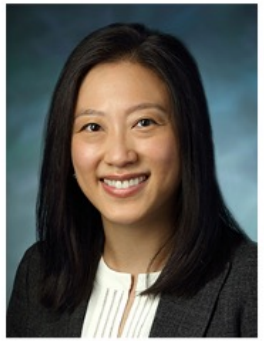
Nov. 19: Evidence Network in Action

The Semaglutide Study



Cindy Cai

Assistant Professor of Ophthalmology
Wilmer Eye Institute at Johns Hopkins Hospital

Topic: Semaglutide and NAION: An OHDSI Network Study

Paul Nagy

Program Director for Graduate Training
in Biomedical Informatics and Data Science
Johns Hopkins University

Topic: Evidence Network

Linying Zhang

Assistant Professor of Biostatistics
Washington University

Topic: Methods

Anthony Sena

Director, Observational Health Data Analytics
Johnson & Johnson

Topic: Strategus

Ben Martin

Postdoctoral Fellow
Johns Hopkins University

Topic: Using the Results Schema

Erik Westlund

Assistant Scientist
Johns Hopkins University

Topic: Using the Results Schema

Wilmer Eye Institute
Johns Hopkins Medicine

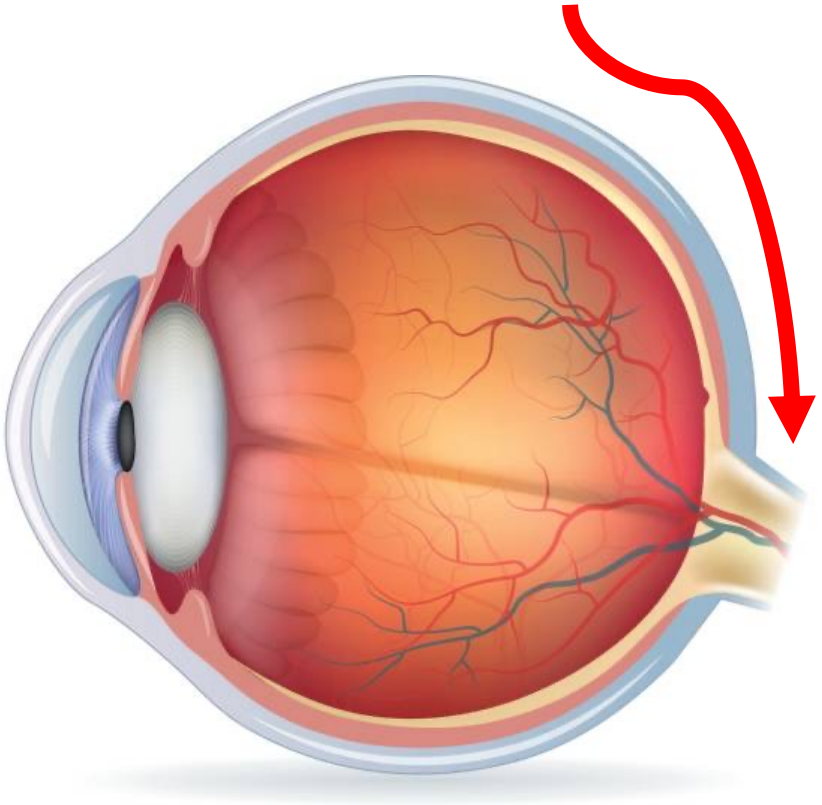
Semaglutide and Nonarteritic Anterior Ischemic Optic Neuropathy: An OHDSI Network Study

Cindy X. Cai, MD
The Jonathan and Marcia Javitt Rising Professor
Assistant Professor of Ophthalmology, Retina Division, The Wilmer Eye Institute
Assistant Professor of Medicine, Biomedical Informatics and Data Science, Division of General Internal Medicine, Department of Medicine
Johns Hopkins University School of Medicine

Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)

- Leading cause of acute optic neuropathy in the elderly
- Significant cause of blindness: 1/4 eyes 20/200 or worse vision
- No definitive treatments

NAION = stroke of the optic nerve



JAMA Ophthalmology | Original Investigation

Risk of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients Prescribed Semaglutide

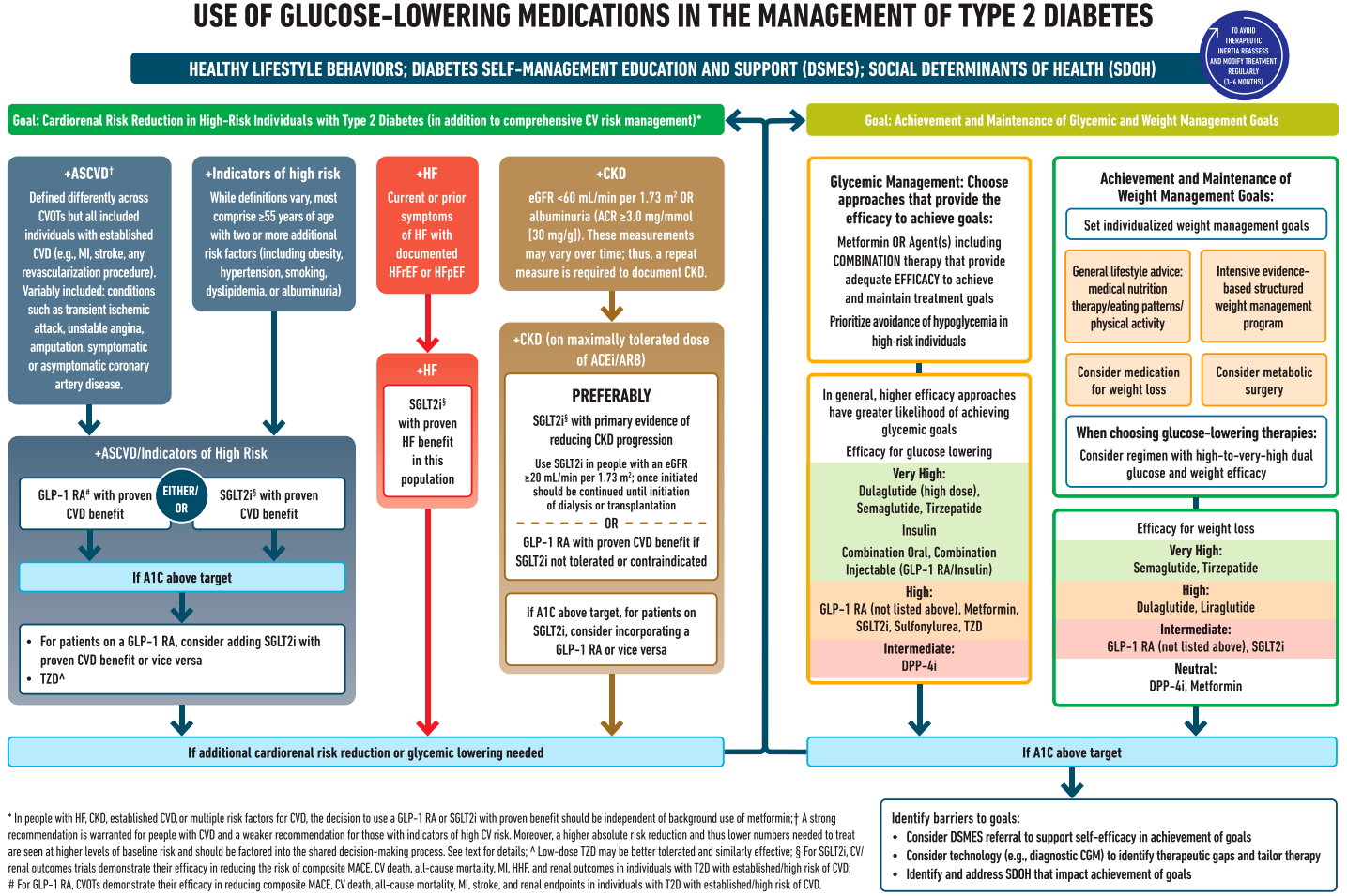
Jimena Tatiana Hathaway, MD, MPH; Madhura P. Shah, BS; David B. Hathaway, MD;
Seyedeh Maryam Zekavat, MD, PhD; Drenushe Krasniqi, BA; John W. Gittinger Jr, MD; Dean Cestari, MD;
Robert Mallery, MD; Bardia Abbasi, MD; Marc Bouffard, MD; Bart K. Chwalisz, MD;
Tais Estrela, MD; Joseph F. Rizzo III, MD

