OHDSI 2025 Collaborator Showcase Lightning Talks Round 2

Linying Zhang, Lu Li, Georgina Kennedy,
Hsin Yi Chen, Katia Verhamme

(I²DB)

Causal Inference with Multi-Modal Foundation Models:

A Case Study of Anti-VEGF Injections in Diabetic Macular Edema

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OHDSI Global Symposium 2025

Oct 8, 2025

Washington University School of Medicine in St.Louis

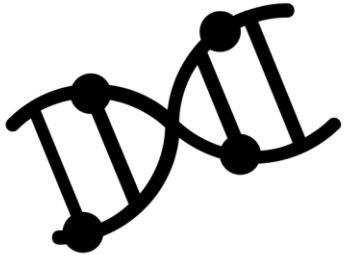
Real-world health data include diverse data modalities.

Electronic Health Records (EHRs)

Demographics Diagnoses Drugs Procedures Labs

Medical Images

Clinical Notes

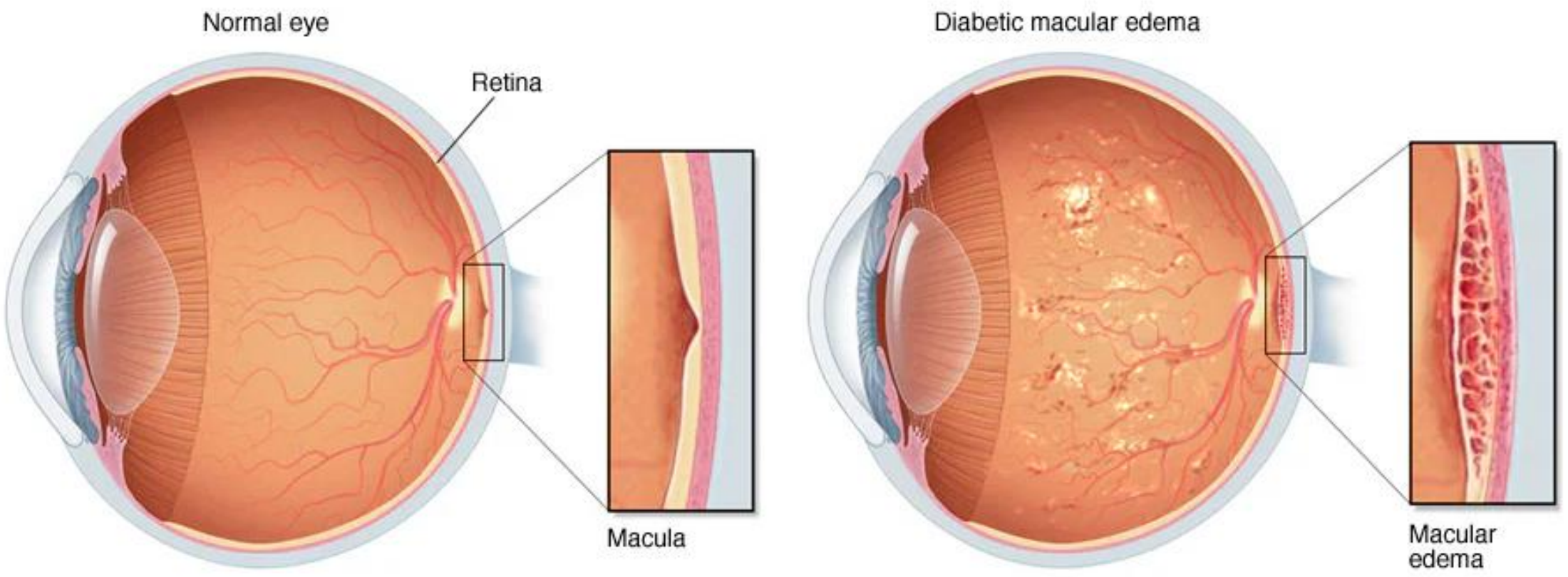


Genomics

Wearables

Surveys

Diabetic Macular Edema (DME)



Macular Optical Coherence Tomography (OCT)

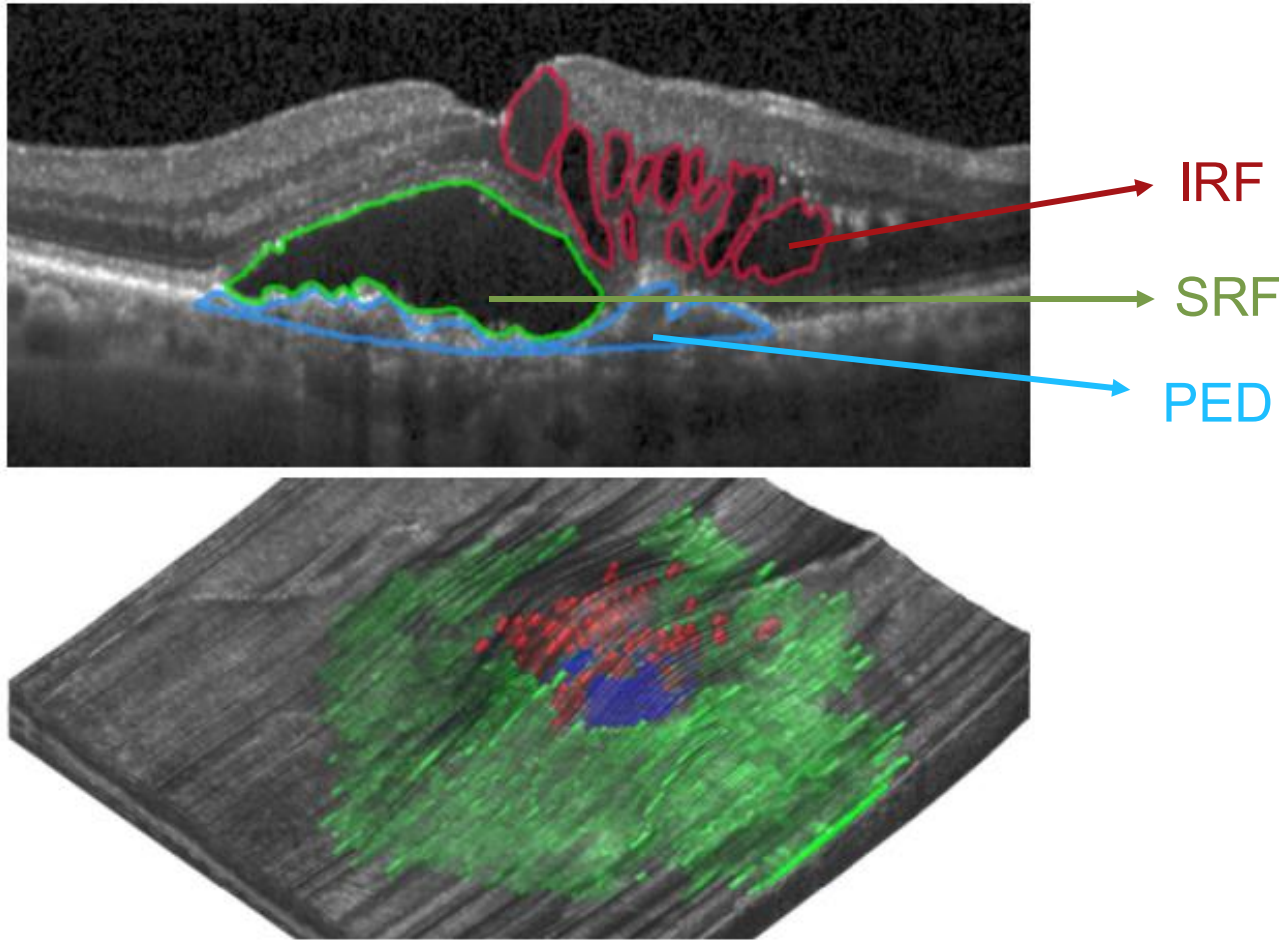
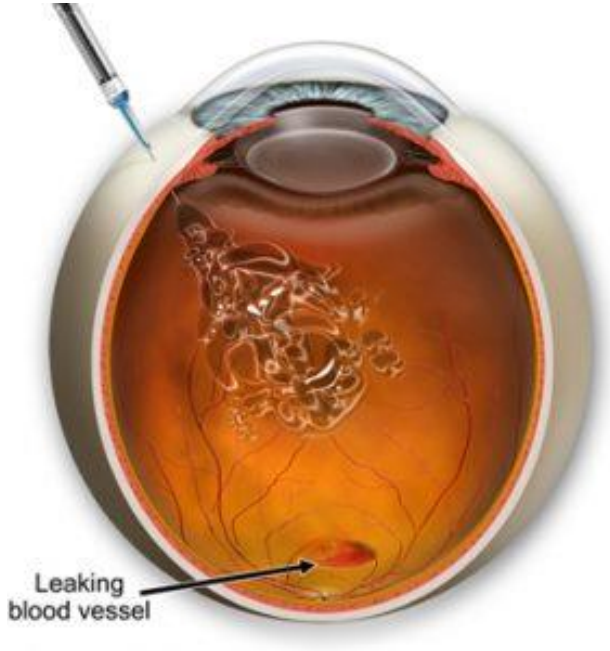


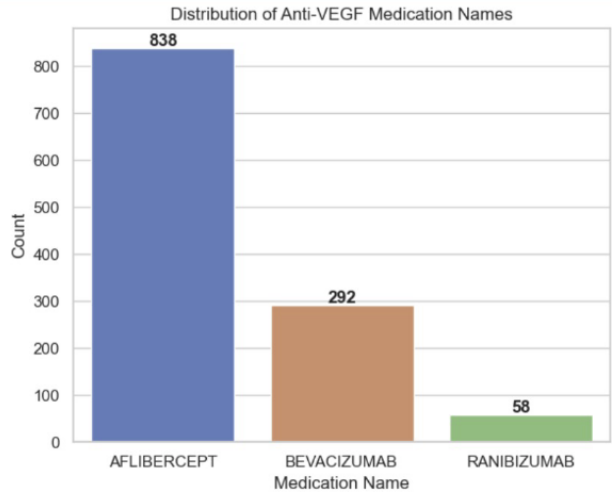
Fig. 2. The three fluid types on a 2D B-scan (above) and as a 3D volume rendering (below): IRF (red), SRF (green) and PED (blue).

Intravitreal Anti-VEGF Injections



There are 3 variations of anti-VEGF injections:

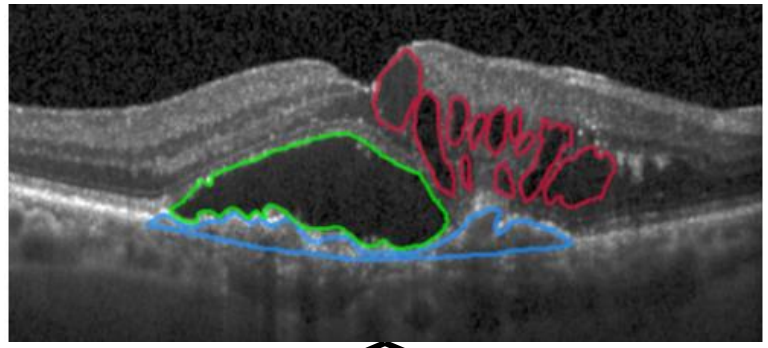
- Aflibercept
- Bevacizumab
- ~~Ranibizumab~~



Question: Is aflibercept more effective than bevacizumab in reducing vision loss?

Confounding Bias

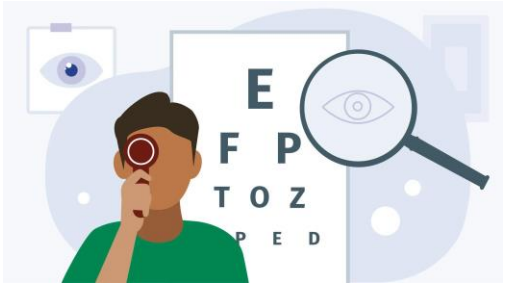
- Confounders are common causes between the treatment and outcome.
- Confounders can lead to bias in effect estimates if unadjusted.



Confounder

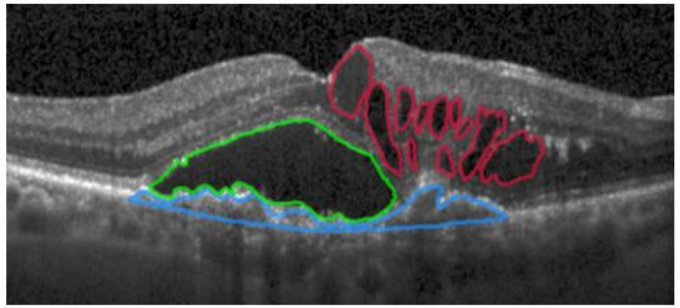
Treatment

?

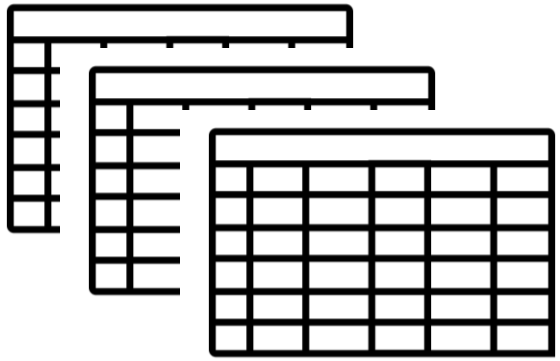


Visual outcome

Multi-modal Causal Inference (MMCI) Pipeline



OCT



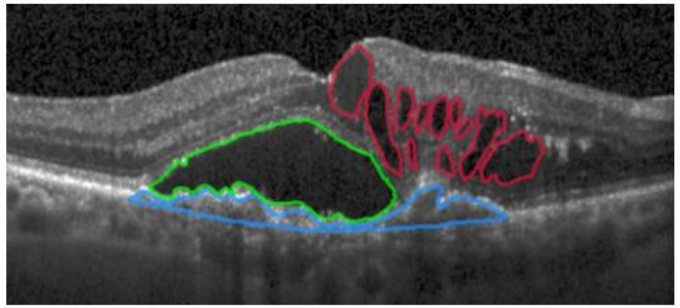
Tabular EHR

(I²DB)

Multi-modal Causal Inference (MMCI) Pipeline

Representation Learning

Treatment Effect Estimation



OCT

Tabular EHR

Image Encoder

EHR Encoder

Latent Representation

Propensity Model

$\hat{e}(X_i)$

$$ATE_{DR} = \frac{1}{n}\sum_{i=1}^{n}\left[\frac{T_i Y_i}{\hat{e}(X_i)} - \frac{\{T_i - \hat{e}(X_i)\}}{\hat{e}(X_i)}\hat{m}_1(X_i)\right] - \frac{1}{n}\sum_{i=1}^{n}\left[\frac{(1-T_i)Y_i}{1-\hat{e}(X_i)} + \frac{\{T_i - \hat{e}(X_i)\}}{1-\hat{e}(X_i)}\hat{m}_0(X_i)\right]$$

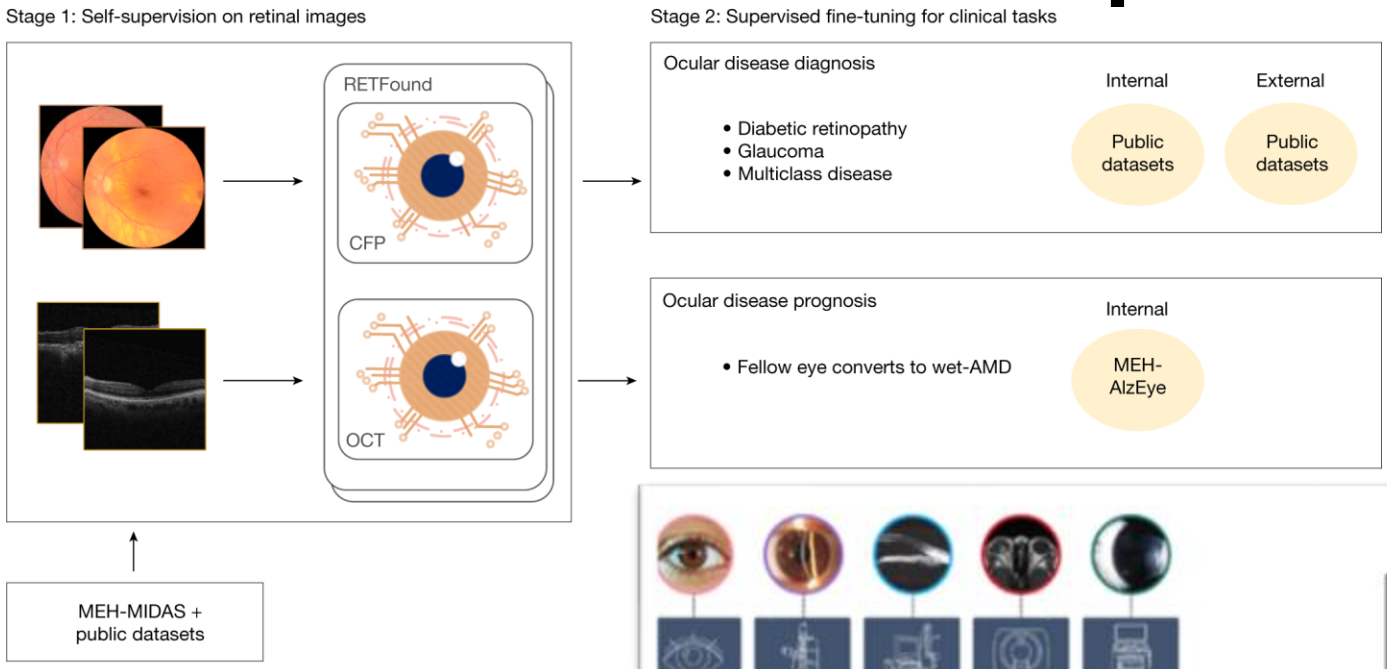
Outcome Model

"Improved vision? Y/N"

$\widehat{m_1}(X_i), \widehat{m_0}(X_i)$

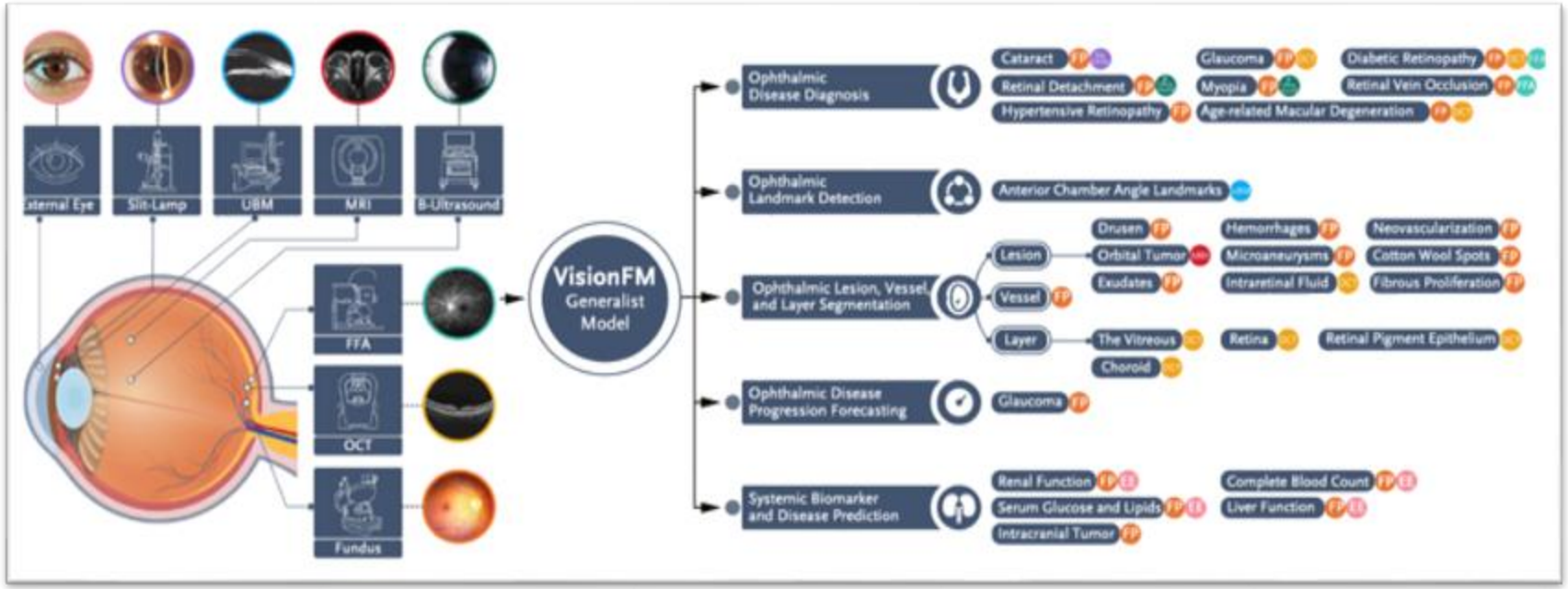
Foundation Models in Ophthalmology

Image Encoder



RETFound

(Zhou et al. *Nature* 2023)



VisionFM

(Qiu et al. *NEJM AI* 2024)

OCT Embeddings

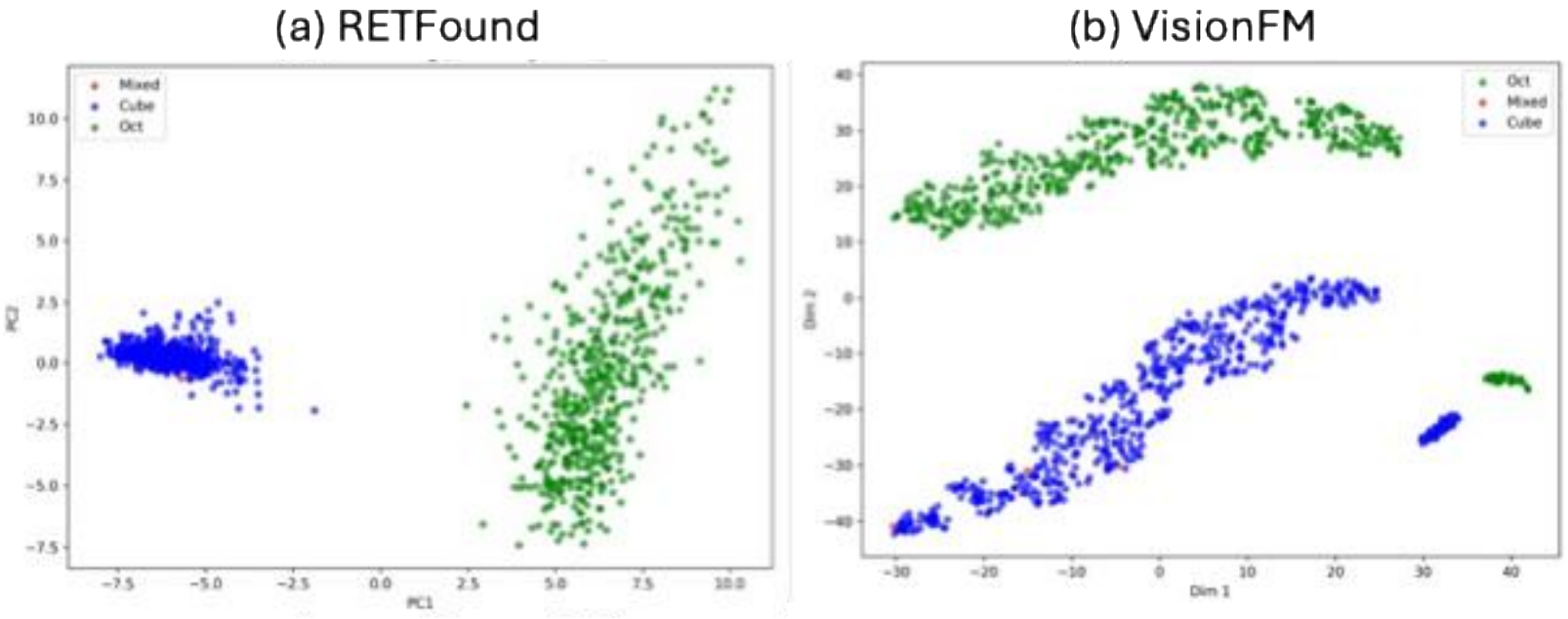


Figure 1. t-SNE visualization of latent embeddings generated by foundation models: (a) RETFound and (b) VisionFM. Each point represents a patient, and colors indicate the OCT imaging device. Clear separation by device suggests that both models capture device-specific features.

