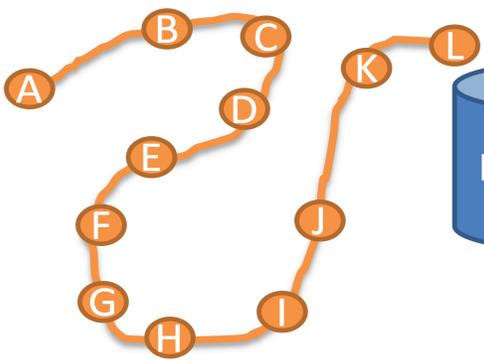
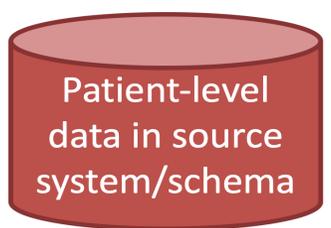




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OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS



OHDSI Standardized Analytics for Evidence Generation

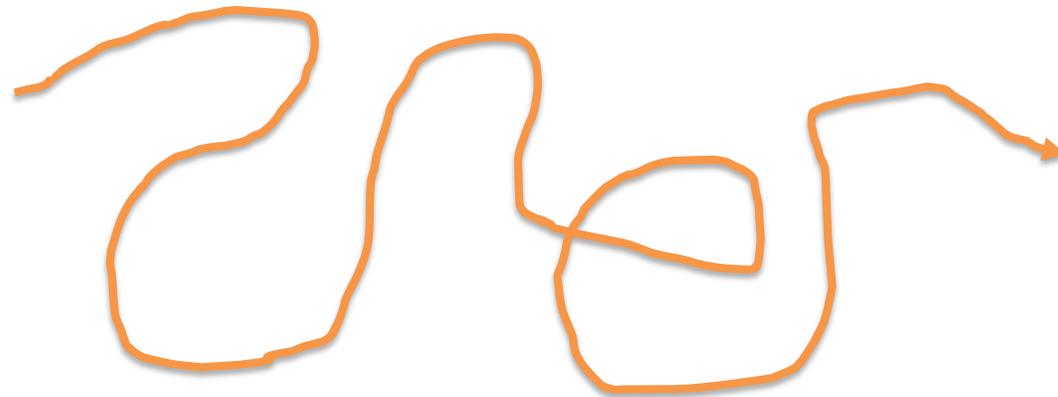
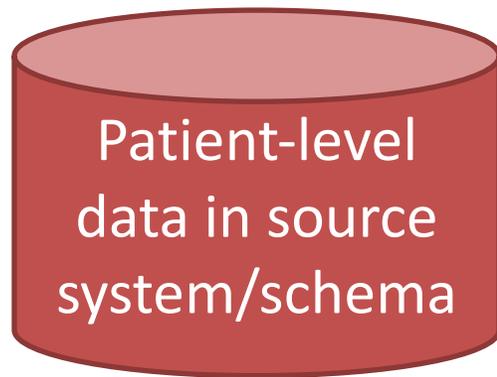
Anthony Sena, Jenna Reps, Martijn Schuemie



The journey through OHDSI's
standardized analytics

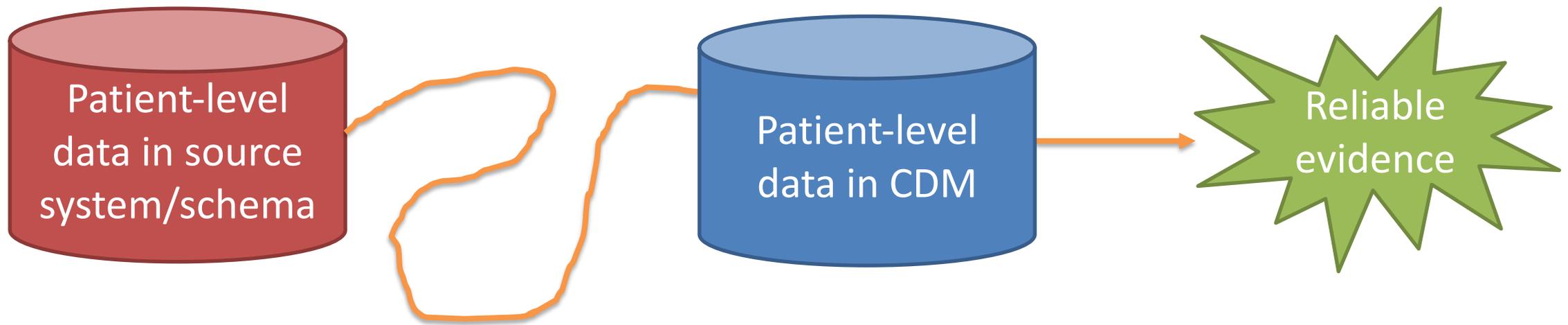


The journey to real-world evidence



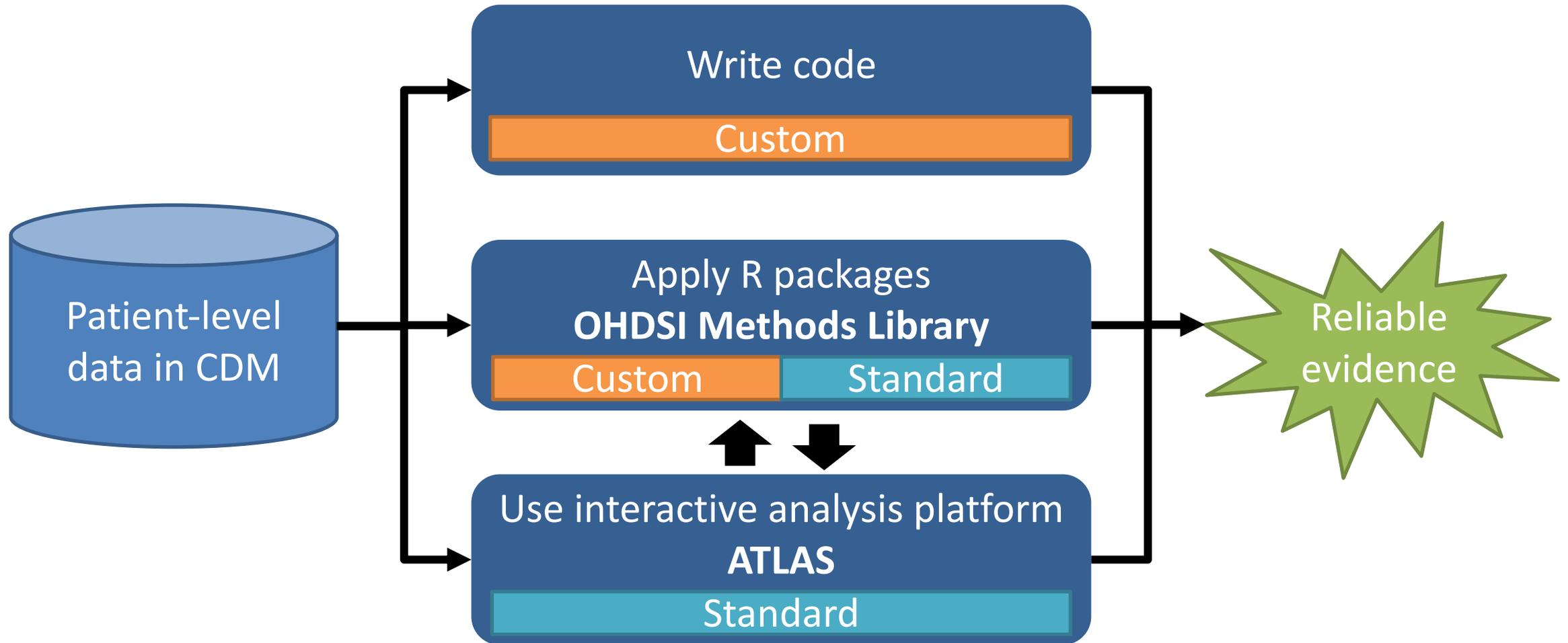


The journey to real-world evidence





The journey to real-world evidence



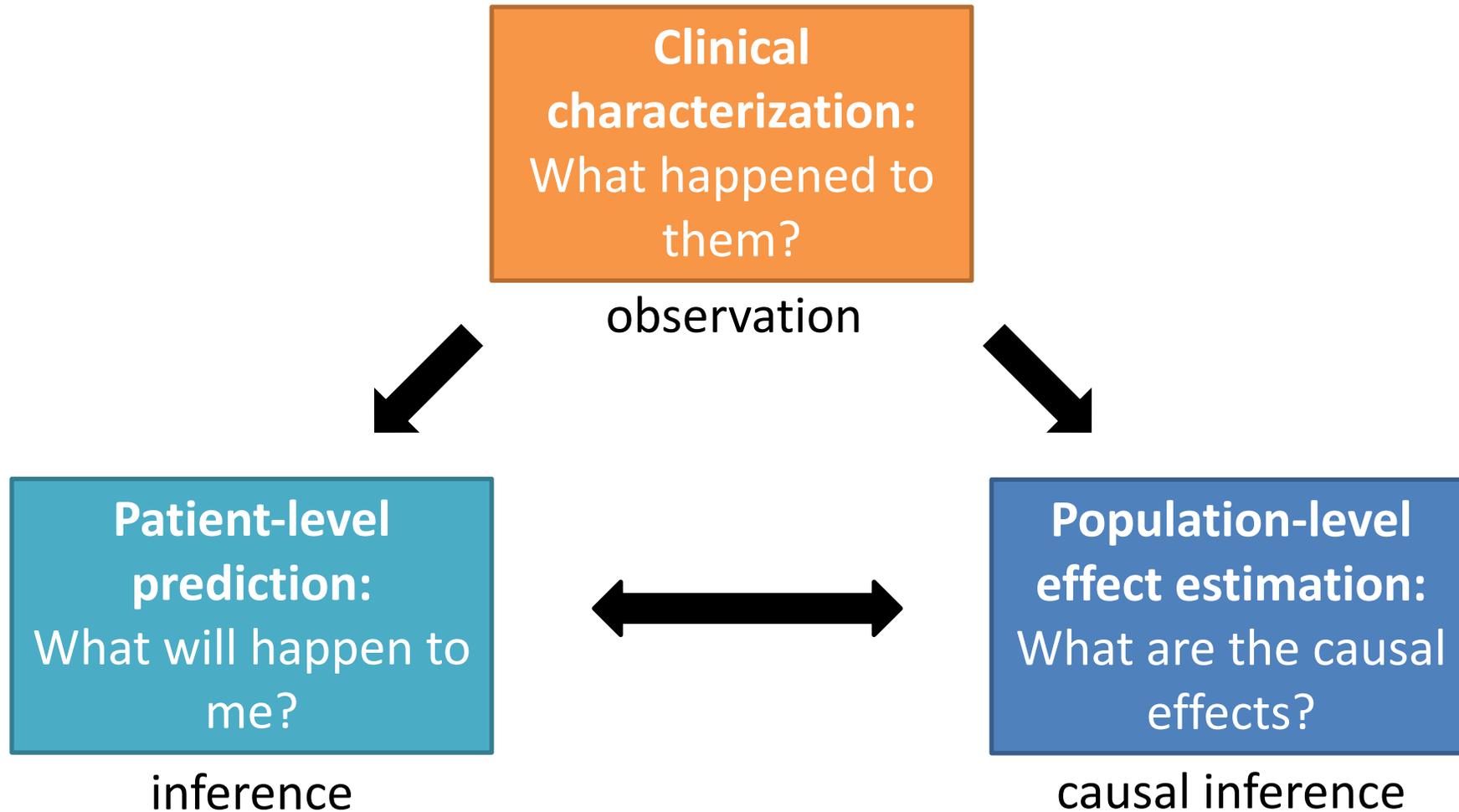


Generating reliable evidence for hypertension

- Hypertension is **prevalent** and a **leading risk factor** for many health outcomes
- There are **many alternative treatments**
 - ACE, Thiazide diuretics, ARB, CCB...
 - Mono vs. combo therapy
- **Multiple potential effects**
 - Intended outcomes (e.g. reduced **acute myocardial infarction**)
 - Adverse drug reactions (e.g. increased **angioedema**)
- **Extensively studied** in clinical trials
 - What can we learn from real-world data?



Complementary evidence to inform the patient journey





The journey through OHDSI's standardized analytics: Clinical Characterization

Anthony Sena

Janssen Research and Development

Erasmus MC

Cohort definition - design



ATLAS

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Cohort #9169

[OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension

Definition | Concept Sets | Generation | Reporting | Export

enter a cohort definition description here

Cohort Entry Events

Events having any of the following criteria:

a drug exposure of **ACE inhibitors** + Add attribute... Delete Criteria

for the first time in the person's history

with continuous observation of at least **365** days before and **0** days after event index date

Limit initial events to: **earliest event** per person.