- Cumulative incidence of NAION for the semaglutide and non–GLP-1 RA cohorts over 36 months was **8.9%** (95% CI, 4.5%-13.1%) and 1.8% (95% CI, 0%-3.5%), respectively
- Hazard Ratio of NAION **4.28** (95% CI: 1.62 – 11.29, P < .001) (compared with non-GLP-1 RA)

Limitations: single academic institution, major referral center for NAION

Semaglutide

- Glucagon-like peptide 1 receptor agonist (GLP-1 RA)
- Benefits in reducing cardiovascular and kidney complications
- Recommended by the ADA as a preferred treatment for T2DM patients with: atherosclerotic cardiovascular disease, chronic kidney disease, or obesity



Purpose of OHDSI Network

- Characterize NAION incidence
- Association of NAION with semaglutide use
  - Compare the risk of NAION associated with semaglutide use against other GLP-1RAs and non-GLP-1RA drugs
  - Investigate NAION incidence rate during semaglutide exposure compared with non-exposure

Build upon a prior OHDSI Network Study: LEGEND-T2DM

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 84, NO. 10, 2024

Comparative Effectiveness of Second-Line Antihyperglycemic Agents for Cardiovascular Outcomes

A Multinational, Federated Analysis of LEGEND-T2DM

Rohan Khera, MD, MS,[a,b,c] Arya Aminorroaya, MD, MPH,[a] Lovedeep Singh Dhingra, MBBS,[a] Phyllis M. Thangaraj, MD, PhD,[a] Aline Pedroso Camargos, PhD,[a] Fan Bu, PhD,[d] Xiyu Ding, MS,[e] Akihiko Nishimura, PhD,[e] Tara V. Anand, BS,[f] Faaizah Arshad, BS,[g] Clair Blacketer, MPH,[h] Yi Chai, PhD,[i] Shounak Chattopadhyay, PhD,[g] Michael Cook, BSc,[e] David A. Dorr, MD, MS,[j] Talita Duarte-Salles, PhD,[k,l] Scott L. DuVall, PhD,[m,n] Thomas Falconer, MS,[f] Tina E. French, RN, CPHQ,[o,p] Elizabeth E. Hanchrow, RN, MSN,[o,p] Guneet Kaur, MS,[q] Wallis C.Y. Lau, BSc, PhD,[r,s,t,u] Jing Li, MS,[v] Kelly Li, BS,[g] Yuntian Liu, MPH,[a,b] Yuan Lu, ScD,[a] Kenneth K.C. Man, BSc, MPH, PhD,[r,s,t,u] Michael E. Matheny, MD, MS, MPH,[o,p] Nestoras Mathioudakis, MD, MHS,[w] Jody-Ann McLeggon, MPH,[f] Michael F. McLemore, RN,[o,p] Evan Minty, MD, MSc,[x] Daniel R. Morales, MD,[q] Paul Nagy, PhD,[w] Anna Ostropolets, MD, PhD,[h] Andrea Pistillo, MSc,[k] Thanh-Phuc Phan, MBA,[y] Nicole Pratt, PhD,[z] Carlen Reyes, MD, PhD,[k] Lauren Richter, MD,[f] Joseph S. Ross, MD, MHS,[b,aa] Elise Ruan, MD,[f] Sarah L. Seager, BS,[bb] Katherine R. Simon, AA,[o,p] Benjamin Viernes, PhD,[m,n] Jianxiao Yang, MS,[cc] Can Yin, MS,[dd] Seng Chan You, MD, PhD,[ee,ff] Jin J. Zhou, PhD,[g,gg] Patrick B. Ryan, PhD,[f] Martijn J. Schuemie, PhD,[hh] Harlan M. Krumholz, MD, SM,[a,b,ii] George Hripcsak, MD, MS,[f] Marc A. Suchard, MD, PhD[g,m,jj,kk]

Indication Cohort:

-T2DM, exclude T1DM

Drug exposures:

Semaglutide (GLP-1 RA)	Dulaglutide (GLP-1 RA)	Exenatide (GLP-1 RA)	Empagliflozin (SGLT2 inhibitor)	Sitagliptin (DPP4 inhibitor)	Glipizide (sulfonylurea)
GLP-1 RA			Non-GLP-1 RA		

Defining NAION

Mobilized the Eye Care and Vision Research Workgroup

- Lack of structured diagnosis codes for NAION
  - 40% of cases coded as ION are not NAION

Outcome Cohorts (NAION):

"Sensitive" NAION -require 1 ION condition	"Specific" NAION -require 2 ION condition

ION diagnosis codes, diagnosis date adjustments (visual field defect, optic disc disorder, optic neuritis, optic disc edema), exclude patients with GCA (x2), exclude patients with traumatic optic neuropathy

Analysis Methods

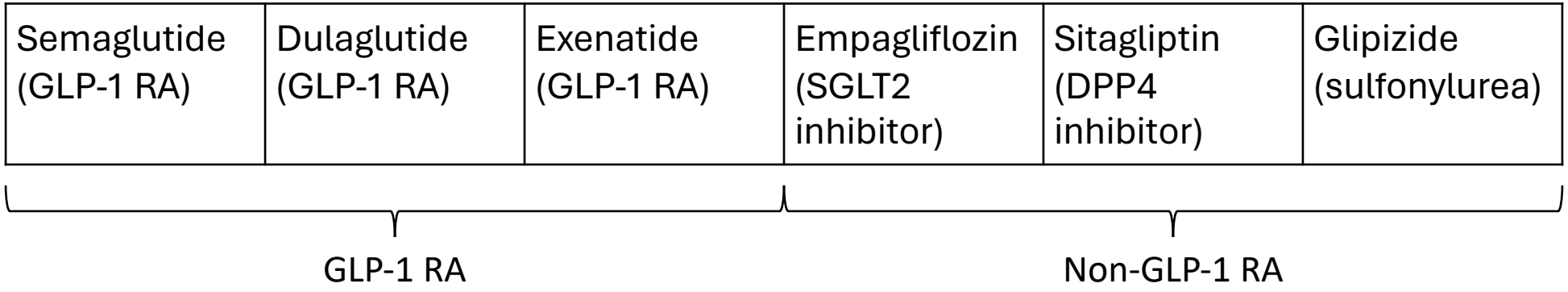
Study start and study end: Dec 2017 to Dec 2023

New-user active-comparator cohort design

-**New-users** of the second-line medications: prior metformin monotherapy, no other prior comparator diabetes medications, 365 days prior observation period, and at most 30 days of insulin exposure
-Compare HR of NAION between drug exposures
-Large-scale **propensity score** models, groups were 1:1 propensity matched
-**Cox proportional hazards model**

Self-controlled case-series

-Cases of T2DM and NAION (diagnosed after first 365 days of observation period): **patient serves as their own control**
-Compare **IRR** of NAION between drug exposure versus control time during observation period
-Exposure time: continuous drug exposure
-Control time: observation time when patient had T2DM and excluded first 365 days of observation period
-**Poisson regression model**
-Pre-exposure window: 30 days before exposure



Only databases and comparisons that pass a rigorous set of study diagnostics contribute to HR and IRR estimates

OHDSI Evidence Network

Administrative Claims (6)

Merative MarketScan® Medicare Supplemental and Coordination of Benefits Database (MDCR)
Merative MarketScan® Commercial Claims and Encounters Database (CCAE)
Merative MarketScan® Multi-State Medicaid Database (MDCD)
IQVIA Open Claims (IQVIA)
Optum® Clinformatics® Data Mart - Extended Data Mart – Socioeconomic Status (Optum Extended SES)
PharMetrics® Plus

EHR (8)

Optum® de-identified Electronic Health Record data set (Optum® EHR)
Johns Hopkins Medical Enterprise (JHME)
Department of Veterans Affairs (VA)
Columbia University Medical Center (CUMC)
Keck Medical Center of University of Southern California (USC)
Oregon Health & Science University (OHSU)
Stanford University (STARR)
Washington University (WashU)

