OHDSI Tools Ecosystem

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Odysseus Data Services

Agenda

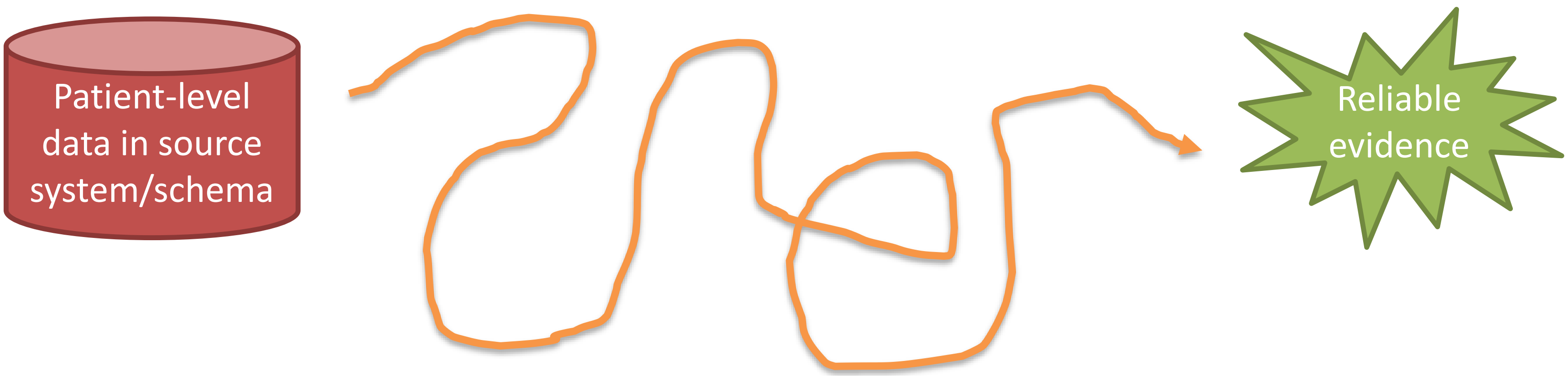
800am-900am	Registration	
900am-1000am	Overview of OHDSI tools ecosystem	Patrick Ryan
1000am-1030am	Vocabulary	Patrick Ryan
1030am-1045am	Break	
1045am-1115am	Data sources (ACHILLES)	Kristin Feeney Kostka
1115am-1230pm	Cohort definition and characterization	Gowtham Rao
1230pm-130pm	Lunch	
130pm-200pm	Incidence rate	Kristin Feeney
200pm-230pm	Population-level effect estimation	Anthony Sena
230pm-300pm	Patient-level prediction	Anthony Sena
300pm-330pm	Break	
330pm-400pm	Network analyses (ARACHNE)	Greg Klebanov
400pm-500pm	Design and implement your own OHDSI study!	Everyone

OHDSI

OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

Overview of the OHDSI tools ecosystem

The journey to real-world evidence



One-time Repeated

The journey to real-world evidence

Patient-level data in source system/schema

<u>Different types of observational data:</u>

- **Populations**
  - Pediatric vs. elderly
  - Socioeconomic disparities
- **Care setting**
  - Inpatient vs. outpatient
  - Primary vs. secondary care
- **Data capture process**
  - Administrative claims
  - Electronic health records
  - Clinical registries
- **Health system**
  - Insured vs. uninsured
  - Country policies

Reliable evidence

One-time Repeated

The journey to real-world evidence

Patient-level data in source system/schema

<u>Types of evidence desired:</u>

- **Cohort identification**
    - Clinical trial feasibility and recruitment
- **Clinical characterization**
    - Treatment utilization
    - Disease natural history
    - Quality improvement
- **Population-level effect estimation**
    - Safety surveillance
    - Comparative effectiveness
- **Patient-level prediction**
    - Precision medicine
    - Disease interception

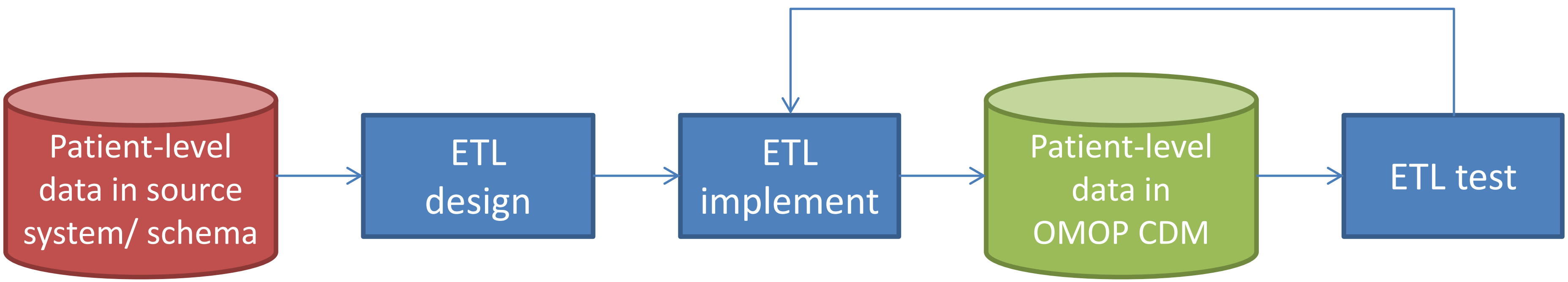
Reliable evidence

One-time

Repeated

What are your research questions?

Structuring the journey from source to a common data model



OHDSI tools built to help

WhiteRabbit: profile your source data

RabbitInAHat: map your source structure to CDM tables and fields

ATHENA: standardized vocabularies for all CDM domains

Usagi: map your source codes to CDM vocabulary

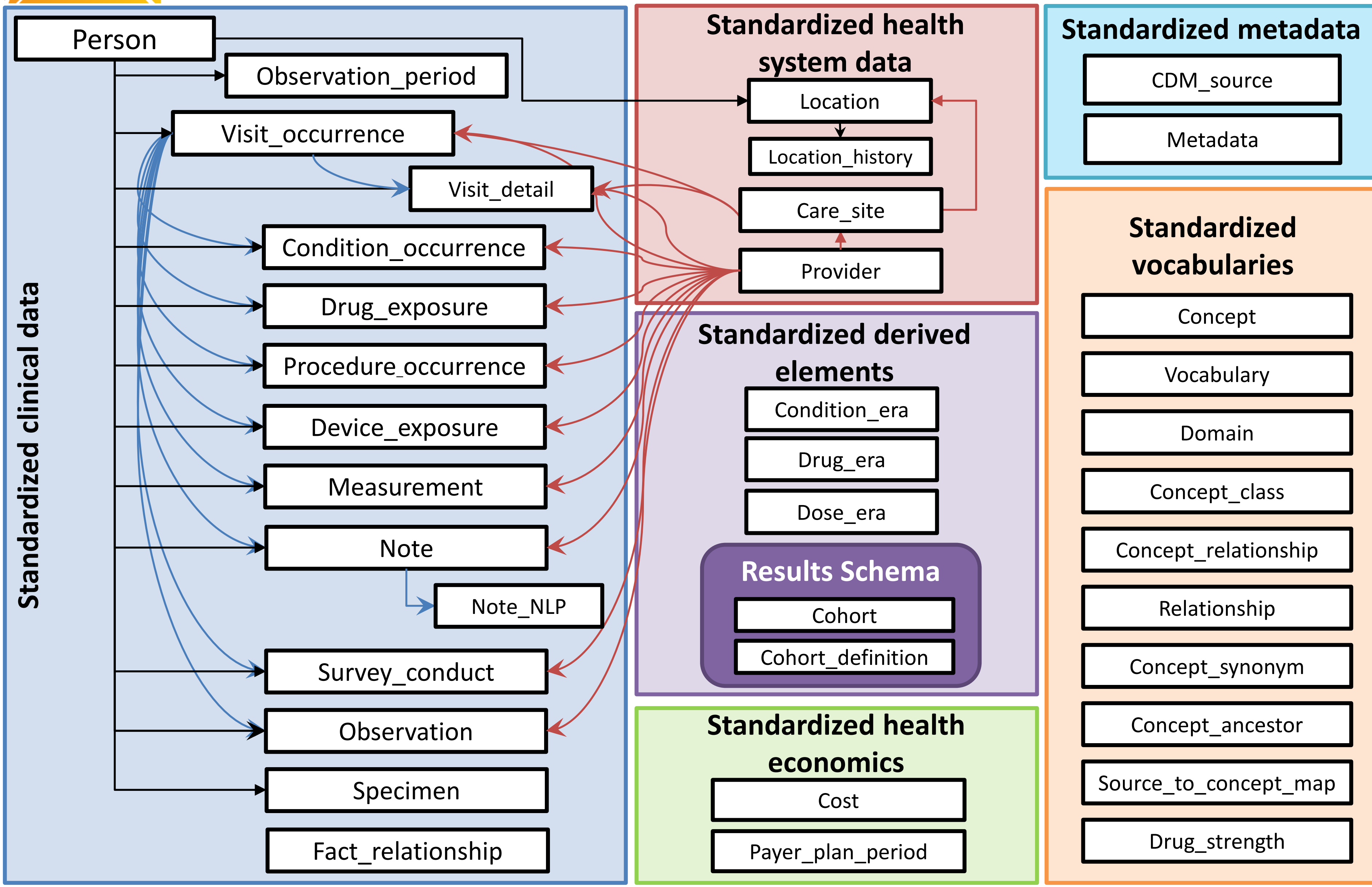
CDM: DDL, index, constraints for various RDBMS flavors; Vocabulary tables with loading scripts

ACHILLES: profile your CDM data; review data quality assessment; explore population-level summaries

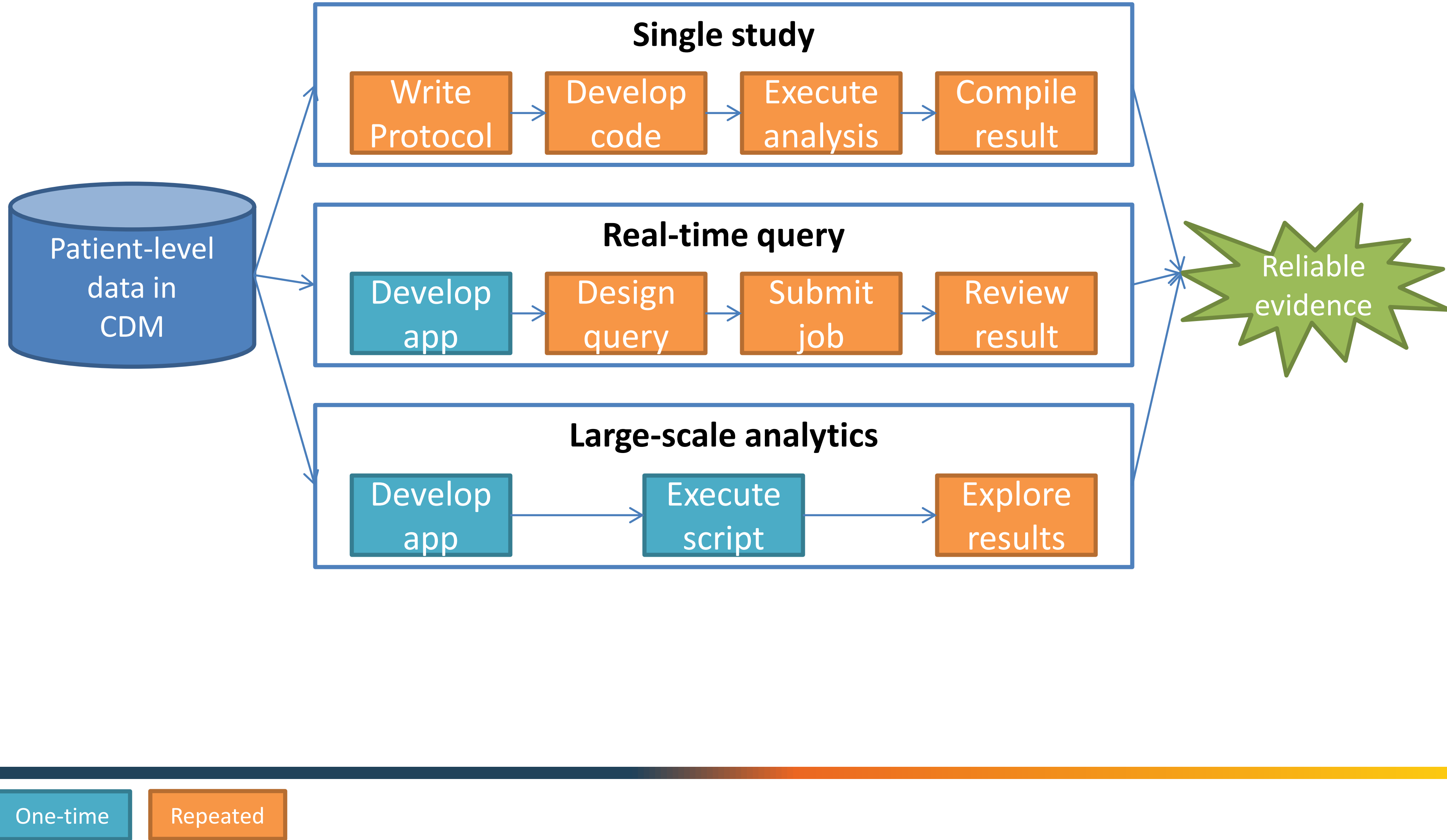
OHDSI Forums: Public discussions for OMOP CDM Implementers/developers