Restrict initial events

Inclusion Criteria

New inclusion criteria has hypertension diagnosis in 1 yr prior to treatment Copy Delete

enter an inclusion rule description

1. has hypertension diagnosis in 1 yr prior to treatment

2. Has no prior antihypertensive drug exposures in medical history

3. Is only taking ACE as monotherapy, with no concomitant combination treatments

having **all** of the following criteria:

with **at least** **1** using **all** occurrences of:

a condition occurrence of **Hypertensive disorder** + Add attribute...

where **event starts** between **365** days **Before** and **0** days **After** **index start date** add additional constraint

restrict to the same visit occurrence

Limit qualifying events to: **earliest event** per person.

Cohort Exit

Event Persistence:

Event will persist until: **end of a continuous drug exposure**

Continuous Exposure Persistence:

Specify a concept set that contains one or more drugs. A drug era will be derived from all drug exposure events for any of the drugs within the concept set, using the specified persistence window as a maximum allowable gap in days between successive exposure events and adding a specified surveillance window to the

Cohort definition - results



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Cohort #9169

[OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension

Definition | Concept Sets | **Generation** | Reporting | Export

Available CDM Sources

Source Name	Generation Status	People	Records	Generated	Generation Duration
▶ Generate Optum Extended SES (v836)	n/a	n/a	n/a	n/a	n/a
▶ Generate Optum Extended SES (v876)	COMPLETE	599,827	599,827	03/24/2019 10:53 AM	00:04:31 View Reports
▶ Generate Optum Panther (v811)	n/a	n/a	n/a	n/a	n/a
▶ Generate Optum Panther (v874)	COMPLETE	736,267	736,267	03/24/2019 10:53 AM	00:05:26 View Reports
▶ Generate Premier (v812)	n/a	n/a	n/a	n/a	n/a
▶ Generate Premier (v877)	n/a	n/a	n/a	n/a	n/a

Inclusion Report for Optum Extended SES (v876)

Inclusion Rule	Summary Statistics:		Total Events		
	Match Rate	Matches	N	% Remain	% Diff
1. has hypertension diagnosis in 1 yr prior to treatment	22.77%	599,827	1,943,297	73.77%	26.23%
2. Has no prior antihypertensive drug exposures in medical history			905,307	34.37%	39.40%
3. Is only taking ACE as monotherapy, with no concomitant combination treatments			599,827	22.77%	11.60%

Attrition Visualization [Switch to intersect view](#)

Cohort characterization - design

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Characterization #248
🔍

Design

Executions

Utilities

Cohort characterization is defined as the process of generating cohort level descriptive summary statistics from person level covariate data. Summary statistics of these person level covariates may be count, mean, sd, var, min, max, median, range, and quantiles. In addition, covariates during a period may be stratified into temporal units of time for time-series analysis such as fixed intervals of time relative to cohort_start_date (e.g. every 7 days, every 30 days etc.), or in absolute calendar intervals such as calendar-week, calendar-month, calendar-quarter, calendar-year.

Cohort definitions

Import

Show entries Search:

ID	Name		
9169	[OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension	Edit cohort	Remove
9170	[OHDSI EU 2019] New users of Thiazide-like diuretics as first-line monotherapy for hypertension	Edit cohort	Remove

Showing 1 to 2 of 2 entries Previous Next

Feature analyses

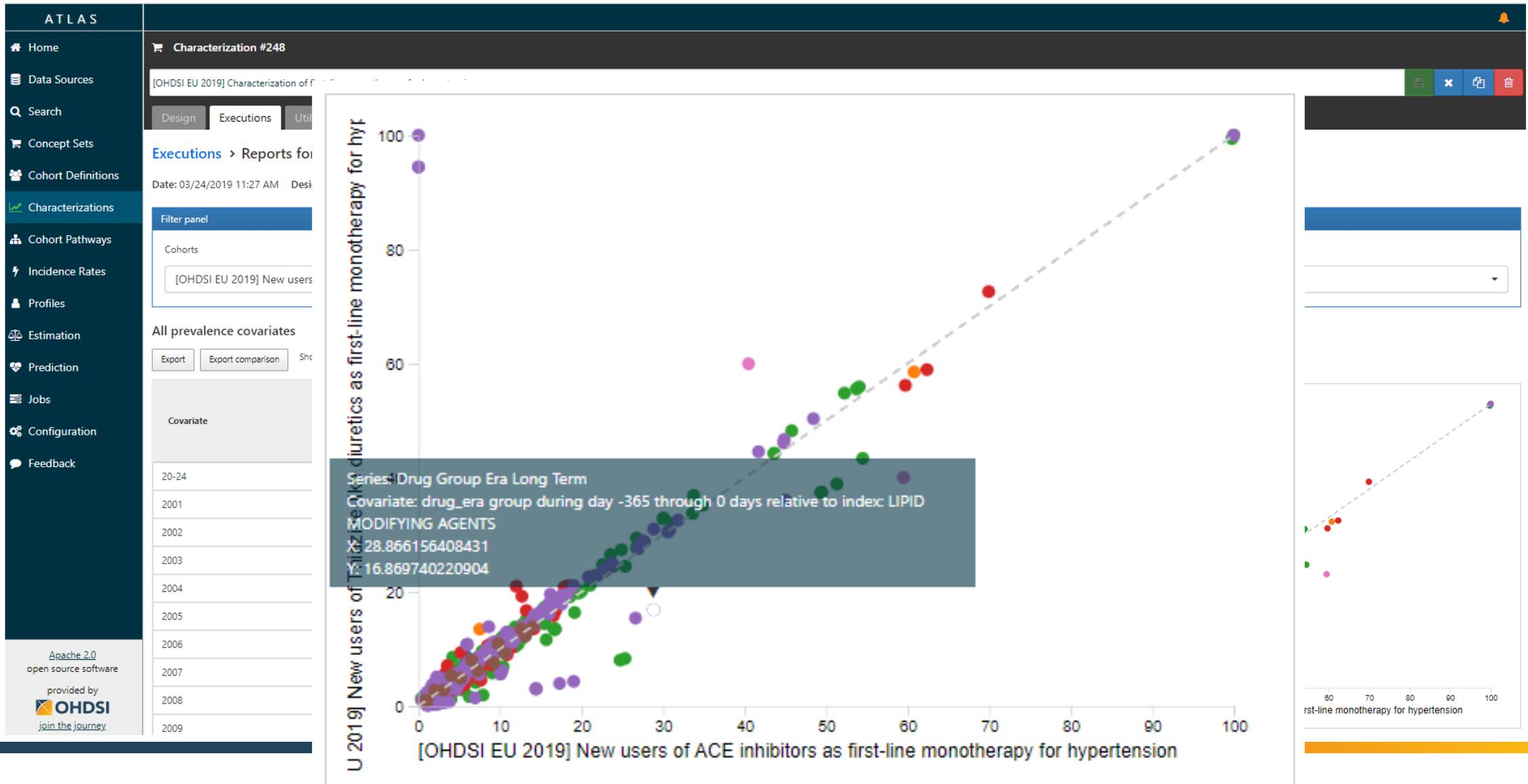
Import

Show entries Search:

ID	Name	Description	Actions
5	Drug Group Era Long Term	One covariate per drug rolled up to ATC groups in the drug_era table overlapping with any part of the long term window.	Remove
30	Condition Group Era Long Term	One covariate per condition era rolled up to groups in the condition_era table overlapping with any part of the long term window.	Remove
49	Charlson Index	The Charlson comorbidity index (Romano adaptation) using all conditions prior to the window end.	Remove
71	Demographics Age Group	Age of the subject on the index date (in 5 year age groups)	Remove
72	Demographics Race	Race of the subject.	Remove
73	Demographics Prior Observation Time	Number of continuous days of observation time preceding the index date.	Remove
74	Demographics Gender	Gender of the subject.	Remove
77	Demographics Age	Age of the subject on the index date (in years).	Remove
70	Demographics Time In Cohort	Number of days of observation time during cohort period	Remove



Cohort characterization - results



Cohort pathways - design

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Cohort Pathway #28

[OHDSI EU 2019] Pathway of antihypertensive drugs

Design Executions Utilities

Cohort Pathway is defined as the process of generating an aggregated sequence of transitions between the Event Cohorts among those people in the Target Cohorts.

Target Cohorts

Each of the Target Cohorts will be analyzed for the pathways through the event cohorts.

Import

Show 10 entries

ID	Name		
9173	[OHDSI EU 2019] Patients initiating first-line therapy for hypertension	Edit cohort	Remove
9184	[OHDSI EU 2019] Patients initiating first-line therapy for hypertension with >3 yr follow-up	Edit cohort	Remove
9185	[OHDSI EU 2019] Patients initiating first-line therapy for hypertension with >3 yr follow-up post-2012	Edit cohort	Remove

Showing 1 to 3 of 3 entries

Previous 1 Next

Event Cohorts

Each Event Cohort defines the step in a pathway that may occur for a person in the Treatment Cohort.

Import

Show 10 entries

ID	Name		
9174	[OHDSI EU 2019] ACE inhibitor use	Edit cohort	Remove
9175	[OHDSI EU 2019] Angiotensin receptor blocker (ARB) use	Edit cohort	Remove
9176	[OHDSI EU 2019] Thiazide diuretic use	Edit cohort	Remove
9177	[OHDSI EU 2019] dihydropyridine Calcium Channel Blocker (dCCB) use	Edit cohort	Remove
9178	[OHDSI EU 2019] non-dihydropyridine Calcium Channel Blocker (ndCCB) use	Edit cohort	Remove
9179	[OHDSI EU 2019] beta blocker use	Edit cohort	Remove
9180	[OHDSI EU 2019] Diuretic-loop use	Edit cohort	Remove



Incidence rate - design

ATLAS

Incidence Rate Analysis #221

[OHDSI EU 2019] Incidence of effects of first-line monotherapy treatments for hypertension

Definition Concept Sets Generation Utilities

Study Cohorts

Target Cohorts

- #9169: [OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension
- #9170: [OHDSI EU 2019] New users of Thiazide-like diuretics as first-line monotherapy for hypertension

Add Target Cohort

Outcome Cohorts

- #9172: [OHDSI EU 2019] Acute myocardial infarction events
- #9171: [OHDSI EU 2019] Angioedema events

Add Outcome Cohort

Time At Risk

Time at risk defines the time window relative to the cohort start or end date with an offset to consider the person 'at risk' of the outcome.

- Time at risk starts with plus days.
- Time at risk ends with plus days.

No study window defined. Add Study Window

Stratify Criteria

You can provide optional stratification criteria to the analysis that will divide the population into unique groups based on their satisfied criteria.

New stratify criteria

- Gender = Female
- Age > 65

Gender = Female Copy Delete

enter an inclusion rule description

having of the following criteria: + Add criteria to group...

with the following event criteria:

+ Add attribute...

with a gender of: Add Import Delete Criteria

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Incidence rate - results

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Incidence Rate Analysis #221

[OHDSI EU 2019] Incidence of effects of first-line monotherapy treatments for hypertension

Definition | Concept Sets | **Generation** | Utilities

Showing target cohort: [OHDSI EU 2019] New users of ACE inhibit... and outcome cohort: [OHDSI EU 2019] Acute myocardial infarcti...

Generate | Export Analysis to CSV

Source Name	Persons	Cases	Proportion [+/-] per 1k persons	Time At Risk (years)	Rate [+/-] per 1k years	Started	Duration
Optum Extended SES (v876)	593,327	2,552	4.30	474,531	5.38	03/24/2019 11:17 AM	00:04:53

Reports | Close

Optum Extended SES (v876)

	Persons	Cases	Proportion [+/-] per 1k persons	Time At Risk (years)	Rate [+/-] per 1k years
Summary Statistics:	593,327	2,552	4.30	474,531	5.38

Stratify Rule	N	Cases	Proportion [+/-] per 1k persons	Time At Risk (years)	Rate [+/-] per 1k years
1. Gender = Female	240,642	938	3.90	195,637	4.79
2. Age > 65	144,733	1,413	9.76	145,206	9.73

771 cases, 68,056 TAR, Rate: 11.33 per 1k years
68,337 (11.52%) people, 1 criteria passed, 1 criteria failed.

2.50 3.48 4.46 5.44 6.42 7.40 8.39 9.37 10.35 11.33 per 1k years



The journey through OHDSI's standardized analytics: Patient-level Prediction

Jenna Reps, PhD

Janssen Research and Development



Journey through Patient-Level Prediction

- At the point in time that I am first given ACE inhibitors for hypertension, what is my risk of experiencing angioedema or acute myocardial infarction within a year?



Characterization can show **Population risk**



Patient-Level Prediction can show **my risk**



Define cohorts

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Cohort #7

[OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension

Definition **?** Concept Sets Generation Reporting Export Messages **3**

enter a cohort definition description here

Cohort Entry Events **?**

Events having any of the following criteria: **+ Add Initial Event ▾**

a drug exposure of **ACE inhibitors ▾** **+ Add attribute... ▾** **Delete Criteria**

✗ for the first time in the person's history

with continuous observation of at least **365 ▾** days before and **0 ▾** days after event index date

Limit initial events to: **earliest event ▾** per person.