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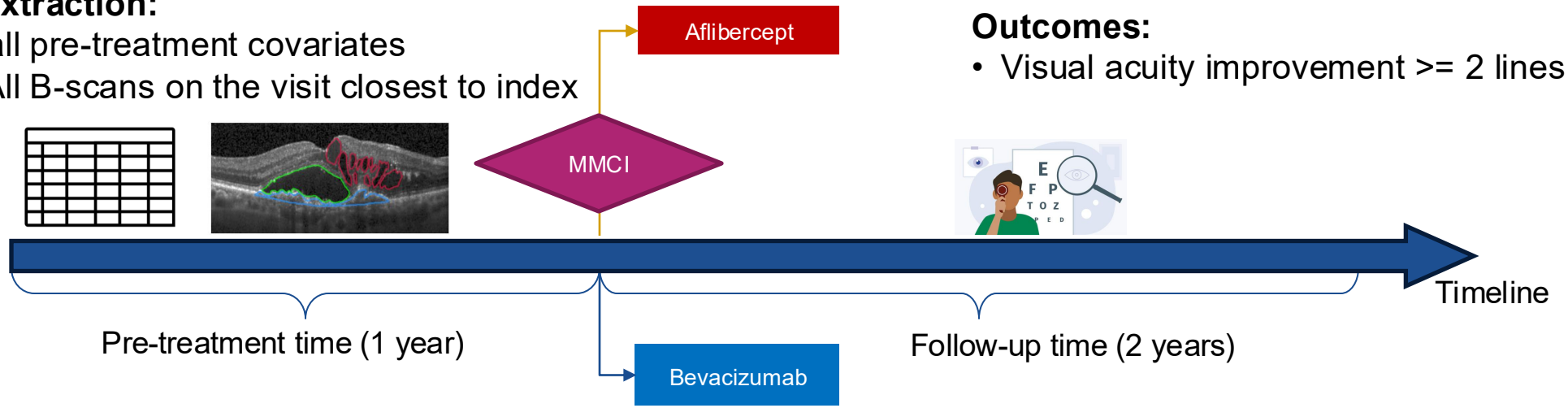
Study Design

- **Data**: EHRs and OCT images were extracted from WashU/BJC HealthCare database.
- **Objective:** Estimate the comparative effectiveness of aflibercept vs bevacizumab in reducing vision loss in DME.

Feature Extraction:
- **EHR:** all pre-treatment covariates
- **OCT**: All B-scans on the visit closest to index date.



Outcomes:
- Visual acuity improvement >= 2 lines

Study Population: New users of aflibercept and bevacizumab (study period: 1/1/2018-12/31/2024)

Inclusion Criteria:
- Adults with diabetic macular edema
- At least 1 year of prior observation.

Evaluation:
We compared the ATE estimates and 95% CI from each model to that from clinical trials.

Comparison of Treatment Effect Estimates

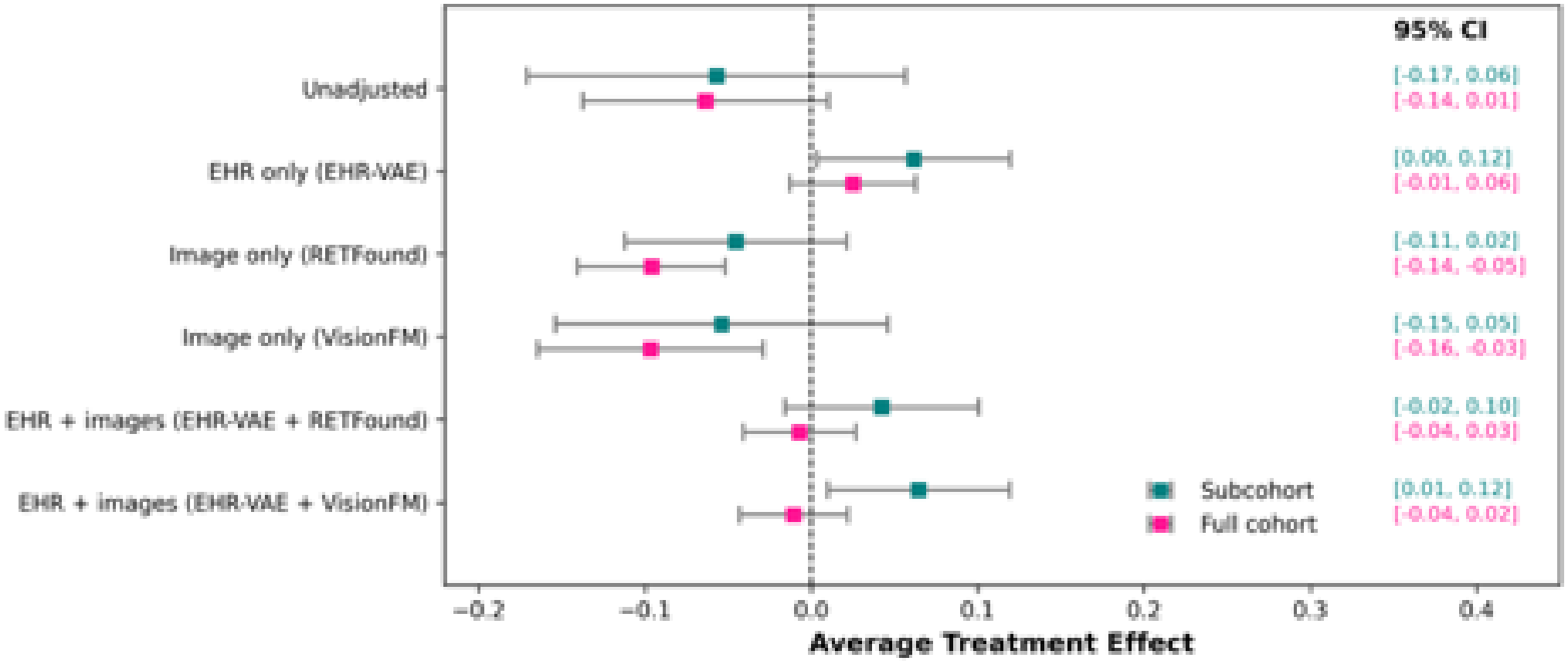


Figure 2. Average treatment effect estimation across adjustment strategies. The full cohort includes all patients in the study population and the sub-cohort includes patients with worse baseline VA. A positive ATE indicates that aflibercept is better at improving vision than bevacizumab.

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Randomized Controlled Trial

ORIGINAL ARTICLE

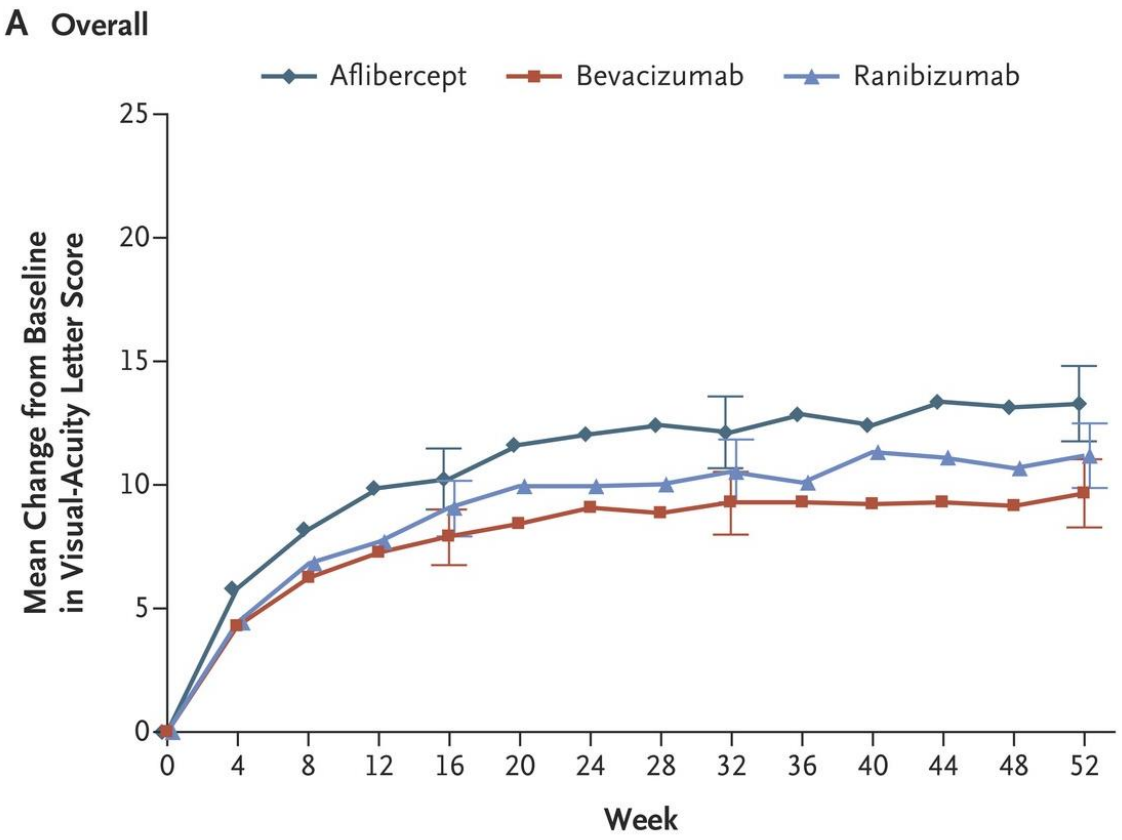
Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema

Author: The Diabetic Retinopathy Clinical Research Network* Author Info & Affiliations

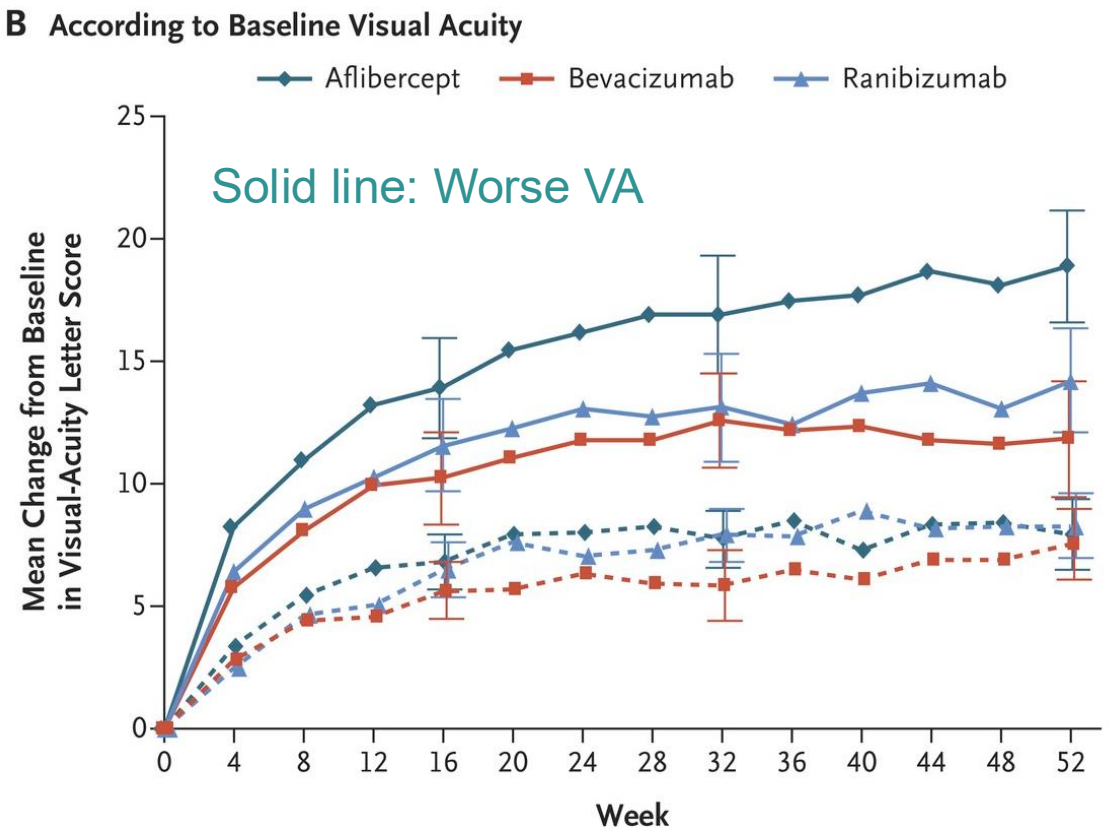
Published March 26, 2015 | N Engl J Med 2015;372:1193-1203 | DOI: 10.1056/NEJMoa1414264 | VOL. 372 NO. 13

Randomized Controlled Trial

Full cohort



Sub-cohort



Conclusions

- Foundation models can be leveraged to include images into causal inference, reducing the risk of unmeasured confounding bias.
- Multi-modal causal inference models produced treatment effect estimates consistent with established RCT evidence.
- Foundation models can robustly learn imaging features that contribute to reliable effect estimation in real-world settings.

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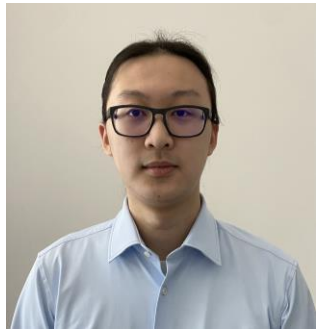
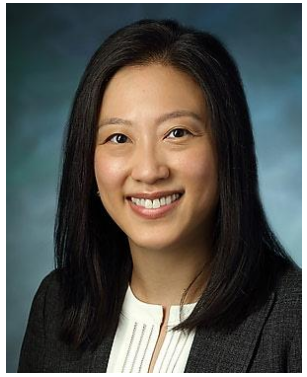
CausAI Lab


Siqi Sun


Ruochong Fan


Saiyu You

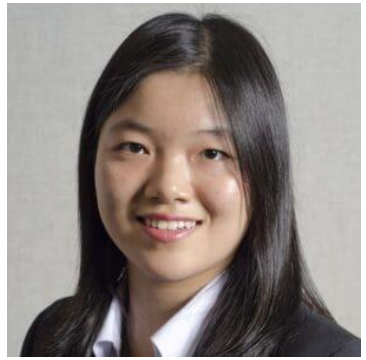
Collaborators


Cindy Cai


Marc Suchard


Diep Tran


Kumar Rao


Yixin Wang

Acknowledgment

WashU RDC
Shinji Naka
Snehil Gupta
Sherry Lassa-Claxton
Albert Lai

WashU I2DB
Philip Payne
Adam Wilcox
Thomas Kannampallil
Joanna Abraham

https://causAiLab.github.io

Washington University School of Medicine in St. Louis

OHDSI 2025 Collaborator Showcase
Lightning Talks Round 2

End: Linying Zhang

Next up: Lu Li

Penn Medicine

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

Department of Biostatistics, Epidemiology and Informatics

LATTE: A One-shot Lossless Algorithm for Federated Target Trial Emulation with Application to Alzheimer's Disease and Related Dementia Drug Repurposing Using Decentralized Data

Lu Li, Ph.D. candidate at the University of Pennsylvania
Advisor: Dr. Yong Chen

2025 OHDSI Symposium

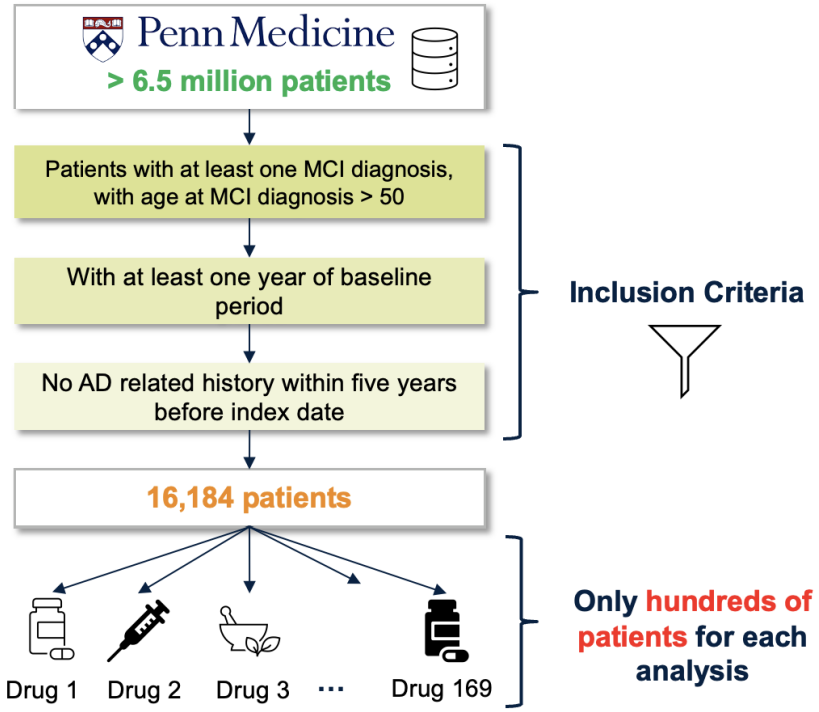
CHASE
Center for Health AI & Synthesis of Evidence

ennCIL
A Computing · Inference · Learning lab at University of Pennsylvania

Li et al. (2025+) The Lancet Digital Health *(Invited Revision)*

Motivation: Reliable Real-World Evidence (RWE) for regulatory decision making

- A key challenge in performing target trial emulation (TTE) using **single site data**:
  - Rigorous eligibility criteria → **substantially smaller sample sizes,** especially for complex conditions such as ADRD, and rare diseases.