http://github.com/OHDSI

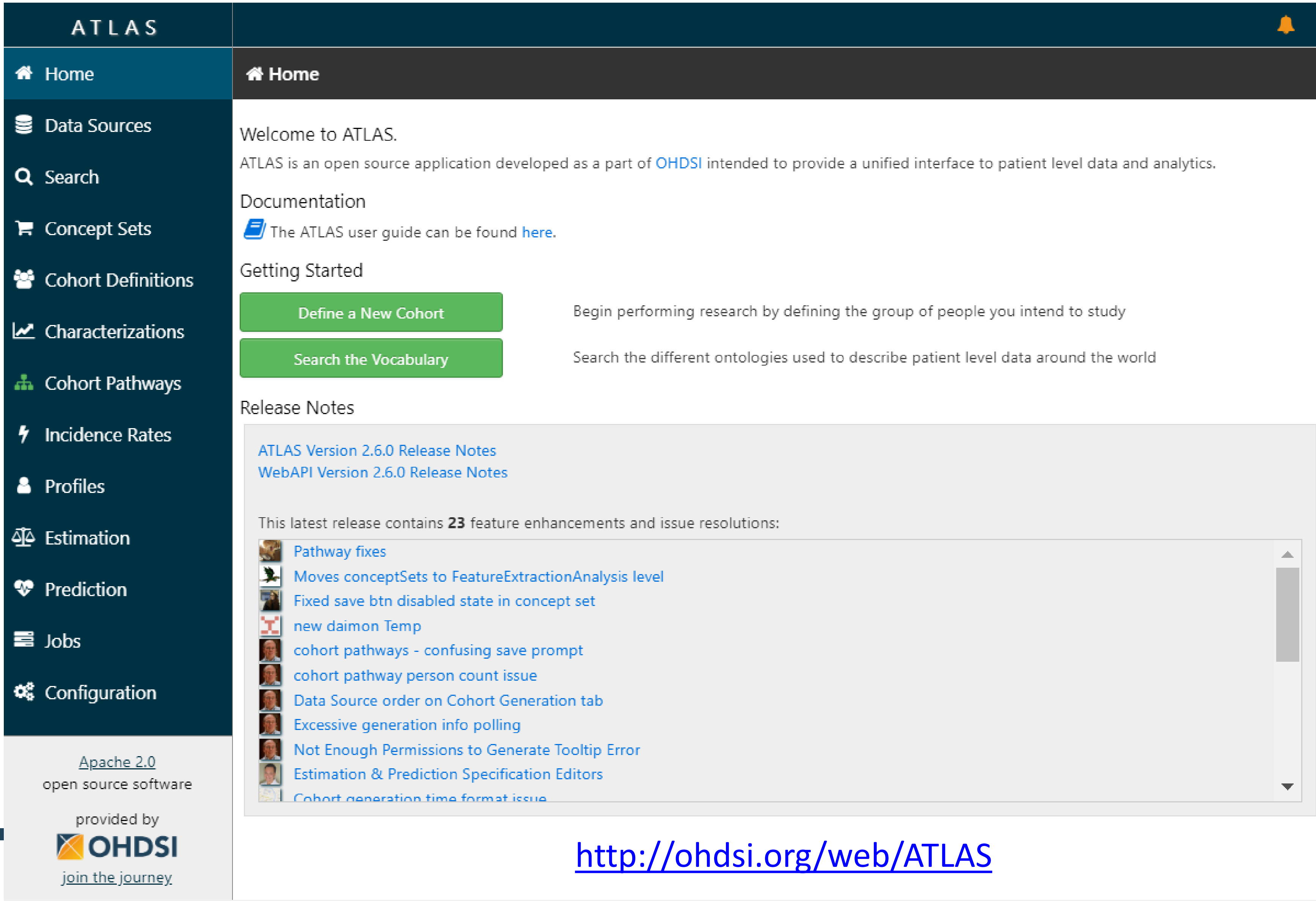
OMOP CDM Version 6



Structuring the journey from a common data model to evidence

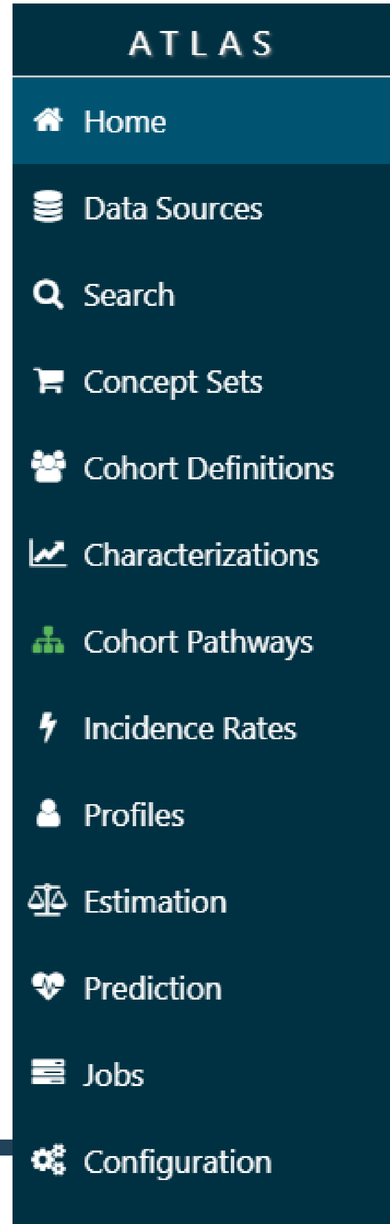


ATLAS – an open-source platform to design and execute observational analyses



http://ohdsi.org/web/ATLAS

Analytic use cases supported in ATLAS



Estimation methods

Cohort Method
New-user cohort studies using large-scale regression for propensity and outcome models

Self-Controlled Case Series
Self-Controlled Case Series analysis using few or many predictors, includes splines for age and seasonality.

Self-Controlled Cohort
A self-controlled cohort design, where time preceding exposure is used as control.

IC Temporal Pattern Disc.
A self-controlled design, but using temporal patterns around other exposures and outcomes to correct for time-varying confounding.

Case-control
Case-control studies, matching controls on age, gender, provider, and visit date. Allows nesting of the study in another cohort.

Case-crossover
Case-crossover design including the option to adjust for time-trends in exposures (so-called case-time-control).

Prediction methods

Patient Level Prediction
Build and evaluate predictive models for user-specified outcomes, using a wide array of machine learning algorithms.

Feature Extraction
Automatically extract large sets of features for user-specified cohorts using data in the CDM.

Method characterization

Empirical Calibration
Use negative control exposure-outcome pairs to profile and calibrate a particular analysis design.

Method Evaluation
Use real data and established reference sets as well as simulations injected in real data to evaluate the performance of methods.

Supporting packages

Database Connector
Connect directly to a wide range of database platforms, including SQL Server, Oracle, and PostgreSQL.

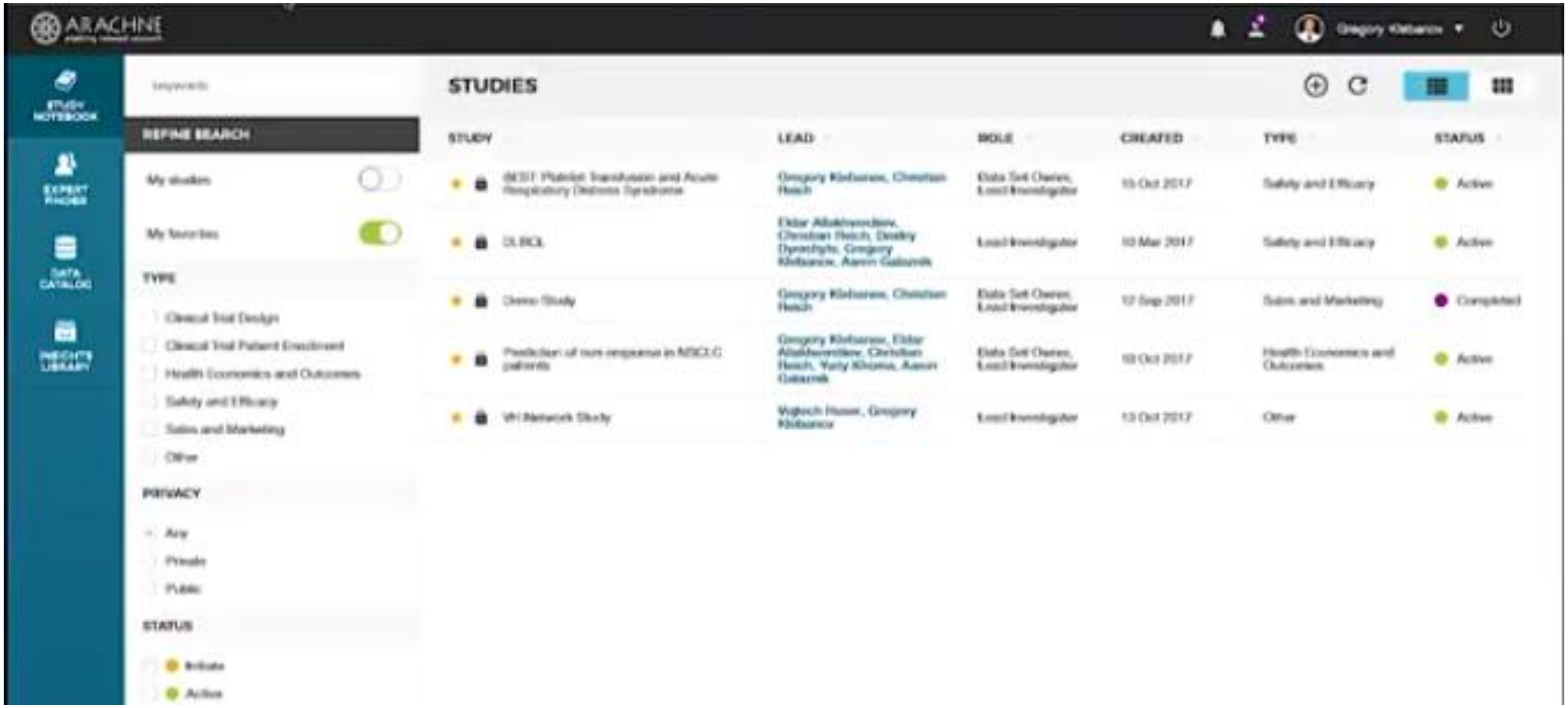
Sql Render
Generate SQL on the fly for the various SQL dialects.

Cyclops
Highly efficient implementation of regularized logistic, Poisson and Cox regression.

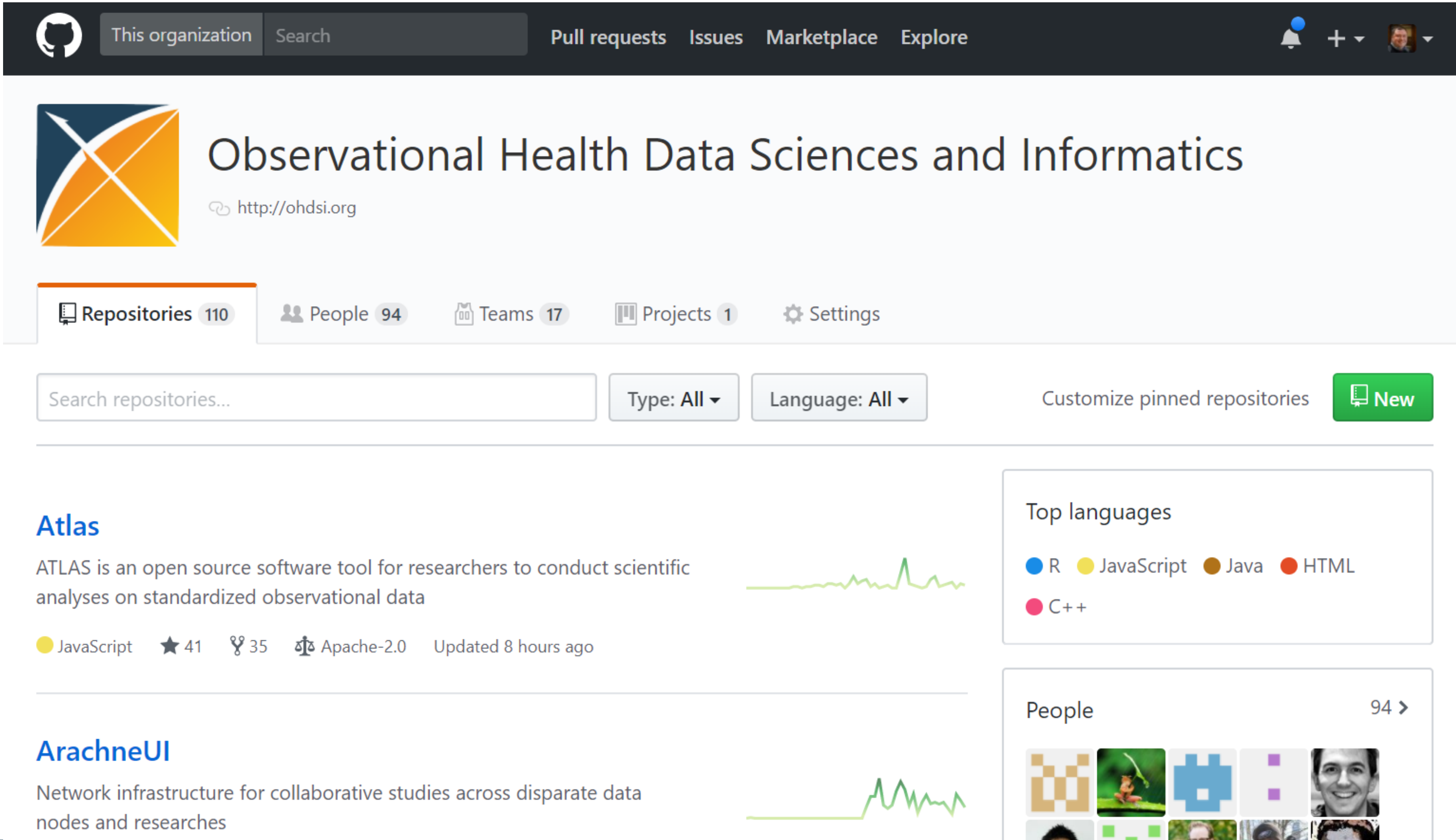
Ohdsi R Tools
Support tools that didn't fit other categories, including tools for maintaining R libraries.