Restrict initial events

Inclusion Criteria **?**

New inclusion criteria

has hypertension diagnosis in 1 yr prior to treatment **Copy** **Delete**

enter an inclusion rule description

having **all ▾** of the following criteria: **+ Add criteria to group... ▾**

with **at least ▾ 1 ▾** using **all** occurrences of:

a condition occurrence of **Hypertensive disorder ▾** **+ Add attribute... ▾** **Delete Criteria**



Patient-level prediction- design

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Patient Level Prediction #53

[OHDSI EU 2019] Prediction of outcomes in 1 year following first-line monotherapy ACE inhibitor treatment for hypertension

Specification Utilities

enter a description here (1000 characters max)

VIEW: All Prediction Problem Settings Analysis Settings Execution Settings Training Settings

Prediction Problem Settings

Target Cohorts

+ Add Target Cohort

Show 10 entries Filter:

Remove	Name
	[OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension

Showing 1 to 1 of 1 entries Previous Next

Outcome Cohorts

+ Add Outcome Cohort

Show 10 entries Filter:

Remove	Name
	[OHDSI EU 2019] Acute myocardial infarction events
	[OHDSI EU 2019] Angioedema events

Showing 1 to 2 of 2 entries Previous Next

Analysis Settings

Model Settings

+ Add Model Settings

Show 10 entries Filter:

Remove	Model	Options
--------	-------	---------



Patient-level prediction- generation

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Patient Level Prediction #53

[OHDSI EU 2019] Prediction of outcomes in 1 year following first-line monotherapy ACE inhibitor treatment for hypertension

Specification Utilities

Review & Download Import Export

Review & Download

Review Full Study Specification

Please review the full study specification below and scroll down the page to download the study package.

Full Analysis List (2) Prediction Problem Settings (2) Analysis Settings (1)

Column visibility Copy CSV Show 10 entries Filter:

Target Cohort Name	Outcome Cohort Name	Model Name	Model Settings	Covariate Settings	Risk Window Start	Risk Window End
Target Cohorts [OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension (2)	[OHDSI EU 2019] Acute myocardial infarction events	LassoLogisticRegressionSettings	{"variance":0.01,"seed":null}	"attr_class":"covariateSettin...	1	365
Outcome Cohorts [OHDSI EU 2019] Angioedema events (1) [OHDSI EU 2019] Acute myocardial infarction events (1)	[OHDSI EU 2019] Angioedema events	LassoLogisticRegressionSettings	{"variance":0.01,"seed":null}	"attr_class":"covariateSettin...	1	365

Showing 1 to 2 of 2 entries Previous 1 Next

Download Study Package

Please provide a name for the study package and click "download" to obtain the study package in ZIP format.

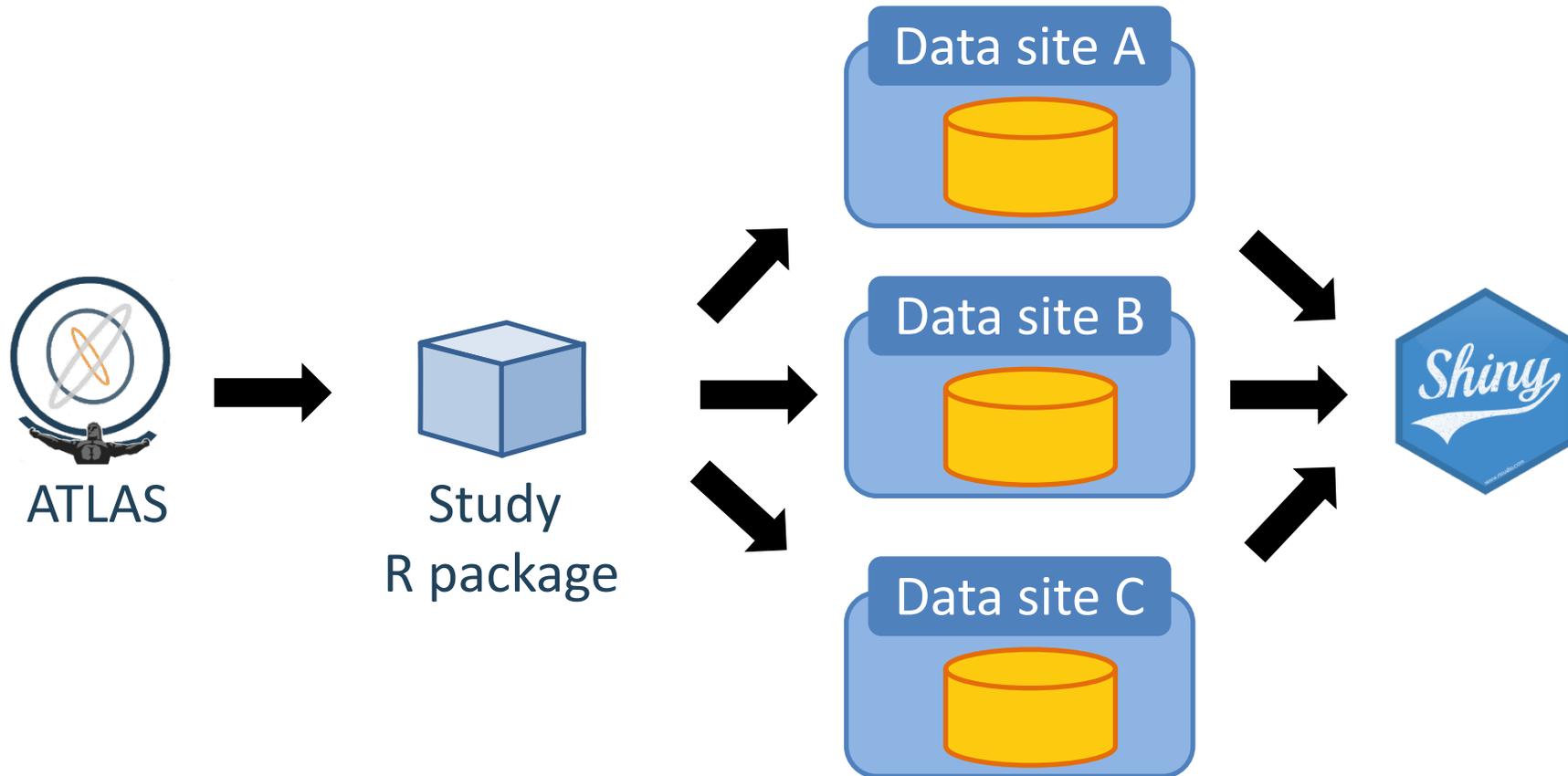
OHDSIEU2019PLP

Please Note: The package name should consist of alphanumeric characters only. No spaces or special characters are permitted.

Download



Study design to results





Results: Overview

Results Model Settings Population Settings Covariate Settings

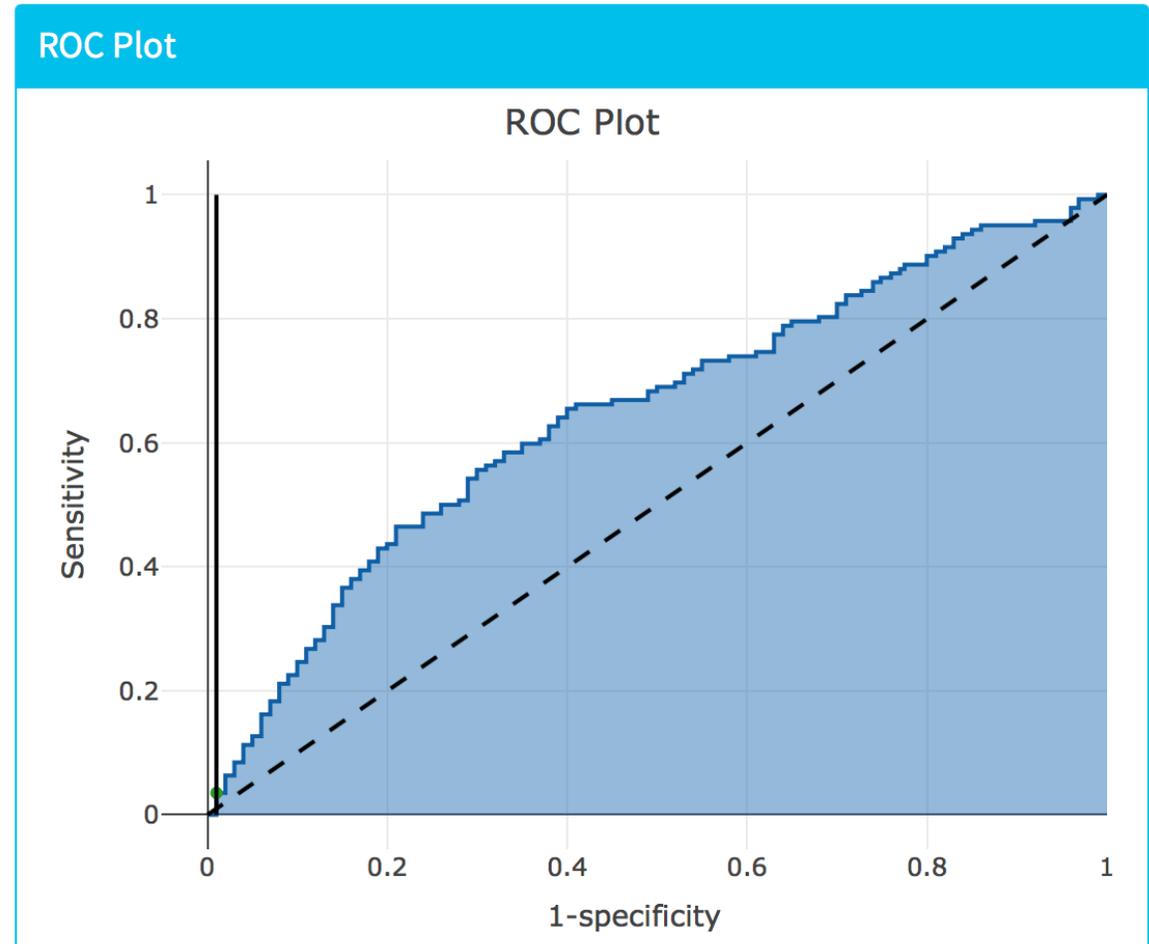
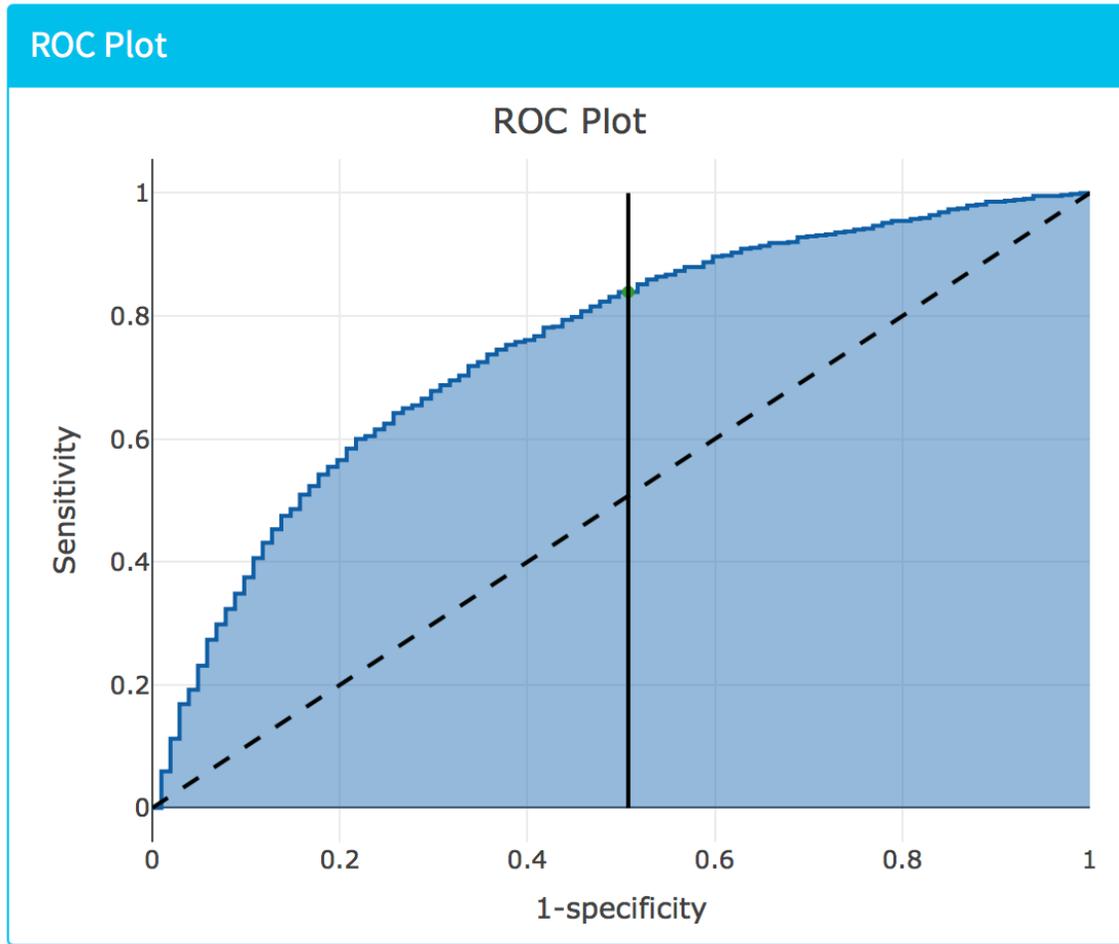
Show 10 entries Search:

