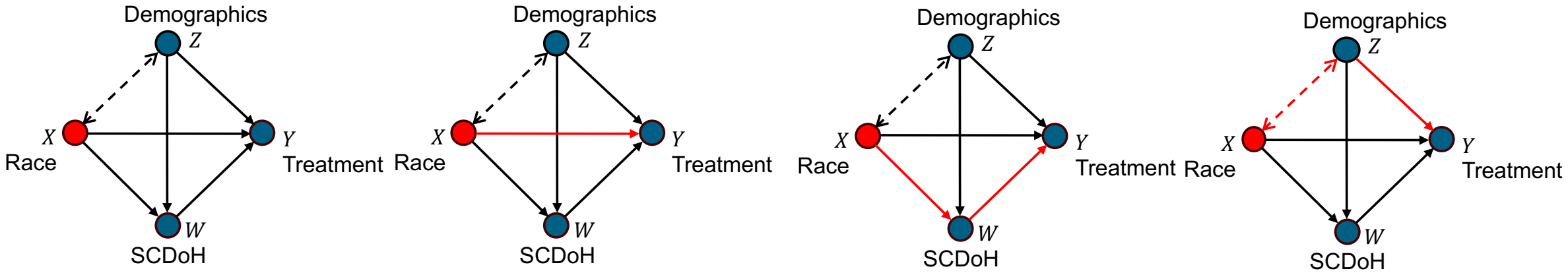
$$TV_{x_0,x_1}(y) = DE_{\mathrm{x_0,x_1}}(y|x_0) + \left(-IE_{\mathrm{x_0,x_1}}(y|x_0)\right) + \left(-CE_{\mathrm{x_0,x_1}}(y)\right)$$

Question: What is the difference in getting the treatment between Black and non-Black patients?

$$TV_{x_0,x_1}(y) = E[Y|X = x_1] - E[Y|X = x_0]$$

(I²DB)

Standard Fairness Model



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Question: What is the direct effect of race on treatment? ⇔What is the difference in treatment probability that is due to the direct effect of changing race from Black to non-Black?

$$DE_{\mathrm{x_0,x_1}}(y|x_0) = E[Y_{x_1,W_{x_0}} \mid x_0] - E[Y_{x_0} \mid x_0]$$

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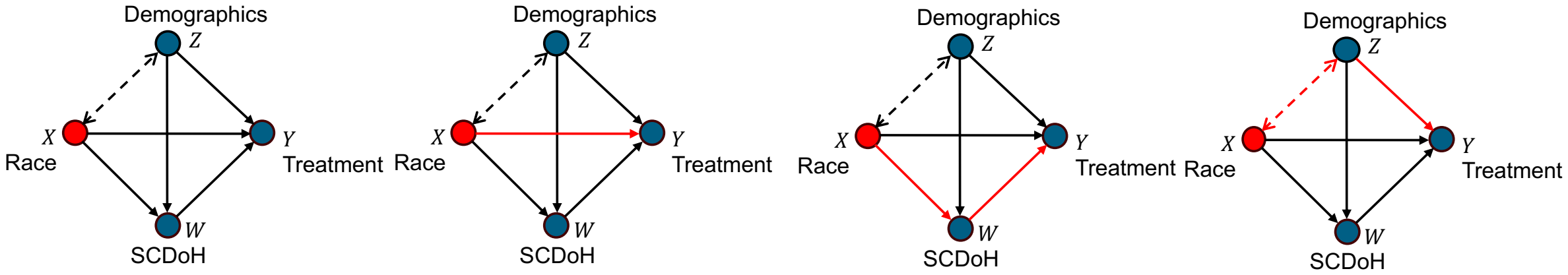
Standard Fairness Model



(a) Causal fairness model (b) Direct effect (c) Indirect effect via SCDoH (d) Confounded effect