Under construction

ARACHNE – an open-source platform to enable analyses across the OHDSI network



All of OHDSI tools are open source and freely available



http://github.com/OHDSI

Cardiovascular, Bleeding, and Mortality Risks in Elderly Medicare Patients Treated With Dabigatran or Warfarin for Nonvalvular Atrial Fibrillation

David J. Graham, MD, MPH; Marsha E. Reichman, PhD; Michael Wernecke, BA; Rongmei Zhang, PhD; Mary Ross Southworth, PharmD; Mark Levenson, PhD; Ting-Chang Sheu, MPH; Katrina Mott, MHS; Margie R. Goulding, PhD; Monika Houstoun, PharmD, MPH; Thomas E. MaCurdy, PhD; Chris Worrall, BS; Jeffrey A. Kelman, MD, MMSc

Background—The comparative safety of dabigatran versus warfarin for treatment of nonvalvular atrial fibrillation in general practice settings has not been established.

Methods and Results—We formed new-user cohorts of propensity score–matched elderly patients enrolled in Medicare who initiated dabigatran or warfarin for treatment of nonvalvular atrial fibrillation between October 2010 and December 2012. Among 134 414 patients with 37 587 person-years of follow-up, there were 2715 primary outcome events. The hazard ratios (95% confidence intervals) comparing dabigatran with warfarin (reference) were as follows: ischemic stroke, 0.80 (0.67–0.96); intracranial hemorrhage, 0.34 (0.26–0.46); major gastrointestinal bleeding, 1.28 (1.14–1.44); acute myocardial infarction, 0.92 (0.78–1.08); and death, 0.86 (0.77–0.96). In the subgroup treated with dabigatran 75 mg twice daily, there was no difference in risk compared with warfarin for any outcome except intracranial hemorrhage, in which case dabigatran risk was reduced. Most patients treated with dabigatran 75 mg twice daily appeared not to have severe renal impairment, the intended population for this dose. In the dabigatran 150-mg twice daily subgroup, the magnitude of effect for each outcome was greater than in the combined-dose analysis.

Conclusions—In general practice settings, dabigatran was associated with reduced risk of ischemic stroke, intracranial hemorrhage, and death and increased risk of major gastrointestinal hemorrhage compared with warfarin in elderly patients with nonvalvular atrial fibrillation. These associations were most pronounced in patients treated with dabigatran 150 mg twice daily, whereas the association of 75 mg twice daily with study outcomes was indistinguishable from warfarin except for a lower risk of intracranial hemorrhage with dabigatran. (*Circulation*. 2015;131:157-164. DOI: 10.1161/CIRCULATIONAHA.114.012061.)

Key Words: anticoagulant ■ pharmacoepidemiology ■ safety ■ thrombin inhibitor ■ warfarin

- Baseline characterization of target and comparator cohort
- Descriptive summaries of:
  - Demographics
  - Medical history (prior conditions)
  - Medication use (prior drugs)
  - Prior procedures
  - Risk scores

Table 1. Sociodemographic Factors, Medical Conditions, and Medication Use at Baseline in Propensity Score–Matched Medicare Beneficiaries Initiating Dabigatran or Warfarin for Atrial Fibrillation, 2010–2012

Characteristic	Dabigatran, % (n=67 207)	Warfarin, % (n=67 207)	Standardized Mean Difference
Age group, y			
65–74	42	41	0.01
75–84	43	43	0.01
≥85	16	16	0.00
Female sex	51	52	0.01
Race/ethnicity			
White	92	92	0.00
Black	3	3	0.00
Other	5	5	0.00
Medical history			
General			
Diabetes mellitus	33	34	0.00
Hypercholesterolemia	74	74	0.00
Hypertension	87	87	0.00
Kidney failure			
Acute	5	5	0.00
Chronic	13	13	0.00
Obesity	11	11	0.00
Peptic ulcer disease	<1	<1	0.00
Prior bleeding event			
Hospitalized	1	1	0.00
Not hospitalized	3	3	0.01
Smoking	16	16	0.01
Cardiovascular disease			
Acute myocardial infarction			
Past 1–30 d	1	1	0.01
Past 31–183 d	1	1	0.00
Coronary revascularization	16	16	0.01
Heart failure			
Hospitalized	4	4	0.01
Outpatient	14	14	0.00
Other ischemic heart disease	48	49	0.01
Stroke			
Past 1–30 d	2	2	0.00
Past 31–183 d	1	2	0.00
Other cerebrovascular disease	13	13	0.00
Transient ischemic attack	7	7	0.00
Cardioablation	2	2	0.00
Cardioversion	9	9	0.02
Other medical conditions			
Falls	5	5	0.00
Fractures	2	2	0.00
Syncope	10	10	0.00
Walker use	3	3	0.00
$CHADS_2$ score*			
0–1	28	28	0.01

(Continued)

Table 1. Continued

Characteristic	Dabigatran, % (n=67 207)	Warfarin, % (n=67 207)	Standardized Mean Difference
2	40	40	0.00
3	21	21	0.01
≥4	10	11	0.01
HAS-BLED score†			
1	9	9	0.01
2	50	50	0.01
3	32	32	0.01
≥4	9	9	0.00
Medication use			
General			
Estrogen replacement	2	3	0.00
H2 antagonists	5	5	0.00
NSAIDs	15	15	0.00
Proton pump inhibitors	26	27	0.01
SSRI antidepressants	13	13	0.01
Cardiovascular			
ACEI/ARB	59	59	0.00
Antiarrhythmics	25	25	0.01
Anticoagulants (injectable)	7	7	0.01
Antiplatelets	17	17	0.01
β-Blockers	70	71	0.00
Calcium channel blockers	42	42	0.01
Digoxin	17	16	0.00
Diuretics			
Loop	28	28	0.00
Potassium sparing	5	5	0.01
Thiazide	29	29	0.00
Nitrates	10	11	0.01
Statins	57	57	0.00
Fibrates	5	5	0.00
Diabetes related			
Insulin	6	6	0.00
Metformin	13	14	0.00
Sulfonylureas	9	10	0.00
Other	6	6	0.00
Metabolic inhibitors‡			
Amiodarone	10	10	0.00
Dronedarone	5	5	0.02
Verapamil	2	2	0.00
Azole antifungals	<1	<1	0.00

Additional factors included in the propensity score model are shown in the online-only Data Supplement. ACEI/ARB indicates angiotensin converting-enzyme inhibitor/angiotensin receptor blocker; NSAIDs, nonsteroidal anti-inflammatory drugs; and SSRI, selective serotonin reuptake inhibitor.

*The $CHADS_2$ score assigns points for the presence of congestive heart failure, hypertension, age≥75 y, diabetes mellitus, stroke, or transient ischemic attack.[11]

†The HAS-BLED score assigns points for the presence of hypertension, abnormal renal or liver function, stroke, bleeding history, labile international normalized ratio, age ≥65 y, and antiplatelet drug or alcohol use.[12,13] Labile international normalized ratio could not be determined from claims data and was excluded from our scoring.

‡Days supply of use overlapped with the date of first prescription for warfarin

Table 2. Outcome Event Counts, Incidence Rates, and Adjusted Hazard Ratios With 95% CIs Comparing Propensity Score–Matched New-User Cohorts of Dabigatran and Warfarin Treated for Nonvalvular Atrial Fibrillation, With Warfarin as the Reference Group

	No. of Events		Incidence Rate per 1000 Person-Years		[redacted]
	Dabigatran	Warfarin	Dabigatran	Warfarin	
Primary outcomes					
Ischemic stroke	205	270	11.3	13.9	
Major hemorrhage	777	851	42.7	43.9	
Gastrointestinal	623	513	34.2	26.5	
Intracranial	60	186	3.3	9.6	
Intracerebral	44	142	2.4	7.3	
Acute myocardial infarction	285	327	15.7	16.9	
Secondary outcomes					
All hospitalized bleeds	1079	1139	59.3	58.8	
Mortality*	603	744	32.6	37.8	

*For 1064 deaths not preceded by a primary study outcome, the adjusted hazard ratio (95% confidence interval [CI]) was 0.89 (0.79–1.00 P=0.051), whereas for 283 deaths occurring within 30 days after a primary outcome, the adjusted hazard ratio (95% CI) was 0.77 (0.61–0.98 P=0.03).

- Incidence rate during target and comparator cohorts based on observing new events during 'time-at-risk' for eight selected outcome cohorts

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	[redacted]	Adjusted Hazard Ratio (95% CI)	*P* Value
Primary outcomes			
Ischemic stroke		0.80 (0.67–0.96)	0.02
Major hemorrhage		0.97 (0.88–1.07)	0.50
Gastrointestinal		1.28 (1.14–1.44)	<0.001
Intracranial		0.34 (0.26–0.46)	<0.001
Intracerebral		0.33 (0.24–0.47)	<0.001
Acute myocardial infarction		0.92 (0.78–1.08)	0.29
Secondary outcomes			
All hospitalized bleeds		1.00 (0.92–1.09)	0.97
Mortality*		0.86 (0.77–0.96)	0.006

*For 1064 deaths not preceded by a primary study outcome, the adjusted hazard ratio (95% confidence interval [CI]) was 0.89 (0.79–1.00; *P*=0.051), whereas for 283 deaths occurring within 30 days after a primary outcome, the adjusted hazard ratio (95% CI) was 0.77 (0.61–0.98; *P*=0.03).

- Population-level effect estimation examining temporal association between target and comparator cohorts and eight selected outcome cohorts

The common building block of all observational analysis: cohorts

Required inputs:

Target cohort:
- Person
- cohort start date
- cohort end date

Comparator cohort:
- Person
- cohort start date
- cohort end date

Outcome cohort:
- Person
- cohort start date
- cohort end date

Desired outputs:

Clinical characterization
- Baseline summary of exposures (treatment utilization)

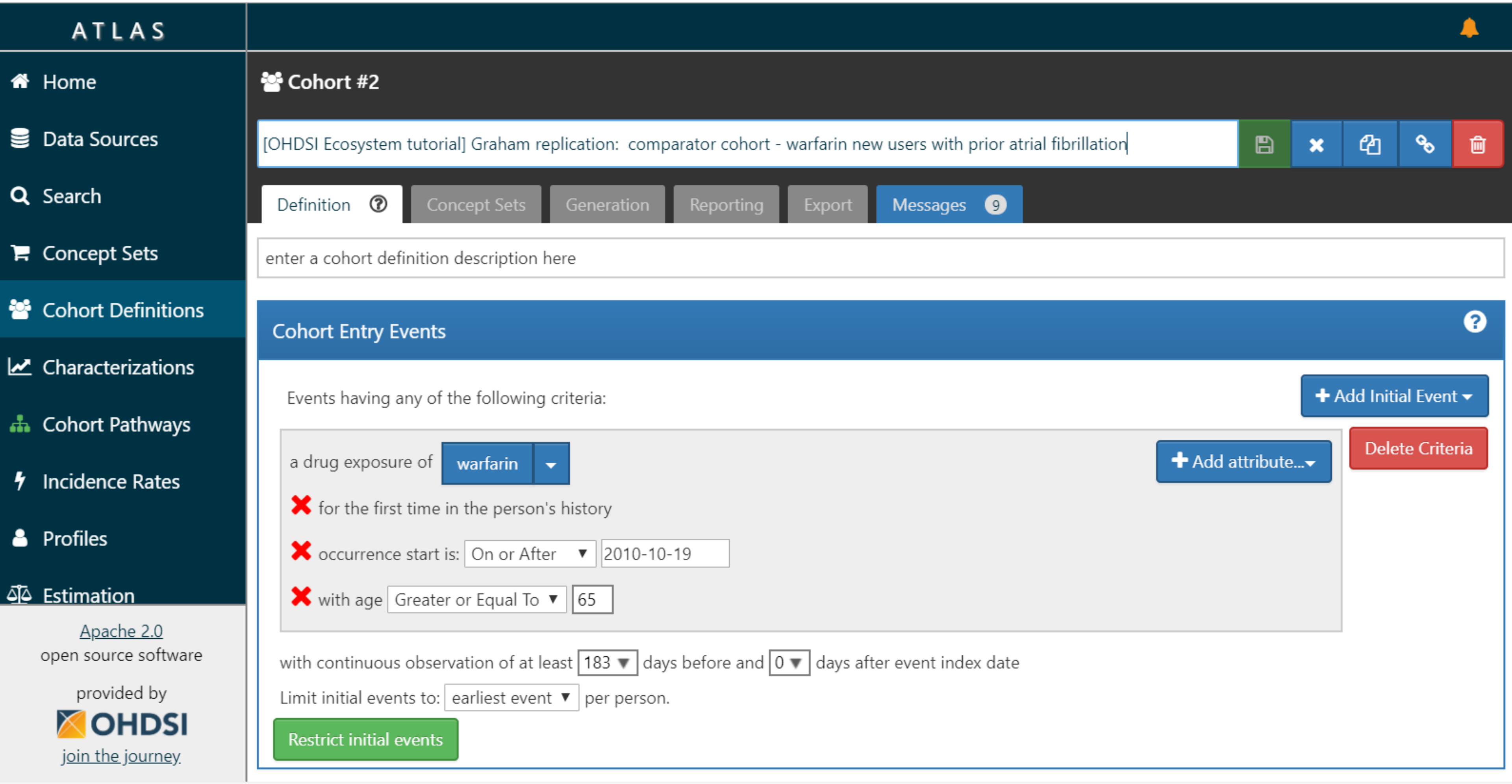
Clinical characterization
- Baseline summary of outcome (disease natural history)