Analysis	Dev	Val	T	O	Model	TAR start	TAR end	AUC	AUPRC	T Size	O Count	Incidence (%)
Analysis_1	friendly database name	friendly database name	[OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension	[OHDSI EU 2019] Acute myocardial infarction events	Lasso Logistic Regression	1	365	0.75642	0.02763	87772	640	0.72916
Analysis_2	friendly database name	friendly database name	[OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension	[OHDSI EU 2019] Angioedema events	Lasso Logistic Regression	1	365	0.65238	0.00355	87637	142	0.16203

Showing 1 to 2 of 2 entries Previous 1 Next



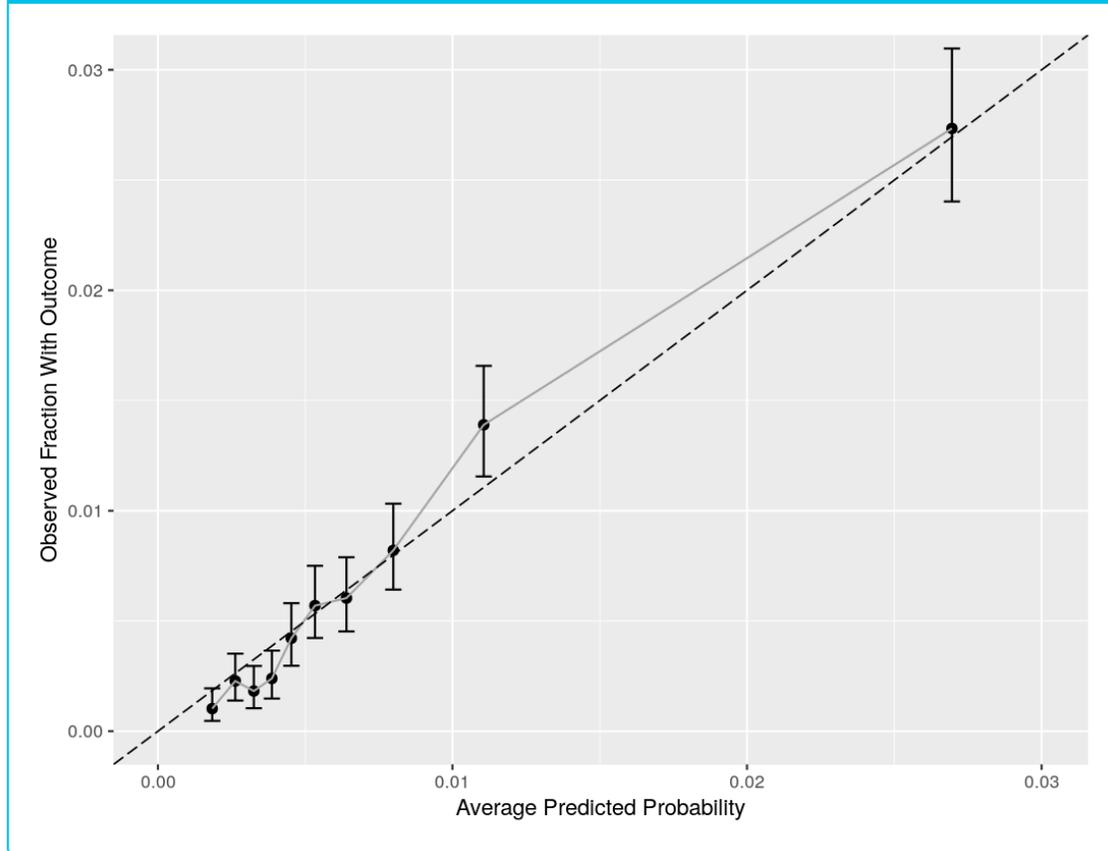
Results: ROC Plots



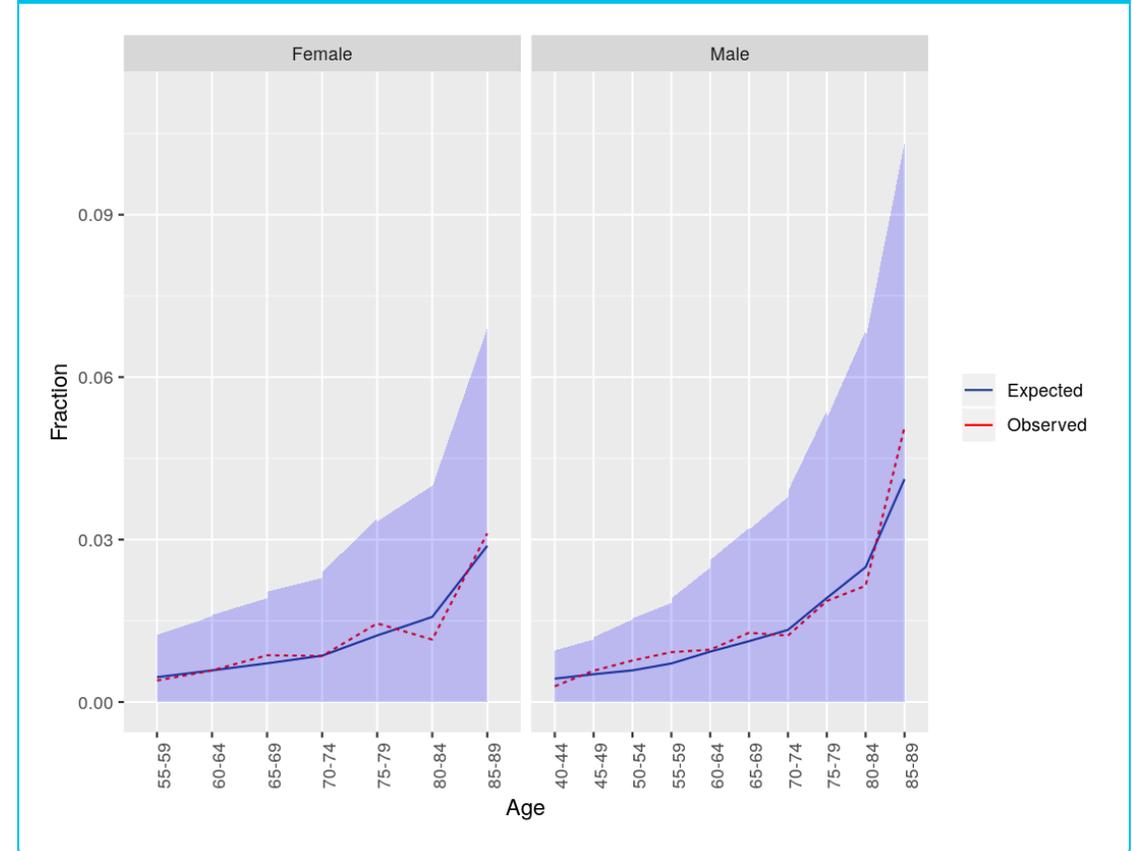


Results: Calibration Plots

Calibration Plot



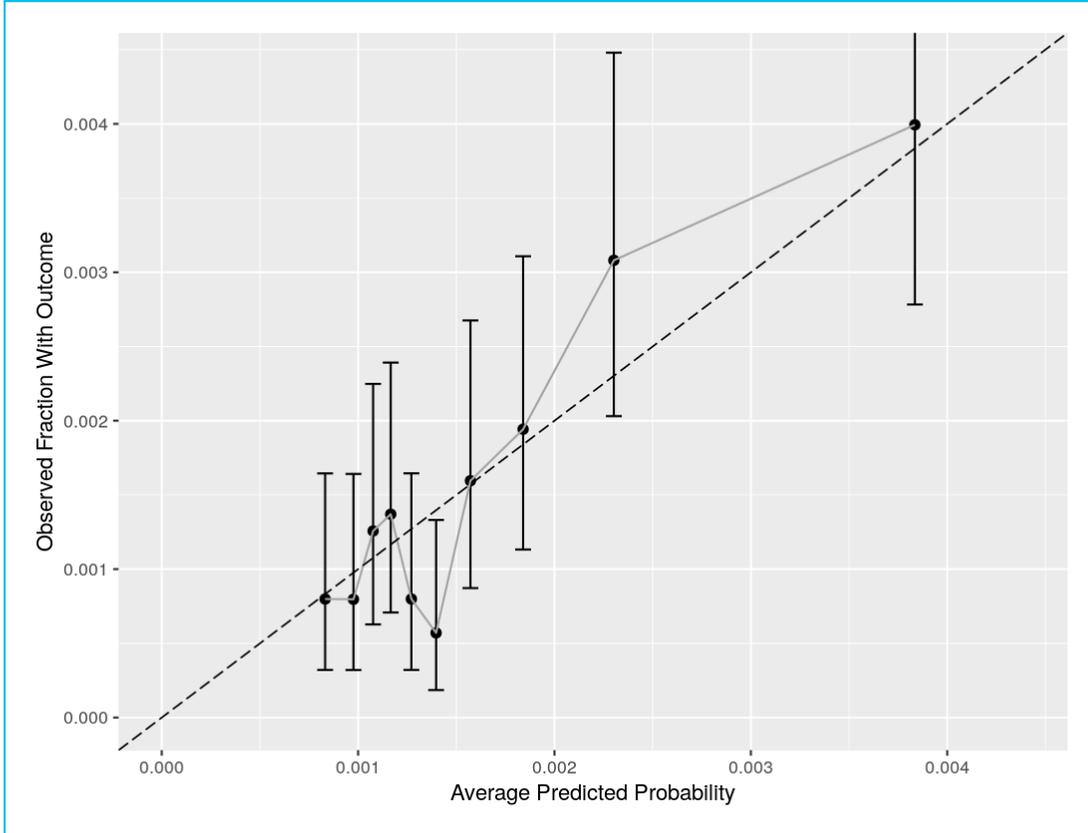
Demographic Plot



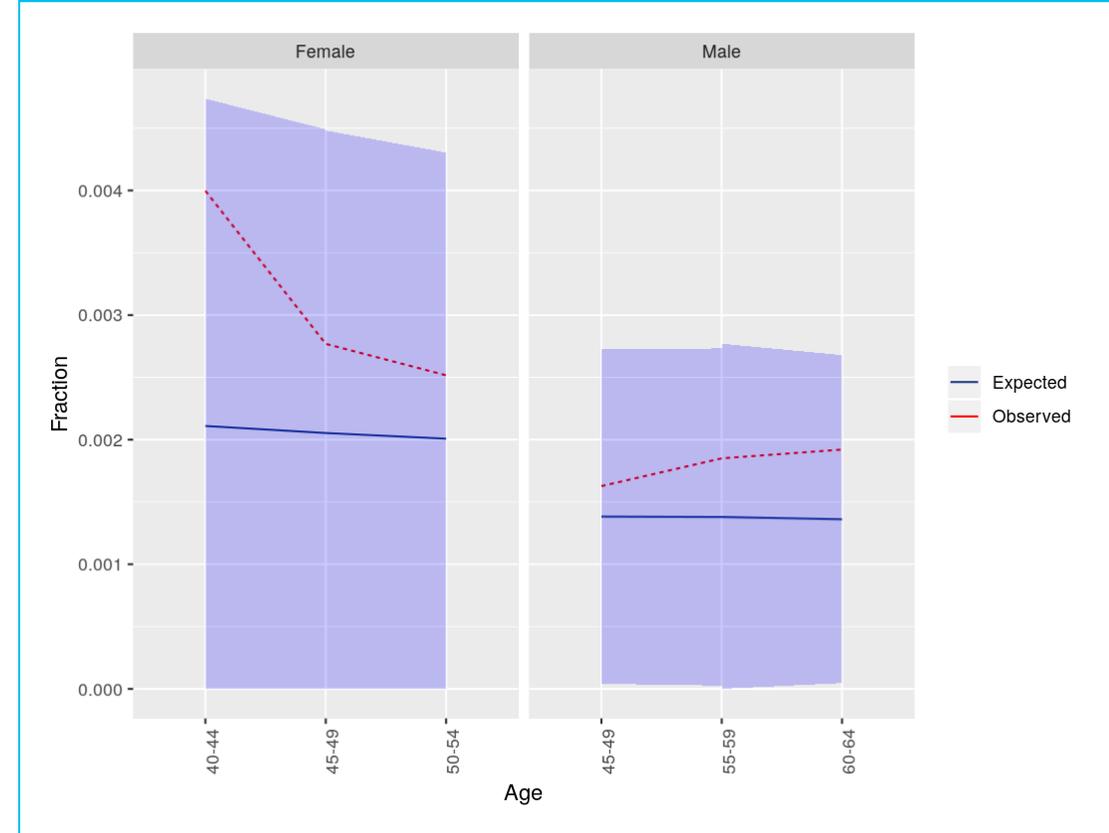


Results: Calibration Plots

Calibration Plot



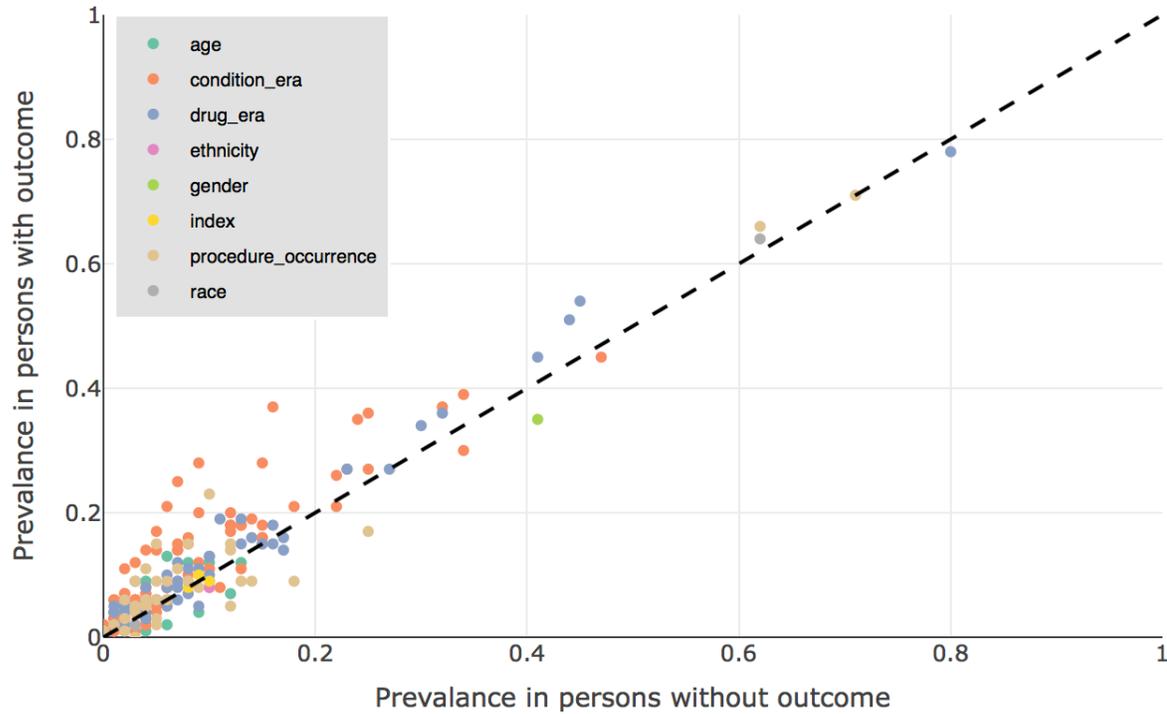
Demographic Plot



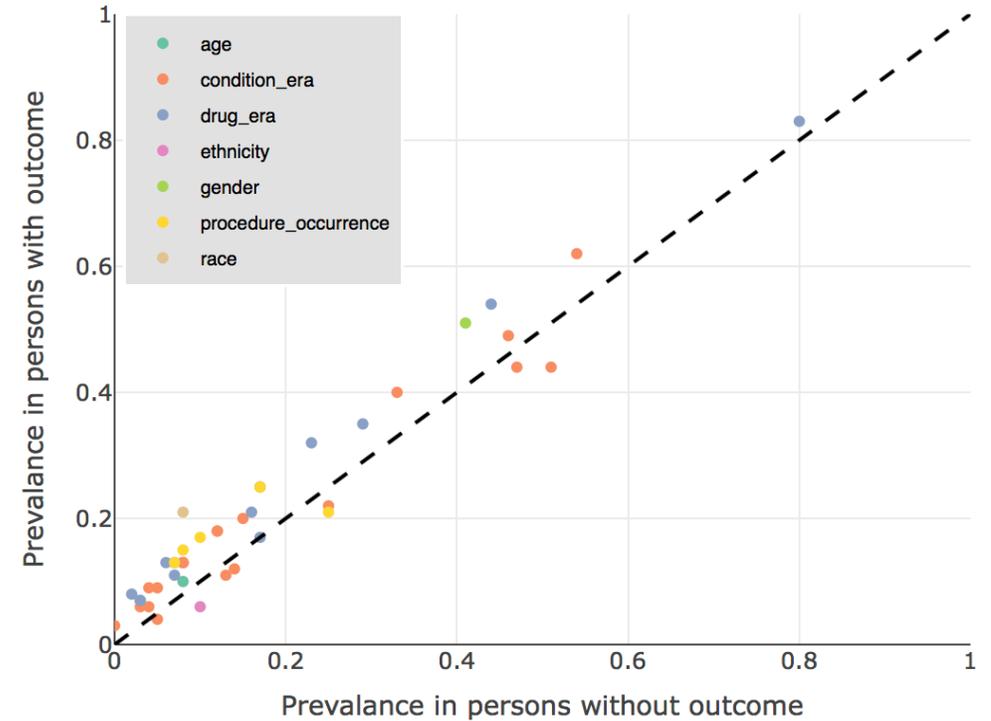


Results: Models

Binary



Binary





Results: Models

Model Table

 Download Model

Show 10  entries

Search:

	Covariate Name	Value	Outcome Mean	Non-outcome Mean
32	age group: 85-89	1.61	0.06	0.01
31	age group: 80-84	1.12	0.09	0.04
30	age group: 75-79	0.93	0.13	0.06
29	age group: 70-74	0.66	0.12	0.08
28	age group: 65-69	0.53	0.13	0.1
26	age group: 60-64	0.4	0.12	0.1
20543	condition_era group during day -365 through 0 days relative to index: Aneurysm of artery of trunk	0.28	0.03	0.01
688	condition_era group during day -365 through 0 days relative to index: Chest pain	0.25	0.28	0.15
23527	condition_era group during day -365 through 0 days relative to index: Nicotine dependence	0.25	0.14	0.07
4	Charlson index - Romano adaptation	0.24	2.49	1.36