<u>Study Timeline</u>

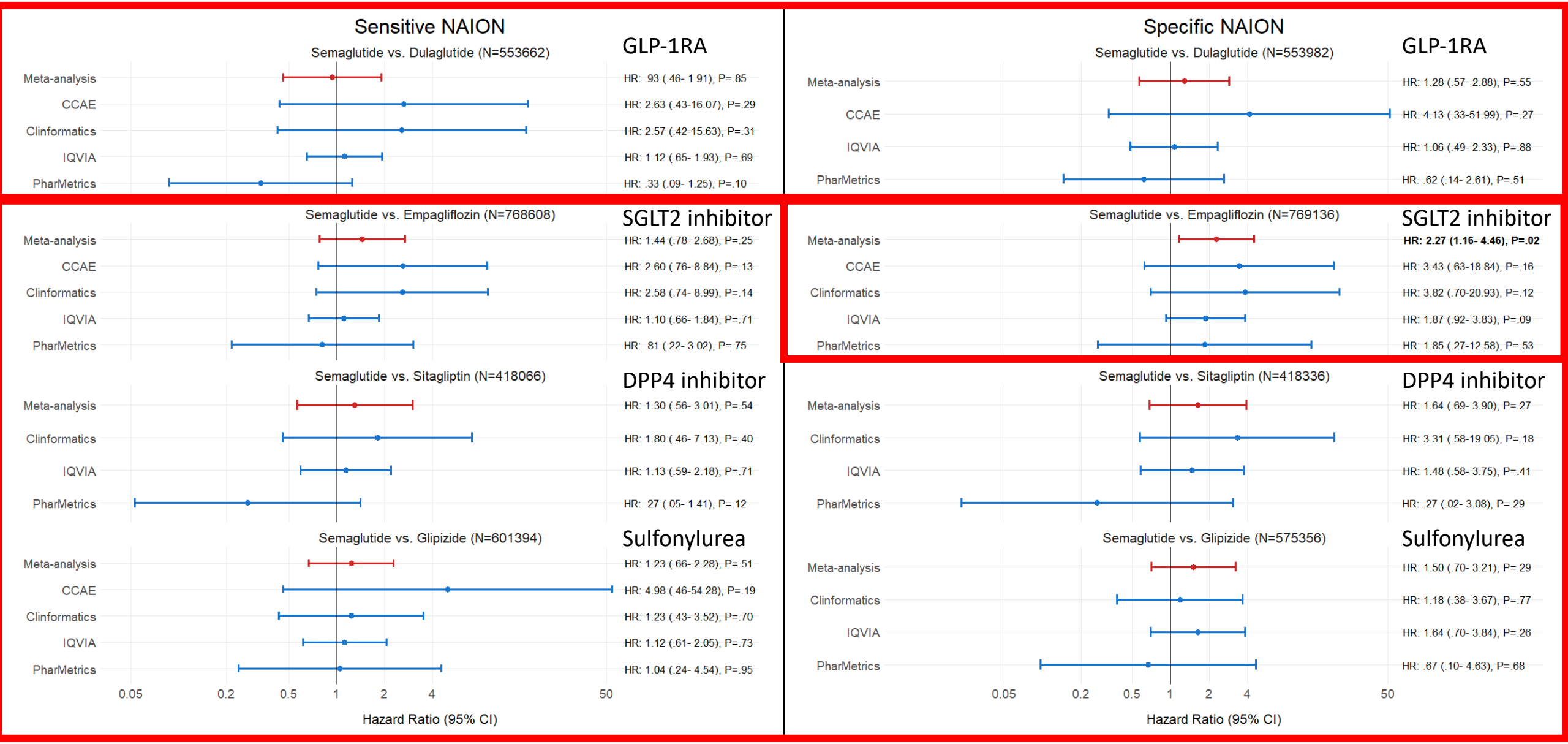
- July 9th, 2024 (Tuesday): OHDSI Community Call
- July 11th, 2024 (Thursday): Eye Care and Vision Research WG
- July 12th, 2024 (Friday): Meeting about Phenotypes
- July 17th, 2024 (Wednesday): Developed Phenotype and Finalized the Protocol
- August 9th, 2024 (Friday): Data Partner to Contribute Data (~4.5 weeks)

Incidence Proportion and Rate of NAION

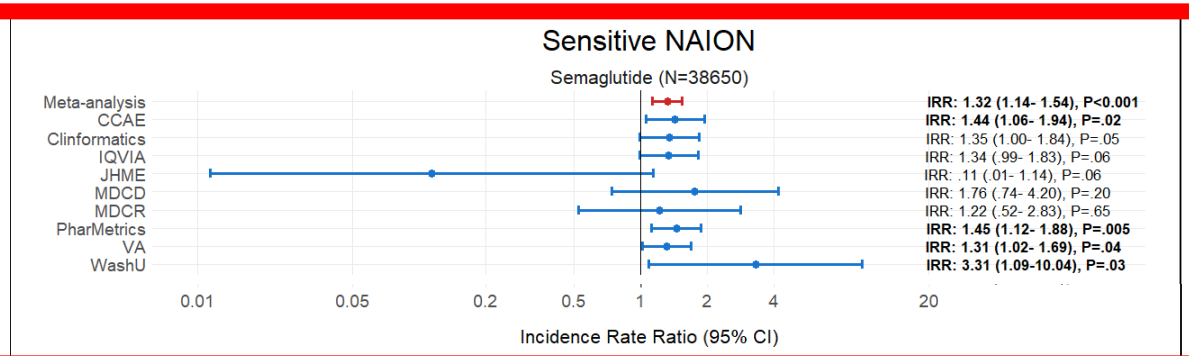
	T2DM	Semaglutide (GLP-1 RA)	Dulaglutide (GLP-1 RA)	Exenatide (GLP-1 RA)	Empagliflozin (SGLT2 inhibitor)	Sitagliptin (DPP4 inhibitor)	Glipizide (sulfonylurea)
Sample Size	37.1M	810390	326282	25936	715802	493563	832295
Incidence Proportion (per 100K persons)	78.3 /32	7.1 / 4.2	7.9 / 3.2	0 / 0	10.4 / 4	12.3 / 4.8	18 / 8.7
Incidence Rate (per 100K person-years)	41 / 16.8	14.5 / 8.7	13.4 / 4.2	0 / 0	13.7 / 5.2	15.1 / 5.9	21.2 / 10.4

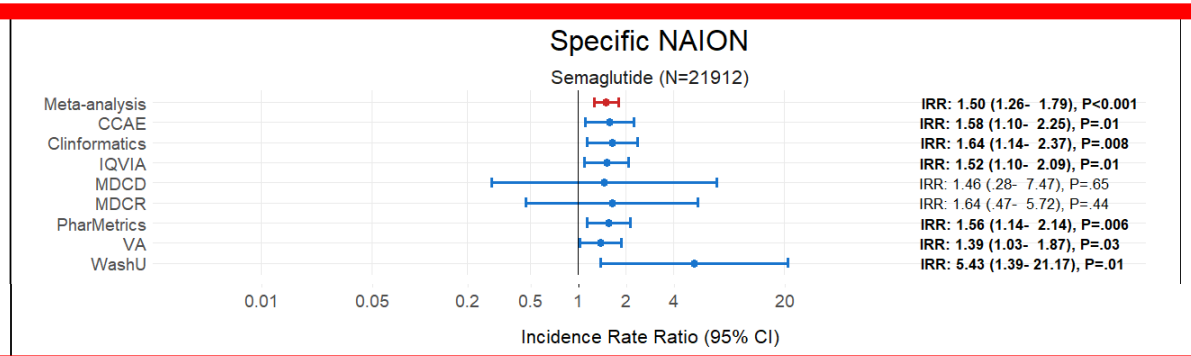
Historically, 2.3 to 11.4 (as high as 82) per 100,000 persons