- FDA guidance on RWE for regulatory decision-making
  - *"Reliability and relevance"*

*"The term relevance includes the availability of data for key study variables (exposures, outcomes, covariates) and **sufficient numbers of representative patients** for the study".*
-- FDA (March 2024)

International multi-site studies

Key challenge: Individual Patient-level Data (IPD) cannot be shared across sites

- Country/region specific laws (HIPAA in the U.S., GDPR in Europe)

OHDSI By The Numbers

- 4,294 collaborators
- 83 countries
- 21 time zones
- 6 continents
- 1 community

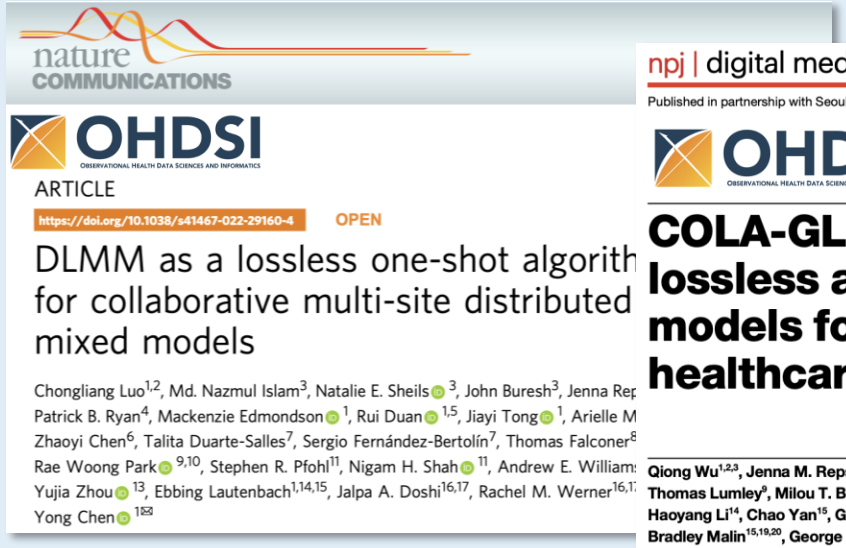
- Diverse population;
- Enlarged sample size;
- Greater statistical power;

→ Relevant and reliable RWE

Privacy-preserving federated learning algorithms

- Enables multi-site studies without sharing IPD
- Allows to enlarge the study sample size to incorporate diverse population

OHDSI Studies using Federated Learning Algorithms for COVID-19 studies


nature COMMUNICATIONS

OHDSI

ARTICLE

https://doi.org/10.1038/s41467-022-29160-4 OPEN

DLMM as a lossless one-shot algorith
for collaborative multi-site distributed
mixed models

Chongliang Luo[1,2], Md. Nazmul Islam[3], Natalie E. Sheils[3], John Buresh[3], Jenna Rep
Patrick B. Ryan[4], Mackenzie Edmondson[1], Rui Duan[1,5], Jiayi Tong[1], Arielle M
Zhaoyi Chen[6], Talita Duarte-Salles[7], Sergio Fernández-Bertolín[7], Thomas Falconer[8]
Rae Woong Park[9,10], Stephen R. Pfohl[11], Nigam H. Shah[11], Andrew E. Williams
Yujia Zhou[13], Ebbing Lautenbach[1,14,15], Jalpa A. Doshi[16,17], Rachel M. Werner[16,17]
Yong Chen[1]✉

(Luo et al. 2022, Nature Communications)


npj | digital medicine Article

Published in partnership with Seoul National University Bundang Hospital

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https://

COLA-GLM: collaborative one-s
lossless algorithms of generali
models for decentralized obser
healthcare data

Qiong Wu[1,2,3], Jenna M. Reps[4,5,6], Lu Li[3,7], Bingyu Zhang[3,7], Yiwen Lu[3,7], Jiayi Tong[2,3,8], Dazheng
Thomas Lumley[9], Milou T. Brand[10], Mui Van Zandt[4,10], Thomas Falconer[11], Xing He[12,13], Yu Hu
Haoyang Li[14], Chao Yan[15], Guojun Tang[16], Andrew E. Williams[17,18], Fei Wang[14], Jiang Bian[12,13],
Bradley Malin[15,19,20], George Hripcsak[11], Martijn J. Schuemie[4,5,21], Yun Lu[22], Steve Drew[16], Jiay
David A. Asch[24,25] & Yong Chen[2,3,24,26,27]✉

(Wu et al. 2025, npj Digital Medicine)


npj | digital medicine Article

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https://doi.org/10.1038/s41746-025-01846-1

Unlocking efficiency in real-world
collaborative studies: a multi-site
international study with one-shot lossless
GLMM algorithm

Check for updates

Jiayi Tong[1,2,3]✉, Jenna M. Reps[4,5,6], Chongliang Luo[7], Yiwen Lu[1,2], Lu Li[1,2], Juan Manuel Ramirez-Anguita[8],
Milou T. Brand[9], Scott L. DuVall[10,11], Thomas Falconer[12], Alex Mayer Fuentes[13], Xing He[14,15],
Michael E. Matheny[16,17], Miguel A. Mayer[8], Bhavnisha K. Patel[16,17], Katherine R. Simon[16,17],
Marc A. Suchard[11,18], Guojun Tang[19], Benjamin Viernes[11], Ross D. Williams[6], Mui van Zandt[9], Fei Wang[20],
Jiang Bian[14,15], Jiayu Zhou[21], David A. Asch[22,23] & Yong Chen[1,2,23]✉

(Tong et al. 2025, npj Digital Medicine)

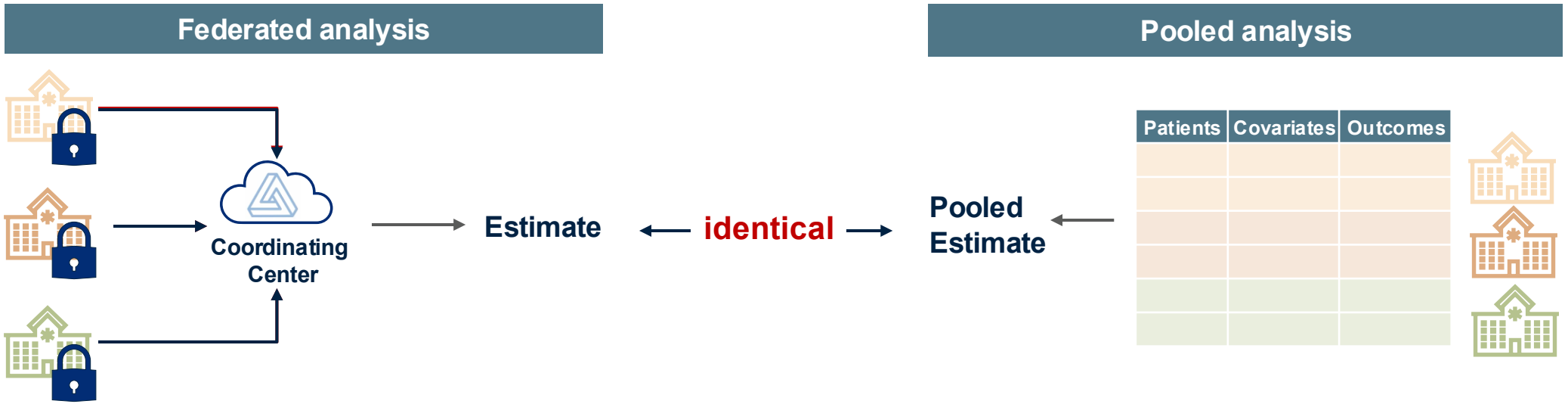
Desirable Properties

One-shot

Only **a single round of communication** is required in practice.

Lossless

Results are **identical** to pooled analysis, with no accuracy loss.



Desirable Properties

One-shot

Only **a single round of communication** is required in practice.

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Results are **identical** to pooled analysis, with no accuracy loss.

However, only a few algorithms have achieved both **lossless and one-shot** properties simultaneously, and they are mainly for **regression tasks**.

We still need **Federated Learning Algorithms** for **Target Trial Emulation (TTE)**.

Desirable Properties

One-shot

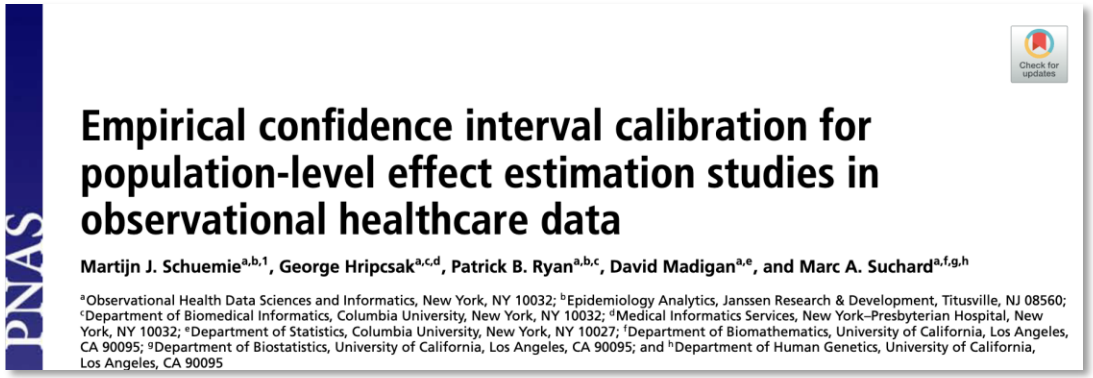
Only **a single round of communication** is required in practice.

Lossless

Results are **identical** to pooled analysis, with no accuracy loss.

Handles Unmeasured Confounding

Mitigates residual systematic bias through a set of negative control outcomes (NCOS).



PNAS

Empirical confidence interval calibration for population-level effect estimation studies in observational healthcare data

Martijn J. Schuemie[a,b,1], George Hripcsak[a,c,d], Patrick B. Ryan[a,b,c], David Madigan[a,e], and Marc A. Suchard[a,f,g,h]

[a]Observational Health Data Sciences and Informatics, New York, NY 10032; [b]Epidemiology Analytics, Janssen Research & Development, Titusville, NJ 08560; [c]Department of Biomedical Informatics, Columbia University, New York, NY 10032; [d]Medical Informatics Services, New York–Presbyterian Hospital, New York, NY 10032; [e]Department of Statistics, Columbia University, New York, NY 10027; [f]Department of Biomathematics, University of California, Los Angeles, CA 90095; [g]Department of Biostatistics, University of California, Los Angeles, CA 90095; and [h]Department of Human Genetics, University of California, Los Angeles, CA 90095

JACC Journals › JACC › Archives › Vol. 84 No. 10

FREE ACCESS | Original Research | 26 August 2024

Comparative Effectiveness of Second-Line Antihyperglycemic Agents for Cardiovascular Outcomes: A Multinational, Federated Analysis of LEGEND-T2DM

Editorial Comment: Finding Truth in Observational and Interventional Studies in Diabetes and Cardiovascular Disease

Authors: Rohan Khera, Arya Aminorroaya, Lovedeep Singh Dhingra, Phyllis M. Thangaraj, Aline Pedroso Camargos, Fan Bu, Xiyu Ding, ... SHOW ALL ... , and Marc A. Suchard | AUTHORS INFO & AFFILIATIONS

Negative control outcome (NCO), known a priori to be unrelated to exposure.

LEGEND-T2DM study (Khera et al. 2024, JACC) used ”tooth loss" as an NCO that is known to be unrelated to the antihyperglycemic.

Our proposed method:

LATTE: **One-shot Lossless** Algorithm for Federated Target Trial Emulation

- Requires only one round of communication (**one shot**)
- Only requires aggregate data (2x2 tables)
- The results obtained is identical to the pooled analysis (**lossless**)

LATTE: **One-shot Lossless** Algorithm for Federated Target Trial Emulation

- Requires only one round of communication (one shot)
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- **Pipeline**

IPD **Summary Statistics**

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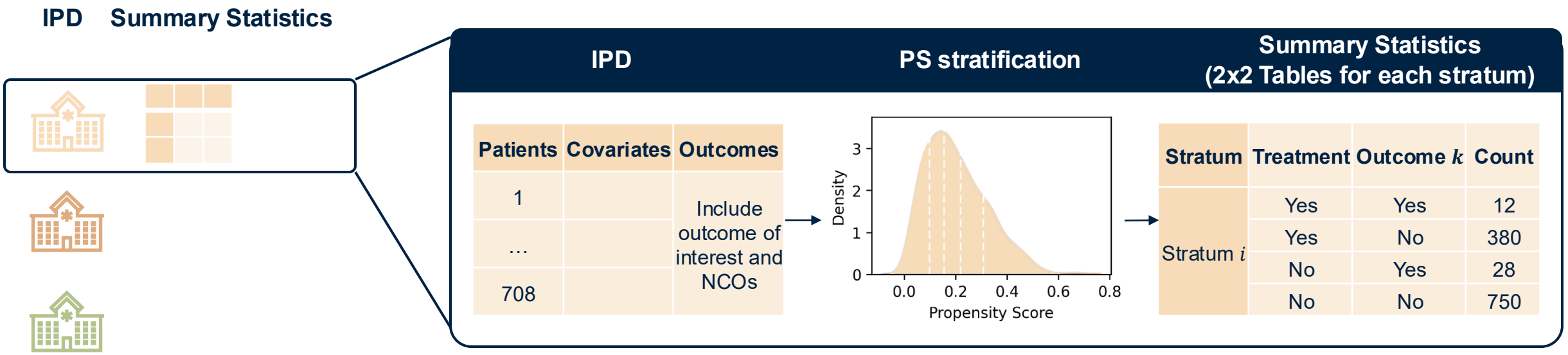

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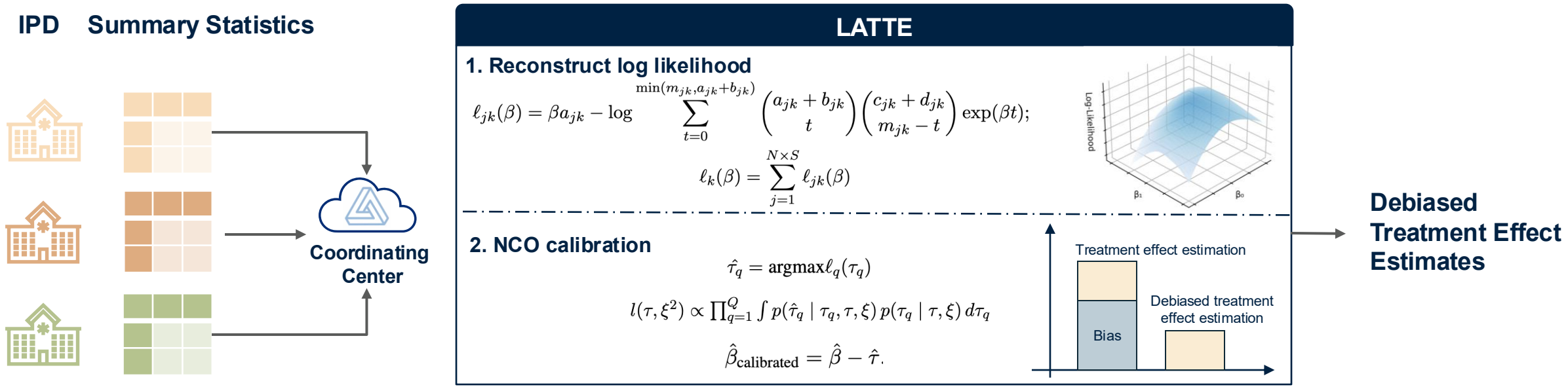
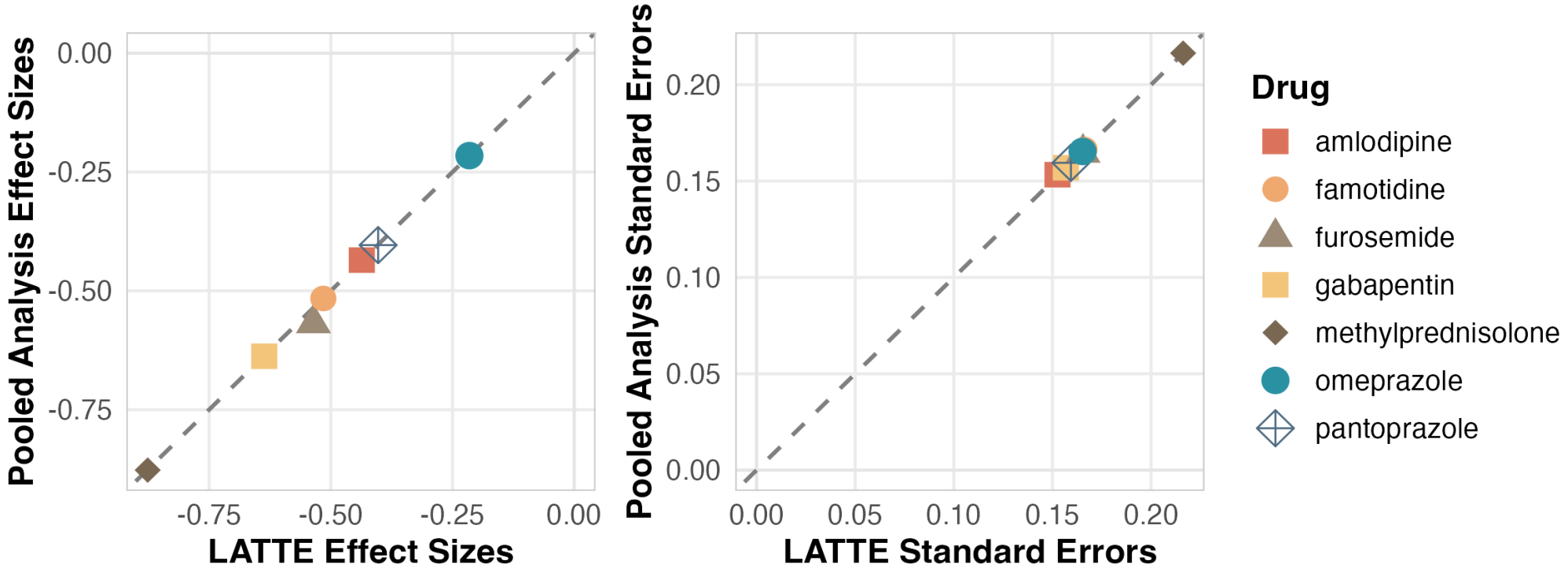


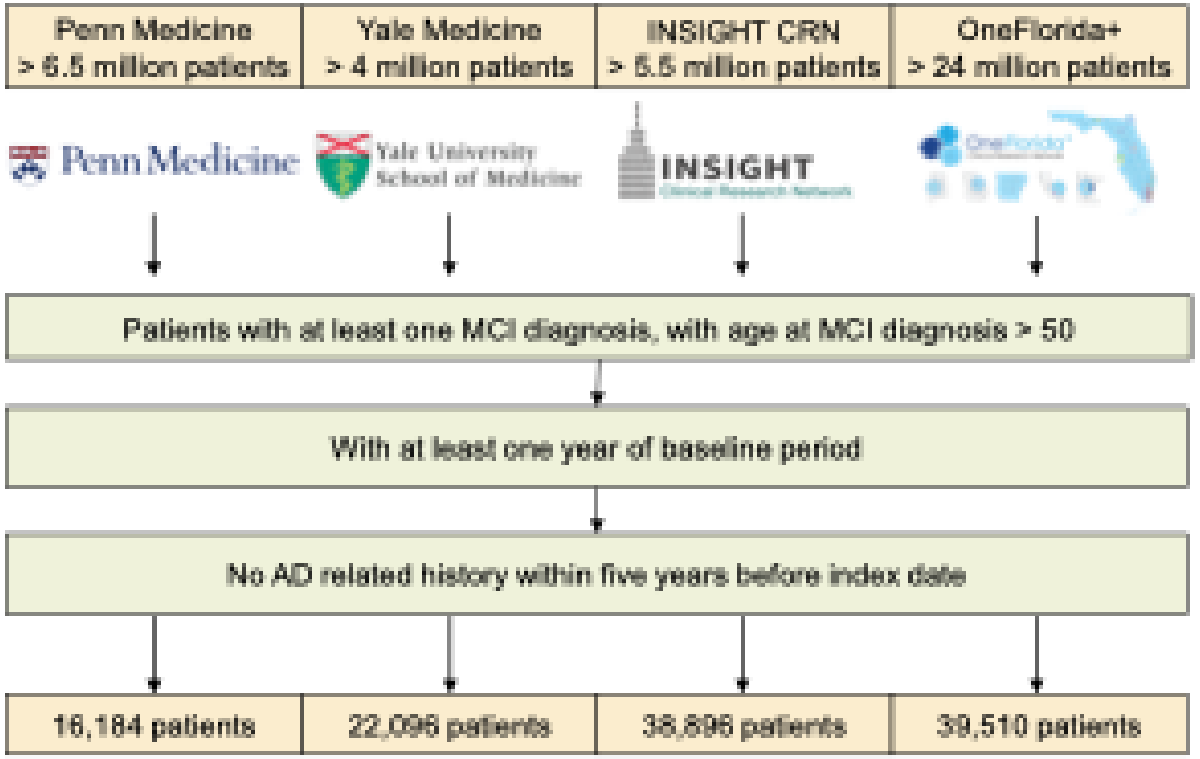
Simulation studies

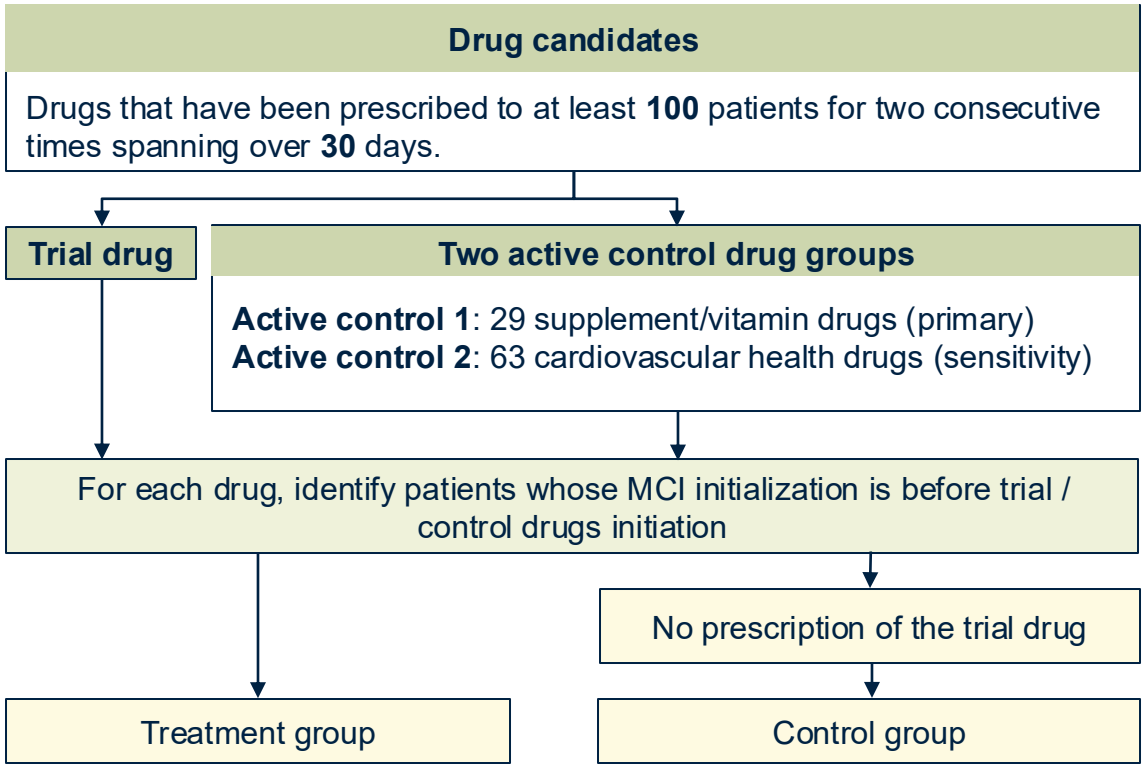
- We randomly split the data at Penn Medicine into 3 sites
- Compared the results from pooled analysis and LATTE