Showing 1 to 10 of 29,137 entries

Previous **1** 2 3 4 5 ... 2914 Next



Results: Models

Model Table

 Download Model

Show 10  entries

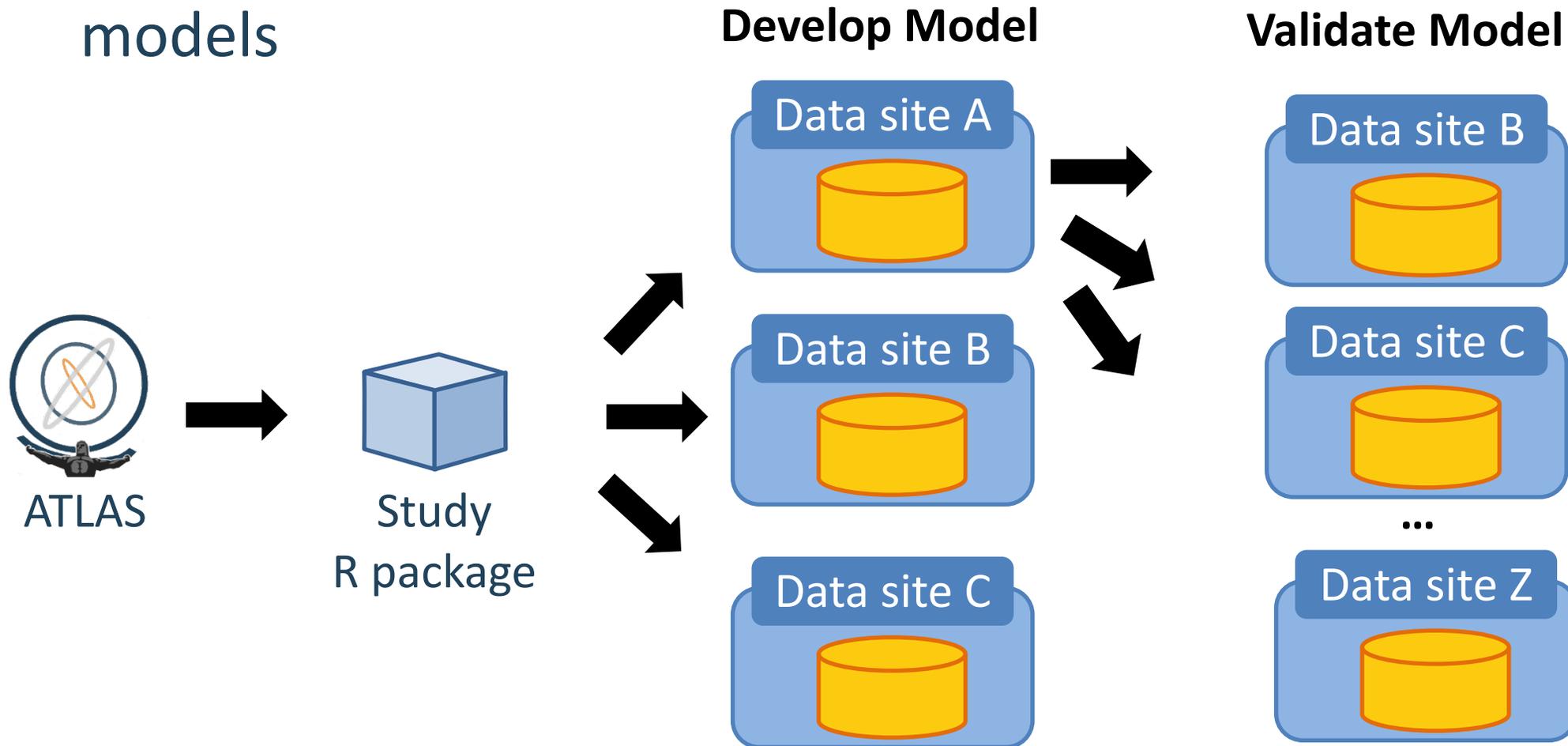
Search:

	Covariate Name	Value	Outcome Mean	Non-outcome Mean
35	race = Black or African American	0.84	0.21	0.08
4263	condition_era group during day -365 through 0 days relative to index: Angioedema	0.64	0.03	0
26059	drug_era group during day -365 through 0 days relative to index: ESTROGENS	0.38	0.13	0.06
4457	condition_era group during day -365 through 0 days relative to index: Edema	0.34	0.09	0.04
8262	drug_era group during day -365 through 0 days relative to index: Prednisone	0.27	0.13	0.07
14895	procedure_occurrence during day -365 through 0 days relative to index: Radiologic examination, chest, 2 views, frontal and lateral	0.26	0.25	0.17
25784	drug_era group during day -365 through 0 days relative to index: ANTIEMETICS AND ANTINAUSEANTS	0.22	0.07	0.03
16014	procedure_occurrence during day -365 through 0 days relative to index: Emergency department visit for the evaluation and management of a patient, which requires these 3 key components: An expanded problem focused history; An expanded problem focused examination; and Medical decision making of moderate complexity. Counseling	0.18	0.13	0.07
23443	condition_era group during day -365 through 0 days relative to index: Mass of trunk	0.17	0.2	0.15
27949	condition_era group during day -365 through 0 days relative to index: Allergic condition	0.15	0.18	0.12



Final thoughts

- Standardization can enable efficient external validation of models



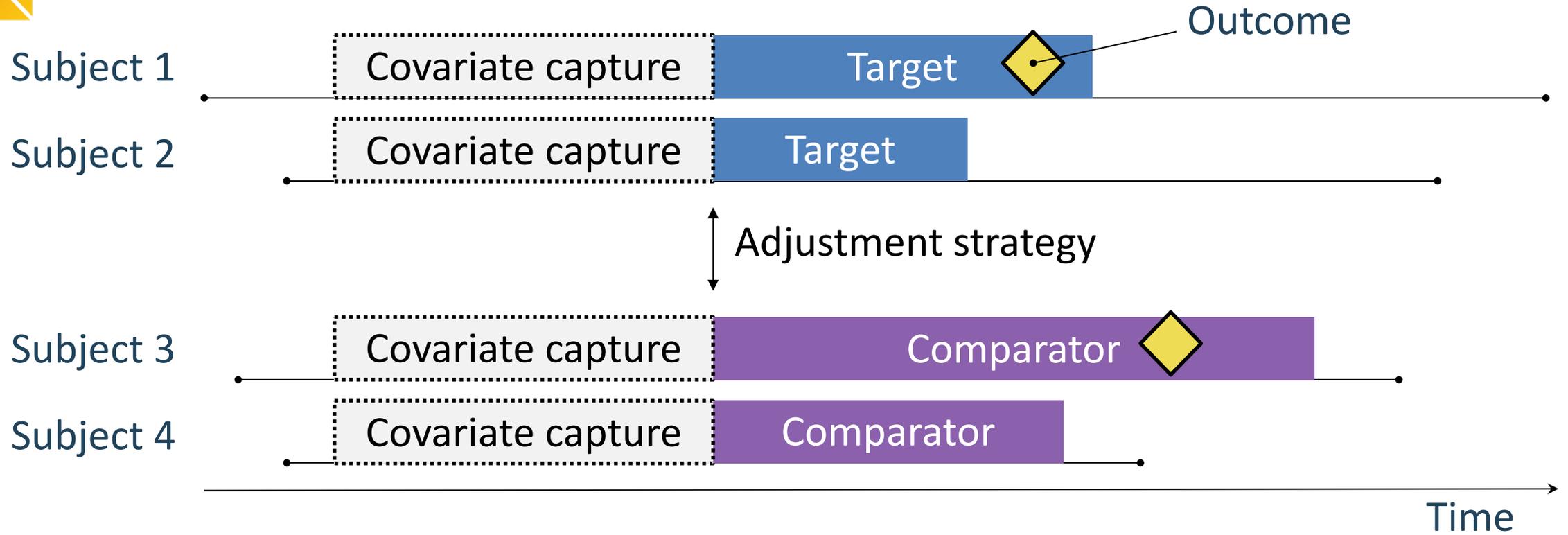


The journey through OHDSI's standardized analytics: Population-level Effect Estimation