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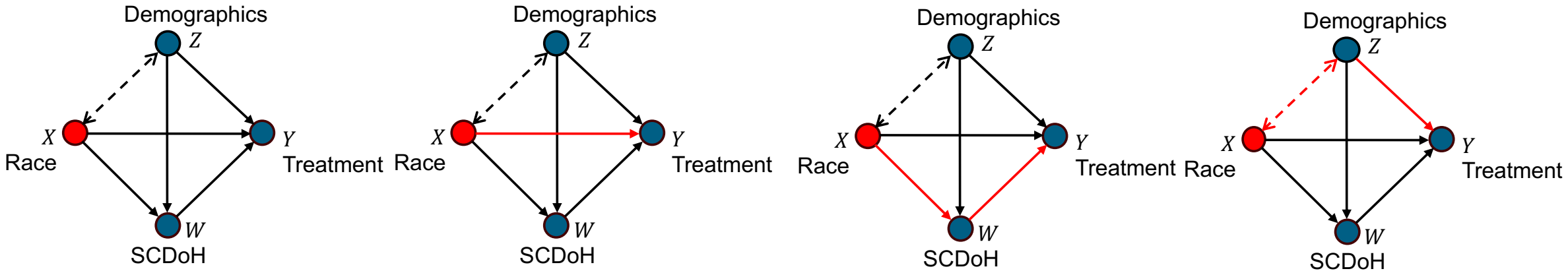
Question: What is the indirect effect of race on treatment?
⇔ What is the difference in treatment probability that is due to the effect of changing race from Black to non-Black on the mediators (ie, social and clinical determinants of health)?

$$IE_{\mathrm{x_0,x_1}}(y|x_0) = E[Y_{x_1,W_{x_0}} \mid x_0] - E[Y_{x_1} \mid x_0]$$

(I²DB)

Standard Fairness Model



(a) Causal fairness model (b) Direct effect (c) Indirect effect via SCDoH (d) Confounded effect

Health disparity decomposition formula:

$$TV_{x_0,x_1}(y) = DE_{\mathrm{x_0,x_1}}(y|x_0) + \left(-IE_{\mathrm{x_0,x_1}}(y|x_0)\right) + \left(-CE_{\mathrm{x_0,x_1}}(y)\right)$$

Question: What is the confounded effect of race on treatment? ⇔ What is the difference in treatment probability that is due to the effect of changing race from Black to non-Black on the confounders (ie, age, sex, etc)?

$$CE_{\mathrm{x_0,x_1}}(y) = E[Y_{x_0} \mid x_1] - E[Y_{x_0} \mid x_0]$$

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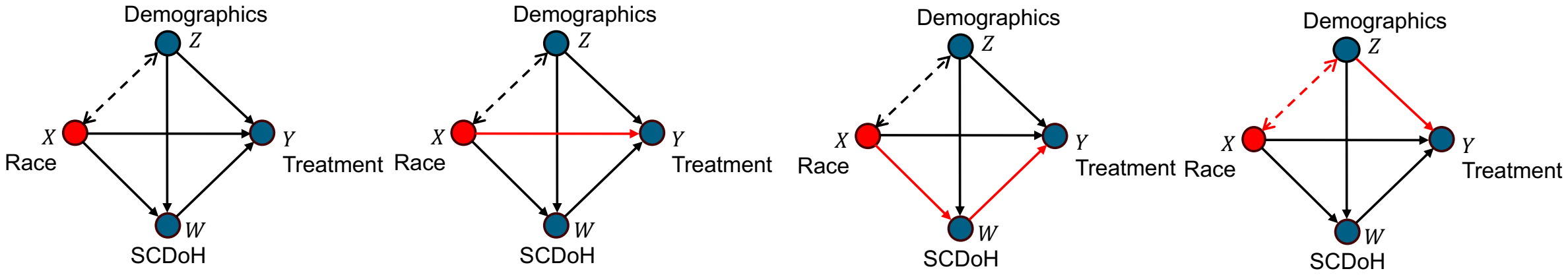
Standard Fairness Model



(a) Causal fairness model (b) Direct effect (c) Indirect effect via SCDoH (d) Confounded effect

Health disparity decomposition formula:

$$TV_{x_0,x_1}(y) = DE_{\mathrm{x_0,x_1}}(y|x_0) + \left(-IE_{\mathrm{x_0,x_1}}(y|x_0)\right) + \left(-CE_{\mathrm{x_0,x_1}}(y)\right)$$

Question: What is the confounded effect of race on treatment? ⇔ What is the difference in treatment probability that is due to the effect of changing race from Black to non-Black on the confounders (ie, age, sex, etc)?