Real-world application to ADRD drug repurposing

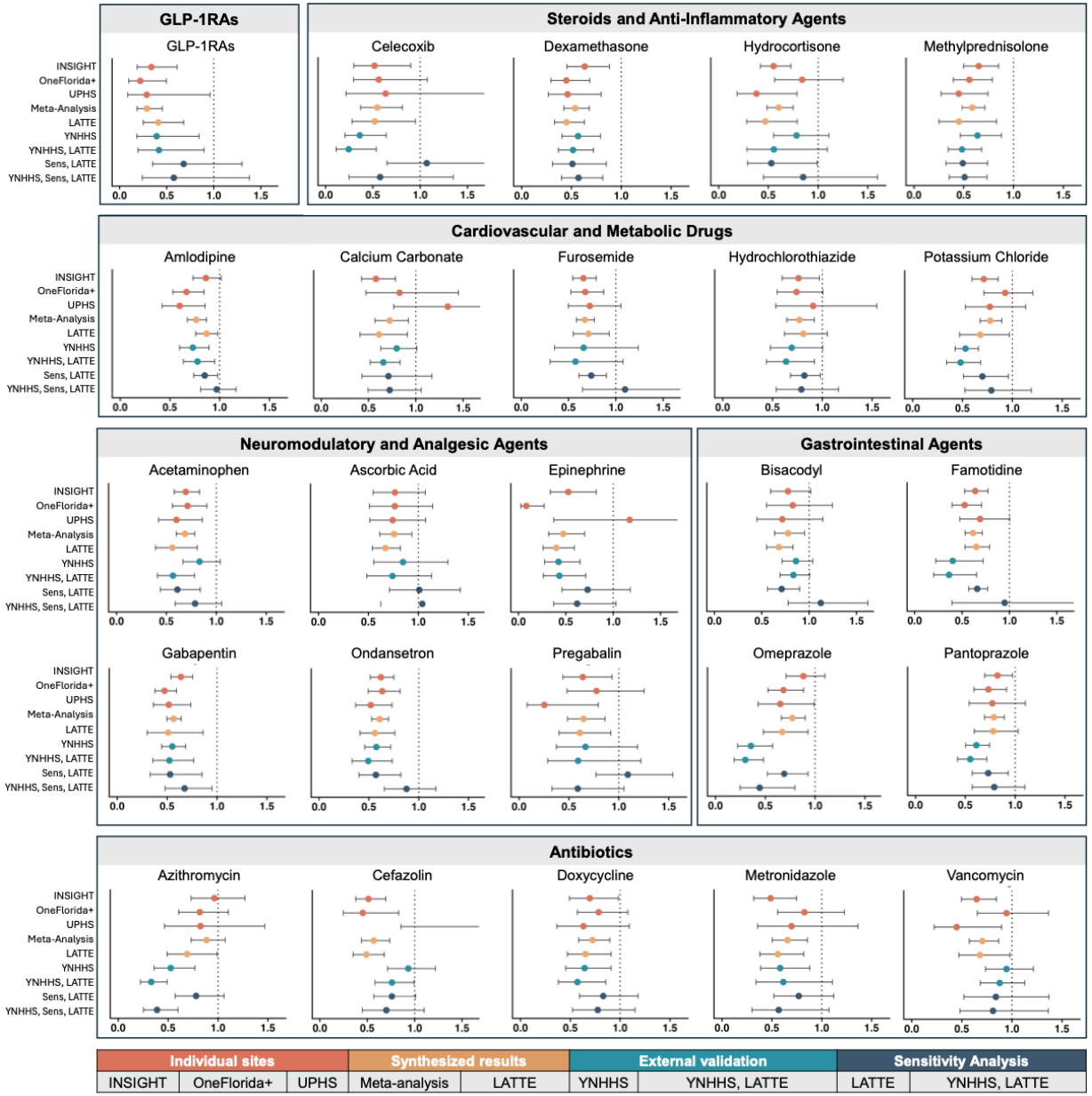
- **Scientific question** Which drugs can potentially be repurposed to slow down progression from MCI to ADRD?
- **Datasets** 4 large-scale academic hospitals, covering **> 40 million** patients.
- **Drug candidates** **112 commonly used drugs** that have been prescribed to at least 100 patients for two consecutive times spanning over 30 days.
- **Empirical calibration** **24 NCOs** selected by domain clinical experts.





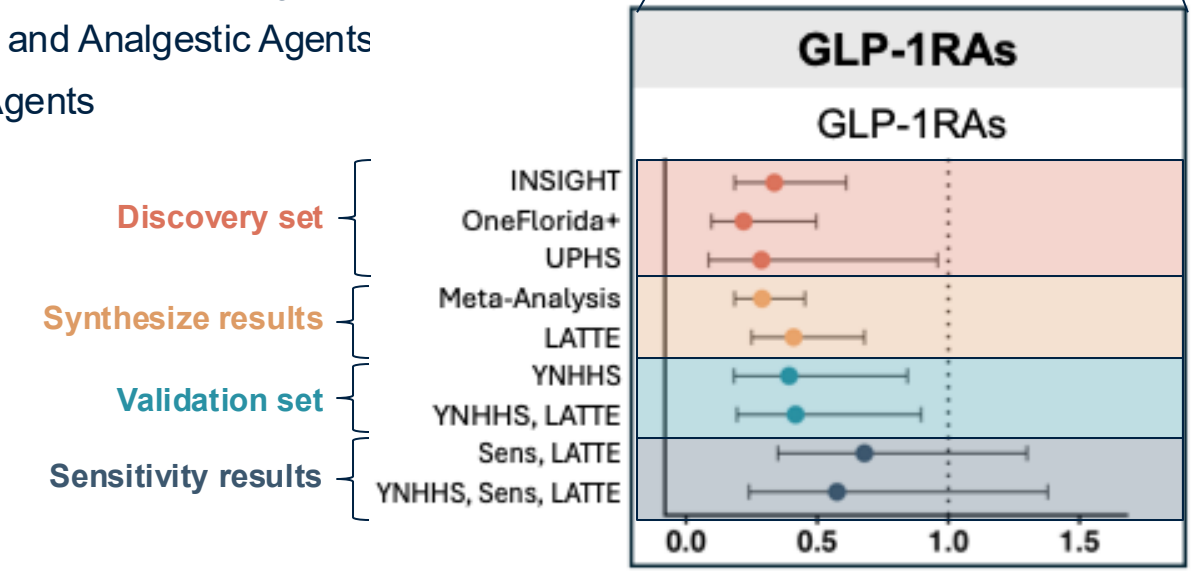
Results

- Identified **25 drugs candidates** from **6 drug classes**
  - GLP-1RAs
    - GLP-1RAs (aOR 0.41, 95% CI: 0.25–0.68)
  - Steroids and Anti-Inflammatory Agents
    - Celecoxib (aOR 0.52, 95% CI 0.28-0.95) …
  - Cardiovascular and Metabolic Drugs
    - Amlodipine (aOR 0.87, 95% CI 0.76-0.98) …
  - Neuromodulatory and Analgestic Agents
    - Ondansetron (aOR 0.56, 95% CI 0.41-0.76) …
  - Gastrointestinal Agents
    - Famotidine (aOR 0.65, 95% CI 0.53-0.79) …
  - Antibiotics
    - Doxycycline (aOR 0.65, 95% CI 0.47-0.91) …



Results

- Identified **25 drugs candidates** from **6 drug classes**
  - GLP-1RAs
  - Steroids and Anti-Inflammatory Agents
  - Cardiovascular and Metabolic Drugs
  - Neuromodulatory and Analgestic Agents
  - Gastrointestinal Agents
  - Antibiotics

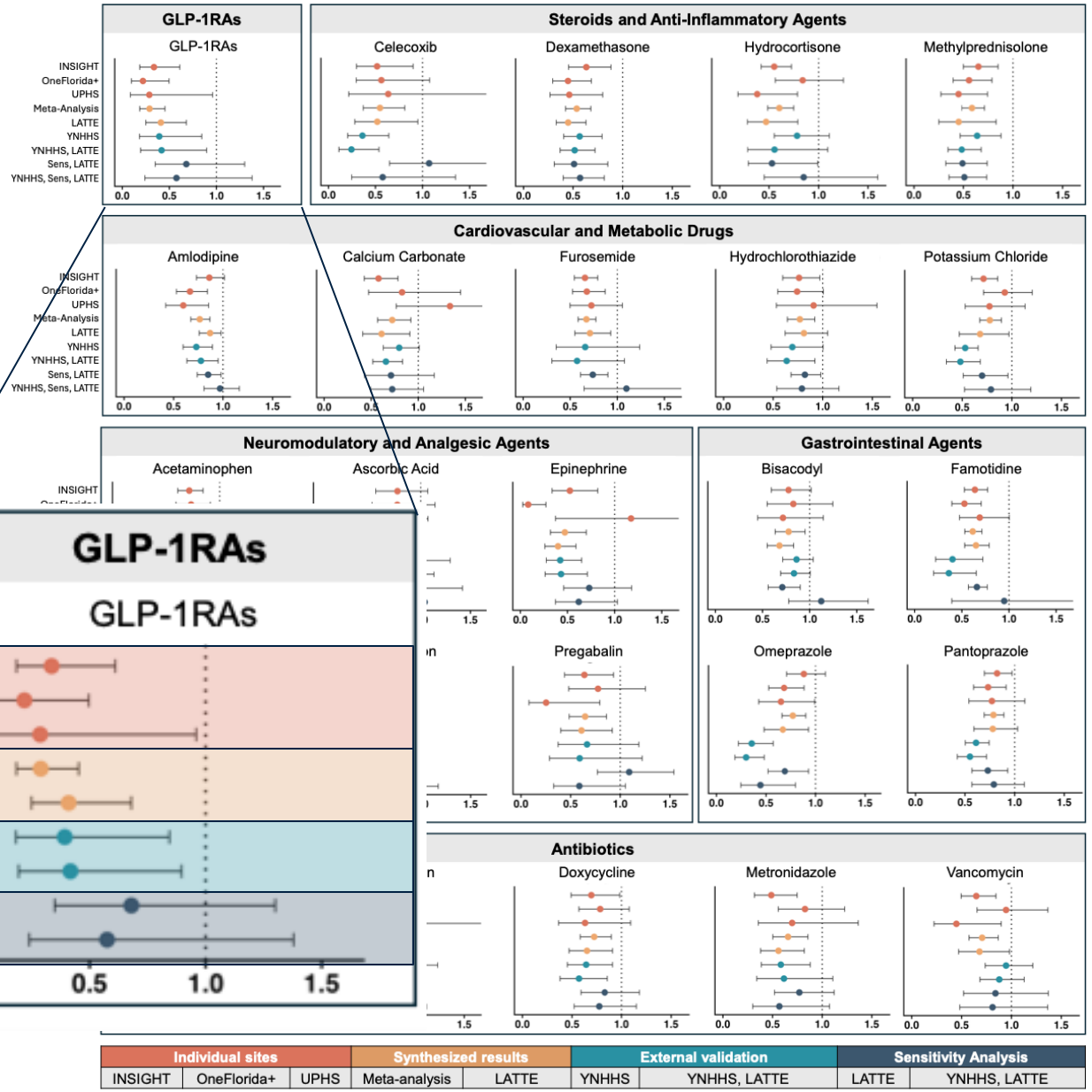


Discovery set

Synthesize results

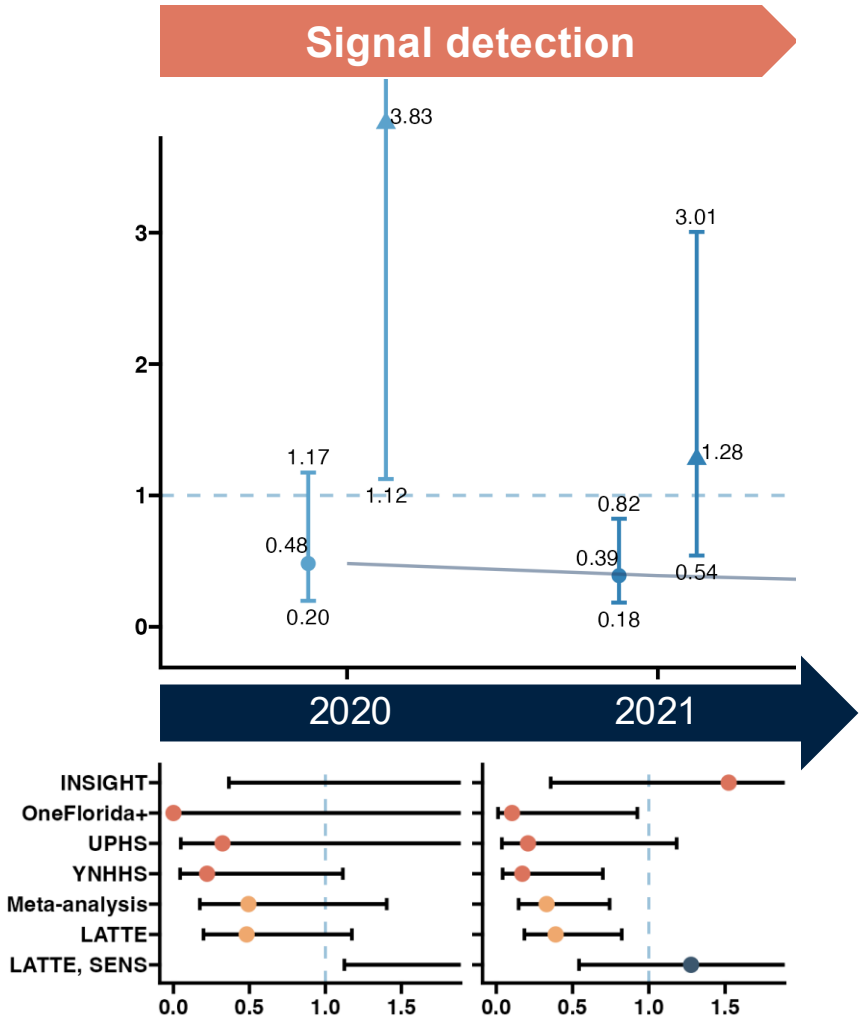
Validation set

Sensitivity results

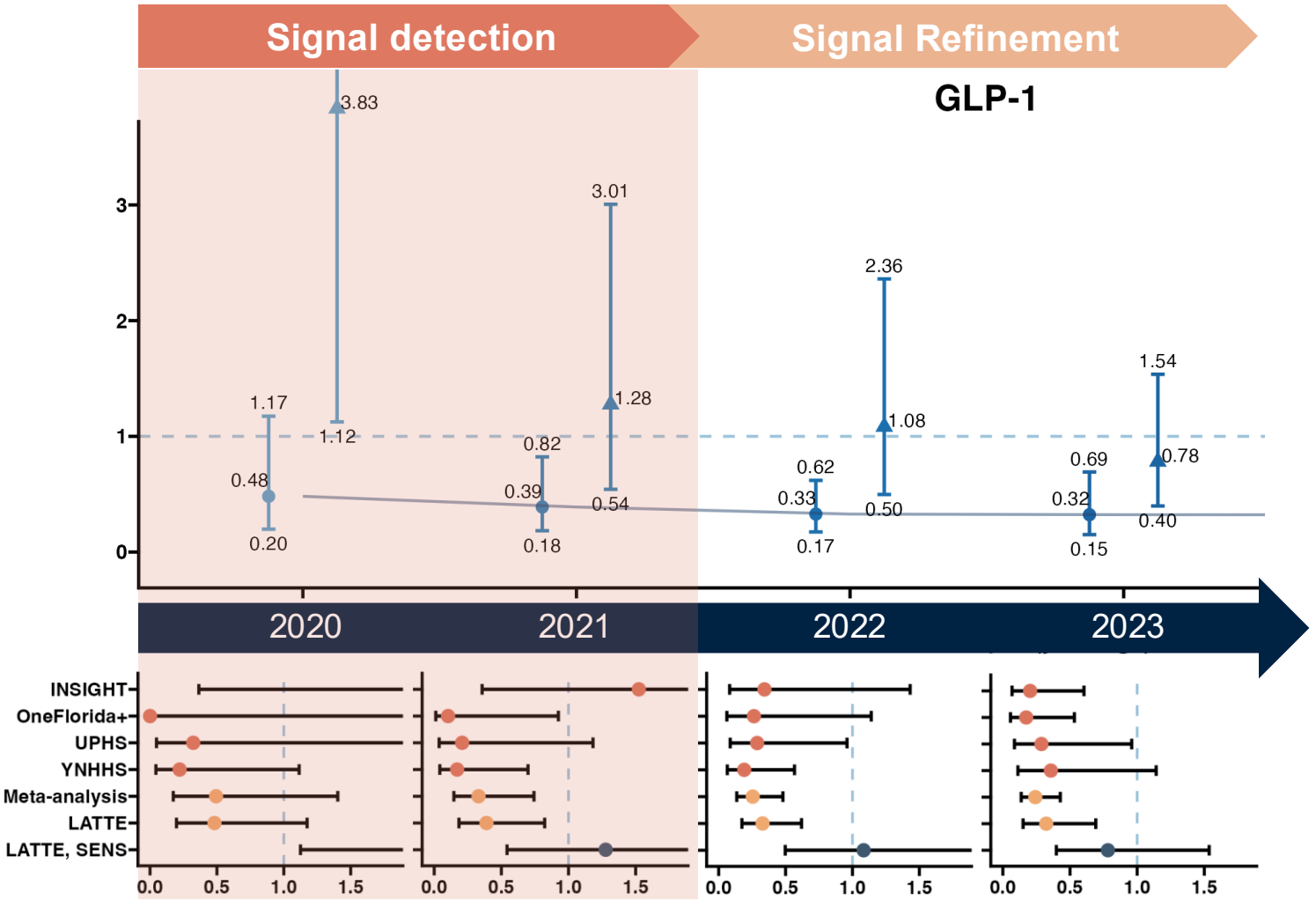


Individual sites			Synthesized results		External validation		Sensitivity Analysis	
INSIGHT	OneFlorida+	UPHS	Meta-analysis	LATTE	YNHHS	YNHHS, LATTE	LATTE	YNHHS, LATTE