Incidence summary
- Proportion/rate of outcome occurring during time-at-risk for exposure

Population-level effect estimation
- Relative risk (HR, OR, IRR) of outcome occurring during time-at-risk for exposure

Patient-level prediction
- Probability of outcome occurring during time-at-risk for each patient in population

OHDSI in action: Cohort definition



OHDSI in action: Cohort characterization

ATLAS

- Home
- Data Sources
- Search
- Concept Sets
- Cohort Definitions
- Characterizations
- Cohort Pathways
- Incidence Rates
- Profiles
- Estimation

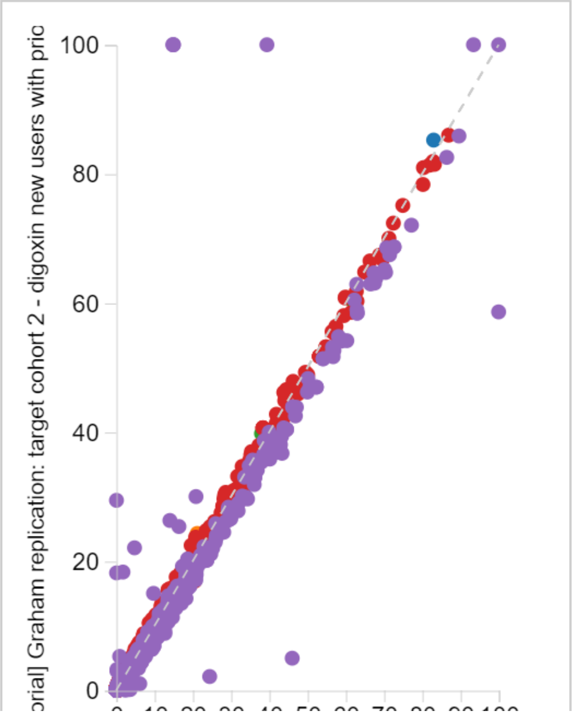
Apache 2.0
open source software

provided by
OHDSI
join the journey

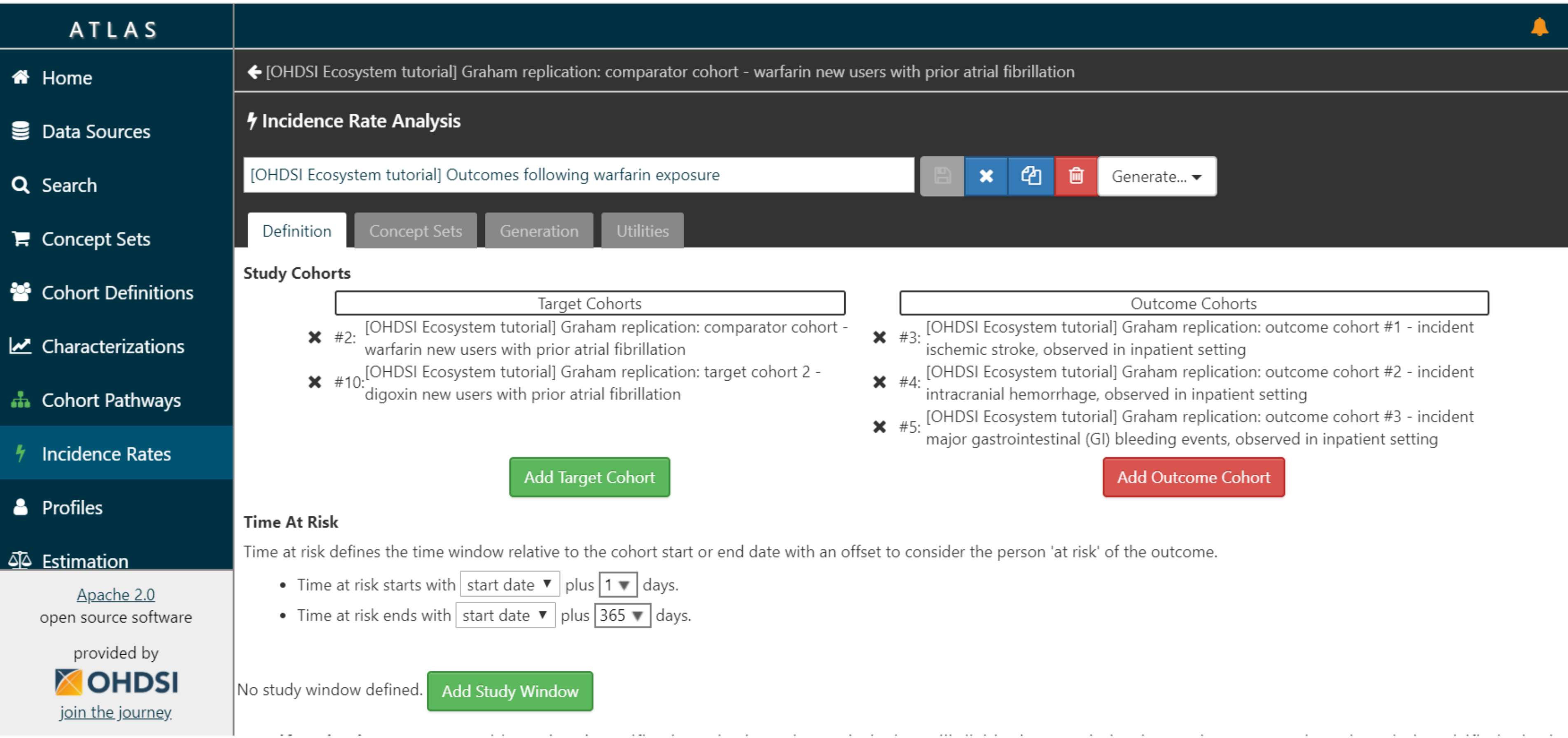
All prevalence covariates

Show 10 entries   Search:

Covariate	[OHDSI Ecosystem tutorial] Graham replication: comparator cohort - warfarin new users with prior atrial fibrillation		[OHDSI Ecosystem tutorial] Graham replication: target cohort 2 - digoxin new users with prior atrial fibrillation		Std diff
	Count	Pct	Count	Pct	
age group: 00-04	54	1.37%	21	1.34%	-0.0020
age group: 65-69	611	15.50%	257	16.36%	0.0153
age group: 70-74	836	21.20%	382	24.32%	0.0461
age group: 75-79	792	20.09%	323	20.56%	0.0074
age group: 80-84	689	17.47%	247	15.72%	-0.0304
age group: 85-89	548	13.90%	173	11.01%	-0.0578
age group: 90-94	272	6.90%	114	7.26%	0.0095
age group: 95-99	141	3.58%	54	3.44%	-0.0052
condition_era group during day -365 through	4	0.10%	3	0.19%	0.0165



OHDSI in action: incidence rate specification



OHDSI in action: incidence rate generation

Incidence Rate Analysis

[OHDSI Europe tutorial] Cardiovascular and Bleeding Risks in Elderly Medicare Patients Treate

Generate...

Definition | Concept Sets | Generation | Utilities

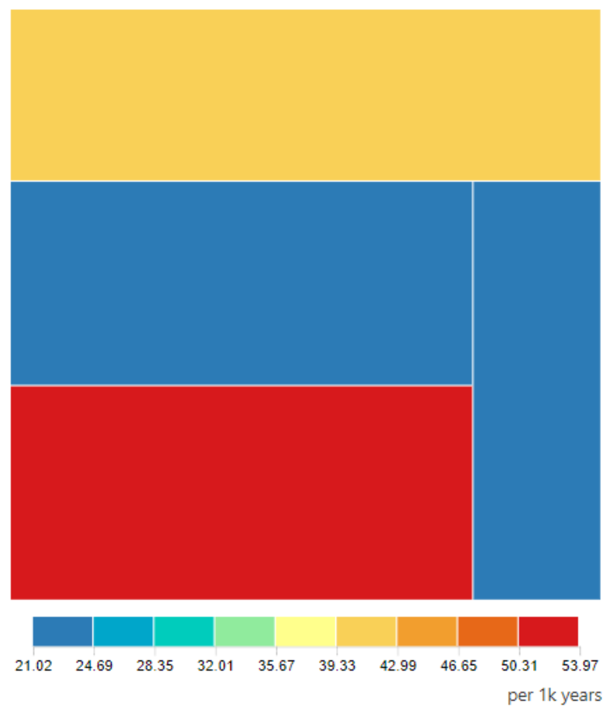
Export Analysis to CSV

Source	Name		Persons	Cases	Proportion [+|-] per 1k persons	Time At Risk (years)	Rate [+|-] per 1k years	Started	Duration	
TRUVENMDCR_V698	Truven MDCR	Execute	19,288	201	10.42	5,606	35.85	2018-03-21, 15:20	00:01:12	Remove

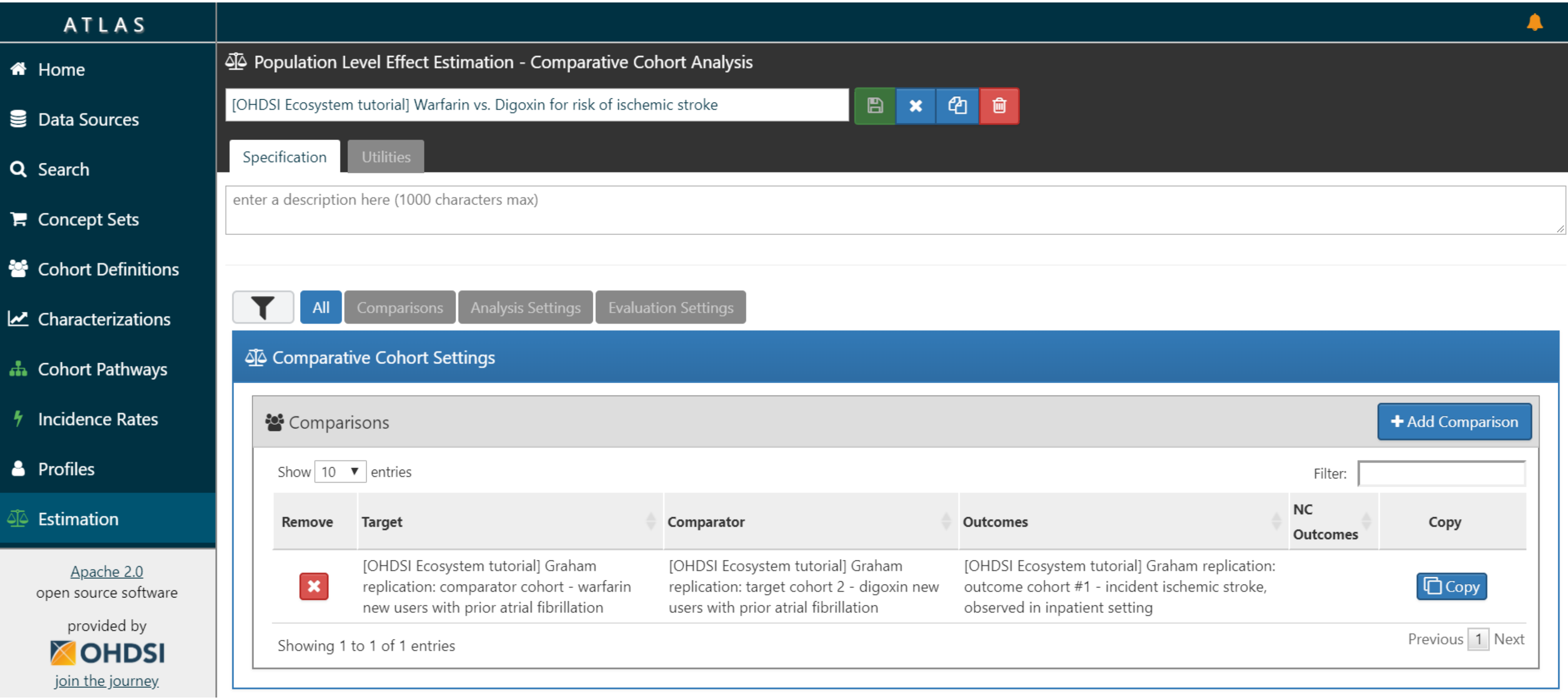
Showing target cohort: [OHDSI Europe tutorial] Graham replicatio and outcome cohort: [OHDSI Europe tutorial] Graham replicatic

	Persons	Cases	Proportion [+|-] per 1k persons	Time At Risk (years)	Rate [+|-] per 1k years
Summary Statistics:	19,288	201	10.42	5,606	35.85

Stratify Rule	N	Cases	Proportion [+|-] per 1k persons	Time At Risk (years)	Rate [+|-] per 1k years
1. Gender = MALE	10,839	99	9.13	3,223	30.72
2. Age >= 75	11,101	150	13.51	3,239	46.31