$$CE_{\mathrm{x_0,x_1}}(y) = E[Y_{x_0} \mid x_1] - E[Y_{x_0} \mid x_0]$$

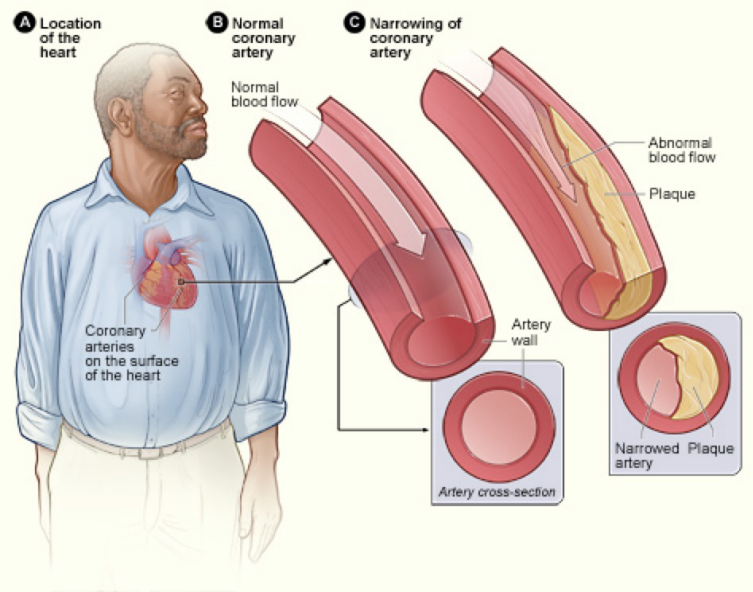
Explaining Treatment Disparities with Causal Modeling

1. Method: Causal fairness model
2. **Application: Revascularization in cardiology**

Coronary artery disease

- **Coronary artery disease** is the most common type of heart disease.
- Patients with coronary artery disease are at higher risk of developing AMI.

Phenotype



Coronary artery disease (CAD)

Outcome

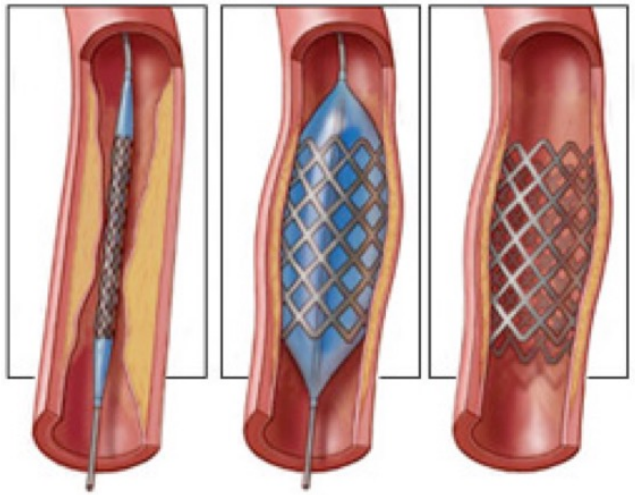


Acute myocardial infarction (AMI)

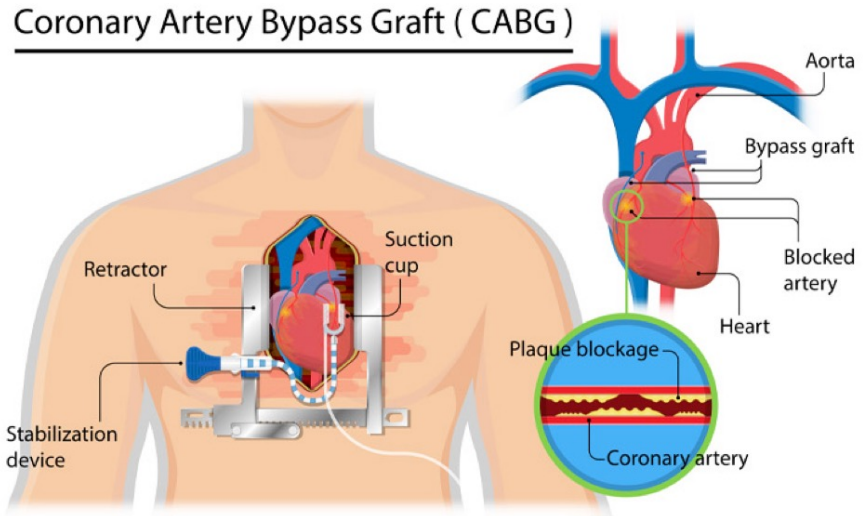
Disparities in CAD Treatments

- **Women**, **racial and ethnic minorities**, patients without **health insurance**, and those who live in **low-income** neighborhoods may have inadequate access to revascularization.