New-user active-comparator cohort design



Self-controlled case-series

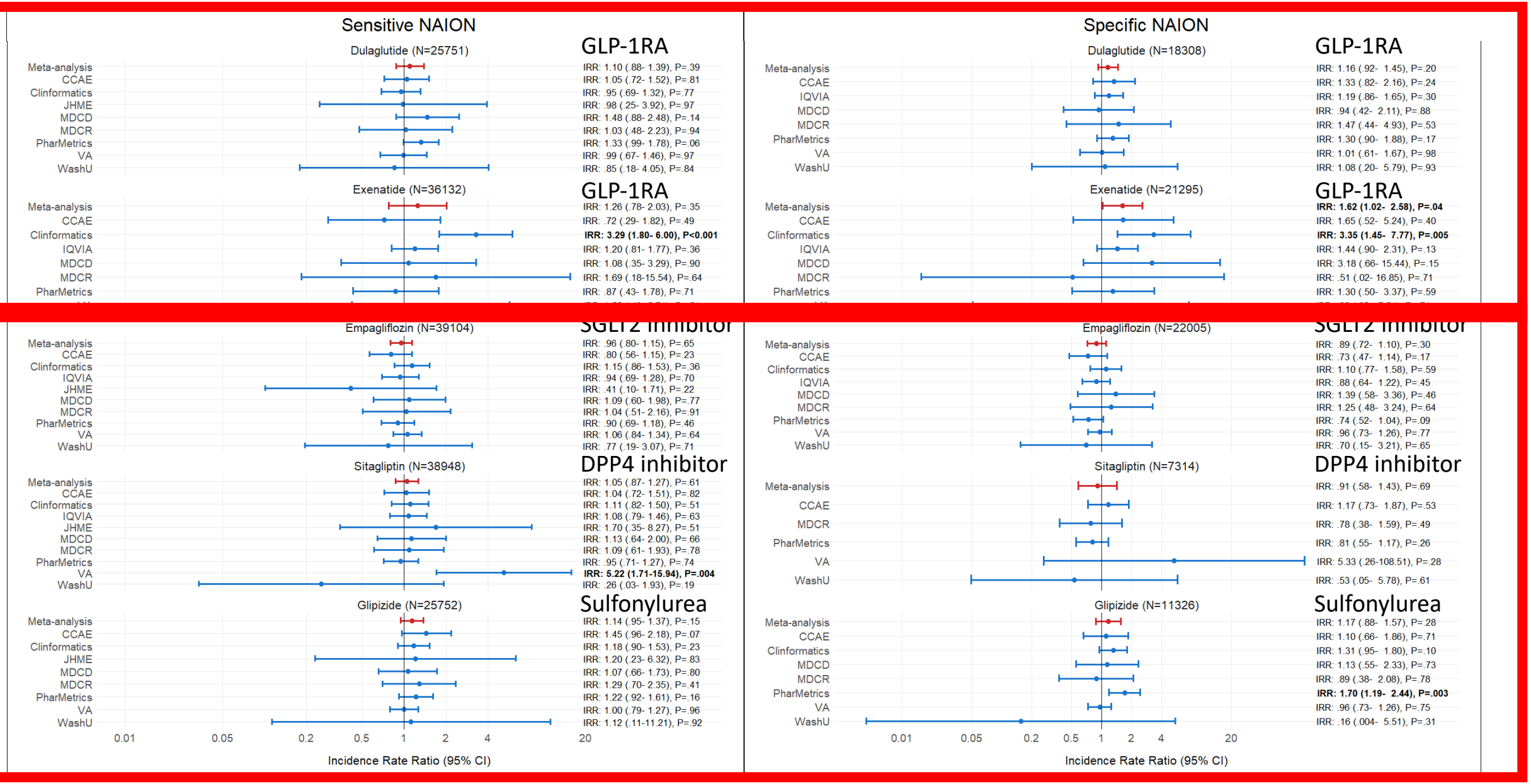




Meta-analysis IRR 1.32

Meta-analysis IRR 1.50

Self-controlled case-series



Wilmer Eye Institute
Johns Hopkins Medicine

Conclusion

- Small increased risk of NAION among T2DM patients exposed to semaglutide
- Additional studies should incorporate ophthalmic risk factors (e.g., cup-to-disc ratio)
- Weigh concern for NAION with therapeutic benefits of semaglutide

Hripcsak	George	Columbia University, New York, NY
Falconer	Thomas	Columbia University, New York, NY
Boland	Michael V.	Harvard Medical School, Boston, MA
Brash	James	IQVIA, Real World Solutions, Brighton, UK
Swerdel	Joel	Janssen Research and Development, Titusville, NJ
Schuemie	Martijn	Janssen Research and Development, Titusville, NJ
Sena	Anthony G.	Janssen Research and Development, Titusville, NJ
Ryan	Patrick B	Janssen Research and Development, Titusville, NJ
Alshammari	Thamir	Jazan University, Jazan, Saudi Arabia
Boyce	Danielle	Johns Hopkins University, Baltimore, MD
Nishimura	Akihiko	Johns Hopkins University, Baltimore, MD
Nagy	Paul	Johns Hopkins University, Baltimore, MD
Martin	Benjamin	Johns Hopkins University, Baltimore, MD
Westlund	Erik	Johns Hopkins University, Baltimore, MD
Mathioudakis	Nestoras	Johns Hopkins University, Baltimore, MD
Chen	John	Mayo Clinic, Rochester, MN
Barkmeier	Andrew	Mayo Clinic, Rochester, MN
Rojas-Carabali	William	Nanyang Technological University, Singapore
Goetz	Kerry	National Eye Institute, National Institutes of Health, Bethesda, MD
Weiskopf	Nicole G.	Oregon Health & Science University, Portland OR
Hribar	Michelle	Oregon Health & Science University, Portland OR
Chen	Aiyin	Oregon Health & Science University, Portland OR
Dorr	David	Oregon Health & Science University, Portland OR
Humes	Izabelle	Oregon Health & Science University, Portland OR
McCoy	David B	Oregon Health & Science University, Portland OR
Adibuzzaman	Mohammad	Oregon Health & Science University, Portland OR
Wang	Sophia	Stanford University, Palo Alto, CA
Leng	Theodore	Stanford University, Palo Alto, CA
Morgan-Cooper	Hannah	Stanford University, Palo Alto, CA
Desai	Priya	Stanford University, Palo Alto, CA
Agrawal	Rupesh	Tan Tock Seng Hospital, Singapore
Suchard	Marc A	University of California - Los Angeles, Los Angeles, CA
Stocking	Jacqueline C.	University of California Davis, Sacramento, CA
Baxter	Sally	University of California San Diego, La Jolla, CA
Swaminathan	Swarup S.	University of Miami, Miami, FL
Ehrlich	Joshua R.	University of Michigan, Ann Arbor, MI
Bu	Fan	University of Michigan, Ann Arbor, MI
Armbrust	Karen R.	University of Minnesota, Minneapolis, MN
Areaux Jr.	Raymond G	University of Minnesota, Minneapolis, MN
Toy	Brian	University of Southern California,Los Angeles, CA
Xu	Benjamin	University of Southern California,Los Angeles, CA
Lee	David A.	University of Texas Health Science Center at Houston, Houston, TX
Lee	Cecilia	University of Washington, Seattle, WA
DuVall	Scott L	VA Informatics and Computing Infrastructure, US Department of Veterans Affairs, Salt Lake City, UT
Matheny	Michael	VA Informatics and Computing Infrastructure, US Department of Veterans Affairs, Salt Lake City, UT
Viernes	Benjamin	VA Informatics and Computing Infrastructure, US Department of Veterans Affairs, Salt Lake City, UT
O'Brien	William	VA Informatics and Computing Infrastructure, US Department of Veterans Affairs, Salt Lake City, UT
Flowers	Alexis	Vanderbilt University Medical Center, Nashville, TN
Brown	Eric N.	Vanderbilt University Medical Center, Nashville, TN
Takkouche	Sahar	Vanderbilt University Medical Center, Nashville, TN
Lee	Lok Hin	Vanderbilt University Medical Center, Nashville, TN
Xie	Yangyiran	Vanderbilt University Medical Center, Nashville, TN
Mawn	Louise	Vanderbilt University Medical Center, Nashville, TN
Zhang	Linying	Washington University in St. Louis, St. Louis, MO
Fan	Ruochong	Washington University in St. Louis, St. Louis, MO
Wilcox	Adam	Washington University in St. Louis, St. Louis, MO
Lai	Albert	Washington University in St. Louis, St. Louis, MO