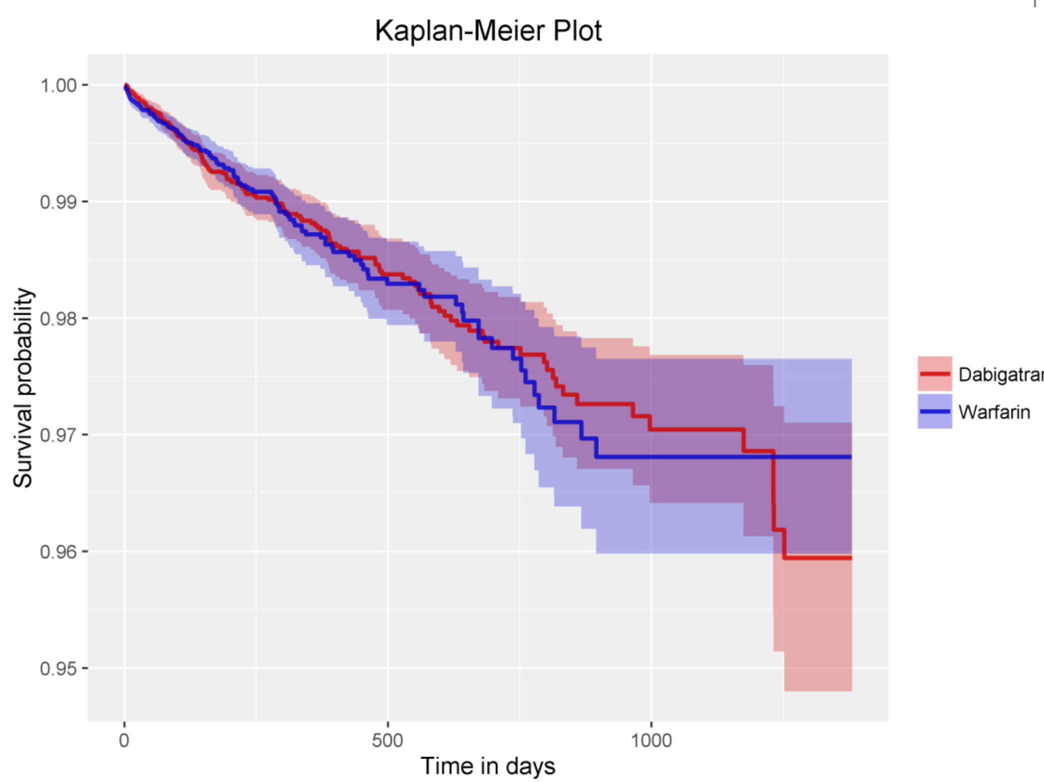


OHDSI in action: Population-level effect estimation design

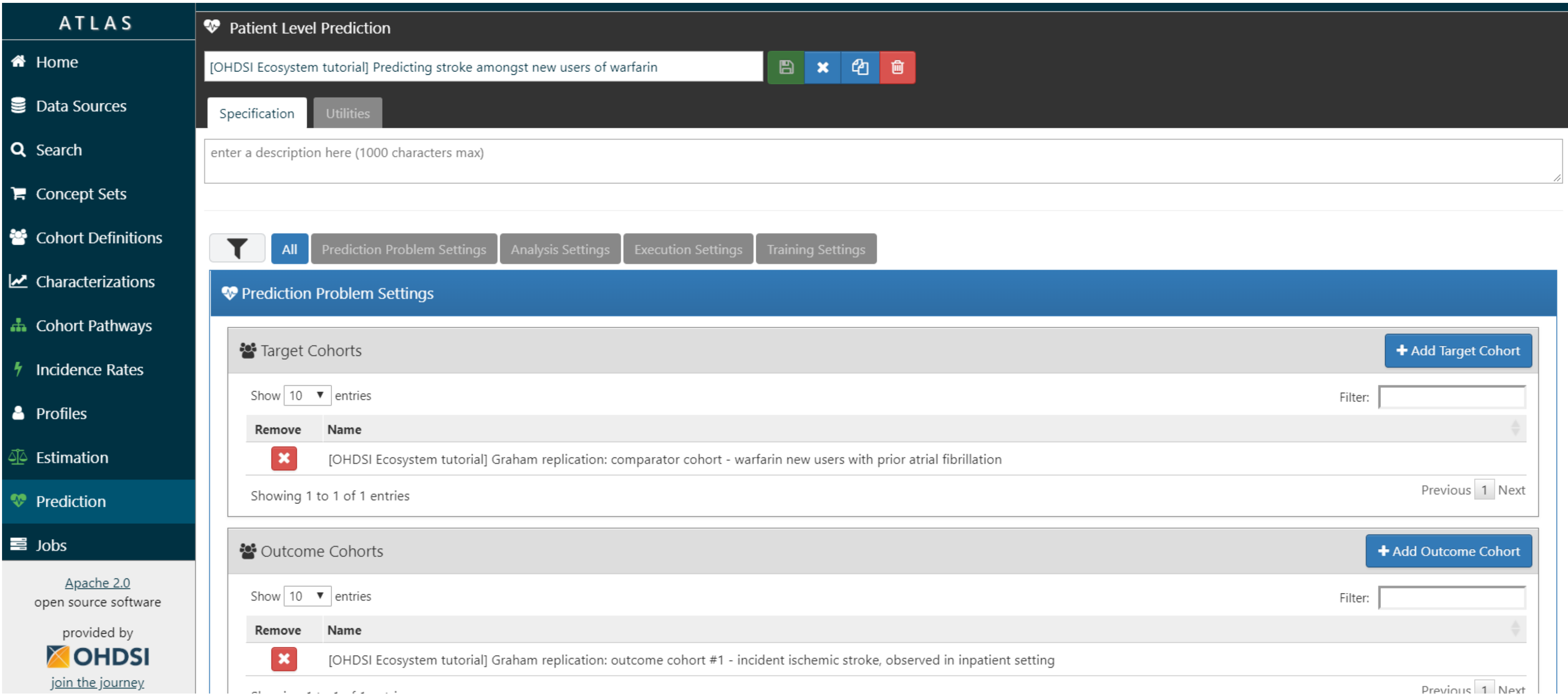


OHDSI in action: Population-level effect estimation implementation

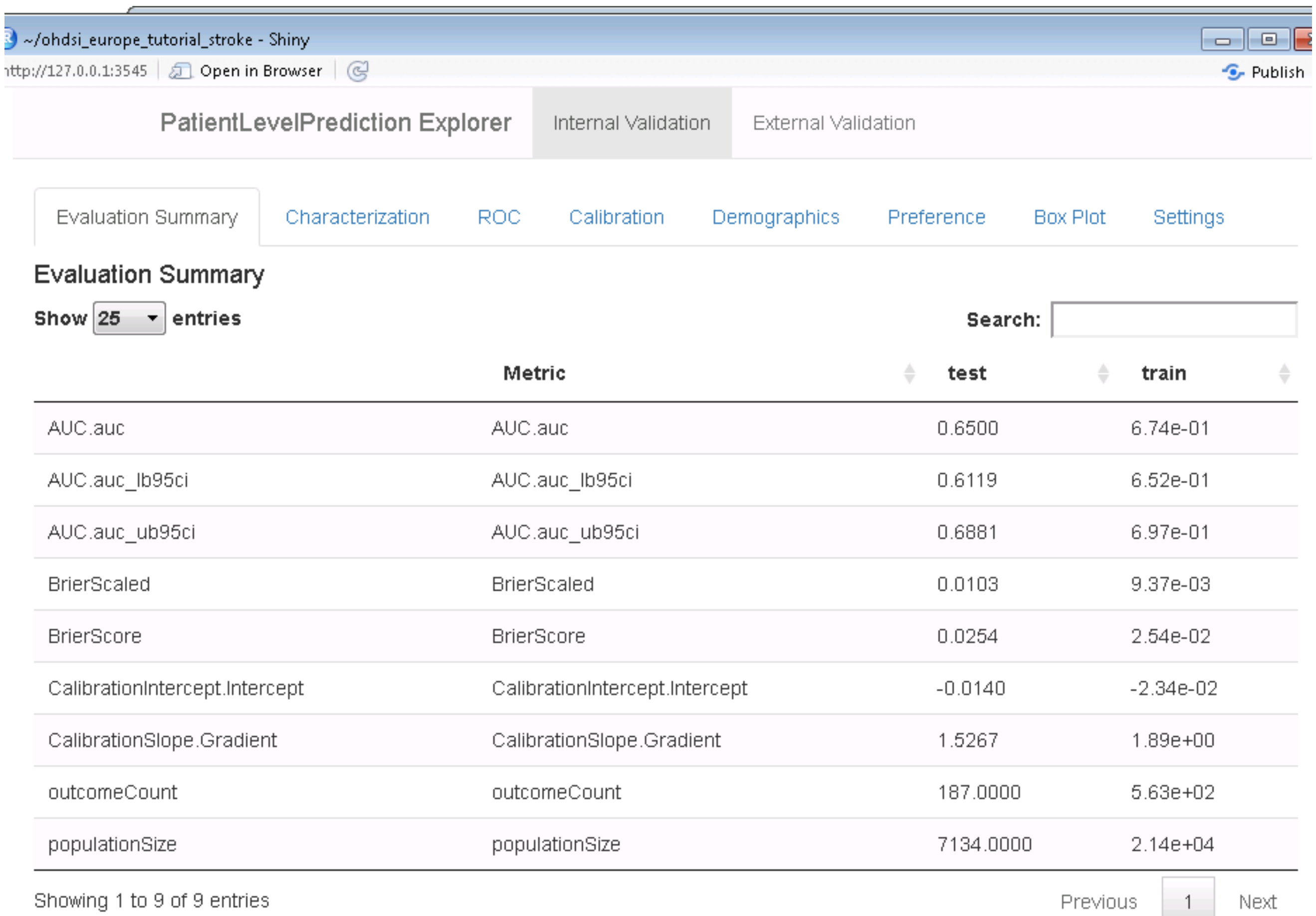
```
Model type: cox
Stratified: FALSE
Use covariates: FALSE
Status: OK

          Estimate  lower .95  upper .95
treatment 0.89626   0.71863    1.11829

Population counts
          treatedPersons       comparatc
Count     17460                17460

Outcome counts
          treatedPersons       comparatc
Count     164                  155

Time at risk
          treatedDays          comparatc
Days      4912947              3954046
```



OHDSI in action:
Patient-level prediction design



OHDSI in action: Patient-level prediction implementation



	Metric	test	train
AUC.auc	AUC.auc	0.6500	6.74e-01
AUC.auc_lb95ci	AUC.auc_lb95ci	0.6119	6.52e-01
AUC.auc_ub95ci	AUC.auc_ub95ci	0.6881	6.97e-01
BrierScaled	BrierScaled	0.0103	9.37e-03
BrierScore	BrierScore	0.0254	2.54e-02
CalibrationIntercept.Intercept	CalibrationIntercept.Intercept	-0.0140	-2.34e-02
CalibrationSlope.Gradient	CalibrationSlope.Gradient	1.5267	1.89e+00
outcomeCount	outcomeCount	187.0000	5.63e+02
populationSize	populationSize	7134.0000	2.14e+04

Vocabulary

Everything is a concept….everything needs to be defined in a common language

Cardiovascular, Bleeding, and Mortality Risks in Elderly Medicare Patients Treated With Dabigatran or Warfarin for Nonvalvular Atrial Fibrillation

David J. Graham, MD, MPH; Marsha E. Reichman, PhD; Michael Wernecke, BA; Rongmei Zhang, PhD; Mary Ross Southworth, PharmD; Mark Levenson, PhD; Ting-Chang Sheu, MPH; Katrina Mott, MHS; Margie R. Goulding, PhD; Monika Houstoun, PharmD, MPH; Thomas E. MaCurdy, PhD; Chris Worrall, BS; Jeffrey A. Kelman, MD, MMSc

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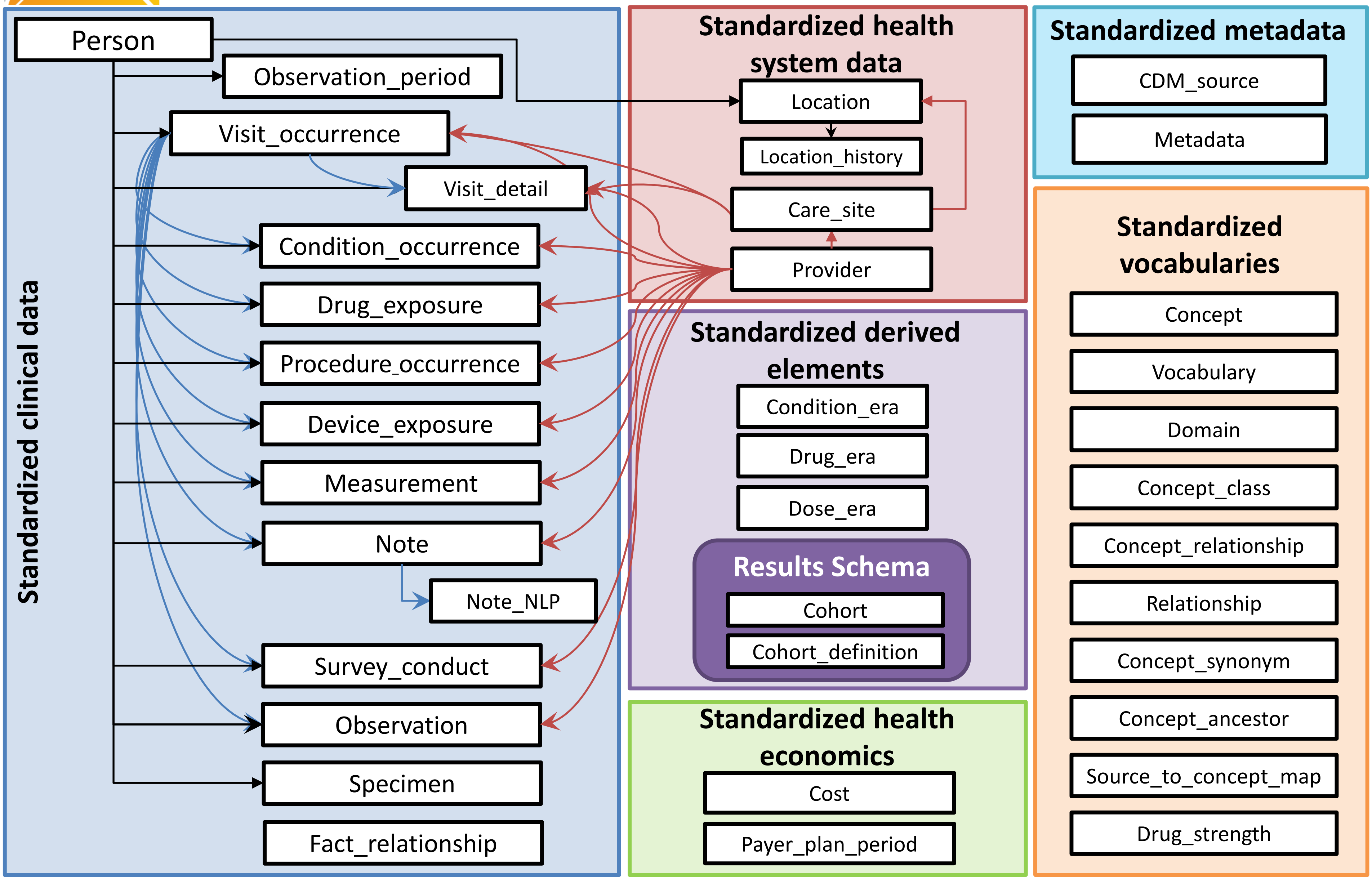
Key Words: anticoagulant ■ pharmacoepidemiology ■ safety ■ thrombin inhibitor ■ warfarin