Treatment



Percutaneous coronary intervention (PCI)



Coronary artery bypass graft (CABG)

- Question: What causes **racial** disparities in allocating revascularization to CAD patients?
- Question: What causes **sex** disparities in allocating revascularization to CAD patients?

Data and Cohort

- Data
  - Source: Columbia University Irving Medical Center (CUIMC) electronic health record (EHR)
  - Format: Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) v5.4
- Cohort
  - The coronary artery disease (CAD) cohort: coronary arteriosclerosis diagnosis codes.
  - Treatment group: Patients treated with either percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).
  - Control group: Patients with CAD but no CABG or PCI.
  - Index date: The index date was the date of the initial treatment in a patient's EHR. The index date for the control group was the latest clinical visit with a coronary arteriosclerosis diagnosis.
  - Patients with missing race or gender were excluded from the study.

Clinical and Social Determinants of Health

- Demographics (race, sex, age)
  - Age
  - Sex
  - Race
- Clinical factors
  - Medical conditions (200+)
- Social determinants of health (SDoH)
  - Health insurance
  - Area deprivation index (ADI) from census data

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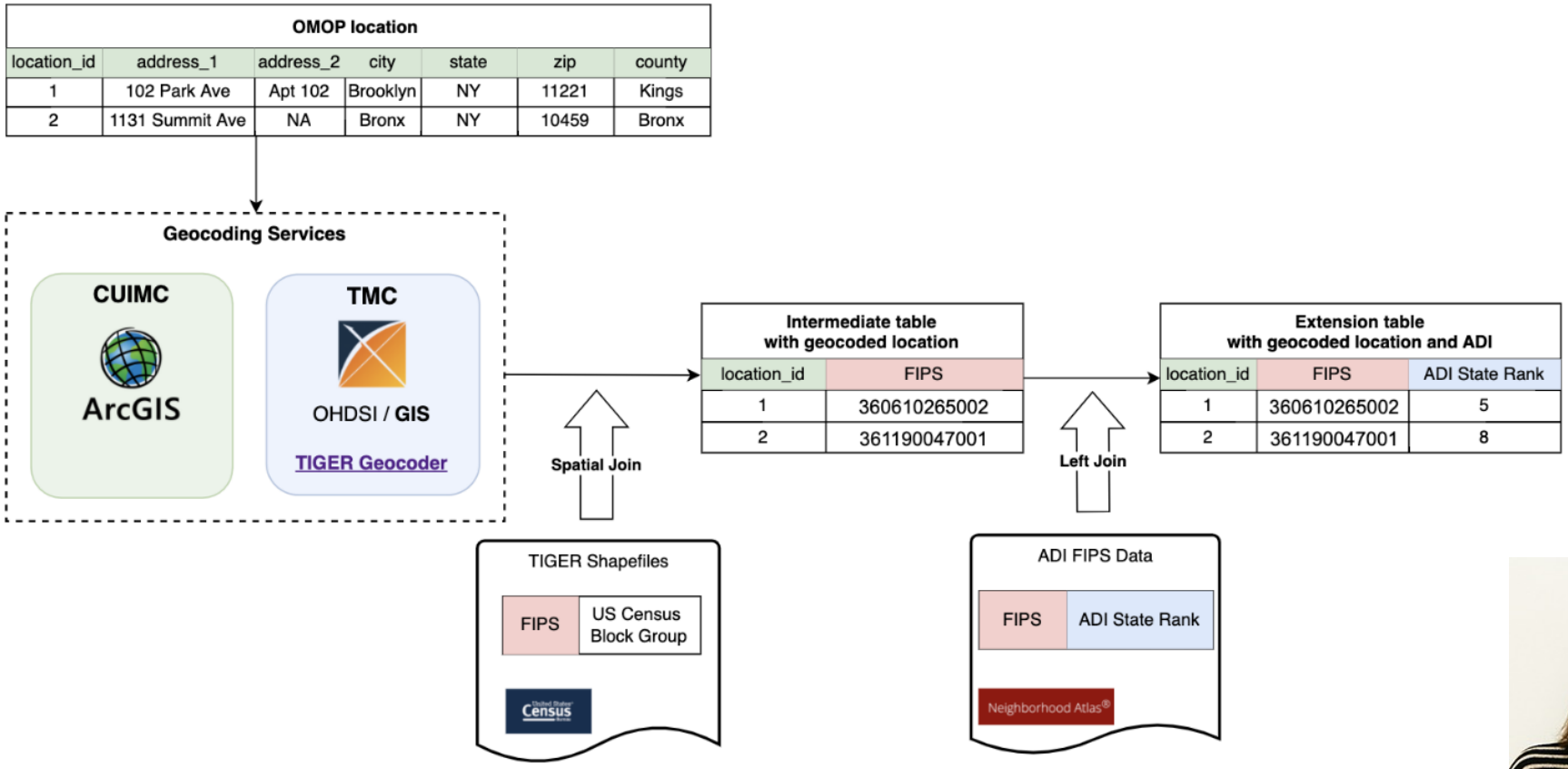
Linking patient record with census data