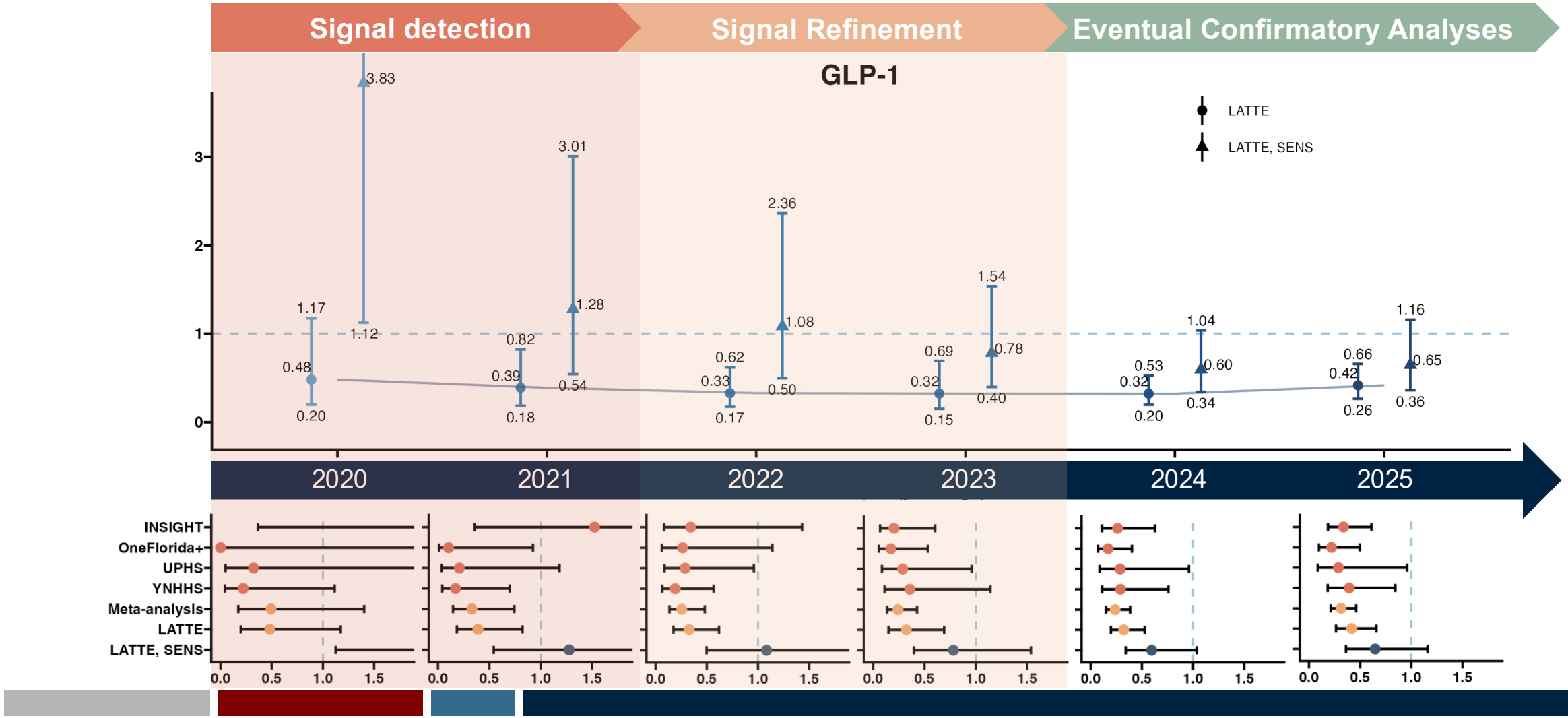
LATTE for Continuous Monitoring



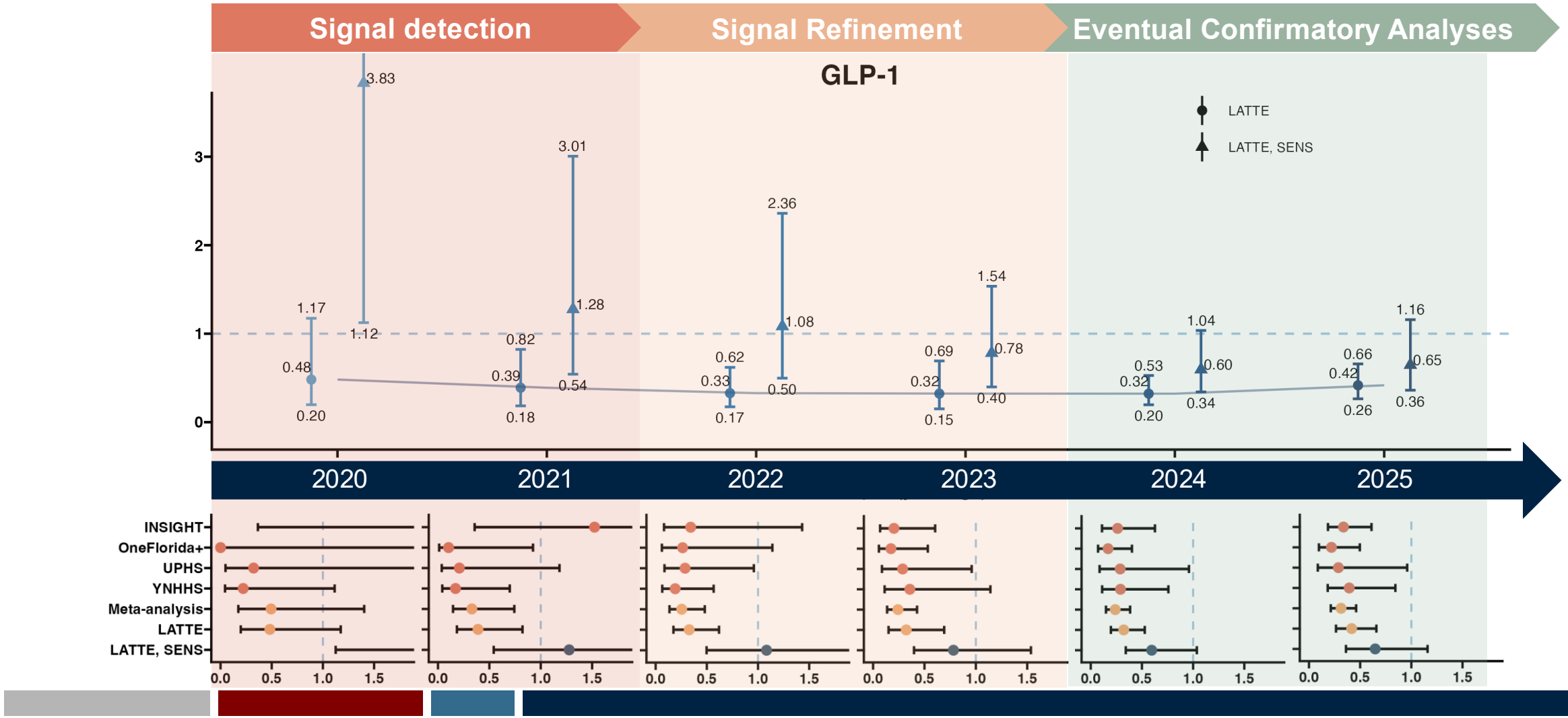
LATTE for Continuous Monitoring



LATTE for Continuous Monitoring



LATTE for Continuous Monitoring



Summary

- **LATTE** performs federated target trial emulation in **one-shot**, **lossless** manner, while **mitigating systematic biases**
- **Summary statistics only**
- **Ready-to-use** within ‘pda’ package

LATTE: Lossless One-shot Algorithm for Federated Target Trial Emulation

R package: ‘pda’

https://github.com/Penncil/pda

Acknowledgments

- Yong Chen, University of Pennsylvania
- David A. Asch, University of Pennsylvania
- Qiong Wu, University of Pittsburgh
- Yiwen Lu, University of Pennsylvania
- Kyra S. O'Brien, University of Pennsylvania
- Bingyu Zhang, University of Pennsylvania
- Ting Zhou, University of Pennsylvania
- Jiayi Tong, University of Pennsylvania
- Dazheng Zhang, University of Pennsylvania
- Yuqing Lei, University of Pennsylvania
- Huilin Tang, University of Pennsylvania
- Haoyang Li, Cornell University
- Zhenxing Xu, Cornell University
- Yu Huang, Indiana University
- Yu Hu, University of Florida
- Yujia Zhou, Yale University
- Fongci Lin, Yale University
- Ying Jiang, Third Affiliated Hospital of Sun Yat-sen University
- Fei Wang, Cornell University
- Jiang Bian, Indiana University
- Hua Xu, Yale University
- Yong Chen, Pfizer Inc
- Jeff D. Williamson, Wake Forest University
- David A. Wolk, University of Pennsylvania
- Yun Lu, Food and Drug Administration

👉 **Poster: # 607**

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OHDSI 2025 Collaborator Showcase
Lightning Talks Round 2

End: Lu Li

Next up: Georgina Kennedy

Maridulu Budyari Gumal | Cancer Clinical Academic Group

OHDSI
Global Symposium
2025

From Data Quality to Clinical Quality

Episodes as Enablers for Next Generation Dashboarding

SPHERE CANCER CLINICAL ACADEMIC GROUP

Dr Georgina Kennedy
Senior Research Fellow, Ingham Institute

CaVa
NSW GOVERNMENT
Proudly supported by Cancer Institute NSW

UNSW SYDNEY
Ingham Institute Applied Medical Research

Health System & Specialty Networks

- Health South Western Sydney Local Health District
- The Sydney children's Hospitals Network
- Health South Eastern Sydney Local Health District
- St Vincent's Hospital Sydney

Additional Support & Partnerships

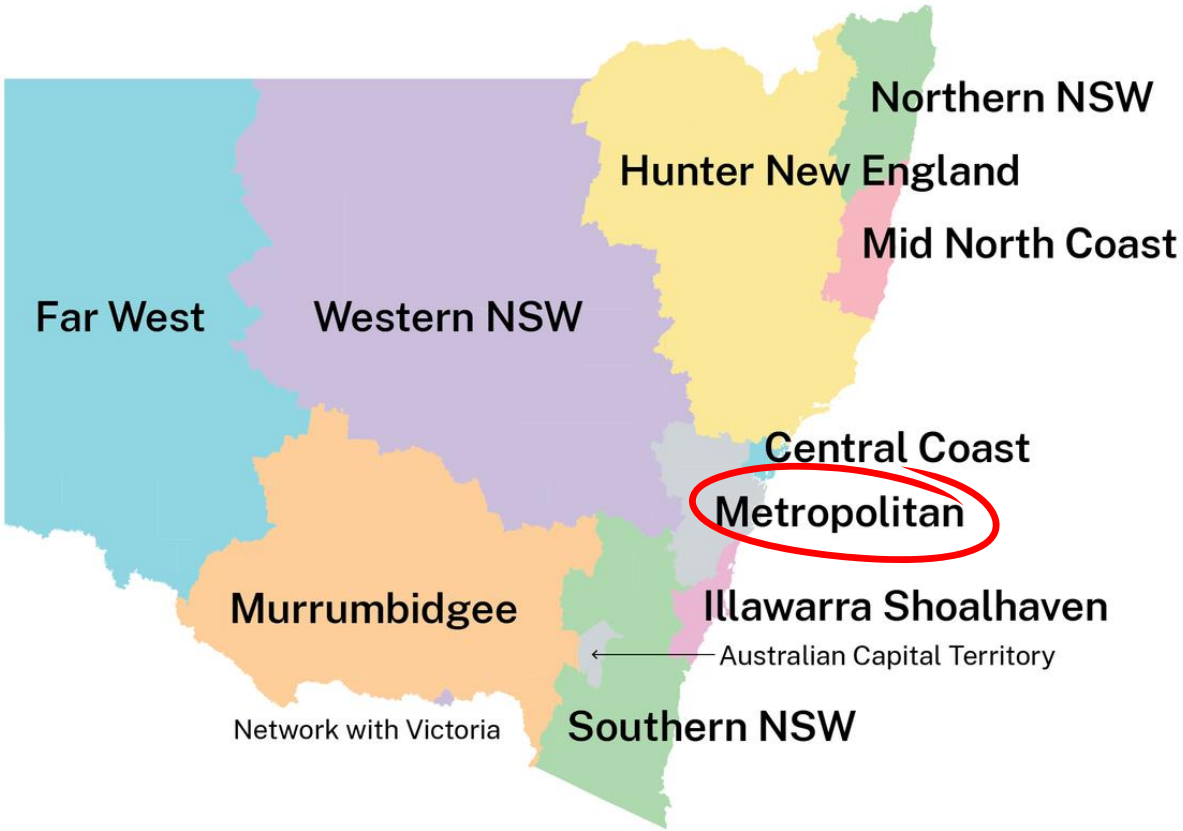
- Maridulu Budyari Gumal — Working together for good health and wellbeing
- Cancer Clinical Academic Group
- Proudly supported by Cancer Institute NSW
- ACDN Australian Cancer Data Network

Universities

- UNSW Sydney
- Western Sydney University
- UTS University of Technology Sydney
- ACU Australian Catholic University

Medical Research Institutes

- Ingham Institute Applied Medical Research
- Garvan Institute of Medical Research
- The George Institute for Global Health
- Children's Cancer Institute
- Black Dog Institute
- NeuRA
- Victor Chang Cardiac Research Institute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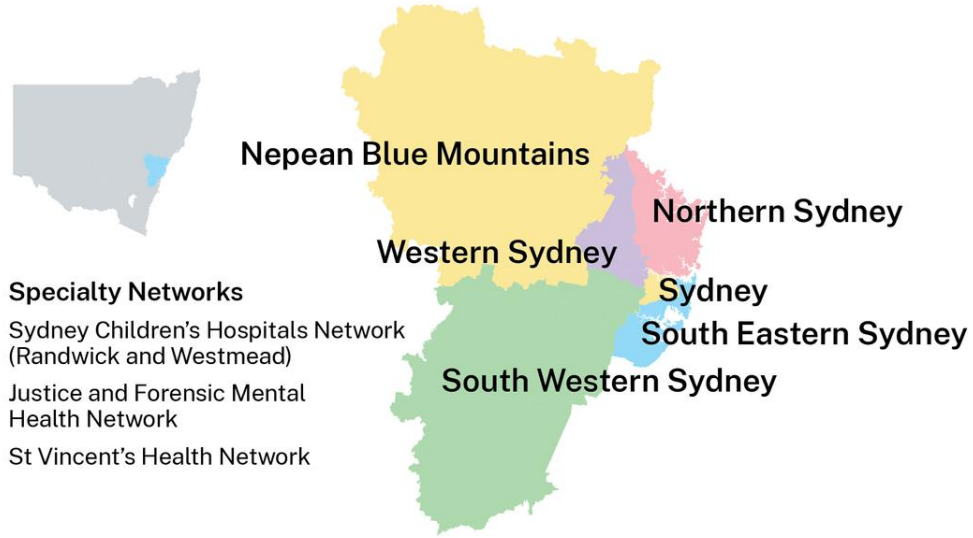
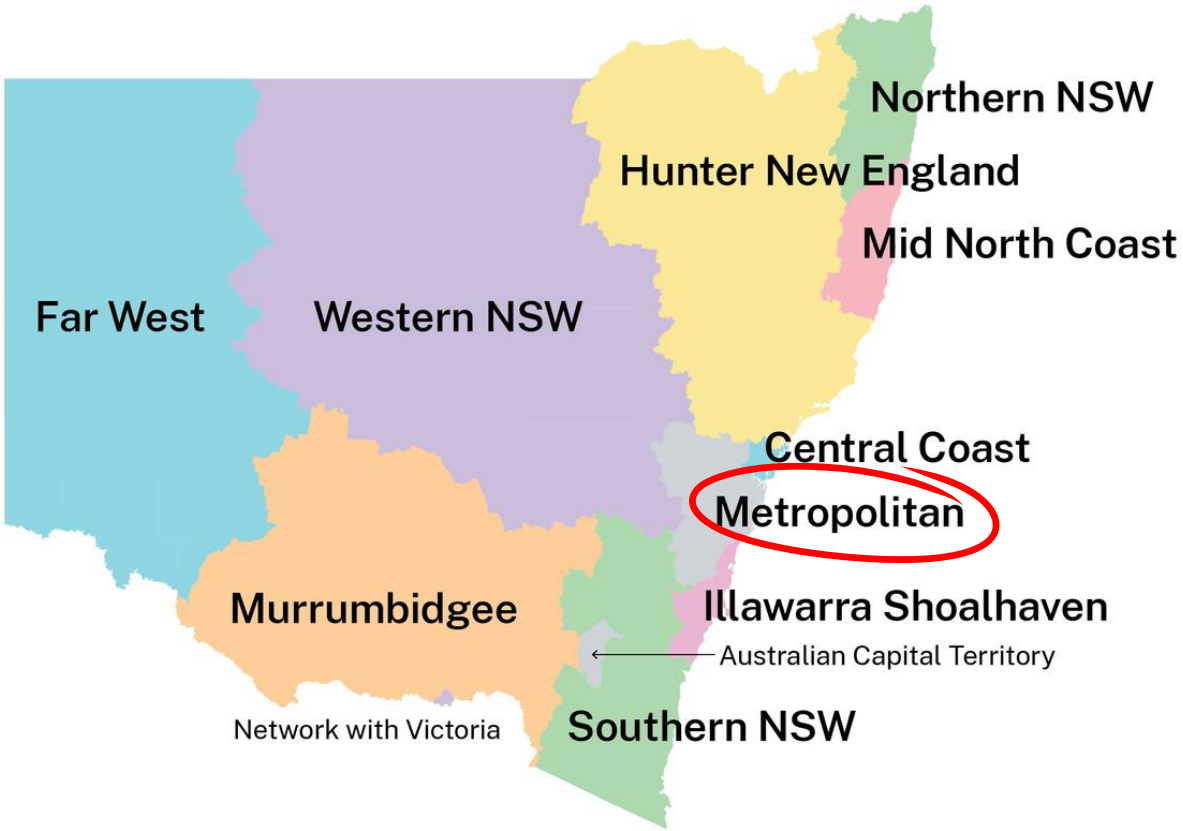
Hunter New England
Mid North Coast
Far West
Western NSW
Central Coast
Metropolitan
Murrumbidgee
Illawarra Shoalhaven
Australian Capital Territory
Network with Victoria
Southern NSW


Nepean Blue Mountains
Northern Sydney
Western Sydney
Sydney
South Eastern Sydney
South Western Sydney
Specialty Networks
Sydney Children's Hospitals Network (Randwick and Westmead)
Justice and Forensic Mental Health Network
St Vincent's Health Network


Northern NSW
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Mid North Coast
Far West
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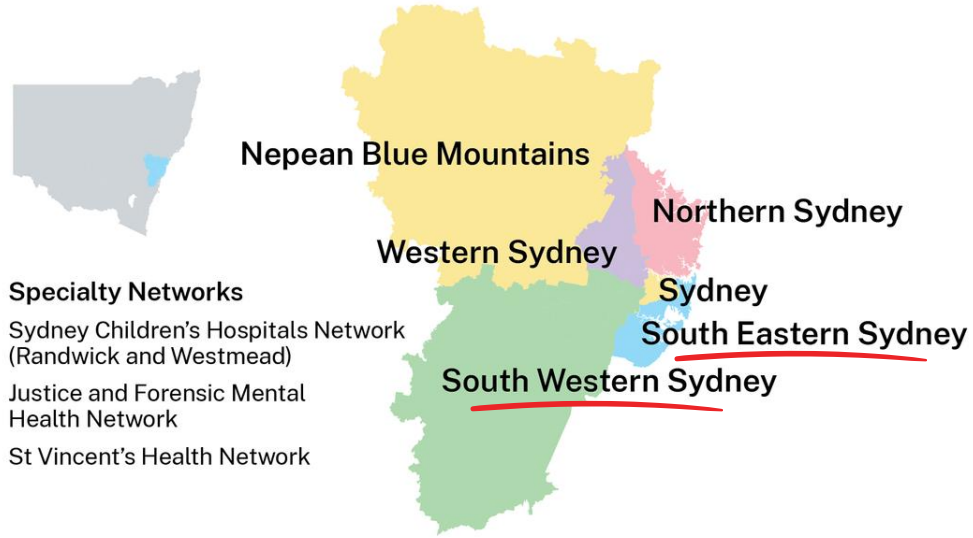
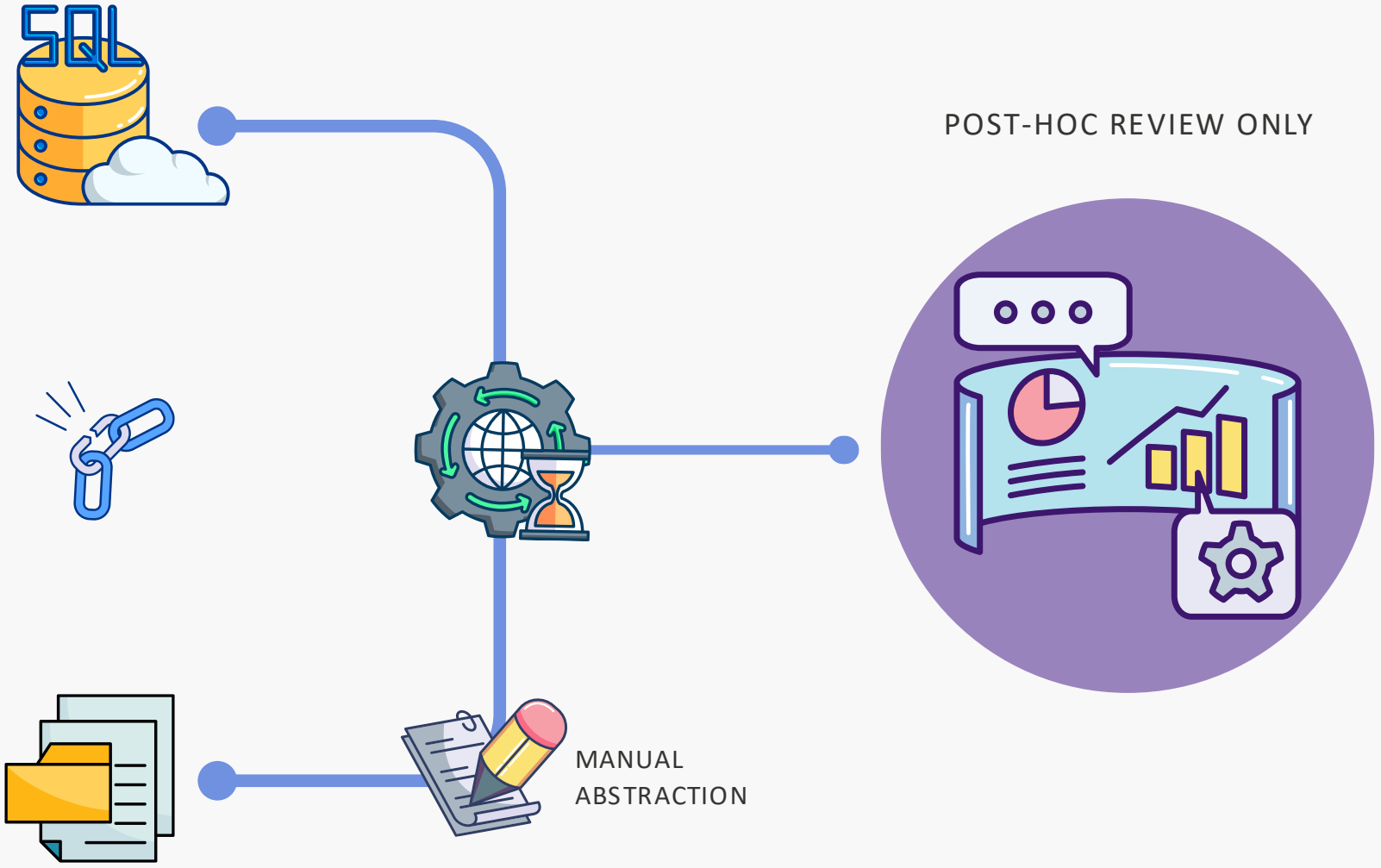
Central Coast
Metropolitan
Murrumbidgee
Illawarra Shoalhaven
Australian Capital Territory
Network with Victoria
Southern NSW


Nepean Blue Mountains
Northern Sydney
Western Sydney
Sydney
South Eastern Sydney
South Western Sydney
Specialty Networks
Sydney Children's Hospitals Network (Randwick and Westmead)
Justice and Forensic Mental Health Network
St Vincent's Health Network

NO HARMONISATION

DISCONNECTED

HETEROGENEOUS; TEXT



POST-HOC REVIEW ONLY

Automation of Clinical Quality Indicators

Functional Requirements

Improved timeliness

Lower manual effort

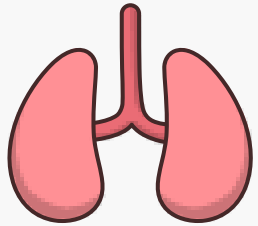
Increased clinical scope

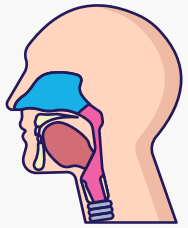
Functional Requirements

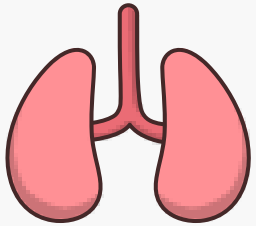
- Improved timeliness
- Lower manual effort
- Increased clinical scope

Technical Requirements

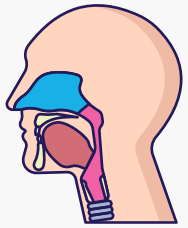
- Modular & configurable
- Extensible; sharable
- Low maintenance costs