Methods for Semaglutide Study

Linying Zhang

OHDSI Community Call

19 November 2024

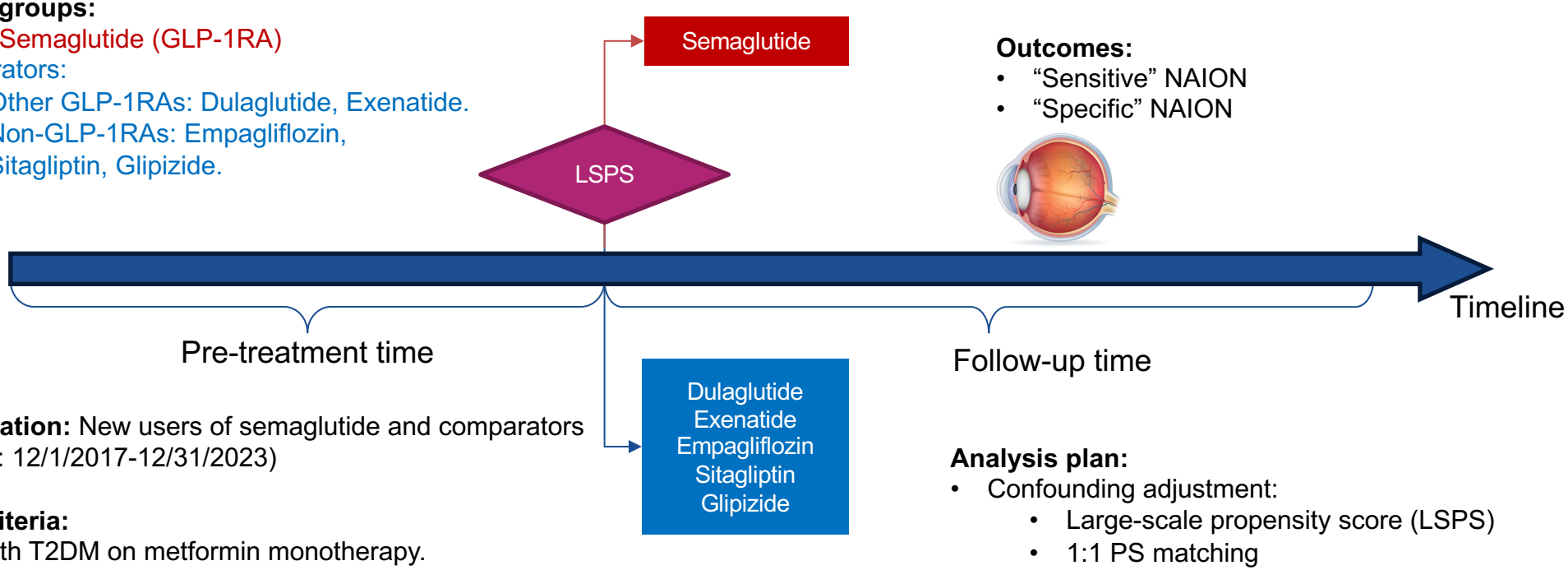
Methods for Semaglutide Study

1. Active-Comparator New-User Cohort Analysis
2. Self-Controlled Case-Series Analysis

Active-Comparator New-User Cohort:
Study Design and Statistical Analysis

Objective:
Estimate the risk of NAION (Non-Arteritic Anterior Ischemic Optic Neuropathy) associated with semaglutide use compared to other diabetes medications.

Exposure groups:
- Target: Semaglutide (GLP-1RA)
- Comparators:
  - Other GLP-1RAs: Dulaglutide, Exenatide.
  - Non-GLP-1RAs: Empagliflozin, Sitagliptin, Glipizide.



Outcomes:
- "Sensitive" NAION
- "Specific" NAION

Study Population: New users of semaglutide and comparators (study period: 12/1/2017-12/31/2023)

Inclusion Criteria:
- Adults with T2DM on metformin monotherapy.
- At least 1 year of prior observation.
- No prior exposure to comparator diabetes medications.
- No more than 30 days of prior insulin use.

Analysis plan:
- Confounding adjustment:
  - Large-scale propensity score (LSPS)
  - 1:1 PS matching
- Hazard ratio estimation:
  - Cox proportional hazards model
- Meta-analysis:
  - Bayesian random-effects model

Active-Comparator New-User Cohort: *Sensitivity Analyses*

- **Sensitivity analysis 1: Alternative cohort definition**
  - Expanded the cohort to include new users of each T2DM medication, regardless of prior exposure to comparator drugs.
- **Sensitivity analysis 2: Temporal stratification**
  - **Objective:** Address potential biases due to external factors, including healthcare utilization patterns and changes in medication prescribing trends.
  - **Approach:** Stratified by calendar time
    - **12/2017 – 1/2020:** Pre-COVID-19.
    - **2/2020 – 6/2021:** COVID-19 pandemic period.
    - **7/2021 – 12/2023:** Post-FDA approval of semaglutide for obesity with a 60% increase in prescriptions.

Active-Comparator New-User Cohort: *Objective Diagnostics*

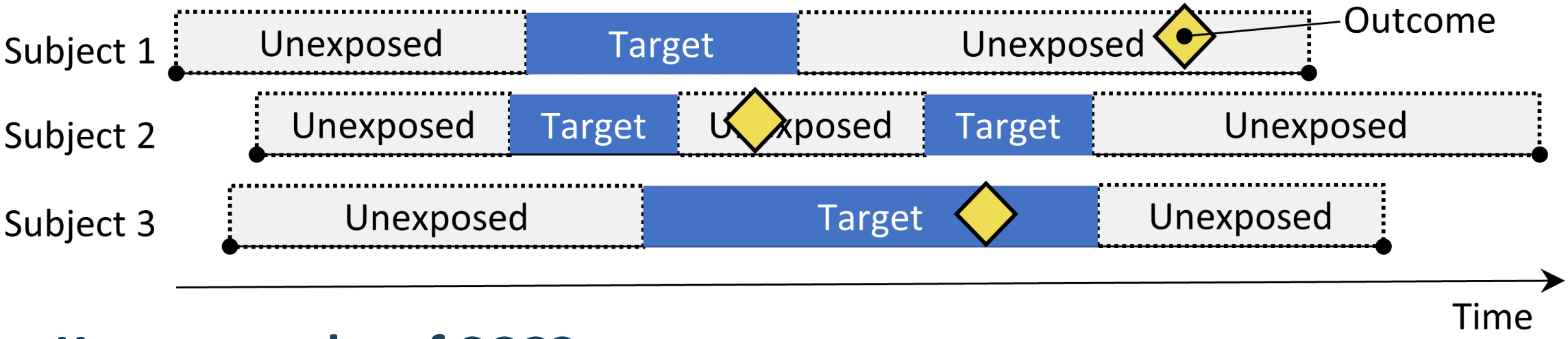
- Empirical equipoise
  - Assess the similarity between target and comparator groups
- Covariate balance
  - Absolute standardized mean difference (ASMD)
  - Unbalanced covariates -> residual bias
- Expected absolute systematic error (EASE)
  - 97 negative control outcomes
  - Assess residual bias
- Minimum detectable relative risk (MDRR)

Only databases that passed all diagnostics were included in the meta-analysis.

Self-Controlled Case-Series (SCCS)
Study Design

- **Exposure group**:
  - Target: Semaglutide (GLP-1RA)

No comparator group: Individuals act as their own control.



- **Key strengths of SCCS:**
  - Robust to between-person confounding
  - Robust to time-invariant confounders *within* individuals.

Figure source: The Book of OHDSI

Self-Controlled Case-Series (SCCS)
Study Design

- **Objective:**
  Estimate the incidence rate ratio (IRR) for NAION during semaglutide exposure compared with unexposed time.
- **Observation period:**
  - Restricted to the period when patients had T2DM.
  - Excluded the first 365 days in the database to improve detection of incident NAION.
- **Pre-exposure control period:**
  - Defined as the 30 days prior to treatment initiation, included in the control time, and adjusted for in the analysis.

Self-Controlled Case-Series (SCCS)
Statistical Analysis

- **Model:** Conditional Poisson regression.
- **Adjustments:**
  - **Seasonality:** Modeled using spline functions of calendar months to control for potential seasonal effects on NAION incidence.
  - **Control period adjustment:** Incorporated a pre-exposure time window to refine estimates.

Self-Controlled Case-Series (SCCS)
Objective Diagnostics

- Time trend diagnostic
  - Detects time trend in the outcome rate.
- Pre-exposure diagnostic
  - The outcome increases the probability of having the exposure ("reverse causality")
  - Detects increased rate of outcome just before the exposure
- Expected absolute systematic error (EASE)
- Minimum detectable relative risk (MDRR)

Only databases that passed all diagnostics were included in the meta-analysis.