Xinzhuo “Zoey” Jiang

Code: https://github.com/cukarthik/CancerTreatmentCharacterization

Washington University School of Medicine in St. Louis

Method for Causal Estimation

- We estimate the direct effect, indirect effect, and confounded effect.
- We used double machine learning to estimate causal quantities in the forms of $E[Y_{x_1}]$ or $E[Y_{x_1,W_{x_0}}]$.
- The estimator is doubly-robust, meaning that the estimator will be consistent as long as one model involved in the estimator is consistent, a highly desired property for estimators.

Results

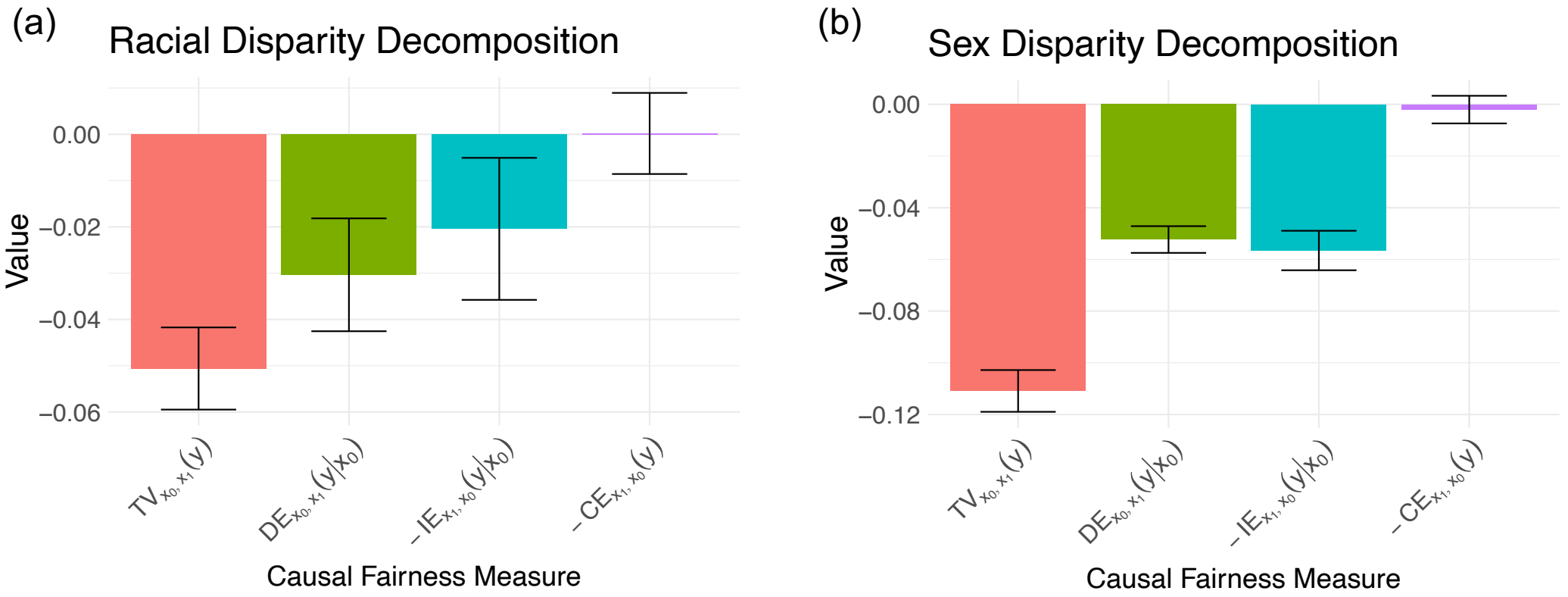


Figure 2. The decomposition of racial and sex disparity on treatment allocation for CAD cohort.