OMOP CDM Version 6



OMOP Common Vocabulary Model

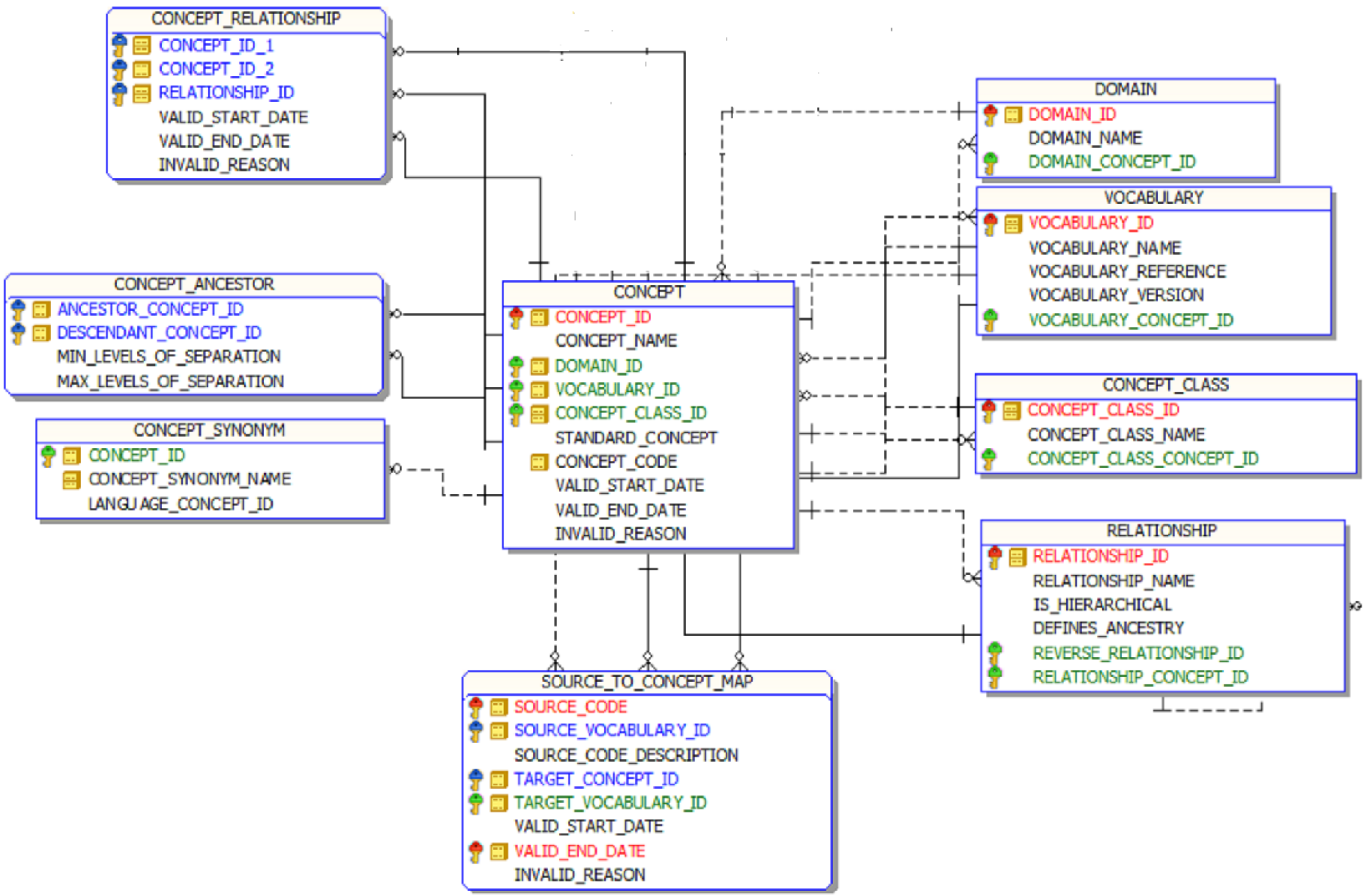
What it is

- **Standardized structure** to house existing vocabularies used in the public domain
- **Compiled standards** from disparate public and private sources and some OMOP-grown concepts

What it's not

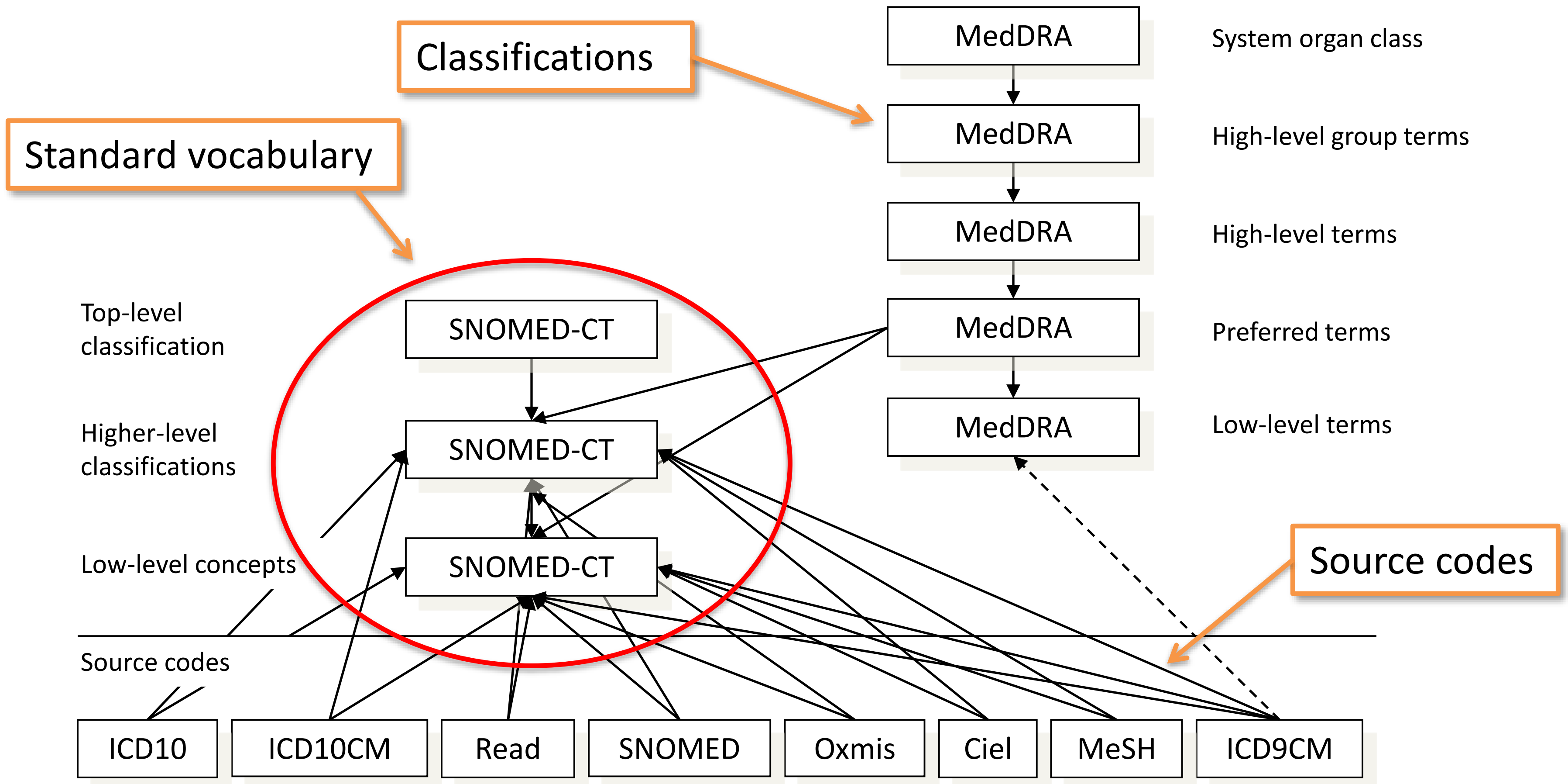
- **Static dataset** – the vocabulary updates regularly to keep up with the continual evolution of the sources
- **Finished product** – vocabulary maintenance and improvement is ongoing activity that requires community participation and support

OMOP Vocabulary CDM

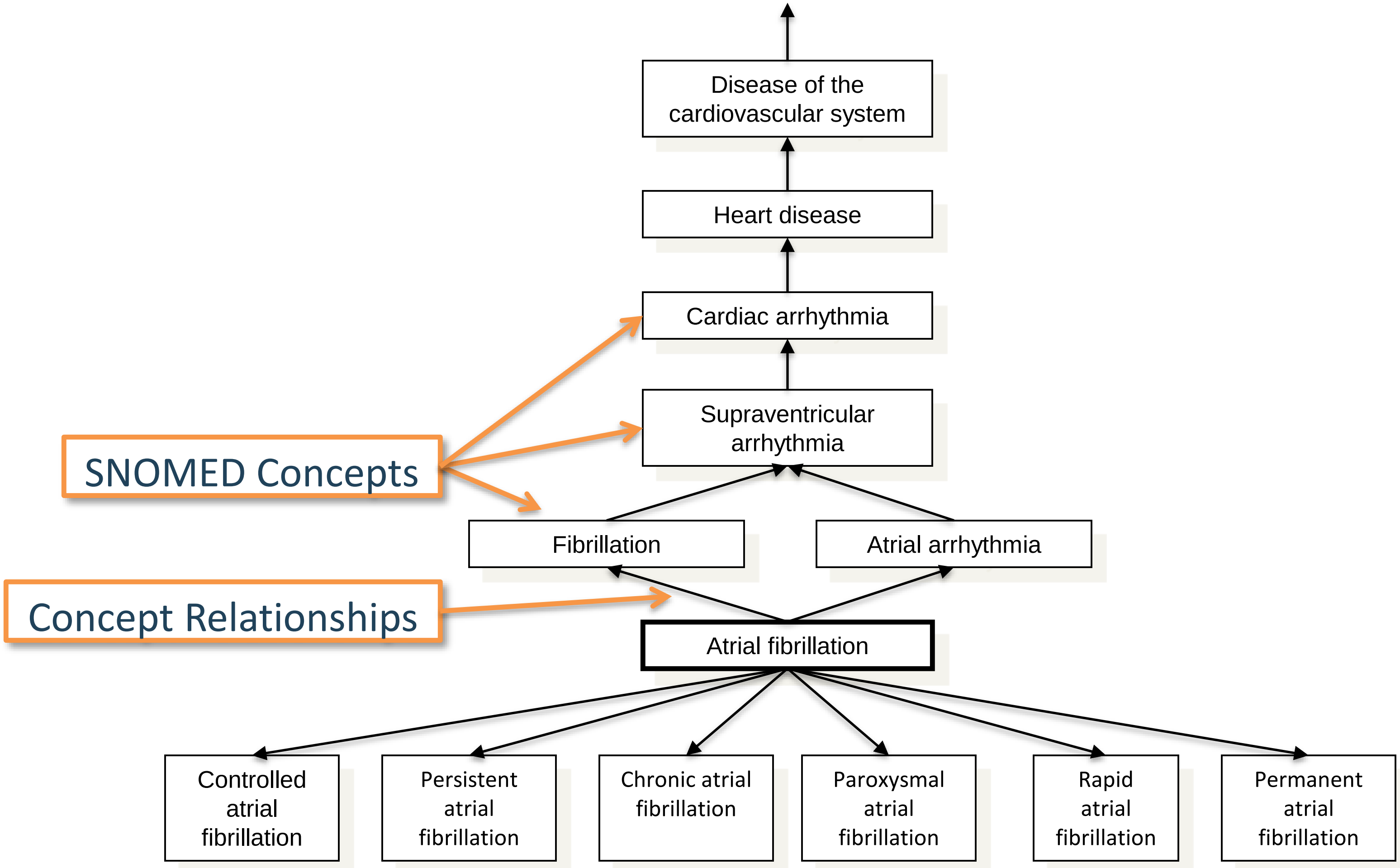


1. All content: concepts in **`concept`** table
2. Direct relationships between concepts listed in **`concept_relationship`**
3. Multi-step hierarchical relationships pre-processed in **`concept_ancestor`**