This network study was brought to you by the letter

OHDSI Evidence Network

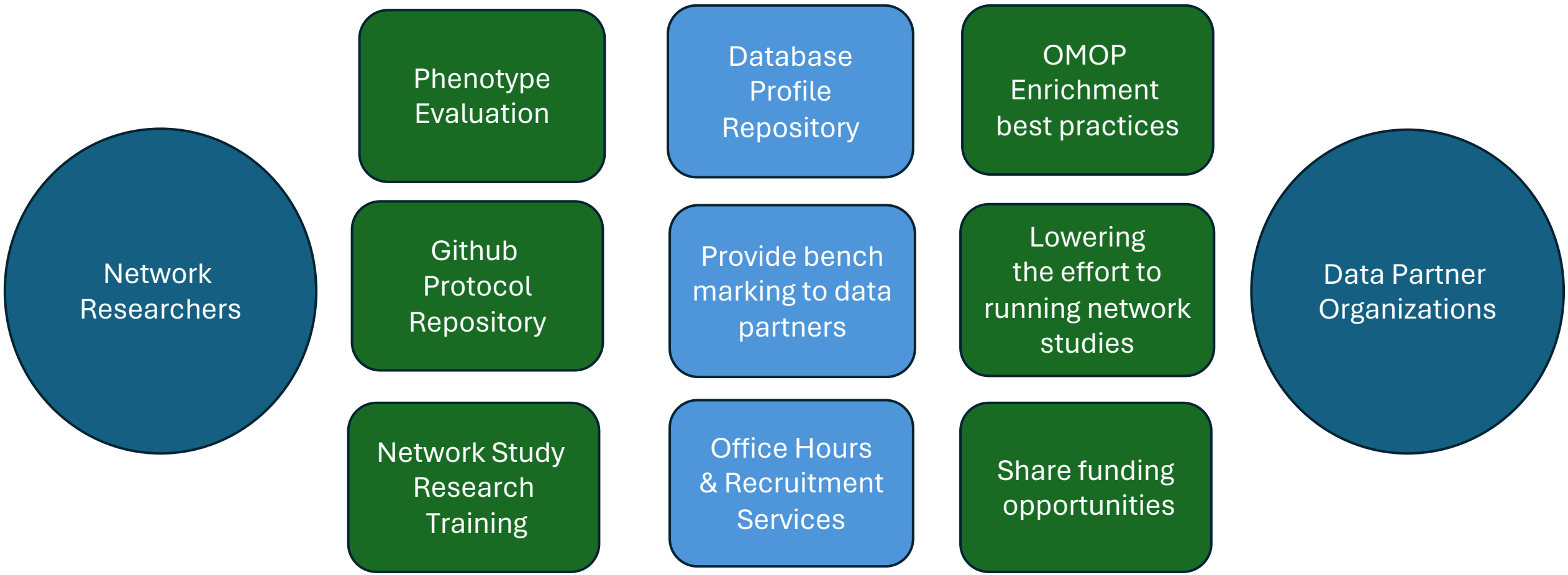
Launched in the spring of 2024, the OHDSI evidence network already has

17 formal data partner organizations representing

37 data sources.

45+ organizations are still going through the onboarding process.

Connecting Researchers with Data Partners



Questions?

We are here to accelerate research!

We host office hours every **Friday from 9am-10am EST** in the Evidence Network teams channel for researchers and data partners.

Data Partners join our Evidence Network Working Group at OHDSI.org. Meets 2x/month on Thursdays at 10 am EST.

Email us at evidencenetwork@ohdsi.org

CB

Strategus & Semaglutide Study

Anthony Sena

OHDSI Community Call

19 November 2024

Elements of an Open OHDSI Network Study*

- All documentation, study code and subsequent results are made publicly available on the OHDSI GitHub.
- Investigators must create and publish a public study protocol detailing the scope and intent of the analysis to be performed.
- **Investigators must create a study package (typically with R or SQL) with code that is CDM compliant.**
- Investigators are encouraged to attend OHDSI Community Calls to promote and recruit collaborators for their OHDSI network study.
- At the end of the analysis, aggregate study results are made available in the OHDSI GitHub.
- Where possible, investigators are encouraged to publish study R Shiny Applications to data.ohdsi.org.

https://ohdsi.github.io/TheBookOfOhdsi

** Book of OHDSI – Chapter 20*

Semaglutide network study using Strategus & HADES

- **Strategus** is an R package for coordinating and executing **HADES analytics packages**.
- Study design choices are documented in machine-readable format (JSON) and used to execute each HADES package.
- We utilize **renv** for reproducible R/Python environment for executing OHDSI network studies.

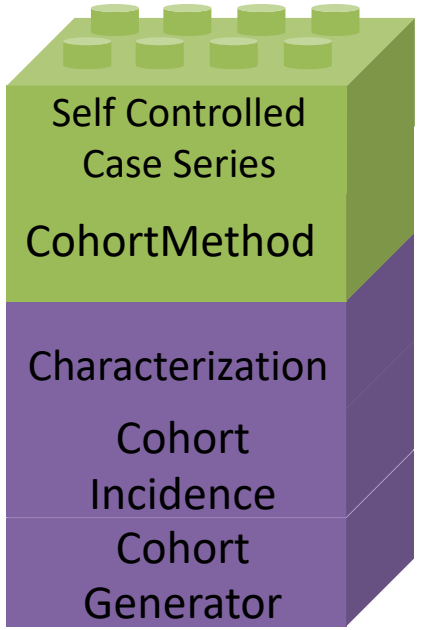
HADES

HADES

HEALTH ANALYTICS DATA-TO-EVIDENCE SUITE

Semaglutide analysis specification

- Strategus contains HADES “modules” the building blocks to create the study analysis specification.
- Semaglutide study team designed the phenotypes and defined analytical choices for the study



Strategus v1.x

[ohdsi-studies/SemaglutideNaion/inst/fullStudyAnalysisSpecification.json]

GitHub

Study Execution

- Download the Semaglutide project from GitHub
- Restore the R execution environment using **renv**
- Configure the connection details to your OMOP CDM
- Execute the study
- Review the results in CSV format
- Share the results with the study coordinator

SemaglutideNaion/StrategusCodeToRun.R

GitHub

Thanks to collaborators!

- Thomas Falconer (Columbia University)
- James Brash (IQVIA)
- Ben Martin (Johns Hopkins University)
- David McCoy (Oregon Health & Science University)
- Hannah Morgan-Cooper (Stanford University)
- Brian Toy (University of Southern California)
- Marc Suchard (Department of Veterans Affairs)
- Ruochong Fan (Washington University)

Areas for collaboration

- Strategus is under active development and has a sub-team as part of the HADES working group.
- Sub-team was formed earlier in 2024. All working group meetings have been recorded and the most recent meeting provided an overview of the sub-team and prior meetings around Strategus design discussion and decisions.
- We welcome those that are interested in the design and development of Strategus and HADES to join the journey!

https://ohdsi.org/workgroups/


OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

Thank you!