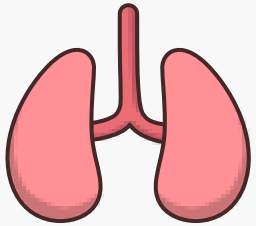


Strong engagement,
mature reporting practice



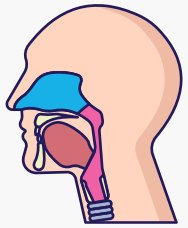
Complex,
high supportive-care needs

Large population,
capacity for improvement



Strong engagement,
mature reporting practice

CQI status: Release candidate

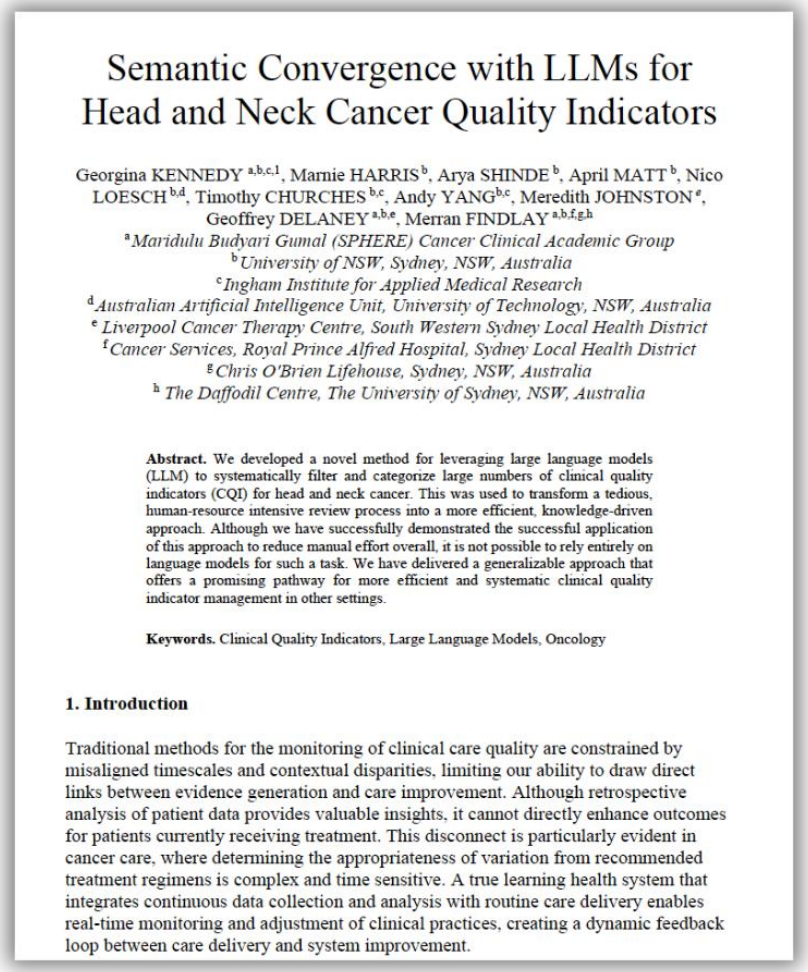


Complex,
high supportive-care needs

CQI status: Alpha definitions

Large population,
capacity for improvement

CQI status: To do



Semantic Convergence with LLMs for Head and Neck Cancer Quality Indicators

Georgina KENNEDY [a,b,c,1], Marnie HARRIS [b], Arya SHINDE [b], April MATT [b], Nico LOESCH [b,d], Timothy CHURCHES [b,c], Andy YANG [b,c], Meredith JOHNSTON [e], Geoffrey DELANEY [a,b,e], Merran FINDLAY [a,b,f,g,h]
[a] *Maridulu Budyari Gumal (SPHERE) Cancer Clinical Academic Group*
[b] *University of NSW, Sydney, NSW, Australia*
[c] *Ingham Institute for Applied Medical Research*
[d] *Australian Artificial Intelligence Unit, University of Technology, NSW, Australia*
[e] *Liverpool Cancer Therapy Centre, South Western Sydney Local Health District*
[f] *Cancer Services, Royal Prince Alfred Hospital, Sydney Local Health District*
[g] *Chris O'Brien Lifehouse, Sydney, NSW, Australia*
[h] *The Daffodil Centre, The University of Sydney, NSW, Australia*

Abstract. We developed a novel method for leveraging large language models (LLM) to systematically filter and categorize large numbers of clinical quality indicators (CQI) for head and neck cancer. This was used to transform a tedious, human-resource intensive review process into a more efficient, knowledge-driven approach. Although we have successfully demonstrated the successful application of this approach to reduce manual effort overall, it is not possible to rely entirely on language models for such a task. We have delivered a generalizable approach that offers a promising pathway for more efficient and systematic clinical quality indicator management in other settings.

Keywords. Clinical Quality Indicators, Large Language Models, Oncology

1. Introduction

Traditional methods for the monitoring of clinical care quality are constrained by misaligned timescales and contextual disparities, limiting our ability to draw direct links between evidence generation and care improvement. Although retrospective analysis of patient data provides valuable insights, it cannot directly enhance outcomes for patients currently receiving treatment. This disconnect is particularly evident in cancer care, where determining the appropriateness of variation from recommended treatment regimens is complex and time sensitive. A true learning health system that integrates continuous data collection and analysis with routine care delivery enables real-time monitoring and adjustment of clinical practices, creating a dynamic feedback loop between care delivery and system improvement.

800+ CLINICAL GUIDELINE-BASED BEST PRACTICE INDICATORS REVIEWED

- CLINICAL CONSENSUS
  - MEASURABILITY
  - IMPACT
  - PRIORITY
- TECHNICAL FEASIBILITY
  - MODULARITY
  - REUSE & GENERALISABILITY

Clinician-led co-design

Improving Lung Cancer Care in Australia

A national collaboration

Lung cancer is the leading cause of cancer death in Australia and has the lowest survival rate.

Lung cancer accounts for 9% of all cancers but is responsible for 18% of deaths from all cancers in Australia. The number of years of potential life lost each year to lung cancer in Australia is estimated to be similar to that of colorectal and breast cancer *combined.* Despite advances in treatments and evidence-based guidelines to inform best clinical practice, the five year survival for all lung cancer in Australia remains terribly low at only 19%.

LUCAP
LUNG CANCER CLINICAL QUALITY DATA PLATFORM

LUCAP drives change to improve standards of lung cancer care

What is LUCAP?

LUCAP is a patient-focused research group who are developing a national clinical quality data platform for lung cancer that collects, analyses and reports on information like how quickly people get lung cancer tests, what sort of tests are done and how quickly people get treatments.

Our Mission

Our mission is to improve the safety, quality and outcomes of health care for all lung cancer patients in Australia.

Our Vision

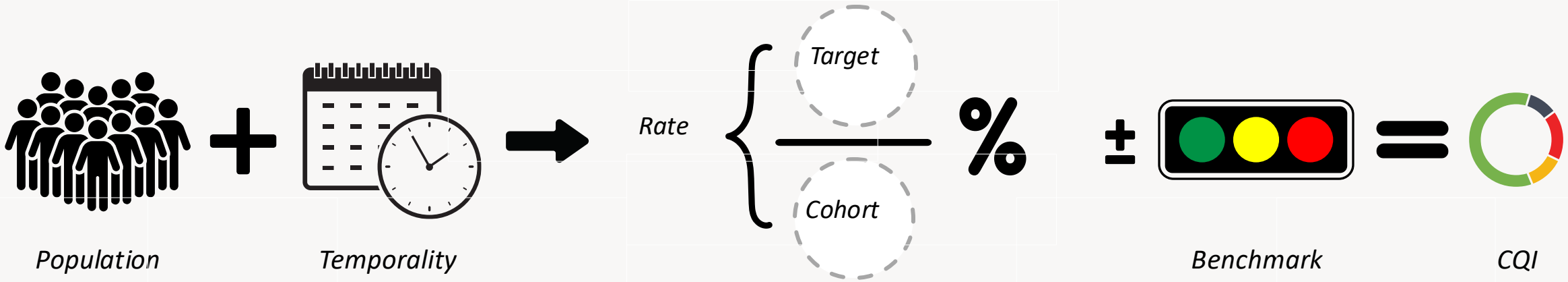
A national data platform that enables the performance of lung cancer service providers to be compared against a set of national standards and supports innovative research in lung cancer care and treatments.

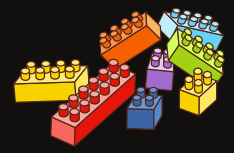
Prof Shalini Vinod
Radiation Oncologist

https://lucap-au.com/

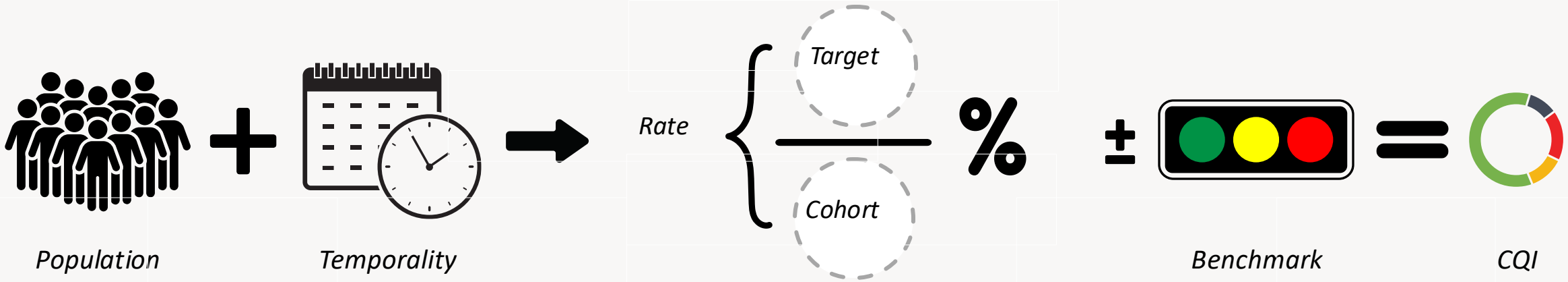
Maridulu Budyari Gumal
Working together for good health and wellbeing

Clinician-led co-design


Target
Rate
Cohort
%
Population
Temporality
Benchmark
CQI



≥80% of patients with Stage I–III SCLC and PS 0–2 should receive chemoradiation



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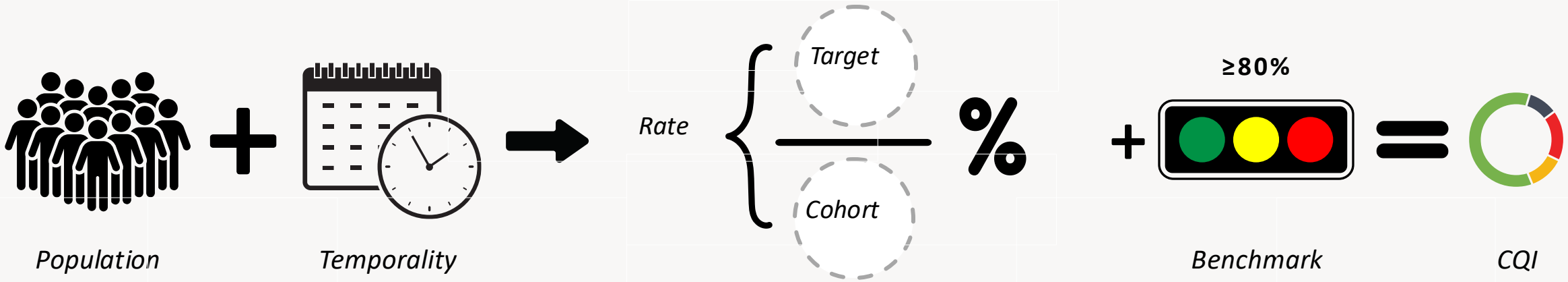

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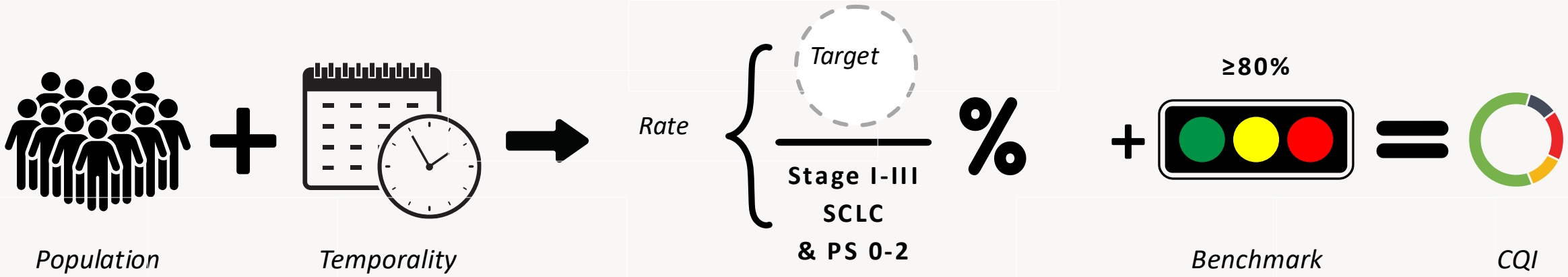

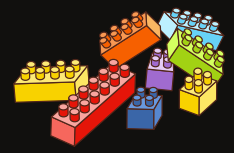

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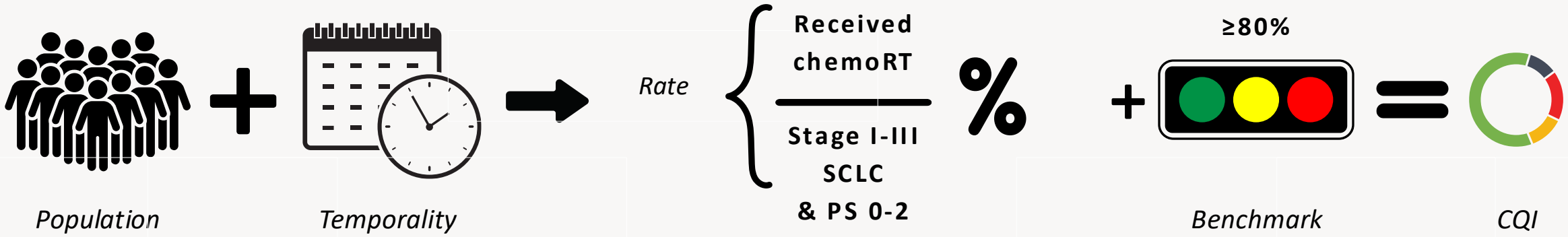
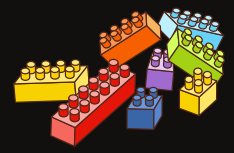
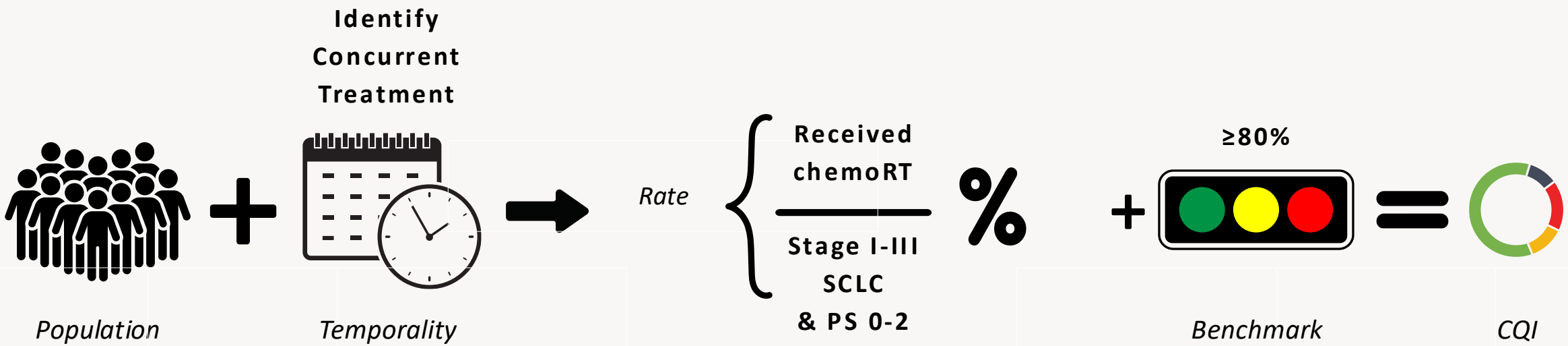
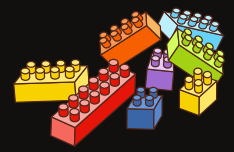




≥80% of patients with Stage I–III SCLC and PS 0–2 should receive chemoradiation

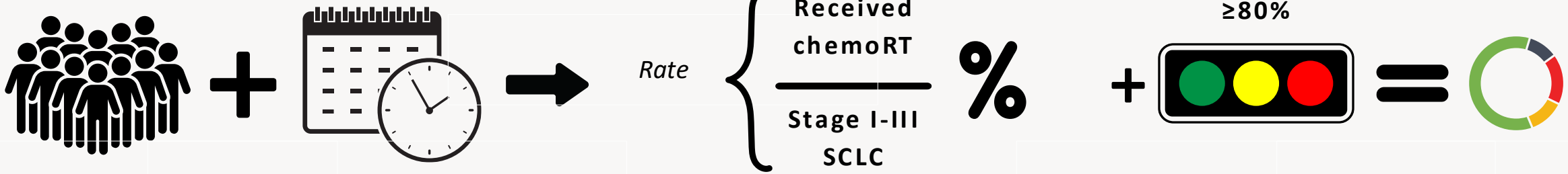




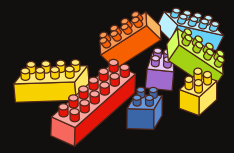
≥80% of patients with Stage I–III SCLC and PS 0–2 should receive chemoradiation

Treatment linked to specific dx

Identify Concurrent Treatment



Population *Temporality* *Benchmark* *CQI*



UX elements filter date range
and sub-cohorts

Cohort Filter

Report

Report Metadata

Cohorts

Measures

Indicators

Measures

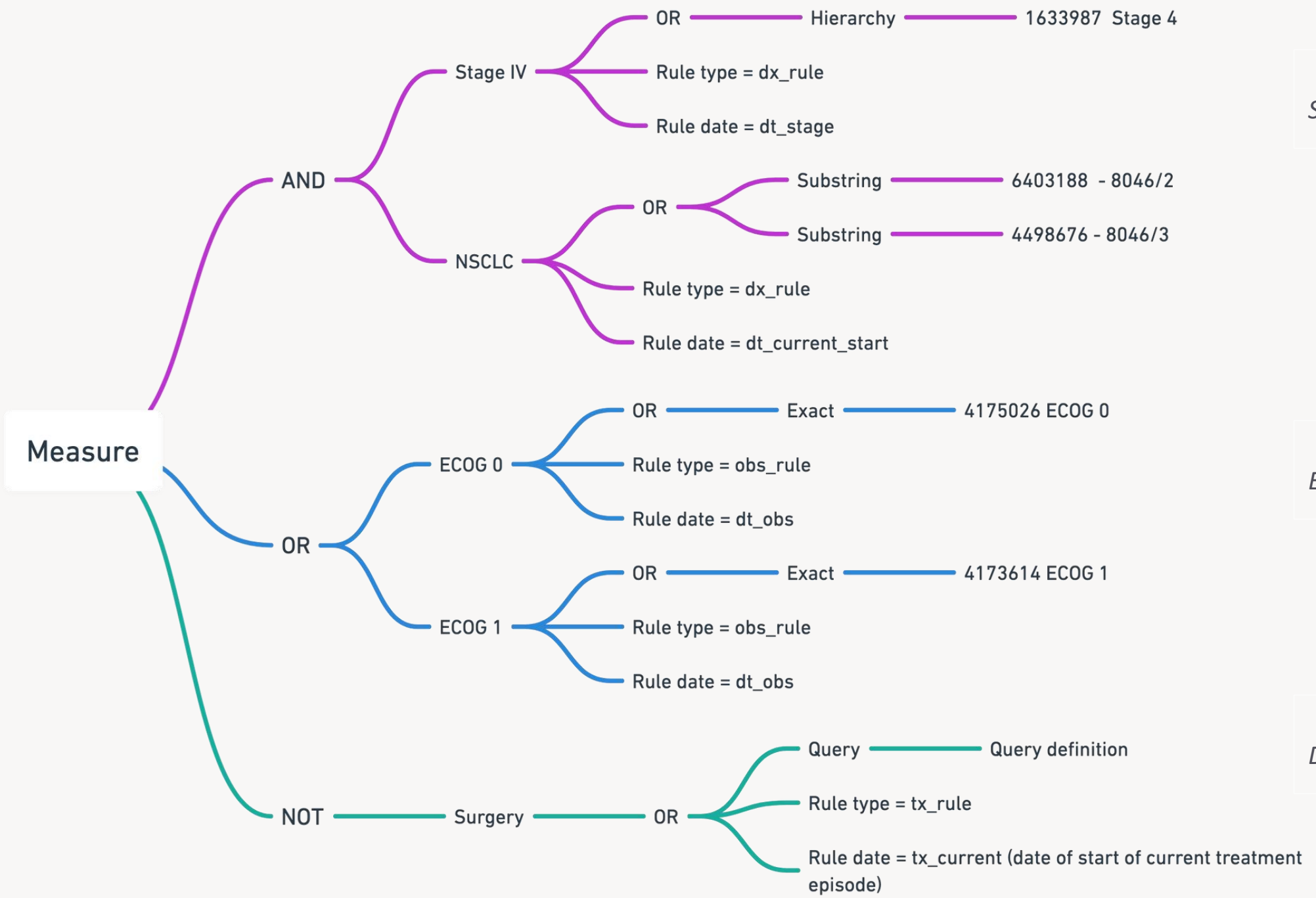
Indicator elements update
to reflect filter selections