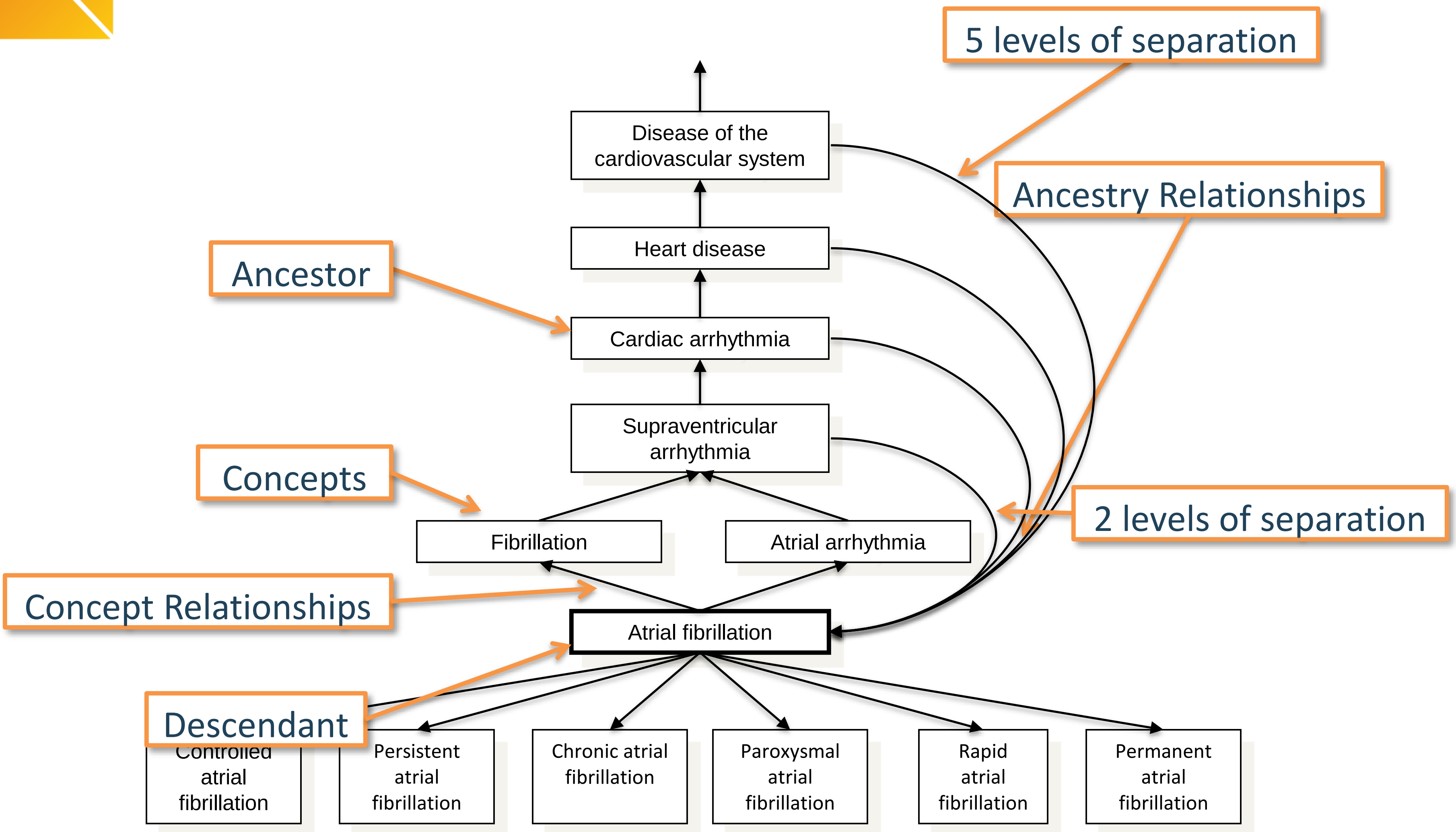
Condition Concepts



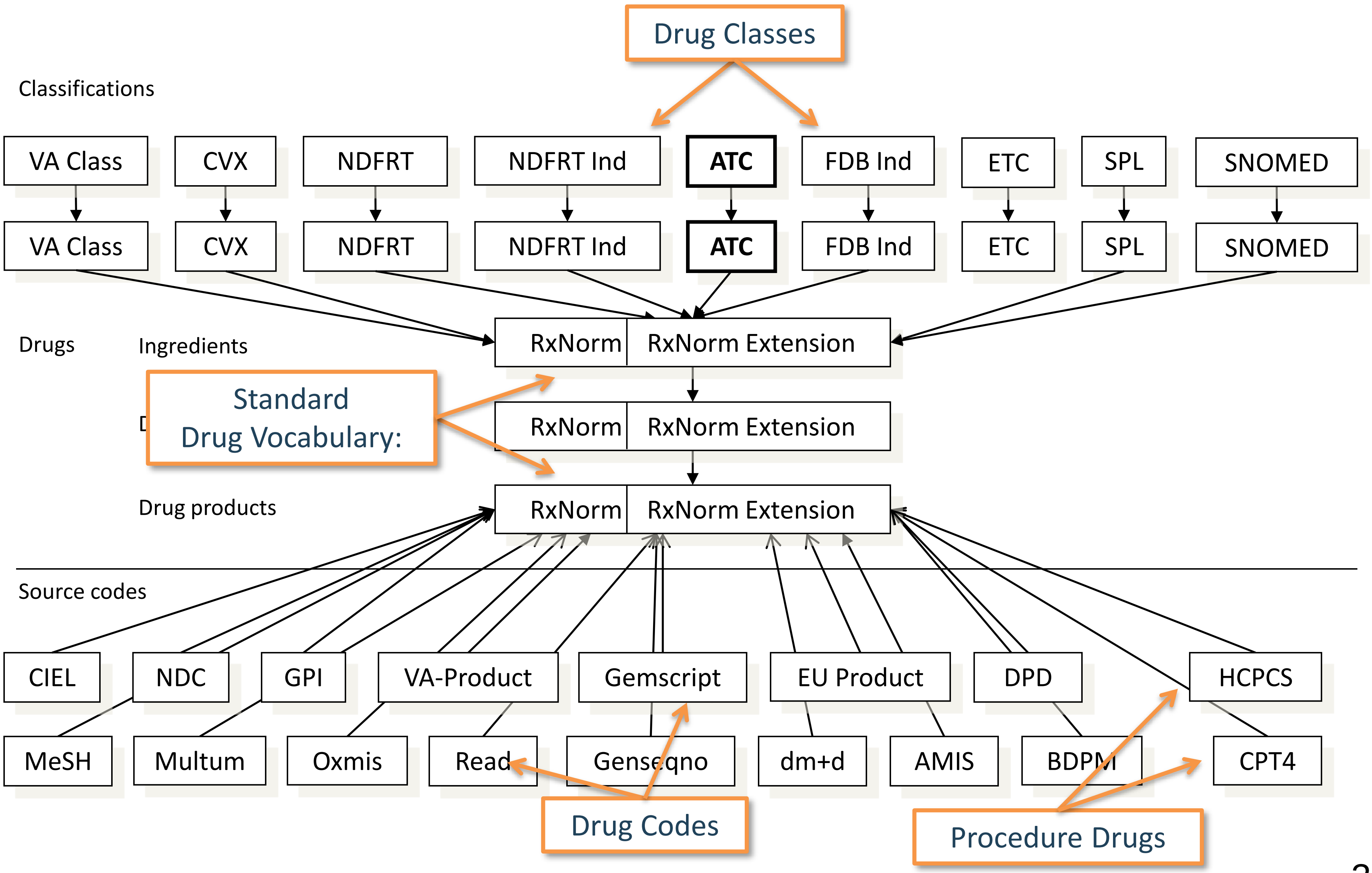
Condition ancestry around “atrial fibrillation“



Ancestry Relationships: Higher-Level Relationships



Drug Hierarchy



Vocabulary classifications improve your efficiency….and your quality!

Health Serv Outcomes Res Method (2013) 13:58–67
DOI 10.1007/s10742-012-0102-1

Applying standardized drug terminologies to observational healthcare databases: a case study on opioid exposure

Frank J. DeFalco · Patrick B. Ryan · M. Soledad Cepeda

- 60% of medication codes and 94% of records are mapped
- 45% of opiate codes covered by one of ATC, ETC, and NDF-RT are covered by all three
    - 15% missed by at least one
- No one classification scheme was better than the others

Vocabulary classifications improve your efficiency….and your quality!

DeFalco HSORM 2013

Table 3 Identification of related 11 digit NDC codes by drug class and vocabulary

Drug class	Vocabulary	System grouping	Ingredients	Clinical drugs	NDC codes	Unique codes
Opioid	ATC	Opioids	23	1,122	11,765	2
Opioid	ETC.	Analgesics–narcotic	20	1,808	19,106	333
Opioid	NDFRT	Opioid agonists	22	1,813	15,912	1,087
Opioid	VA	Opioid analgesics	24	1,750	17,113	450
NSAID	ATC	Antiinflam and antirheumatic products, non-steroids	52			
NSAID	ETC.	NSAID analgesics	23			
NSAID	NDFRT	NSAID analgesics	23			
NSAID	VA	Nonsalicylate NSAIDs, antirheumatic	24			
Antidiabetic	ATC	Drugs used in diabetes	53			
Antidiabetic	ETC.	Oral antidiabetic agents	19			
Antidiabetic	NDFRT	Insulin receptor agonists	42			
Antidiabetic	VA	Oral hypoglycemic agents	18			
Antidepressant	ATC	Antidepressants	47			
Antidepressant	ETC.	Antidepressants	29			
Antidepressant	NDFRT	Serotonin uptake inhibitors, norepinephrine uptake inhibitors, dopamine uptake inhibitors	40			
Antidepressant	VA	Antidepressants	29			

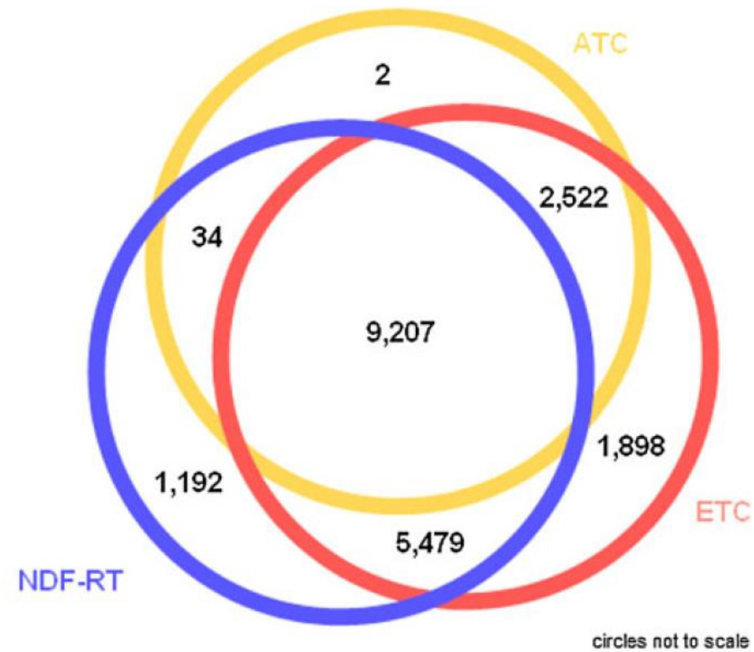


Fig. 1 Overlap in coverage of 'opioid' NDC drug codes by classification system

If we try to speak the same language, will there be loss in translation?

Journal of Biomedical Informatics 45 (2012) 689–696

Contents lists available at SciVerse ScienceDirect

Journal of Biomedical Informatics

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

ELSEVIER

Evaluation of alternative standardized terminologies for medical conditions within a network of observational healthcare databases ☆

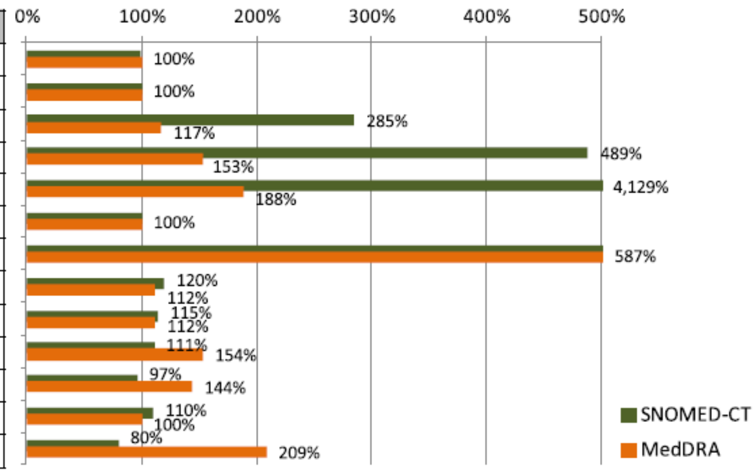
Christian Reich [a,*], Patrick B. Ryan [a,b,1], Paul E. Stang [a,b,1], Mitra Rocca [c,2]

[a] *Observational Medical Outcomes Partnership, Foundation for the National Institutes of Health, 9650 Rockville Pike, Bethesda, MD 20814, USA*
[b] *Janssen Research & Development, LLC, 1125 Trenton-Harbourton Road, PO Box 200, MS K304, Titusville, NJ 08560, USA*
[c] *Office of Translational Sciences, Center for Drug Evaluation and Research (CDER), US Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 21, Rm. 4608, Silver Spring, MD 20933, USA*

Changing language may change your codelist, that may change your cohort depending on the disease...