Using The Results Schema

Erik Westlund & Benjamin Martin

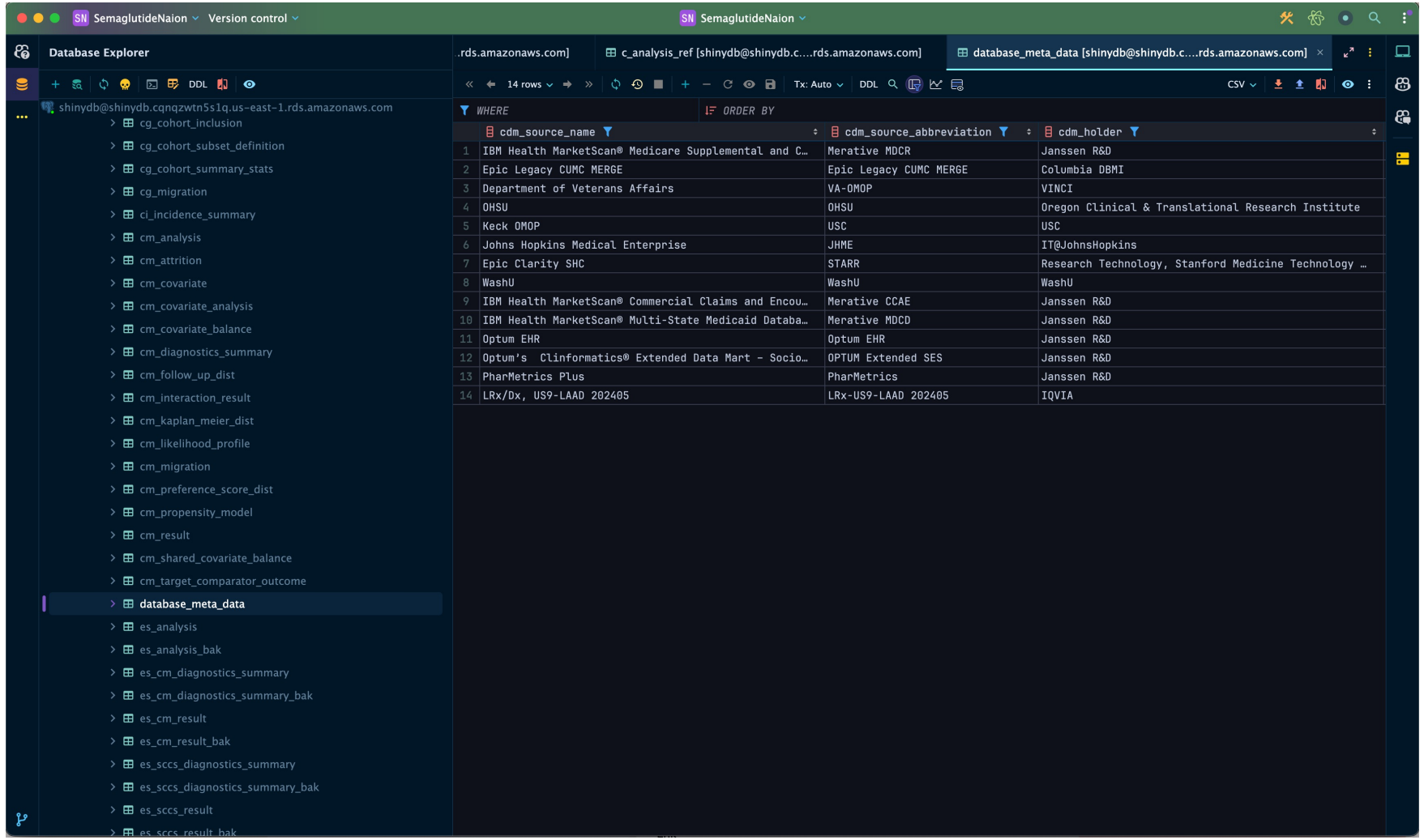
Our Tasks

- Get the results out of the database
- Format for publication
  - Tables
  - Figures

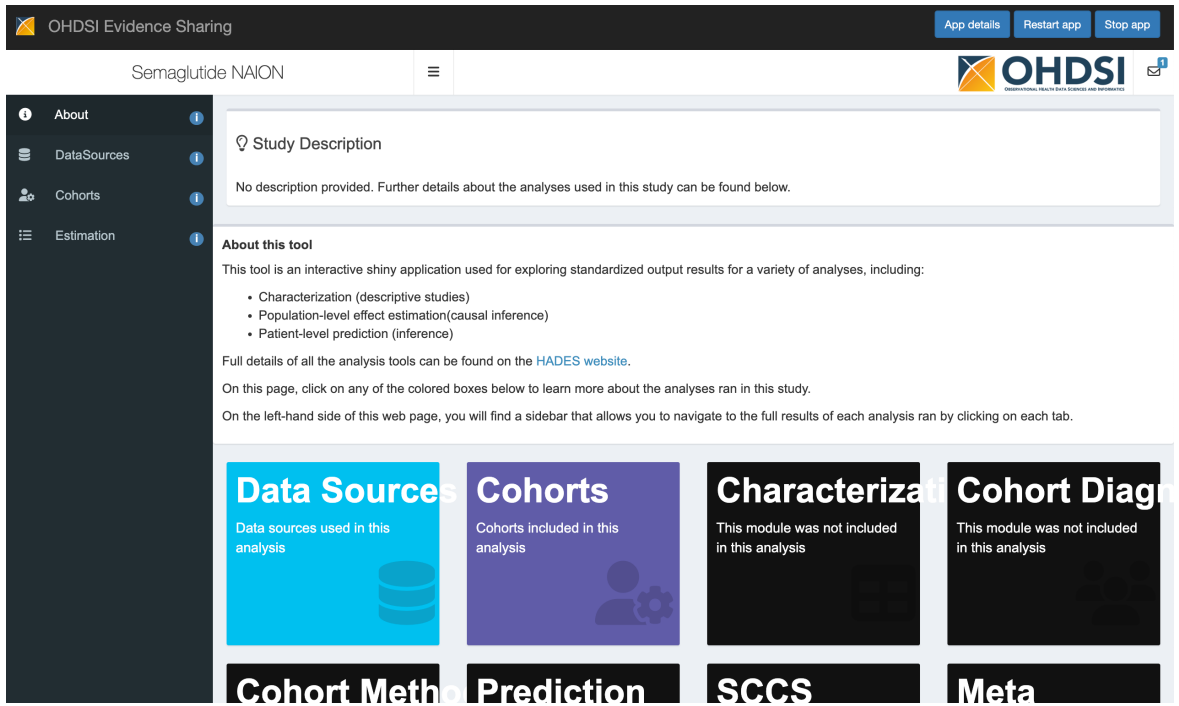
Approach

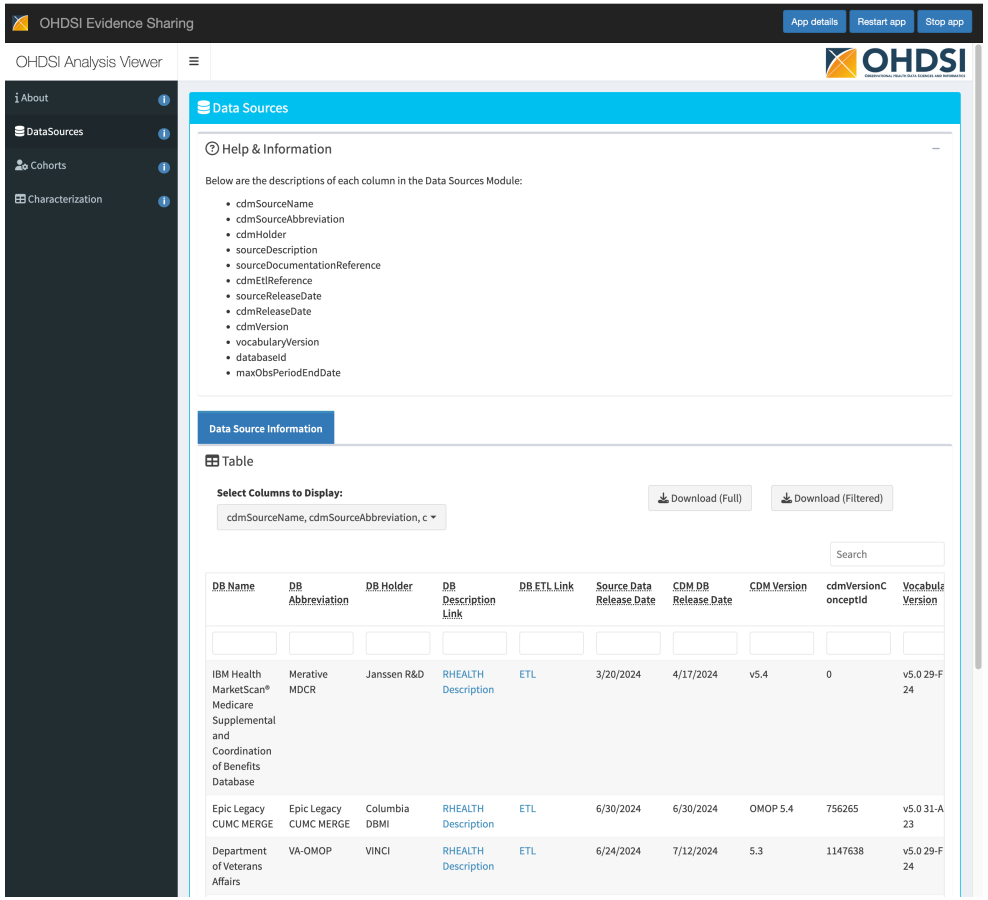
- The Strategus pipeline created results which are uploaded to a Postgres database
- Shiny apps are created
- Results can be extracted from the results schema

The Results Schema



The Shiny Apps





The Job

- Extract information that needs to be reported
- Format into tables and figures

The Challenge

- There is a lot of data:
  - Two NAION phenotypes
  - Two analytical approaches (CM, SCCS)
  - Multiple analyses within each (20 T/C drug pairs, 6 SCCS drugs)
  - Hundreds of diagnostics
- In numbers:
  - Table 1 has ~150 results/aggregations
  - Table 2 has ~1050 reported results/aggregations
- Moving target: we added databases midway
- Must automate. No tool yet ready to automate this process.