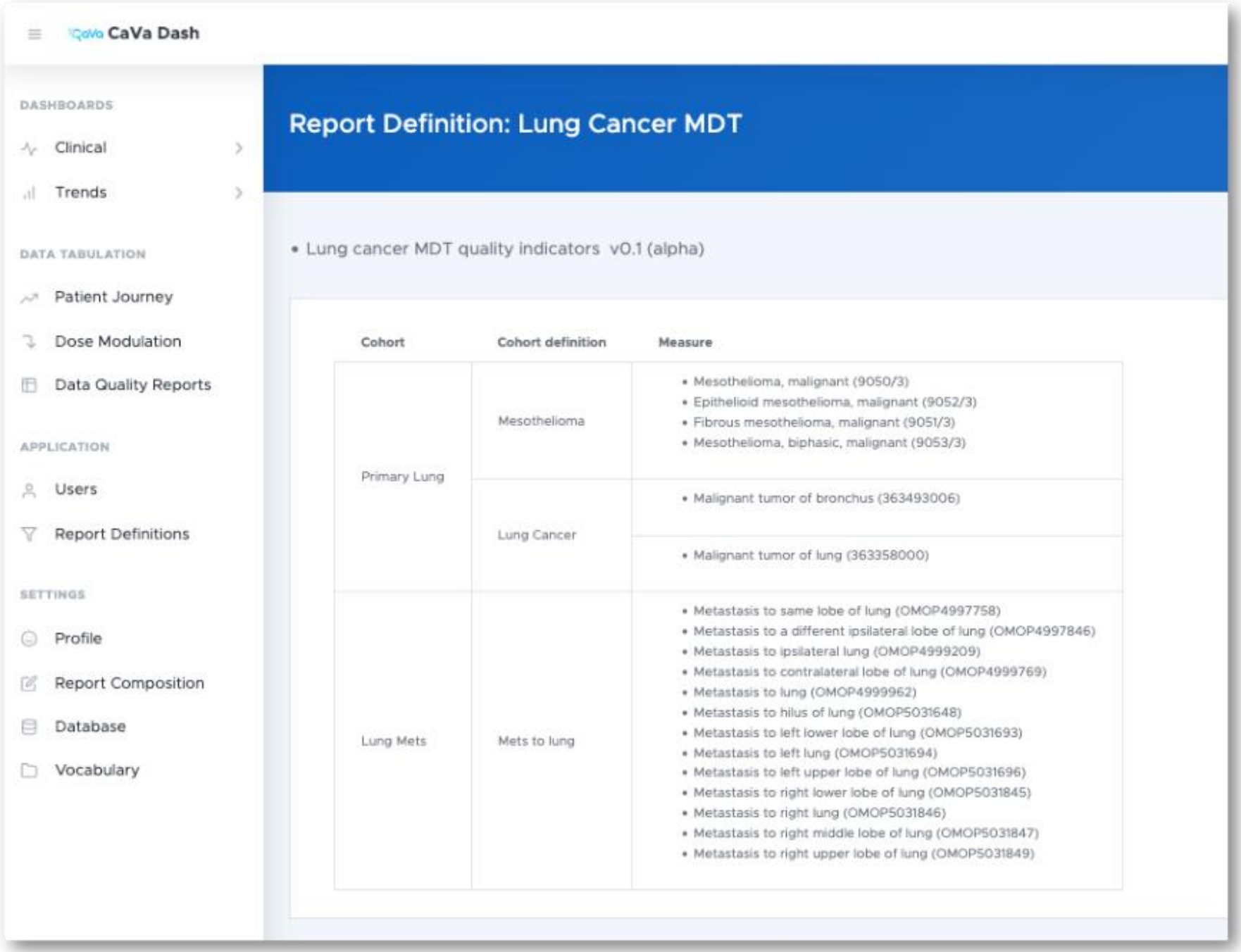
Temporal buckets offer
trend analysis

Report Data

Measures

Measure Members


Measure
AND
Stage IV
OR
Hierarchy
1633987 Stage 4
Rule type = dx_rule
Rule date = dt_stage
NSCLC
OR
Substring
6403188 - 8046/2
Substring
4498676 - 8046/3
Rule type = dx_rule
Rule date = dt_current_start
OR
ECOG 0
OR
Exact
4175026 ECOG 0
Rule type = obs_rule
Rule date = dt_obs
ECOG 1
OR
Exact
4173614 ECOG 1
Rule type = obs_rule
Rule date = dt_obs
NOT
Surgery
OR
Query
Query definition
Rule type = tx_rule
Rule date = tx_current (date of start of current treatment episode)
Stage IV NSCLC Patients
ECOG 0-1
Did not have surgery


CaVa Dash
DASHBOARDS
Clinical
Trends
DATA TABULATION
Patient Journey
Dose Modulation
Data Quality Reports
APPLICATION
Users
Report Definitions
SETTINGS
Profile
Report Composition
Database
Vocabulary
Report Definition: Lung Cancer MDT
• Lung cancer MDT quality indicators v0.1 (alpha)
Cohort
Cohort definition
Measure
Primary Lung
Mesothelioma
• Mesothelioma, malignant (9050/3)
• Epithelioid mesothelioma, malignant (9052/3)
• Fibrous mesothelioma, malignant (9051/3)
• Mesothelioma, biphasic, malignant (9053/3)
Lung Cancer
• Malignant tumor of bronchus (363493006)
• Malignant tumor of lung (363358000)
Lung Mets
Mets to lung
• Metastasis to same lobe of lung (OMOP4997758)
• Metastasis to a different ipsilateral lobe of lung (OMOP4997846)
• Metastasis to ipsilateral lung (OMOP4999209)
• Metastasis to contralateral lobe of lung (OMOP4999769)
• Metastasis to lung (OMOP4999962)
• Metastasis to hilus of lung (OMOP5031648)
• Metastasis to left lower lobe of lung (OMOP5031693)
• Metastasis to left lung (OMOP5031694)
• Metastasis to left upper lobe of lung (OMOP5031696)
• Metastasis to right lower lobe of lung (OMOP5031845)
• Metastasis to right lung (OMOP5031846)
• Metastasis to right middle lobe of lung (OMOP5031847)
• Metastasis to right upper lobe of lung (OMOP5031849)

Apache Airflow

plotly | Dash

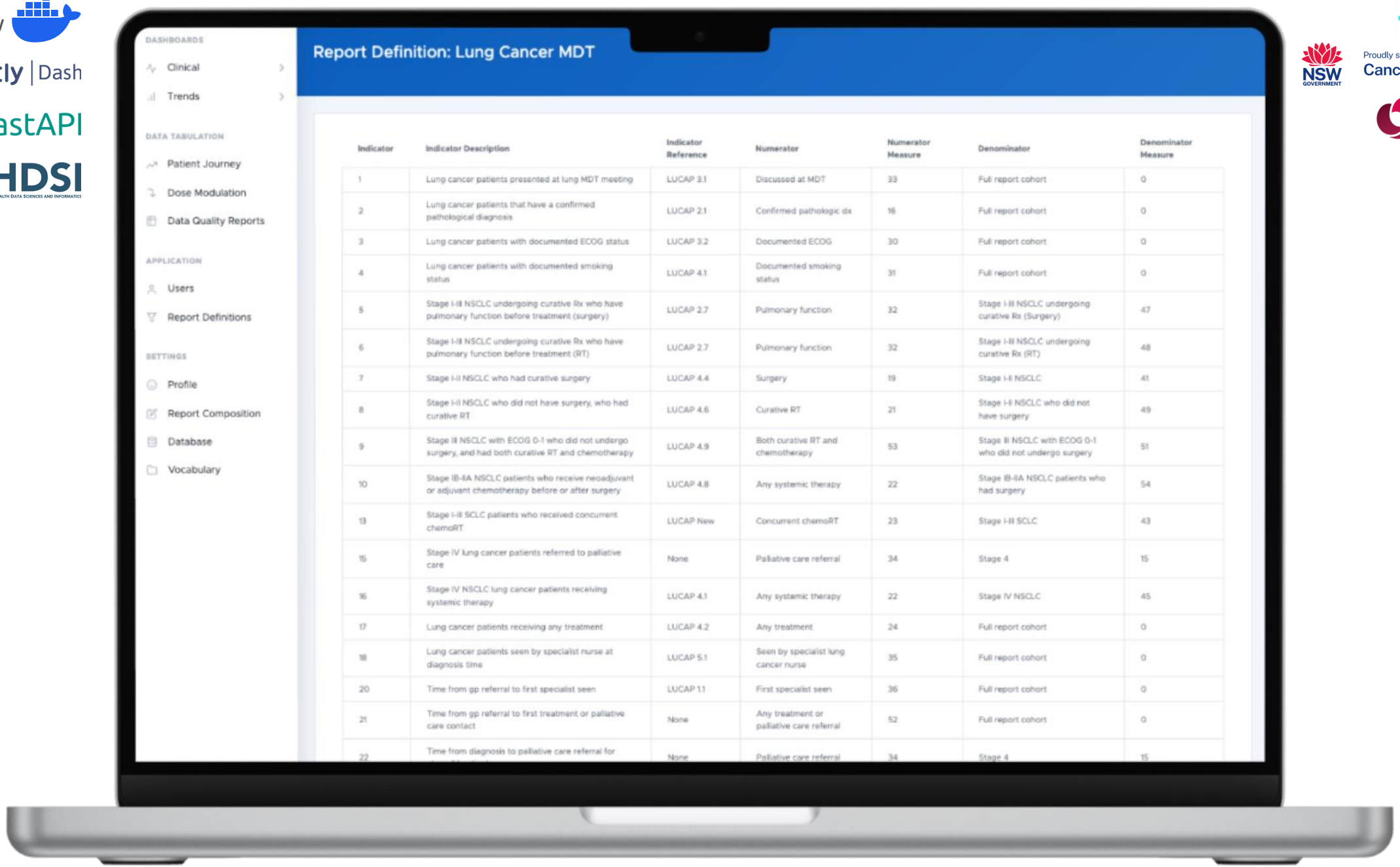
FastAPI

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

QaVa

Proudly supported by
NSW GOVERNMENT
Cancer Institute NSW

HCF



Indicator	Indicator Description	Indicator Reference	Numerator	Numerator Measure	Denominator	Denominator Measure
1	Lung cancer patients presented at lung MDT meeting	LUCAP 3.1	Discussed at MDT	33	Full report cohort	0
2	Lung cancer patients that have a confirmed pathological diagnosis	LUCAP 2.1	Confirmed pathologic dx	16	Full report cohort	0
3	Lung cancer patients with documented ECOG status	LUCAP 3.2	Documented ECOG	30	Full report cohort	0
4	Lung cancer patients with documented smoking status	LUCAP 4.1	Documented smoking status	31	Full report cohort	0
5	Stage I-II NSCLC undergoing curative Rx who have pulmonary function before treatment (surgery)	LUCAP 2.7	Pulmonary function	32	Stage I-II NSCLC undergoing curative Rx (Surgery)	47
6	Stage I-II NSCLC undergoing curative Rx who have pulmonary function before treatment (RT)	LUCAP 2.7	Pulmonary function	32	Stage I-II NSCLC undergoing curative Rx (RT)	48
7	Stage I-II NSCLC who had curative surgery	LUCAP 4.4	Surgery	19	Stage I-II NSCLC	41
8	Stage I-II NSCLC who did not have surgery, who had curative RT	LUCAP 4.6	Curative RT	21	Stage I-II NSCLC who did not have surgery	49
9	Stage II NSCLC with ECOG 0-1 who did not undergo surgery, and had both curative RT and chemotherapy	LUCAP 4.9	Both curative RT and chemotherapy	53	Stage II NSCLC with ECOG 0-1 who did not undergo surgery	51
10	Stage IB-IIA NSCLC patients who receive neoadjuvant or adjuvant chemotherapy before or after surgery	LUCAP 4.8	Any systemic therapy	22	Stage IB-IIA NSCLC patients who had surgery	54
13	Stage I-III SCLC patients who received concurrent chemoRT	LUCAP New	Concurrent chemoRT	23	Stage I-III SCLC	43
15	Stage IV lung cancer patients referred to palliative care	None	Palliative care referral	34	Stage 4	15
16	Stage IV NSCLC lung cancer patients receiving systemic therapy	LUCAP 4.1	Any systemic therapy	22	Stage IV NSCLC	45
17	Lung cancer patients receiving any treatment	LUCAP 4.2	Any treatment	24	Full report cohort	0
18	Lung cancer patients seen by specialist nurse at diagnosis time	LUCAP 5.1	Seen by specialist lung cancer nurse	35	Full report cohort	0
20	Time from gp referral to first specialist seen	LUCAP 1.1	First specialist seen	36	Full report cohort	0
21	Time from gp referral to first treatment or palliative care contact	None	Any treatment or palliative care referral	52	Full report cohort	0
22	Time from diagnosis to palliative care referral for	None	Palliative care referral	34	Stage 4	15

Dates filter underlying report data

Columns in the report correspond to a measure and associated measure date. Each measure may be a True/False boolean type, or have a single associated scalar value.

Indicators

Indicator visualisations correspond to measure definitions (columns) in underlying dash report

From

To

Underlying report data

Dash Report

Person	Cohort Date	Measure 1	Measure Date	Measure 2	Measure Date
1	YYYY-MM-DD	10	YYYY-MM-DD		
2	YYYY-MM-DD			TRUE	YYYY-MM-DD
3	YYYY-MM-DD	11	YYYY-MM-DD	TRUE	YYYY-MM-DD
4	YYYY-MM-DD				
5	YYYY-MM-DD				
6	YYYY-MM-DD			TRUE	YYYY-MM-DD
7	YYYY-MM-DD				
8	YYYY-MM-DD				
9	YYYY-MM-DD				
10	YYYY-MM-DD				
11	YYYY-MM-DD	3	YYYY-MM-DD	TRUE	YYYY-MM-DD
12	YYYY-MM-DD				
13	YYYY-MM-DD			TRUE	YYYY-MM-DD
14	YYYY-MM-DD				

Report cohort: 1 row per person who meets the qualifying cohort measure criteria

Report Cohort

Indicators are typically process / quality specific - bulk operations and drill down for details only when outliers identified

Date that this person qualified for the report cohort, as expressed by the cohort measure - used to include or exclude the person from dashboard summary when applying date range filters.

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OMOP_ALCHEMY

```python
class Treatment_Window(Base):
    """
    This mapper returns the bounds of a treatment window, looking for earliest and latest RT/SACT events

    Note that surgical procedures are not currently mapped into episodes, but current mappings
    are only for manually entered, relevant surgical procedures, so this is robust at the person level.

    """

    __table__ = dx_treatment_window
    person_id = dx_treatment_window.c.person_id
    episode_id = dx_treatment_window.c.episode_id
    episode_start_datetime = so.column_property(dx_treatment_window.c.episode_start_datetime)
    death_datetime = so.column_property(dx_treatment_window.c.death_datetime)
    rt_start = so.column_property(dx_treatment_window.c.rt_start)
    sact_start = so.column_property(dx_treatment_window.c.sact_start)
    rt_end = so.column_property(dx_treatment_window.c.rt_end)
    sact_end = so.column_property(dx_treatment_window.c.sact_end)
    procedure_datetime = so.column_property(dx_treatment_window.c.procedure_datetime)

    @sa.ext.hybrid.hybrid_property
    def latest_treatment(self):
        treat_ends = [d for d in [self.rt_end, self.sact_end, self.procedure_datetime] if d is not None]
        if not(treat_ends):
            return None
        return max(treat_ends)

    @sa.ext.hybrid.hybrid_property
    def treatment_days_before_death(self):
        latest_treatment = self.latest_treatment
        if not(latest_treatment) or not(self.death_datetime):
            return None
        delta = self.death_datetime.date() - latest_treatment
        return delta.days

    @latest_treatment.expression
    def latest_treatment(cls):
        return sa.func.greatest(
            sa.case((cls.rt_end != None, cls.rt_end), else_=None),
            sa.case((cls.sact_end != None, cls.sact_end), else_=None),
            sa.case((cls.procedure_datetime != None, sa.cast(cls.procedure_datetime, sa.Date)), else_=None))

    @treatment_days_before_death.expression
    def treatment_days_before_death(cls):
        return sa.cast(cls.death_datetime, sa.Date) - cls.latest_treatment
```

ITERATIVELY BUILD COMPLEXITY → COMPOSABLE MAPPERS DEFINE TESTABLE CONVENTIONS

OA_COHORTS

```python
class Measure(Base):
    """Measure class can combine child measures using boolean logic to an arbitrary depth in order to build complex definitions.

    A measure that contains a subquery should be the root measure definition and therefore not contain any child measures of its own.

    An example measure may have the sub-queries _Lung Cancer_ **and** _Stage IV_, to select all patients with Stage IV lung cancer,
    or it could be broken down further with sub-query _Lung Cancer_ **and** a child measure representing the combination (_Stage I_
    **or** _Stage 2_).
    """
    __tablename__ = 'measure'
    measure_id: so.Mapped[int] = so.mapped_column(primary_key=True)
    id = so.synonym('measure_id')

    measure_name: so.Mapped[str] = so.mapped_column(sa.String(250))
    measure_combination: so.Mapped[int] = so.mapped_column(sa.Enum(RuleCombination)) # rule_and, rule_or, rule_except
    subquery_id: so.Mapped[Optional[int]] = so.mapped_column(sa.ForeignKey('subquery.subquery_id'), nullable=True)
    person_ep_override: so.Mapped[bool] = so.mapped_column(sa.Boolean)

    subquery: so.Mapped["Subquery"] = so.relationship("Subquery", foreign_keys=[subquery_id], back_populates='measures')
    in_dash_cohort: so.Mapped[List['Dash_Cohort_Def']] = so.relationship("Dash_Cohort_Def", back_populates="dash_cohort_measure")

    child_measures: so.Mapped[List["Measure_Relationship"]] = so.relationship("Measure_Relationship",
                                                                              foreign_keys="Measure_Relationship.parent_measure_id",
                                                                              viewonly=True)
    parent_measures: so.Mapped[List["Measure_Relationship"]] = so.relationship("Measure_Relationship",
                                                                               foreign_keys="Measure_Relationship.child_measure_id",
                                                                               viewonly=True)
    def get_measure(self, ep_override=False):
        ep_override = self.person_ep_override or ep_override
        if self.subquery:
            return self.subquery.get_subquery_any(ep_override)
        elif self.measure_combination==RuleCombination.rule_or:
            return sa.union_all(*[m.get_measure(ep_override) for m in self.children])
        else:
            return self.get_measure_first_qualifying(ep_override)

    def get_measure_any(self, ep_override=False):
        ep_override = self.person_ep_override or ep_override
        if self.subquery:
            return self.subquery.get_subquery_any(ep_override)
        else:
            return sa.union(*[m.get_measure_any(ep_override) for m in self.children])

    def get_measure_earliest(self, ep_override=False):
        ...
        return earliest

    def get_measure_first_qualifying(self, ep_override=False):
        ...
        return combined

    def execute_measure(self, db, people=[], force_refresh=False):
        if not force_refresh and len(self._members) > 0:
            return self._members
        query = self.get_measure()
        if len(people) > 0:
            query = sa.select(query.subquery()).filter(sa.column('person_id').in_(people))
        self._members = db.execute(query).all()
        return self._members
```

OHDSI 2025 Collaborator Showcase
Lightning Talks Round 2

End: Georgina Kennedy

Next up: Cindy Chen

Heterogeneity of Treatment Effects Across Nine Glucose-Lowering Drug Classes in Type 2 Diabetes

Extension of the LEGEND-T2DM Network Study

Hsin Yi Chen, Thomas Falconer, Anna Ostropolets, Tara V. Anand, Xinzhuo Jiang, David Dávila-García, Linying Zhang, Ruochong Fan, Hannah Morgan-Cooper, George Hripcsak

Motivation

- Type 2 diabetes (T2DM) affects more than 525 million people globally
- OHDSI's LEGEND-T2DM study (Khera et. al 2024) investigated the relative treatment effects of different antihyperglycemic agents
- However, T2DM patients are a heterogeneous group:
  - Different demographics and baseline risks can modify the benefits and risks associated with different drugs

Do risks of health outcomes differ based on patient characteristics?

Extend LEGEND T2DM → Stratify treatment effect estimation by clinical and demographic subgroups.

Methods: Study Design

- Target Cohorts: Adults (≥18 years of age) diagnosed with T2DM who initiated treatment with a drug agent from one of the nine specified glucose-lowering drug classes: (1) Alpha-Glucosidase Inhibitors, (2) Biguanides, (3) DPP-4 inhibitors, (4) GIP and GLP-1 RA, (5) GLP-1RA, (6) Meglitinides, (7) SGLT-2 inhibitors, (8) Sulfonylureas, and (9) Thiazolidinediones.

Methods: Study Design

- Target Cohorts: Adults (≥18 years of age) diagnosed with T2DM who initiated treatment with a drug agent from one of the nine specified glucose-lowering drug classes: (1) Alpha-Glucosidase Inhibitors, (2) **Biguanides**, (3) **DPP-4 inhibitors**, (4) GIP and GLP-1 RA, (5) **GLP-1RA**, (6) Meglitinides, (7) **SGLT-2** inhibitors, (8) **Sulfonylureas**, and (9) Thiazolidinediones.
- Outcomes of interest: Acute myocardial infarction, acute renal failure, hospitalization for heart failure, stroke, abnormal weight gain, acute pancreatitis, diabetic ketoacidosis, diarrhea, hypoglycemia, vomiting, and hepatic failure.
- Subgroups of interest: Age, sex, renal impairment, obesity, poorly controlled diabetes, HTN, HLD, diabetic ketoacidosis, diabetic retinopathy, MASLD

How we quantified "heterogeneity of treatment effect"

- Calculated pair-wise hazard ratios for each target-comparator-outcome-subgroup combination

- Example of a HR interpretation:
  - Target = Sulfonylureas
  - Comparator = GLP-1 RA
  - A HR of 1.5 would mean that the **risk of the outcome is 1.5 times higher for SU vs. GLP-1 RA**

$$HR = \frac{h_{target}(t)}{h_{comparator}(t)}$$

How we quantified "heterogeneity of treatment effect"

- To quantify "heterogeneity of treatment effect", we calculated the difference in log transformed HRs between two subgroups
- Then, we performed meta-analysis on $\Delta ln(HR)$ for available databases

$$HR = \frac{h_{target}(t)}{h_{comparator}(t)}$$

$$\Delta ln(HR) = ln\left(HR_{subgroup1}\right) - ln\left(HR_{subgroup2}\right)$$

How we quantified "heterogeneity of treatment effect"

Hyperlipidemia (HLD) Subgroups (HLD vs. No HLD)					
Outcome	Target	Comparator	HR (HLD)	HR (No HLD)	p-value
Stroke	Biguanide	SGLT-2i	1.76 (0.91,3.43)	0.73 (0.44,1.23)	0.04

Subgroups: HR for the group with hyperlipidemia, different?

p-value of $\Delta ln(HR)$: i.e. are the subgroups *different with* (is there HTE?)