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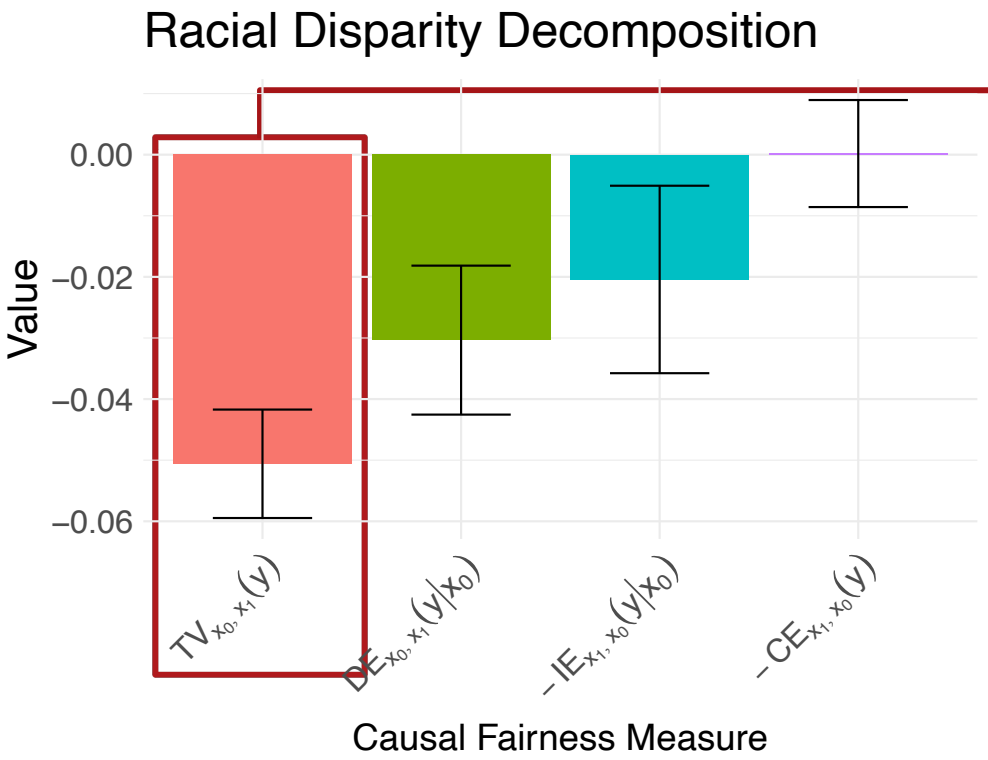
Results



Total disparity: Black patients were 5.0% [95%CI: 4.1% to 6.0%] less likely to receive revascularization treatment compared to non-Black patients.

- The final cohort consists of 41,630 patients,
  - Treatment: 8,428 (20.2%) patients; Control: 33,202 (79.8%) patients
  - Black or African American: 6298 patients (15.2%)