Martijn Schuemie, PhD
Janssen Research & Development
UCLA



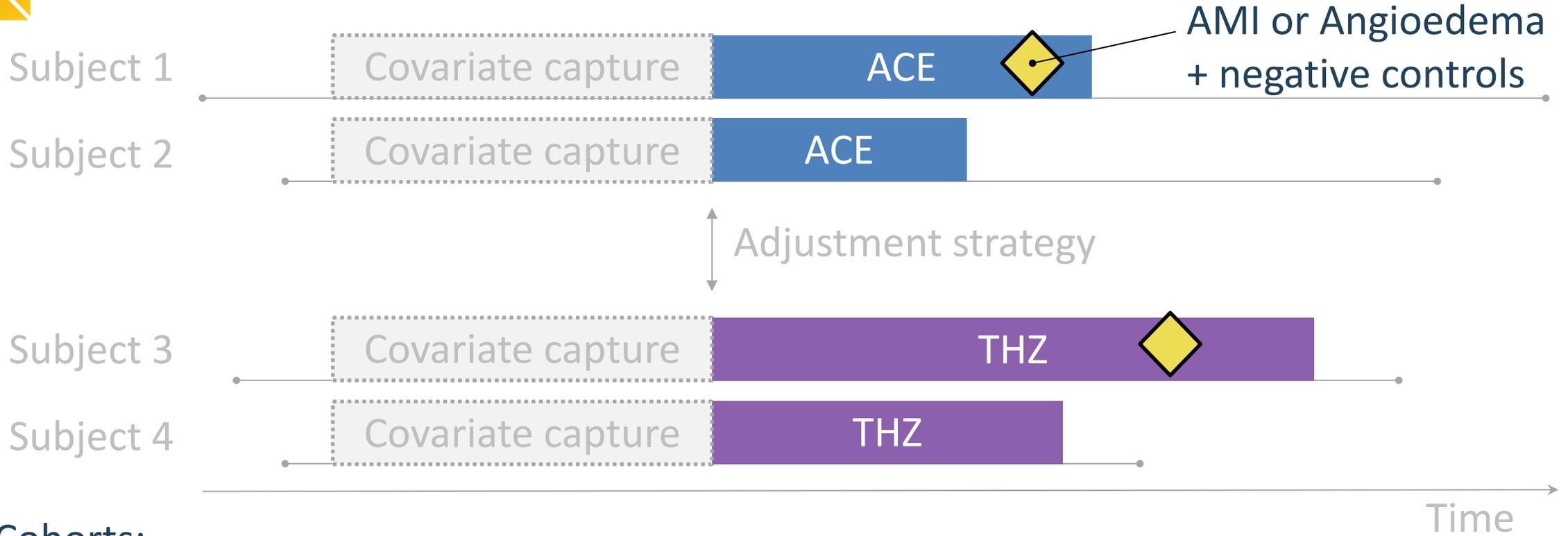
New-user cohort method



Compare the hazard of the **Outcome** in **Target** to **Comparator**



Hypertension



Cohorts:

- New users of ACE
- New users of THZ
- AMI
- Angioedema



Define cohorts

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Cohort #7

[OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension

Definition **?** | Concept Sets | Generation | Reporting | Export | Messages **3**

enter a cohort definition description here

Cohort Entry Events **?**

Events having any of the following criteria: + Add Initial Event ▾

a drug exposure of **ACE inhibitors** + Add attribute... ▾ Delete Criteria

✗ for the first time in the person's history

with continuous observation of at least **365** days before and **0** days after event index date

Limit initial events to: **earliest event** per person. Restrict initial events

Inclusion Criteria **?**

New inclusion criteria has hypertension diagnosis in 1 yr prior to treatment Copy Delete

enter an inclusion rule description

having **all** of the following criteria: + Add criteria to group... ▾

with **at least** **1** using **all** occurrences of:

a condition occurrence of **Hypertensive disorder** + Add attribute... ▾ Delete Criteria

Design study



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Population Level Effect Estimation - Comparative Cohort Analysis #43

[OHDSI EU 2019] Comparative effectiveness of first-line ACE inhibitor monotherapy vs first-line thiazide diuretic monotherapy for treatment of hypert

Specification

Utilities

Comparing ACE inhibitors to Thiazide and thiazide-like diuretics for the outcomes of acute myocardial infarction and angioedema.

VIEW:

Full Specification

Comparisons

Analysis Settings

Evaluation Settings

Comparative Cohort Settings

Comparisons

+ Add Comparison

Show 10 entries

Filter:

Remove	Target	Comparator	Outcomes	NC Outcomes	Copy
	[OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension	[OHDSI EU 2019] New users of Thiazide-like diuretics as first-line monotherapy for hypertension	[OHDSI EU 2019] Acute myocardial infarction events (1+ more outcome)	[OHDSI EU 2019] Negative controls	

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Effect Estimation Analysis Settings



Study package generation

ATLAS

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← [OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension

Population Level Effect Estimation - Comparative Cohort Analysis #2

[OHDSI EU 2019] Comparative effectiveness of first-line ACE inhibitor monotherapy vs first-line thiazide diuretic monotherapy for treatment of I

Specification Utilities

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Review Full Study Specification

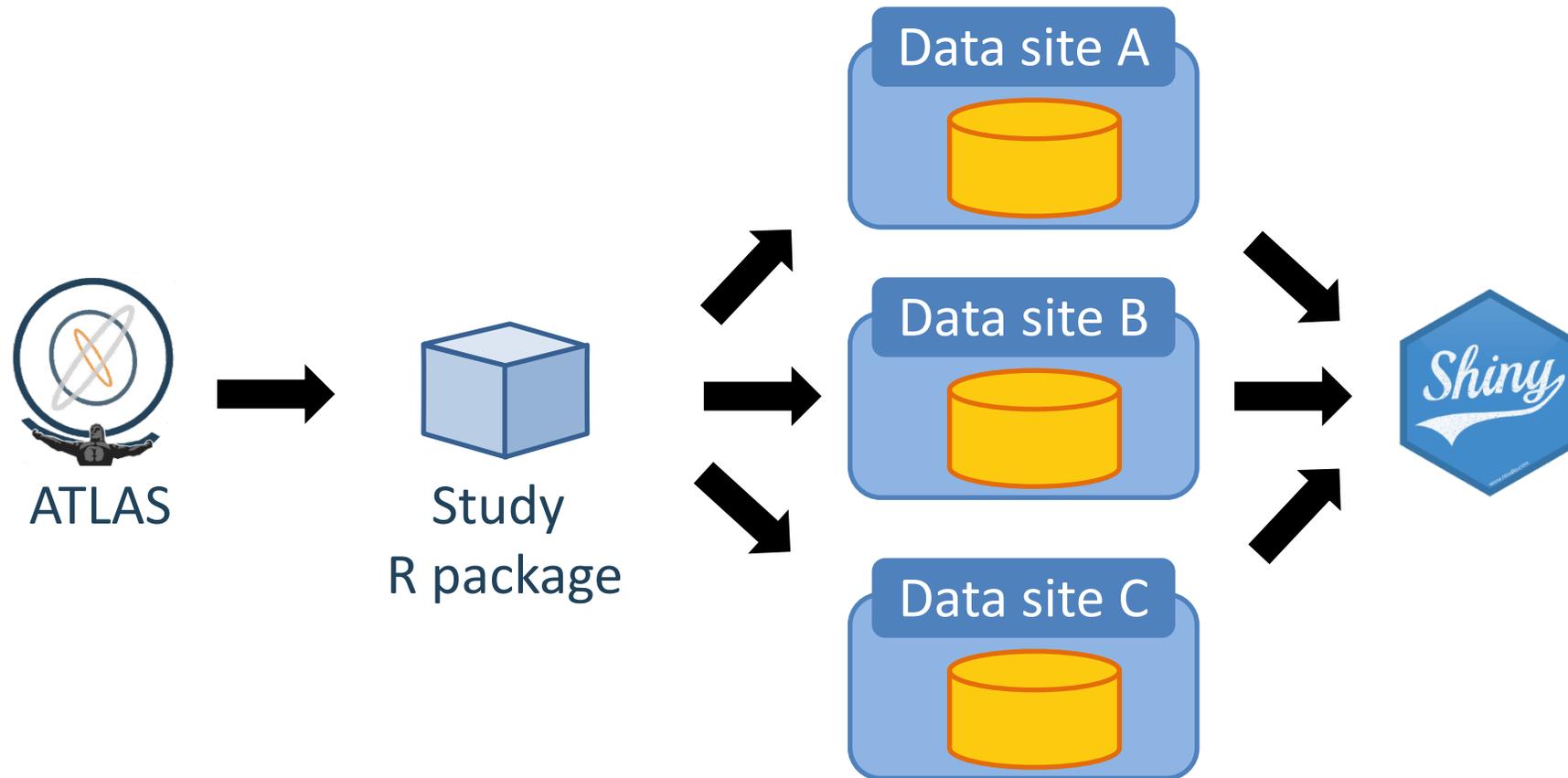
Column visibility Copy CSV Show 10 entries Filter:

Target Cohort Name	Comparator Cohort Name	Outcome Cohort Name	Analysis Name	Time At Risk	Outcome Model
[OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension (8)	[OHDSI EU 2019] New users of Thiazide-like diuretics as first-line monotherapy for hypertension	[OHDSI EU 2019] Acute myocardial infarction events	PS stratification, on-treatment	1-0d (min: 1d)	cox
[OHDSI EU 2019] New users of Thiazide-like diuretics as first-line monotherapy for hypertension (8)	[OHDSI EU 2019] New users of ACE inhibitors as first-line monotherapy for hypertension	[OHDSI EU 2019] Acute myocardial infarction events	PS stratification, intent-to-treat	1-99999d (min: 1d)	cox

[OHDSI EU 2019] [OHDSI EU 2019] New



Study design to results



Results: Overview

LEGEND basic viewer

About Specific research questions

Indication

Hypertension

Exposure group

Drug class

Include combination exposures

Target

ACE inhibitors

Comparator

Thiazide or thiazide-like diuretics

Outcome

Acute myocardial infarction

Data source

- CCAE
- CUMC
- IMSC
- JMDC
- MDCD
- MDCR
- NHIS_NSC
- Optum
- Panther
- Meta-analysis

Analysis

- PS stratification, on-treatment
- PS stratification, intent-to-treat
- PS matching, on-treatment
- PS matching, intent-to-treat

Show 15 entries

Analysis	Data source	HR	LB	UB	P	Cal.HR	Cal.LB	Cal.UB	Cal.P
PS stratification, on-treatment	CCAIE	1.12	0.99	1.26	0.07	1.17	0.97	1.46	0.10
PS stratification, on-treatment	CUMC	0.94	0.59	1.51	0.79	1.03	0.65	1.76	0.84
PS stratification, on-treatment	MDCD	1.43	1.02	2.06	0.04	1.45	1.03	2.09	0.03
PS stratification, on-treatment	MDCR	1.07	0.91	1.27	0.42	1.10	0.91	1.36	0.29
PS stratification, on-treatment	Meta-analysis	1.16	1.08	1.23	0.00	1.19	1.04	1.40	0.01
PS stratification, on-treatment	NHIS_NSC	0.79	0.30	2.13	0.64	0.75	0.27	2.06	0.54
PS stratification, on-treatment	Optum	1.19	1.08	1.32	0.00	1.23	1.05	1.49	0.01
PS stratification, on-treatment	Panther	1.22	1.02	1.46	0.03	1.20	0.97	1.59	0.03

Showing 1 to 8 of 8 entries

Previous 1 Next

Power Propensity scores Covariate balance Systematic error Forest plot

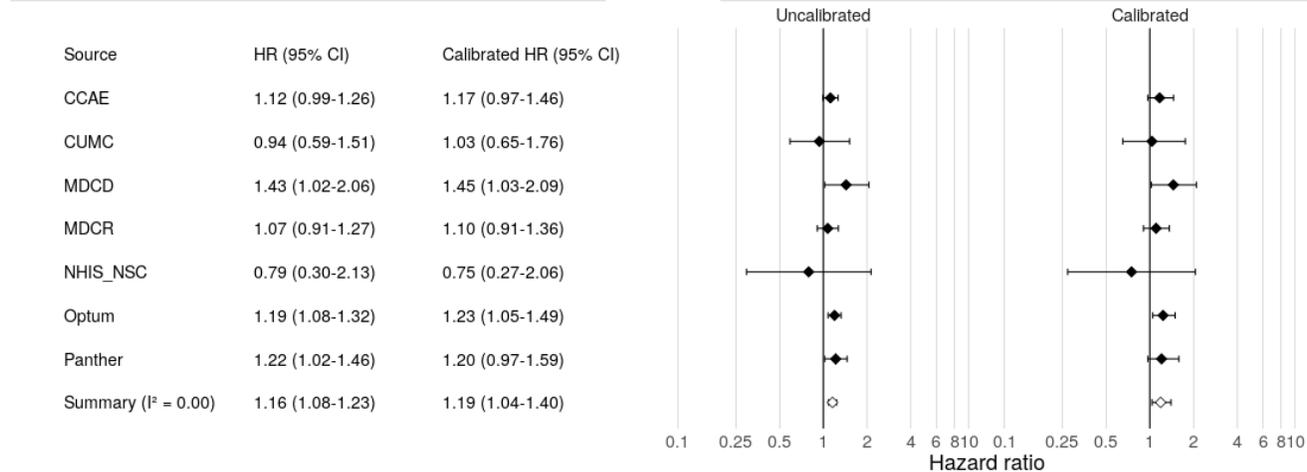


Figure 6. Forest plot showing the per-database and summary hazard ratios (and 95 percent confidence intervals) comparing ACE inhibitors to Thiazide or thiazide-like diuretics for the outcome of Acute myocardial infarction, using stratification. Estimates are shown both before and after empirical calibration. The I2 is computed on the uncalibrated estimates.