Interpretation: There is a **differential effect** in the HLD vs. Non-HLD groups when comparing Biguanide and SGLT-2i for stroke

Results

- 6 Different databases, 5 of which passed diagnostics
- Hyperlipemia, Hypertension, Obesity, Sex, and Age (>60y vs. 21-60y) passed diagnostics
  - Many other subgroups (ex: renal impairment, diabetic ketoacidosis, etc.) did not pass diagnostics
  - All subgroups but age had some evidence of outcomes with HTE

Some Interesting Subgroup Comparisons!

- In general: aligns with known pharmacologic patterns
- Obesity Subgroup
  - Obese patients have a *greater benefit* on biguanide (vs. DPP-4i) against hospitalization with heart failure events
- Sex Subgroup
  - Female patients have a higher risk of diarrhea on GLP-1 RA (vs. DPP-4i), and SU (vs. DPP-4i).
  - Female patients have a lower risk of stroke on SGLT-2i (vs. DPP-4i)

Key Takeaways & Next Steps

- Hypothesis generating study—lots of null results, some databases/comparisons did not pass diagnostics
  - However: there is potential evidence of treatment heterogeneity!
- Potential for personalized T2DM treatments in the future
- The power of OHDSI and large-scale studies!

More @ Poster #609!

Contact: hc3292@cumc.columbia.edu

Thank you to the Hripcsak Lab, Columbia Department of Biomedical Informatics, and the OHDSI community for making this project possible!

OHDSI 2025 Collaborator Showcase
Lightning Talks Round 2

End: Cindy Chen

Next up: Katia Verhamme

DARWIN EU

Coordination Centre

A multi-national network cohort and self-controlled case series study of the effect of doxycycline on the risk of suicidality, depression and anxiety in individuals with acne

Nicholas B. Hunt, Guido J. van Leeuwen, Maarten van Kessel, Anna Palomar-Cros, Antonella Delmestri, Agustina Giuliodori, Talita Duarte Salles, Mandickel Kamtengeni, Ross D. Williams, Daniel Prieto Alhambra, **Katia Verhamme (presenter)**

OHDSI Global 2025

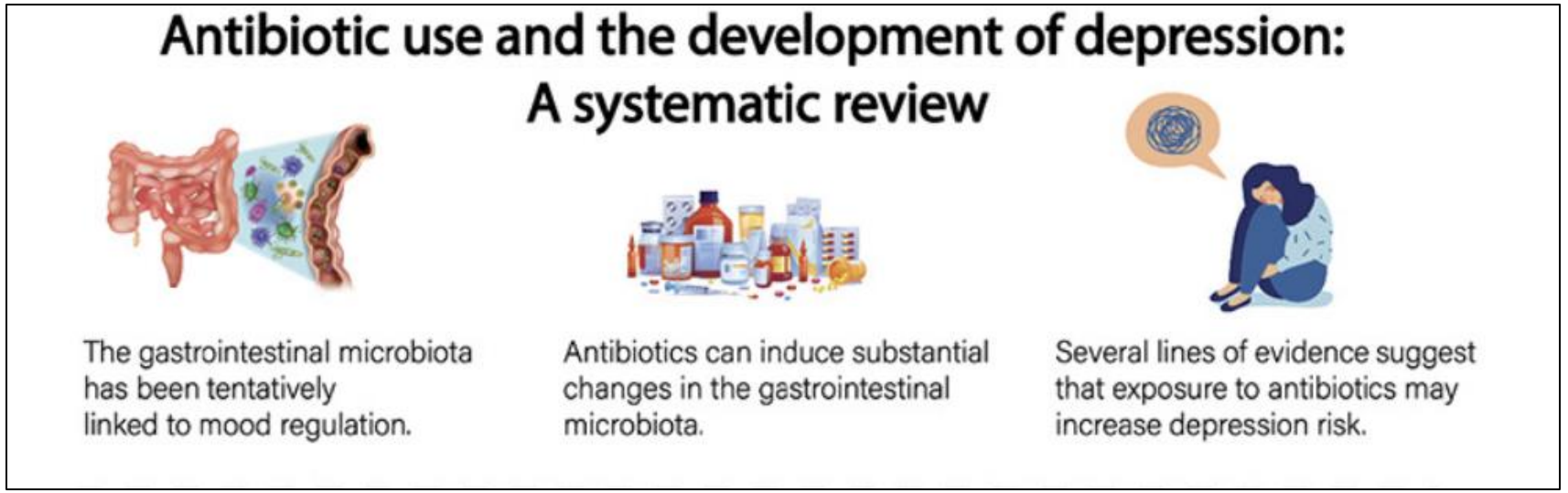
Disclosure

This study was funded by EMA and performed via DARWIN EU®. The study funder was involved in revising the study protocol and the objectives and reviewing the study report including the results. Data partners' role is only to execute code at their data source. They do not have an investigator role.

This communication represents the views of the DARWIN EU® Coordination Centre only and cannot be interpreted as reflecting those of the EMA or the European Medicines Regulatory Network

Background

- Doxycycline is a tetracycline antibiotic which is widely used for treating acne, upper respiratory tract infections, sexually transmittable diseases and rosacea
- There are case reports about a potential association between doxycycline and suicide



- EMA commissioned a study to be conducted within the DARWIN EU® network

Objective: to estimate the risk of suicide-related events, anxiety and depression during doxycycline use for the treatment of acne

Methods

Study design: **new-user active comparator cohort** and **self-controlled case series study** (SCCS) to assess the association between doxycycline and the composite outcome of suicide-related events, depression, and anxiety in <u>individuals with acne</u>

Primary care EHR data sources: IPCI (Netherlands), CPRD GOLD (UK) and SIDIAP (Spain)

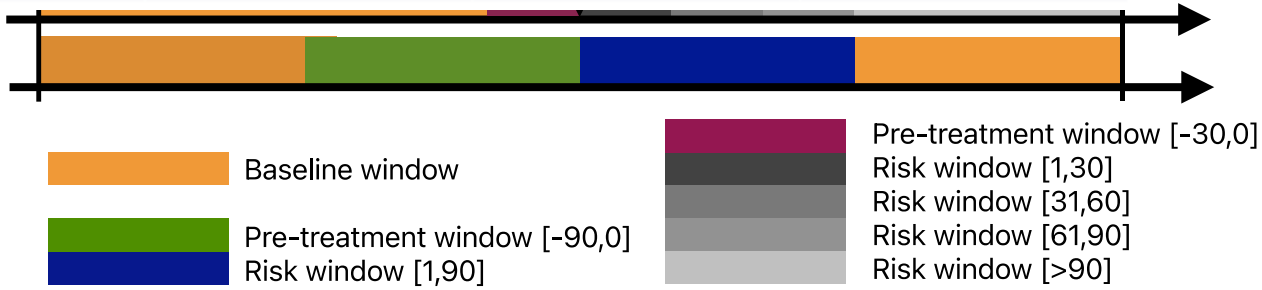
CohortMethod and *SelfControlledCaseSeries*

	CPRD GOLD (UK)		IPCI (Netherlands)		SIDIAP (Spain)	
Cohort	Doxycycline	Erythromycin	Doxycycline	Erythromycin	Doxycycline	Erythromycin
Subjects (n)	18,054	30,682	778	793	12,265	16,998
Cohort	Doxycycline	Isotretinoin	Doxycycline	Isotretinoin	Doxycycline	Isotretinoin
Subjects (n)	655	1,064	2,757	3,534	6,090	9,350

Pro

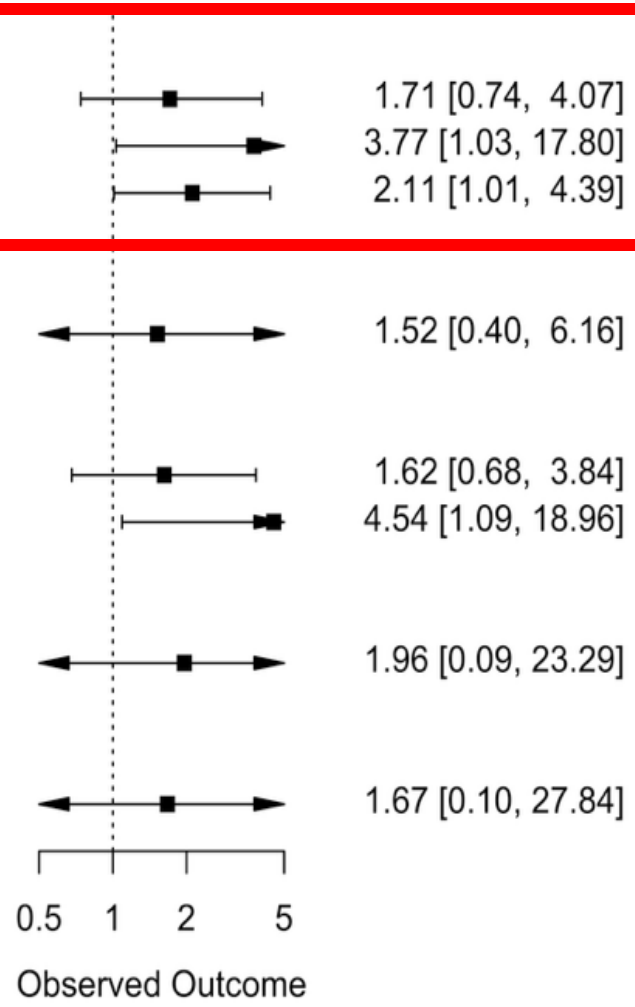
1. Doxycycline vs erythromycin
2. Doxycycline vs isotretinoin

Sub-analyses: individuals with a history of depression and calibration by negative control outcomes



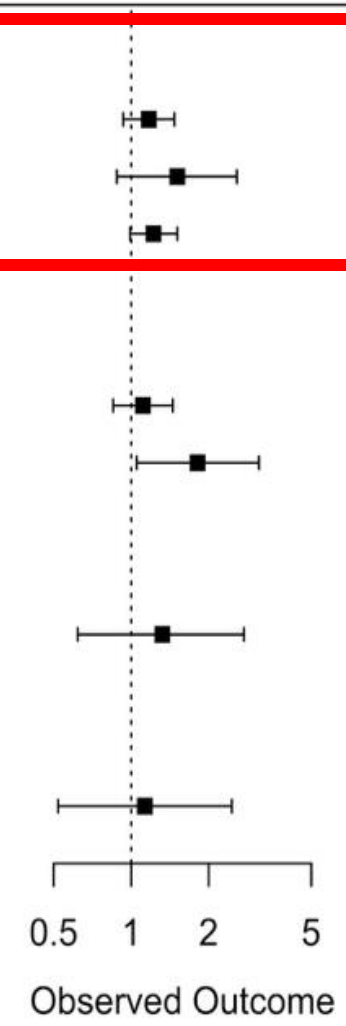
Cohort study results - suicide-related events as outcome

Analysis	Doxycycline outcomes	Doxycycline person-years	Comparator outcomes	Comparator person-years	Hazard ratio [95% CI]
Doxycycline versus erythromycin					
CPRD GOLD	12	3909	10	5437	1.71 [0.74, 4.07]
SIDIAP	7	2963	≤5	5328	3.77 [1.03, 17.80]
Meta-analysis					2.11 [1.01, 4.39]
Subjects with a history of depression					
CPRD GOLD	5	501	≤5	589	1.52 [0.40, 6.16]
Caibrated analysis					
CPRD GOLD	12	3909	10	5437	1.62 [0.68, 3.84]
SIDIAP	7	2963	≤5	5328	4.54 [1.09, 18.96]
Doxycycline versus isotretinoin					
IPCI	≤5	511	≤5	1403	1.96 [0.09, 23.29]
Caibrated analysis					
IPCI	≤5	511	≤5	1403	1.67 [0.10, 27.84]



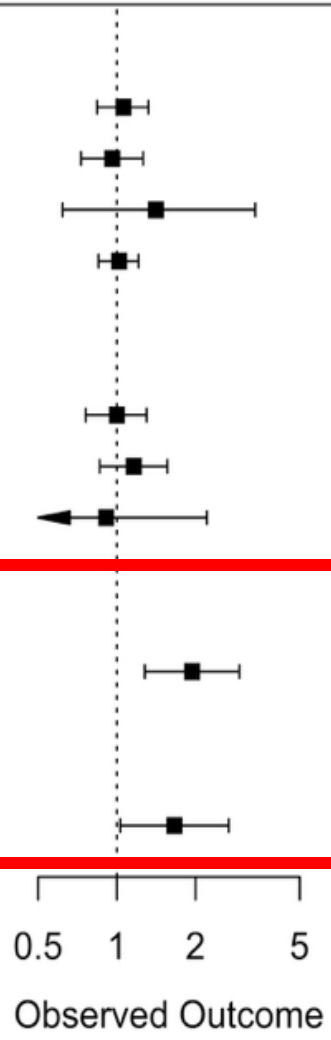
Cohort study results – depression as outcome

Analysis	Doxycycline outcomes	Doxycycline person-years	Comparator outcomes	Comparator person-years	Hazard ratio [95% CI]
Doxycycline versus erythromycin					
CPRD GOLD	131	3442	168	4846	1.17 [0.93, 1.47]
SIDIAP	27	2886	31	5185	1.51 [0.88, 2.57]
Meta-analysis					1.22 [0.99, 1.51]
Calibrated analysis					
CPRD GOLD	131	3442	168	4846	1.11 [0.85, 1.45]
SIDIAP	27	2886	31	5185	1.81 [1.05, 3.13]
Doxycycline versus isotretinoin					
IPCI	13	473	19	1314	1.32 [0.62, 2.74]
Calibrated analysis					
IPCI	13	473	19	1314	1.13 [0.52, 2.46]



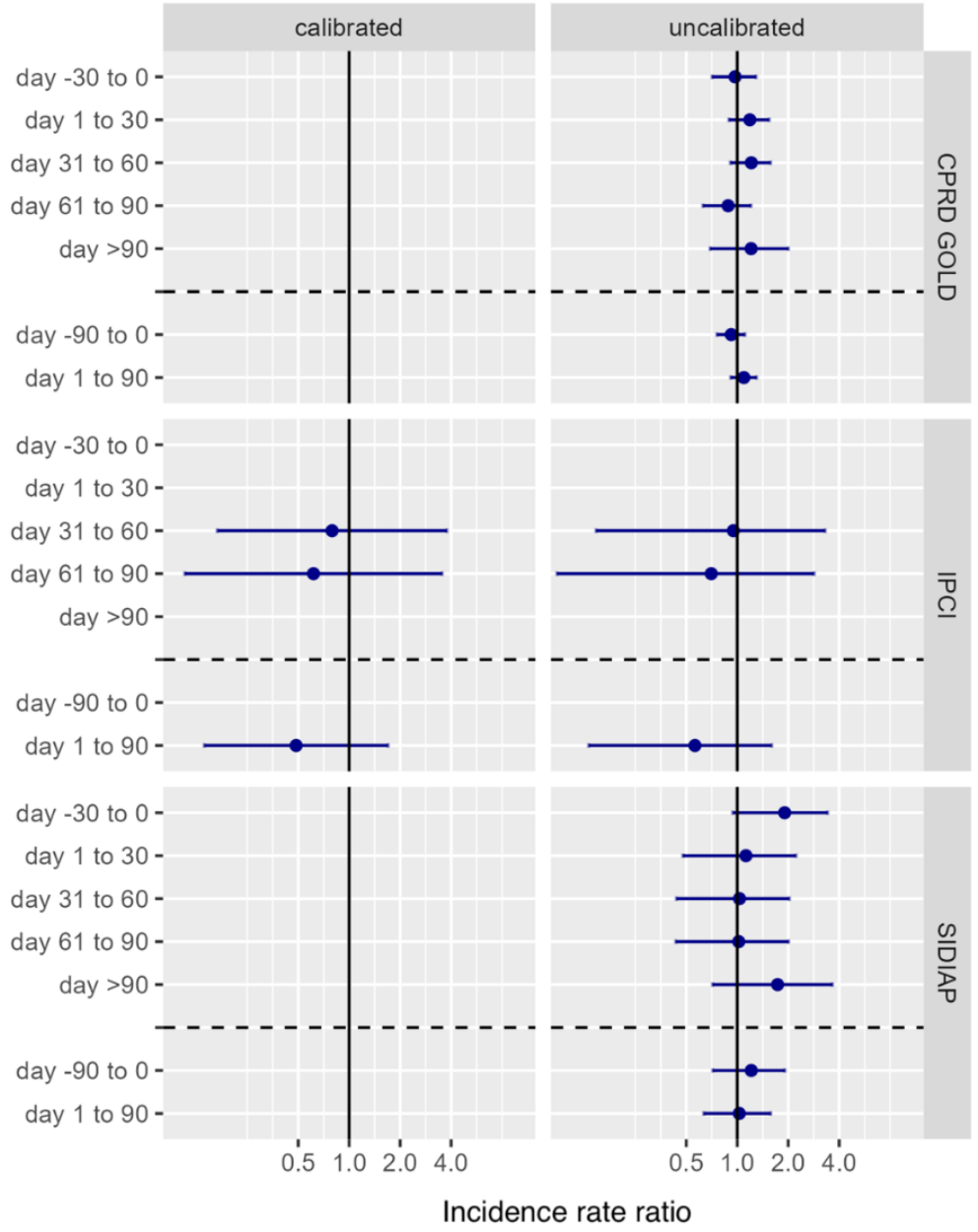
Cohort study results – anxiety as outcome

Analysis	Doxycycline outcomes	Doxycycline person-years	Comparator outcomes	Comparator person-years	Hazard ratio [95% CI]
Doxycycline versus erythromycin					
CPRD GOLD	129	3512	185	4935	1.06 [0.84, 1.32]
SIDIAP	82	2550	146	4664	0.96 [0.73, 1.26]
IPCI	14	106	9	100	1.41 [0.62, 3.38]
Meta-analysis					1.02 [0.85, 1.21]
Calibrated analysis					
CPRD GOLD	129	3512	185	4935	1.00 [0.76, 1.30]
SIDIAP	82	2550	146	4664	1.16 [0.86, 1.56]
IPCI	14	106	9	100	0.91 [0.38, 2.21]
Doxycycline versus isotretinoin					
IPCI	47	413	59	1128	1.94 [1.28, 2.94]
Calibrated analysis					
IPCI	47	413	59	1128	1.66 [1.03, 2.68]



Self-controlled case series

- Non-fatal suicide-related events: **there were no associations identified**
- Depression [1,90 days] window: CPRD GOLD (**IRR 0·90, 95%CI [0·84-0·97]**)
- Anxiety 1,90 days] window: CPRD GOLD (**IRR 0·94, 95%CI [0·88-1·00]**) and IPCI (**IRR 0·91, 95%CI [0·80-1·02]**)



Discussion

Cohort study results

- Two-fold increased risk of suicide-related events with doxycycline use compared to erythromycin use across CPRD GOLD and SIDIAP.
- Increased association of depression with doxycycline use compared to erythromycin. (CPRD GOLD and SIDIAP)
- Small but increased association of anxiety with doxycycline use compared to erythromycin or isotretinoin use. (IPCI only)

SCCS results

- No associations identified for suicide-related events.
- (Small) protective effect on anxiety and depression outcomes in some of the time-frames.

Limitations: (1) underreporting of outcome, (2) inconsistent time trends leading to censored analyses, (3) SCCS did not take prescription duration into account, (4) confounding by (acne)-severity

Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 25-28 November 2024

Share

29 November 2024

Doxycycline: currently available evidence not supporting link with risk of suicidality

News Human Medicines Pharmacovigilance Referrals

Doxycycline: currently available evidence not supporting link with risk of suicidality

EMA's safety committee (PRAC) has concluded that the currently available evidence is not sufficient to establish a causal relationship between the use of the antibiotic doxycycline and the risk of suicidality.

Doxycycline is a broad-spectrum antibiotic, widely used to treat a wide range of infections caused by bacteria such as acne, urinary and lower respiratory tract infections, dental infections, and skin infections. It is also used to prevent the development of certain infections, such as malaria.

A safety signal on the risk of suicidality, suicidal thoughts or actions with doxycycline was raised based on cases reported to the Finnish national competent authority, as well as further cases reported to EudraVigilance, the centralised European database of suspected side effects reports, and the medical literature.

The PRAC started its review in November 2023 and requested the marketing authorisation holders for doxycycline to perform a cumulative review of the data from all relevant sources.

The PRAC also requested a study based on real-world evidence, which includes data from electronic health records and disease registries, through DARWIN EU to facilitate the assessment of the signal. After reviewing all available evidence from spontaneous reports, the literature, the discussion on possible mechanisms and the study performed via DARWIN EU, the PRAC considered that the evidence is not sufficient to establish a causal relationship and that no update to the product information of doxycycline is warranted.

Suicide-related events in relation to doxycycline will be closely monitored and any new evidence will be discussed in the Periodic Safety Update Reports (PSURs).

DARWIN EU® Coordination Centre

Executive Director
Prof. Peter Rijnbeek

Contractor

Thank you on behalf of the whole Darwin EU®

Coordination Centre