Process

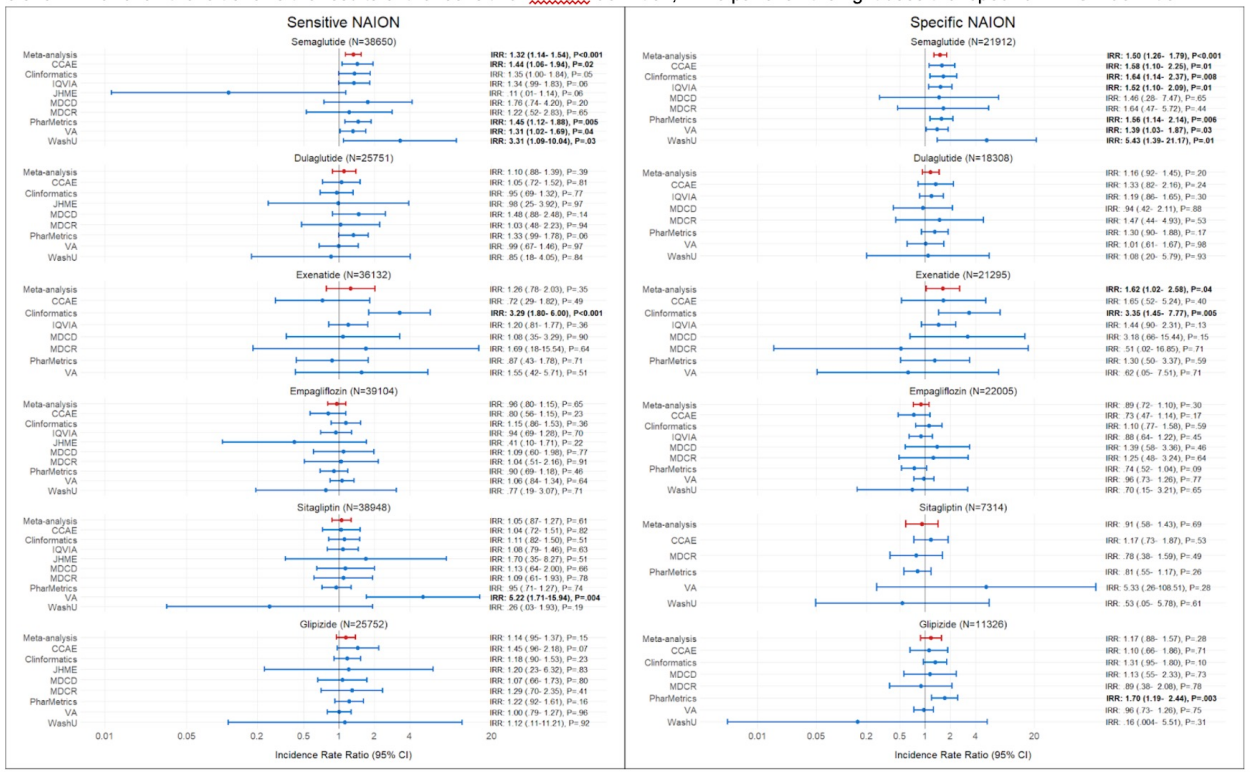
- Studied the Shiny app and consulted with experts (namely, Anthony Sena – thank you)
- We created pipelines in R notebooks to extract results directly from the results schema
- These were processed into tables and figures using tidyverse tools
- The tables and figures were shared with other team members

The Output

Table 2: The incidence proportion and incidence rate of NAION among adults with T2DM and in each T2DM drug exposure cohort (semaglutide, dulaglutide, exenatide, empagliflozin, sitagliptin, glipizide) across all databases.

		"Sensitive" NAION definition[&]					"Specific" NAION definition[&]				
Cohort	Database	Patients at Risk*	On-Treatment Time (Person-Years)	Number of Outcomes	Incidence Proportion (per 100,000 Persons)	Incidence Rate (per 100,000 Person-Years)	Patients at Risk*	On-Treatment Time (Person-Years)	Number of Outcomes	Incidence Proportion (per 100,000 Persons)	Incidence Rate (per 100,000 Person-Years)
T2DM	**Total**[%]	37076692	75093073	26501	78.3	41	37096287	75165063	10473	32	16.8
	CCAE	2126003	3427034	1185	55.7	34.6	2126453	3428658	541	25.4	15.8
	Clinformatics	4010797	7443649	6269	156.3	84.2	4013178	7454714	2392	59.6	32.1
	CUMC	99138	213381.6	39	39.3	18.3	99183	213523.4	16	16.1	7.5
	IQVIA	20155571	43536250	9976	49.5	22.9	20167656	43576868	3892	19.3	8.9
	JHME	138751	227697.3	79	56.9	34.7	138833	227892	30	21.6	13.2
	MDCD	867613	1650953	826	95.2	50	868099	1652770	256	29.5	15.5
	MDCR	501145	824223.2	851	169.8	103.2	501599	825674.9	327	65.2	39.6
	OHSU	54958	122074.7	32	58.2	26.2	55019	122219.7	19	34.5	15.5
	Optum EHR	2516415	4303811	562	22.3	13.1	2516877	4305088	307	12.2	7.1
	PharMetrics	5619829	10736023	5348	95.2	49.8	5621567	10744401	2225	39.6	20.7
	STARR	68735	153558	31	45.1	20.2	68757	153655.9	17	24.7	11.1
	USC	41431	47863	21	50.7	43.9	41445	47886.4	10	24.1	20.9
	VA	753008	2053014	1235	164	60.2	754240	2057853	416	55.2	20.2
	WashU	123298	353541.1	47	38.1	13.3	123381	353858.1	25	20.3	7.1
Semaglutide (GLP-1 RA)	**Total**[%]	810390	400136.6	89	7.1	14.5	810937	400423.9	51	4.2	8.7
	CCAE	50173	26646.6	11	21.9	41.3	50194	26657.4	6	12	22.5
	Clinformatics	43555	20212.7	13	29.8	64.3	43588	20228.6	10	22.9	49.4
	CUMC	1794	1491.4	0	0	0	1796	1492.4	0	0	0
	IQVIA	581923	290882.1	52	8.9	17.9	582336	291103.7	30	5.2	10.3
	JHME	1473	1003.5	<5	NA	NA	1473	1003.6	0	0	0
	MDCD	2108	680.2	0	0	0	2111	681	0	0	0
	MDCR	3665	1710.4	0	0	0	3670	1712.4	0	0	0
	OHSU	602	384.1	0	0	0	603	384.2	0	0	0
	Optum EHR	38711	12501.5	<5	[NA]	NA	38719	12507.5	<5	NA	NA
	PharMetrics	76572	38014.4	8	10.4	21	76618	38037.7	5	6.5	13.1
	STARR	979	791.1	<5	NA	NA	979	791.1	<5	NA	NA
	USC	196	57.5	0	0	0	196	57.5	0	0	0

Figure 2: Forest plot for the self-controlled case-series analysis. Incidence Rate Ratio (IRR) and 95% confidence interval (CI) estimate for the risk of NAION while on-treatment with one of the T2DM medications compared with control time, not on treatment with the medication of interest. Results are shown for semaglutide, other GLP-1 RAs (dulaglutide, exenatide), and non-GLP-1 RA medications (empagliflozin, sitagliptin, glipizide). Results from databases that passed study diagnostics are provided, as well as the meta-analytic estimates.* The total number of patients included is shown. Panel on the left shows the results of the "sensitive" NAION definition, while panel on the right uses the "specific" NAION definition.[&]



Challenges

- Currently, not all information one wants is able to be easily extracted, particularly around characterization
- Database is heavily normalized; requires expertise in SQL in general and the results schema in particular
- Sanity tests with Shiny app are laborious

Challenges

- Journal submissions requirements sometimes at odds with automation: arbitrary needs, manual uploading, etc.
- The Shiny results viewer is a great and comprehensive, but it should not be used to put results in a paper
  - Don’t try copying and pasting
  - Graphics are useful but not publication ready
- Condensing information and formatting for idiosyncrasies of specific study
- Testing and quality control

Future Software

- A general-purpose table and figure generation tool would be helpful
- Studies have idiosyncrasies that determine presentation (e.g., our multiple phenotypes) – how to be useful for everyone?
- Potential solution
  - Utilities to extract key results in a “tidy”, composable way
  - These could be composed into tables and figures for specific journal needs
  - Testing utilities to ensure the correct information extracted
  - Vignettes/repository of common uses