Results: Power

Power

Attrition

Population characteristics

Propensity scores

Covariate balance

Systematic error

Kaplan-Meier

Table 1a. Number of subjects, follow-up time (in years), number of outcome events, and event incidence rate (IR) per 1,000 patient years (PY) in the target (*ACE inhibitors*) and comparator (*Thiazide or thiazide-like diuretics*) group after stratification, as well as the minimum detectable relative risk (MDRR). Note that the IR does not account for any stratification.

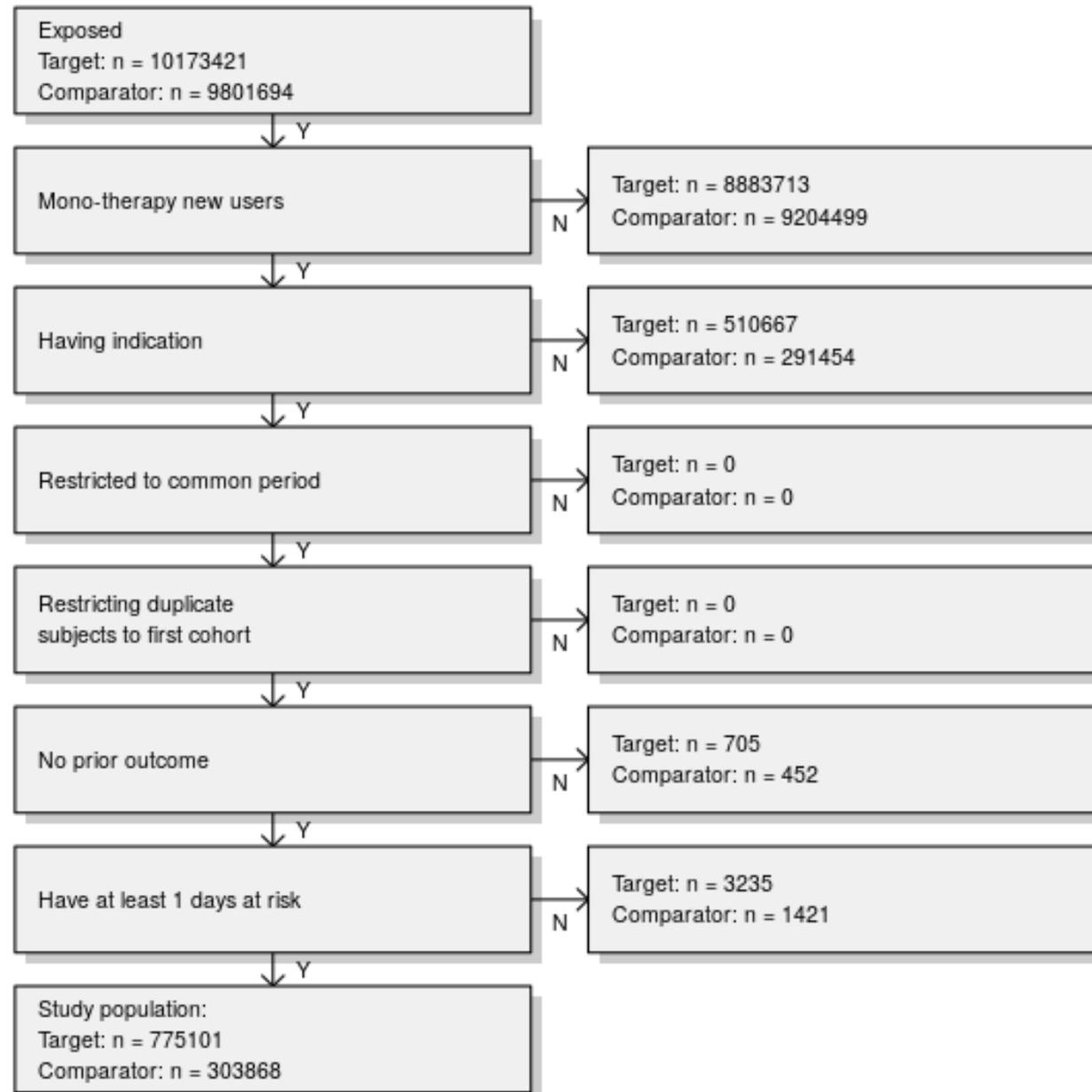
Target subjects	Comparator subjects	Target years	Comparator years	Target events	Comparator events	Target IR (per 1,000 PY)	Comparator IR (per 1,000 PY)	MDRR
775,101	303,868	588,000	213,511	784	169	1.33	0.79	1.22

Table 1b. Time (days) at risk distribution expressed as minimum (min), 25th percentile (P25), median, 75th percentile (P75), and maximum (max) in the target (*ACE inhibitors*) and comparator (*Thiazide or thiazide-like diuretics*) cohort after stratification.

Cohort	Min	P10	P25	Median	P75	P90	Max
Target	1	29	38	116	530	721	6,218
Comparator	1	29	29	95	486	676	6,101



Results: Attrition





Results: Patient characteristics

[Power](#)[Attrition](#)[Population characteristics](#)[Propensity scores](#)[Covariate balance](#)[Systematic error](#)[Kaplan-Meier](#)

Table 2. Select characteristics before and after stratification, showing the (weighted) percentage of subjects with the characteristics in the target (*ACE inhibitors*) and comparator (*Thiazide or thiazide-like diuretics*) group, as well as the standardized difference of the means.

Characteristic	Before stratification			After stratification		
	Target	Comparator	Std. diff	Target	Comparator	Std. diff
	%	%		%	%	
Age group						
10-14	0.2	0.1	0.02	0.1	0.1	0.00
15-19	0.7	0.6	0.02	0.7	0.7	0.00
20-24	1.4	1.6	-0.02	1.4	1.5	0.00
25-29	2.6	3.5	-0.06	2.8	2.7	0.00
40-44	12.1	13.4	-0.04	12.4	12.3	0.00
45-49	16.1	16.3	-0.01	16.2	15.9	0.01
50-54	18.7	17.7	0.03	18.5	18.4	0.00
55-59	18.3	16.2	0.06	17.8	18.0	0.00
60-64	15.5	13.2	0.06	15.0	15.3	-0.01
65-69	1.3	1.1	0.02	1.3	1.3	0.00
Gender: female	38.4	60.7	-0.46	44.7	45.2	-0.01
Medical history: General						
Acute respiratory disease	24.5	26.1	-0.04	25.0	25.4	-0.01
Attention deficit hyperactivity disorder	1.0	1.1	-0.01	1.1	1.0	0.00



Results: Propensity score

Power

Attrition

Population characteristics

Propensity scores

Covariate balance

Systematic error

Kaplan-Meier

ACE inhibitors Thiazine or thiazide-like diuretics

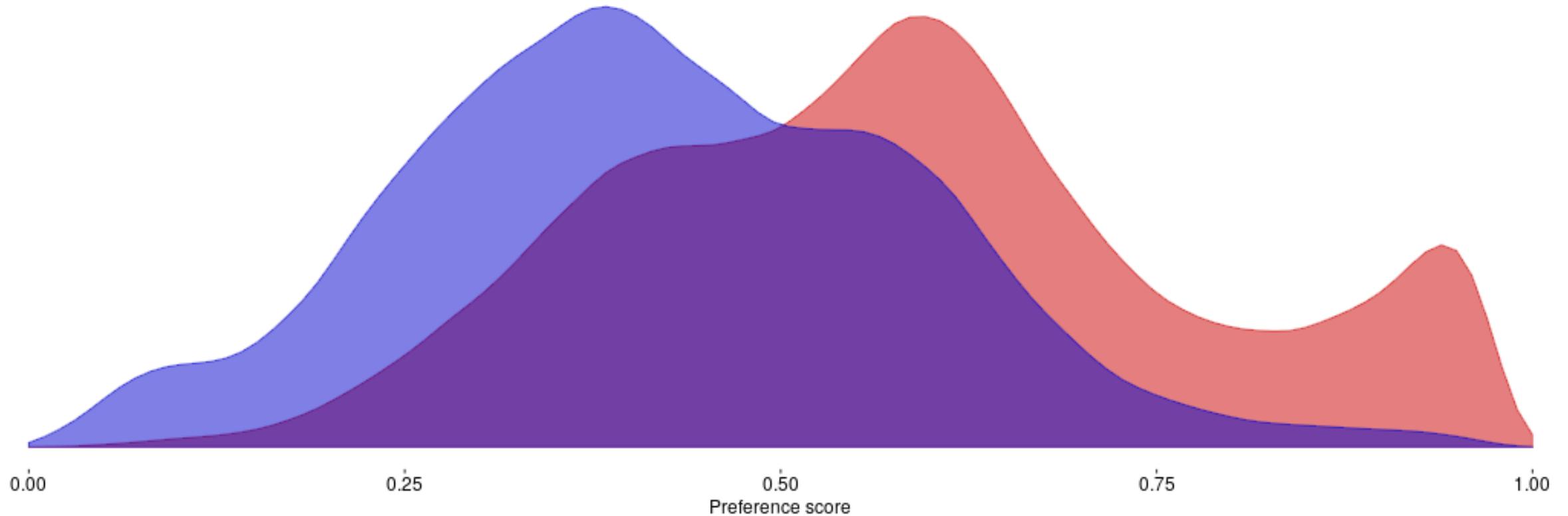


Figure 2. Preference score distribution. The preference score is a transformation of the propensity score that adjusts for differences in the sizes of the two treatment groups. A higher overlap indicates subjects in the two groups were more similar in terms of their predicted probability of receiving one treatment over the other.



Results: Covariate balance

Power Attrition Population characteristics Propensity scores **Covariate balance** Systematic error Kaplan-Meier

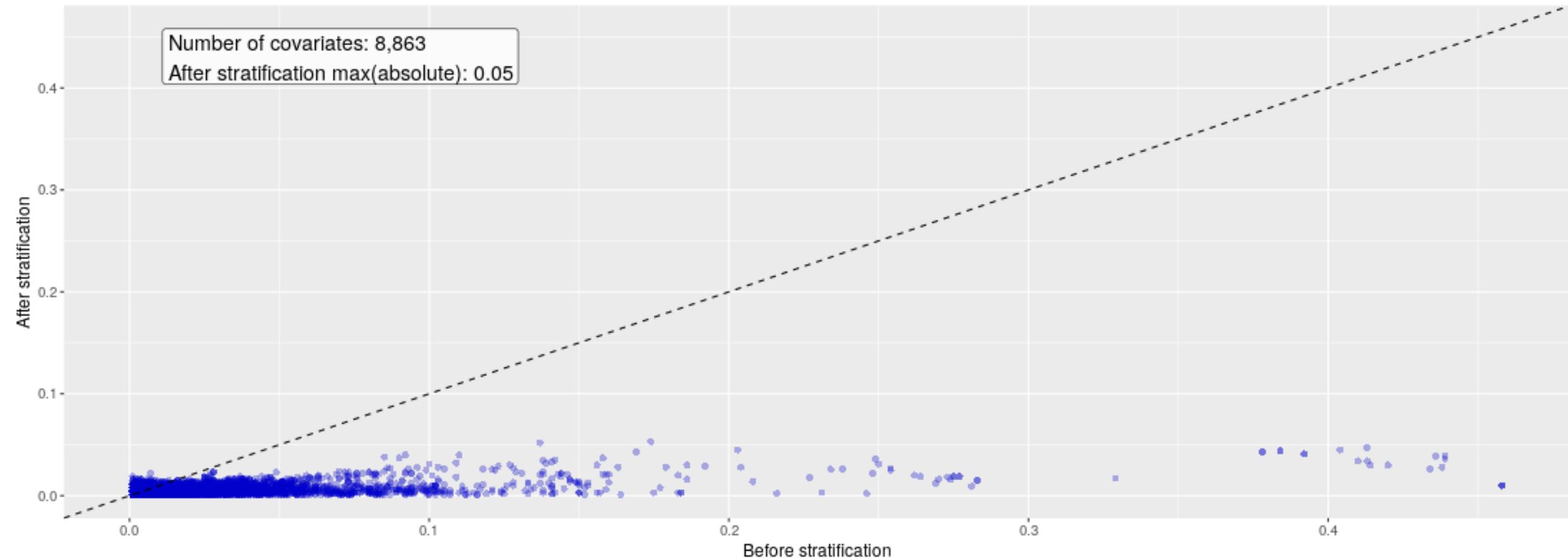


Figure 3. Covariate balance before and after stratification. Each dot represents the standardized difference of means for a single covariate before and after stratification on the propensity score. Move the mouse arrow over a dot for more details.