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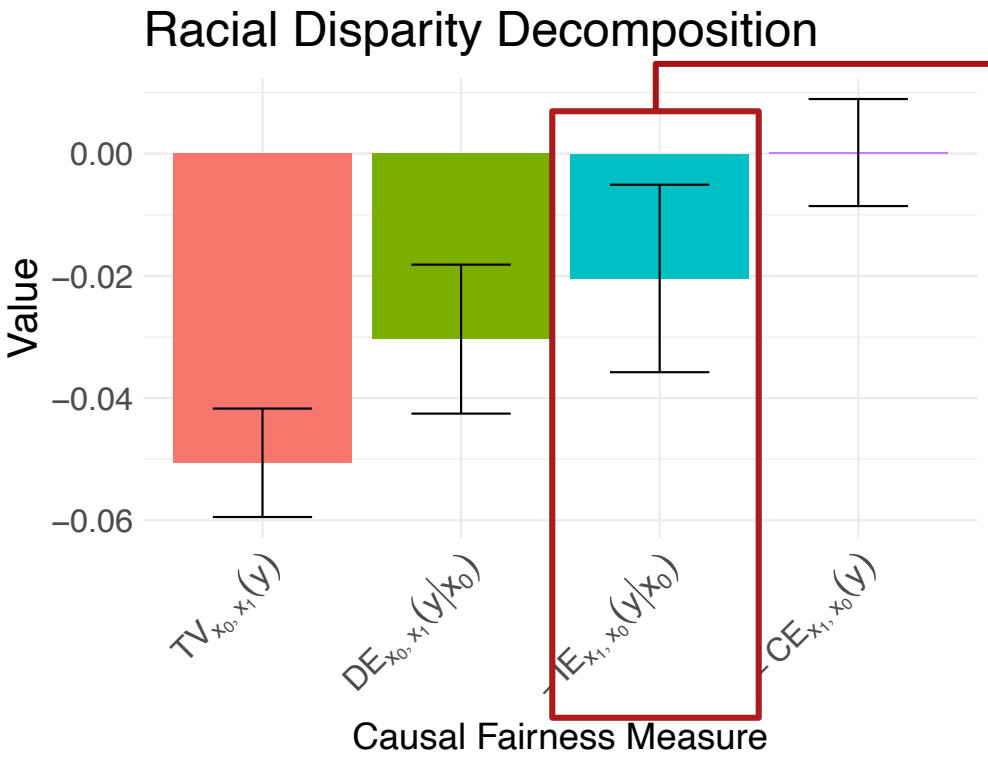
Results



- Indirect effect: If a non-Black patient were Black, their probability of receiving treatment would have decreased by 2.2% [95%CI: 1.0% to 3.5%].
- This indicates the impact of race on treatment allocation that is mediated through clinical conditions and SDoH.

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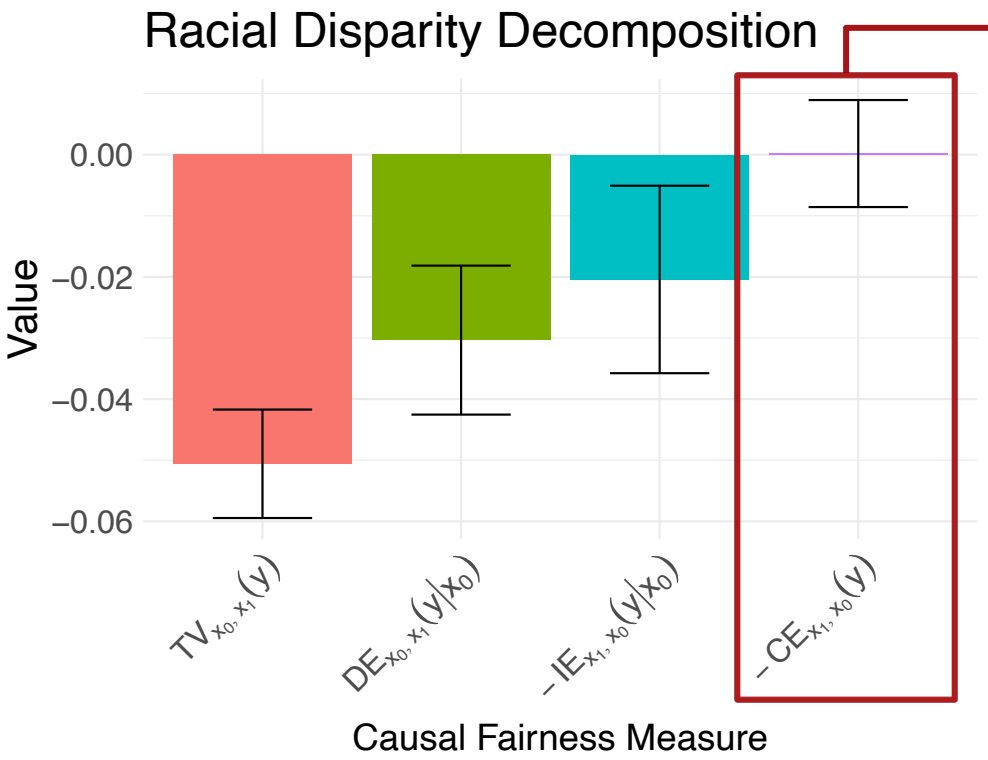
Results



Confounded effect: Other demographic factors contributed 0.0% [95%CI: -1.0% to 1.0%], difference in probability of receiving treatment between Black and non-Black patients.