Results: Estimates for negative and positive controls

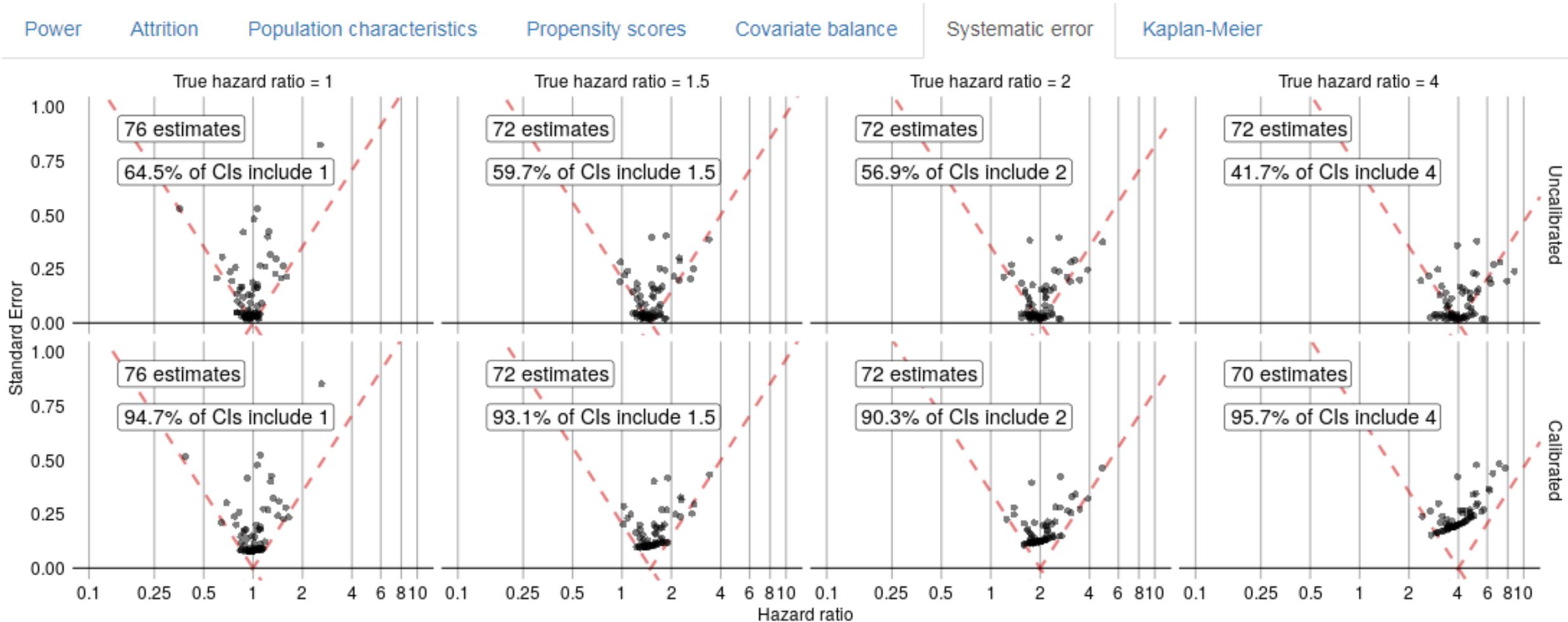
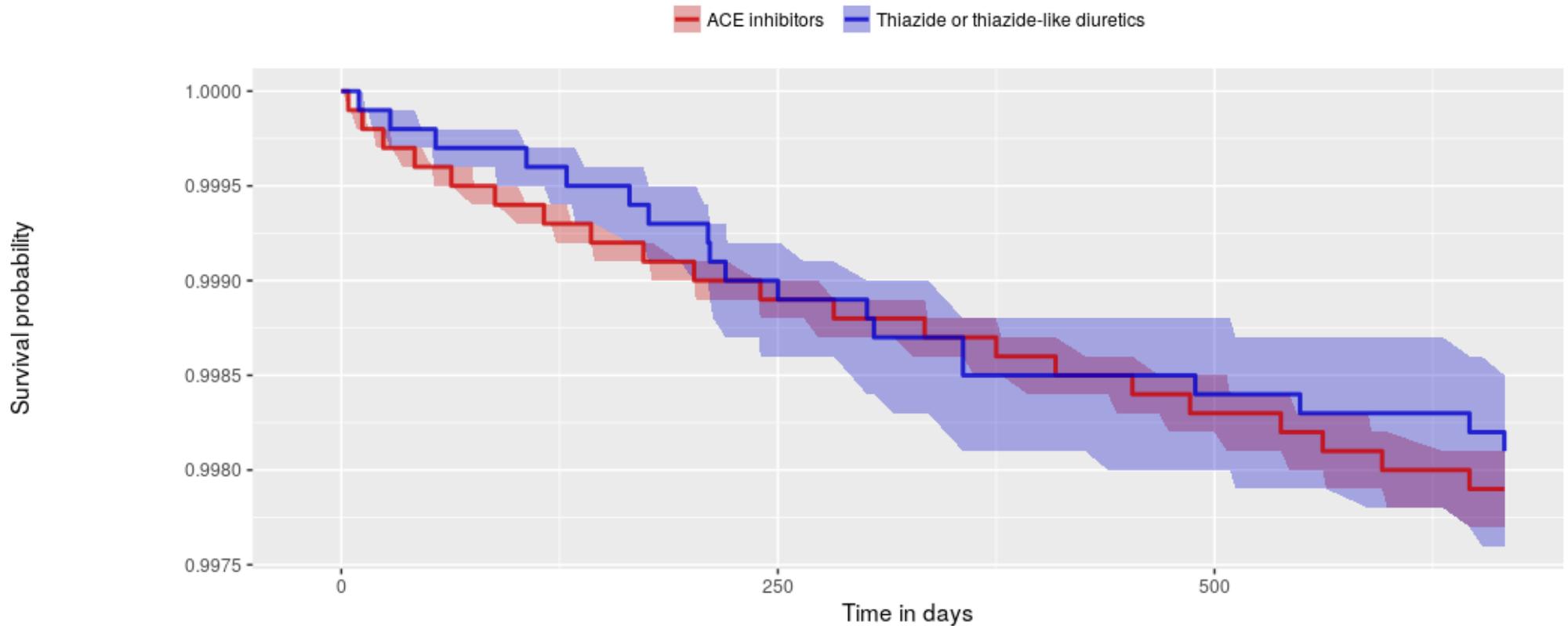


Figure 4. Systematic error. Effect size estimates for the negative controls (true hazard ratio = 1) and positive controls (true hazard ratio > 1), before and after calibration. Estimates below the diagonal dashed lines are statistically significant ($\alpha = 0.05$) different from the true effect size. A well-calibrated estimator should have the true effect size within the 95 percent confidence interval 95 percent of times.



Result: Kaplan-Meier plot

Power Attrition Population characteristics Propensity scores Covariate balance Systematic error Kaplan-Meier



Number at risk			
ACE inhibitors	775,101	241,666	124,241
Thiazide or thiazide-like diuretics	303,868	85,093	44,191

Figure 5. Kaplan Meier plot, showing survival as a function of time. This plot is adjusted for the propensity score stratification: The target curve (*ACE inhibitors*) shows the actual observed survival. The comparator curve (*Thiazide or thiazide-like diuretics*) applies reweighting to approximate the counterfactual of what the target survival would look like had the target cohort been exposed to the comparator instead. The shaded area denotes the 95 percent confidence interval.



Result: Forest plot

Power Propensity scores Covariate balance Systematic error Forest plot

Source	HR (95% CI)	Calibrated HR (95% CI)
CCAEC	1.96 (1.65-2.34)	2.01 (1.55-2.80)
CUMC	1.08 (0.52-2.29)	1.17 (0.60-2.49)
MDCD	4.57 (3.00-7.19)	4.52 (2.85- NA)
MDCR	2.44 (1.52-4.13)	2.46 (1.49-4.17)
Optum	1.99 (1.62-2.47)	2.03 (1.56-2.80)
Panther	2.70 (1.97-3.78)	2.31 (1.62-4.03)
Summary ($I^2 = 0.73$)	2.32 (1.79-3.00)	2.26 (1.68-3.30)

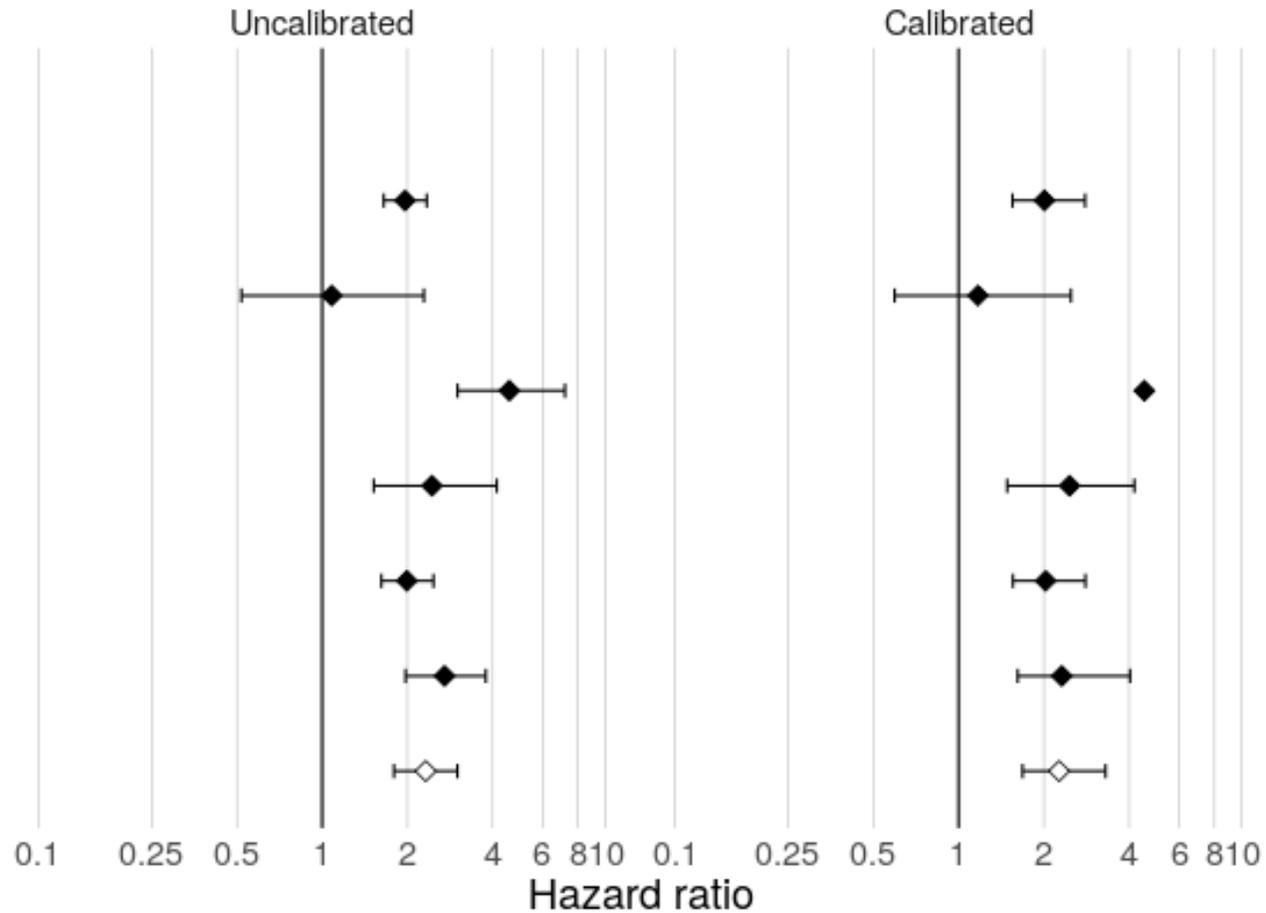


Figure 6. Forest plot showing the per-database and summary hazard ratios (and 95 percent confidence intervals) comparing ACE inhibitors to Thiazide or thiazide-like diuretics for the outcome of Angioedema, using stratification. Estimates are shown both before and after empirical calibration. The I^2 is computed on the uncalibrated estimates.



Final thoughts

- Standardization does not mean one-size-fits-all
- Exposes design choices
- Enables:
 - Consistency
 - Transparency
 - Reproducibility
 - Efficiency