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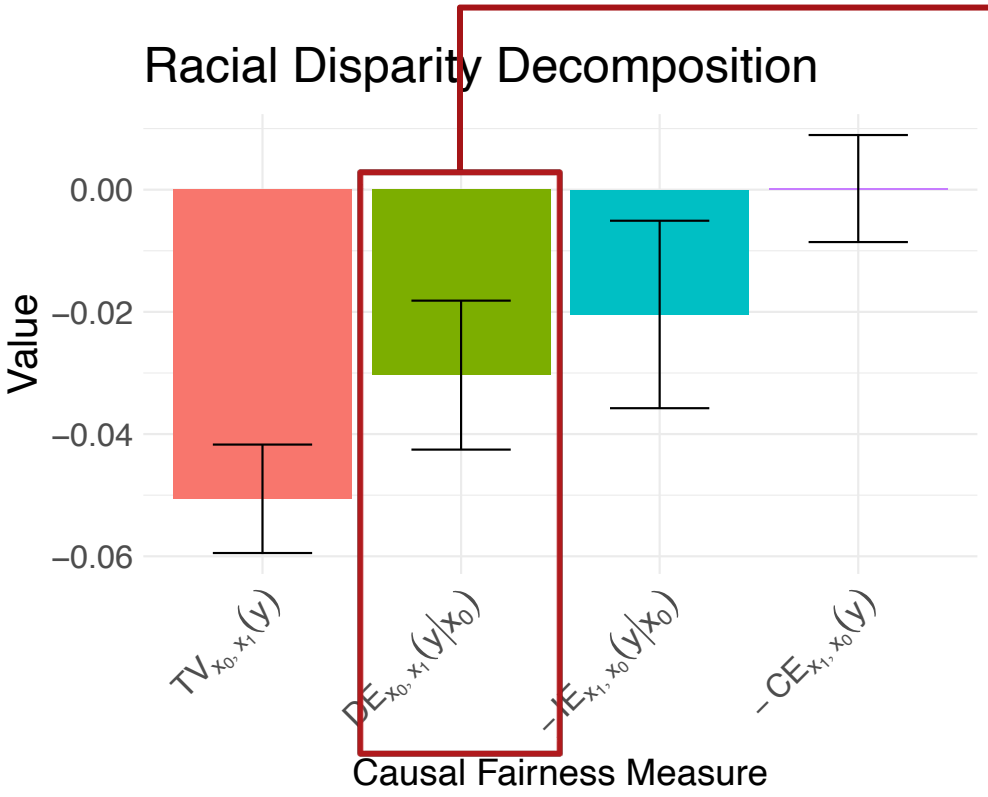
Results



- Direct effect measures any residual impact of race on treatment allocation that is not accounted by the other demographic factors (confounded), medical conditions, and SDoH (indrect).
- Direct effect: 3.0% [95%CI: 4.1% to 1.9%], suggesting that if a non-Black patient were Black, their probability of receiving treatment would have decreased by 3.0%, assuming all other features remain the same.
- Race has a statistically significant direct effect on the treatment allocation.

Summary

In this study, we

- Adapted a causal fairness analysis framework to better understand the causes and their impact on treatment disparities.
  - Coronary artery disease
- Quantified the effect of race on treatment allocation by decomposing the effect of race into
  - Direct effect
  - Indirect effect (via baseline medical conditions and social determinants of health (SDoH))
  - Confounded effect (via age and sex)

References

This work:

- Zhang L, Jiang X, Natarajan K, Hripcsak G, Explaining Treatment Disparities from a Causal Perspective with EHRs, *AMIA Annual Symp*, 2023.

Related work:

- Plečko D and Bareinboim E, Causal Fairness Analysis, *Foundations and Trends® in Machine Learning*. 2024.
- Jiang X, Beaton MA, Gillberg J, Williams A, Natarajan K. Feasibility of Linking Area Deprivation Index Data to the OMOP Common Data Model. *AMIA Annu Symp Proc.* 2022.

Acknowledgments



Xinzhou (Zoey) Jiang, MS



Karthik Natarajan, PhD



George Hripcsak, MD, MS

Zhang L, Jiang X, Natarajan K, Hripcsak G, Explaining Treatment Disparities from a Causal Perspective with EHRs, *AMIA Annual Symp*, 2023.

The goal is to integrate causal modeling with machine learning to generate reliable real-world evidence and to build an equitable healthcare system.

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