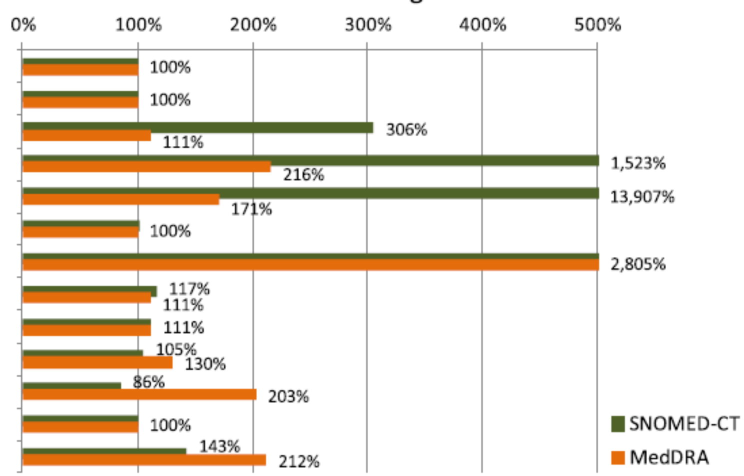
Cohort size of HOI in MSLR for different terminologies

Condition	#
Angioedema	1
Aplastic Anemia	1
Acute Liver Failure	1
	2
	7
Acute Renal Failure	1
	4
Bleeding	1
	3
Hip Fracture	1
Acute myocardial Infarction	1
	2
Upper GI Ulcer Hospitalization	1



Cohort size of HOI in GE for different terminologies

Condition	#
Angioedema	1
Aplastic Anemia	1
Acute Liver Failure	1
	2
	7
Acute Renal Failure	1
	4
Bleeding	1
	3
Hip Fracture	1
Acute myocardial Infarction	1
	2
Upper GI Ulcer Hospitalization	1



…but in practice, running an estimation analysis using source vs. standard vocabulary yields similar results

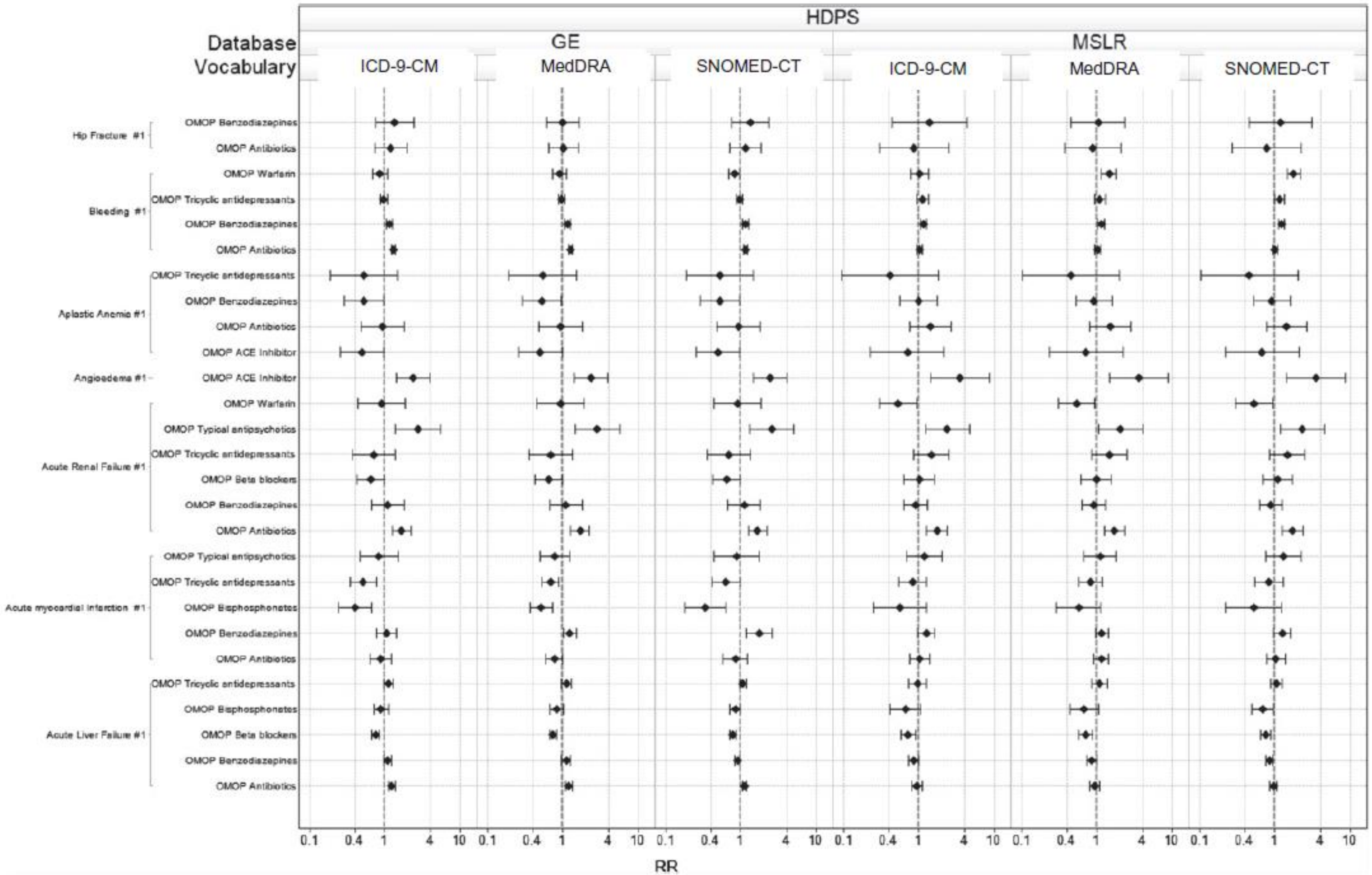


Fig. 3. Effect estimates and 95% confidence intervals for incident user design applied to MSLR and GE using ICD-9-CM, SNOMED-CT, and MedDRA as standard terminologies. Each dot represents the estimate of the effect of an individual HOI-drug combination (on the X-axis).

Demo: Searching the vocabulary in ATLAS

Follow along at:

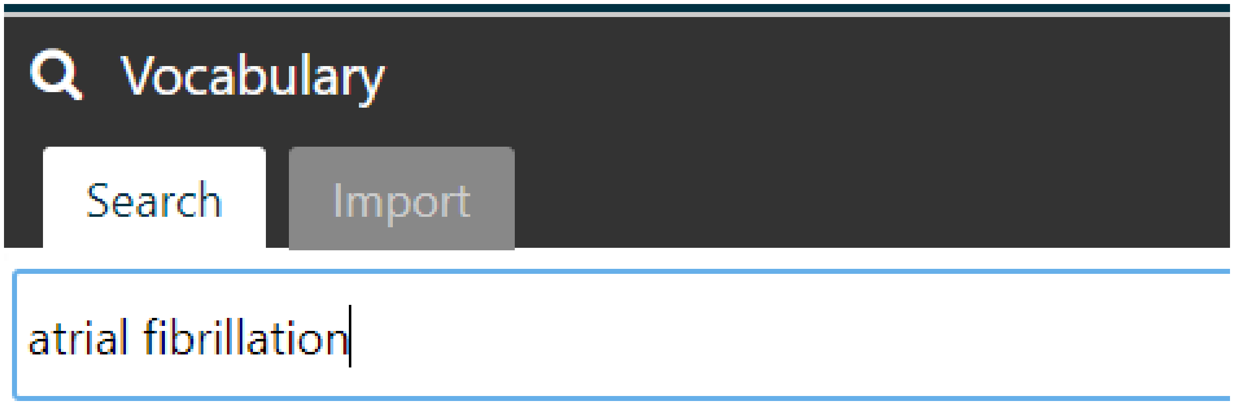
(during training)

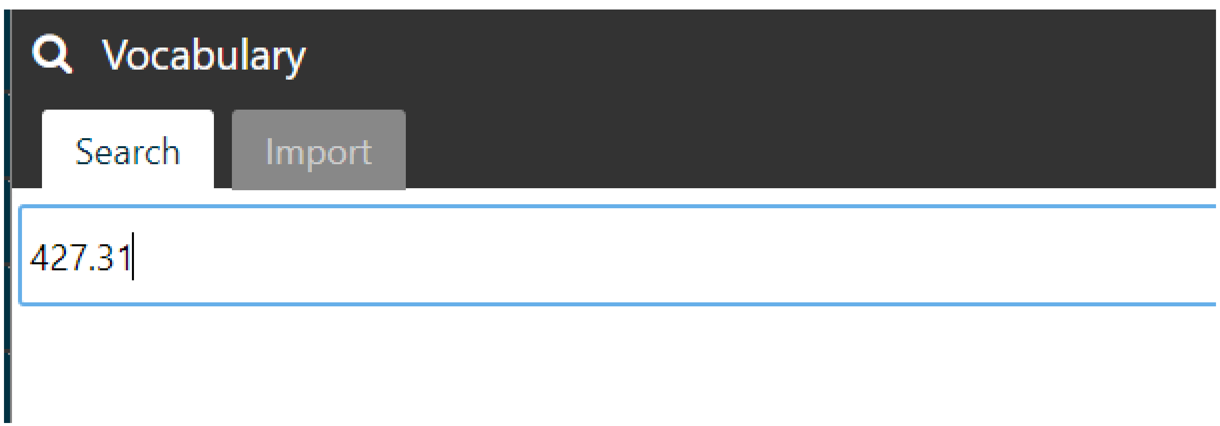
https://overview.ohdsi.amazingawsdemos.com

(public demo environment)

http://ohdsi.org/web/ATLAS

Demo: vocabulary search





Search for concept names, concept IDs, or source codes across any domain in the OMOP CDM

Demo: vocabulary search results

Vocabulary

Search | Import

atrial fibrillation

Advanced Options

Column visibility | Copy | CSV | Show 15 entries

Filter:

Showing 1 to 15 of 208 entries

Previous 1 2 3 4 5 ... 14 Next

Vocabulary
- SNOMED (52)
- NDC (48)
- Read (29)
- MedDRA (14)
- Indication (12)

Class
- 11-digit NDC (48)
- Read (29)
- Clinical Finding (27)
- Procedure (17)
- HLT (12)

Domain
- Condition (76)
- Drug (67)
- Observation (41)

Id	Code	Name	Class	RC	DRC	Domain	Vocabulary
21013671	00013671	Ventricular Rate Control in Atrial Fibrillation	Indication	0	136,810,452	Drug	Indication
4344544	N0000000507	Atrial Fibrillation	Ind / CI	0	133,648,447	Drug	NDFRT
21013672	00013672	Prevention of Post Cardio-Thoracic Surgery Atrial Fibrillation	Indication	0	85,818,852	Drug	Indication
313217	49436004	Atrial fibrillation	Clinical Finding	32,938,949	38,400,483	Condition	SNOMED
35204953	10003658	Atrial fibrillation	PT	0	38,400,483	Condition	MedDRA
500002401	500002401	OMOP Atrial Fibrillation 1	Cohort	0	38,400,483	Condition	Cohort
21005673	00005673	Prevention of Thromboembolism in Chronic Atrial Fibrillation	Indication	0	23,812,247	Drug	Indication
21003018	00003018	Cardioversion of Atrial Fibrillation	Indication	0	5,175,583	Drug	Indication
21013390	00013390	Prevention of Recurrent Atrial Fibrillation	Indication	0	4,866,791	Drug	Indication

Demo: vocabulary concept selection

Vocabulary › Concept

Atrial fibrillation

Details | Related Concepts | Hierarchy | Record Counts

Property	Value
Concept Name	Atrial fibrillation
Domain Id	Condition
Concept Class Id	Clinical Finding
Vocabulary Id	SNOMED
Concept Id	313217
Concept Code	49436004
Invalid Reason	Valid
Standard Concept	Standard

Demo: Concept relationship exploration

Vocabulary > Concept

Atrial fibrillation

Details | Related Concepts | Hierarchy | Record Counts

Column visibility | Copy | CSV | Show 15 entries | Filter:

Vocabulary
- SNOMED (50)
- MedDRA (25)
- Indication (18)
- CIEL (10)

Standard Concept
- Classification (46)
- Standard (45)
- Non-Standard (37)

Invalid Reason
- Valid (122)
- Invalid (6)

Class
- Clinical Finding (42)

Showing 1 to 5 of 5 entries

Previous 1 Next

Id	Code	Name	Class	RC	DRC	Distance	Domain	Vocabulary
321588	56265001	Heart disease	Clinical Finding	1,212,872	193,512,502	3	Condition	SNOMED
44784217	698247007	Cardiac arrhythmia	Clinical Finding	655,834	59,608,937	2	Condition	SNOMED
4248028	72654001	Supraventricular arrhythmia	Clinical Finding	0	44,910,236	2	Condition	SNOMED
4068155	17366009	Atrial arrhythmia	Clinical Finding	0	42,808,095	1	Condition	SNOMED
4226399	40593004	Fibrillation	Clinical Finding	0	38,592,904	1	Condition	SNOMED

Showing 1 to 5 of 5 entries

Previous 1 Next

Demo: Concept hierarchy

Vocabulary > Concept

Atrial fibrillation

Details | Related Concepts | Hierarchy | Record Counts

Parents

Id	Code	Name	Class	RC	DRC	Distance	Domain	Vocabulary
500001801	500001801	OMOP Qt Prolongation/Torsade De Pointes 1	Cohort	0	57,981,637	1	Condition	Cohort
35202455	10042600	Supraventricular arrhythmias	HLT	0	44,910,236	1	Condition	MedDRA
4068155	17366009	Atrial arrhythmia	Clinical Finding	0	42,808,095	1	Condition	SNOMED
4226399	40593004	Fibrillation	Clinical Finding	0	38,592,904	1	Condition	SNOMED
35204969	10061592	Cardiac fibrillation	PT	0	38,592,904	1	Condition	MedDRA
35204953	10003658	Atrial fibrillation	PT	0	38,400,483	1	Condition	MedDRA
500002401	500002401	OMOP Atrial Fibrillation 1	Cohort	0	38,400,483	1	Condition	Cohort

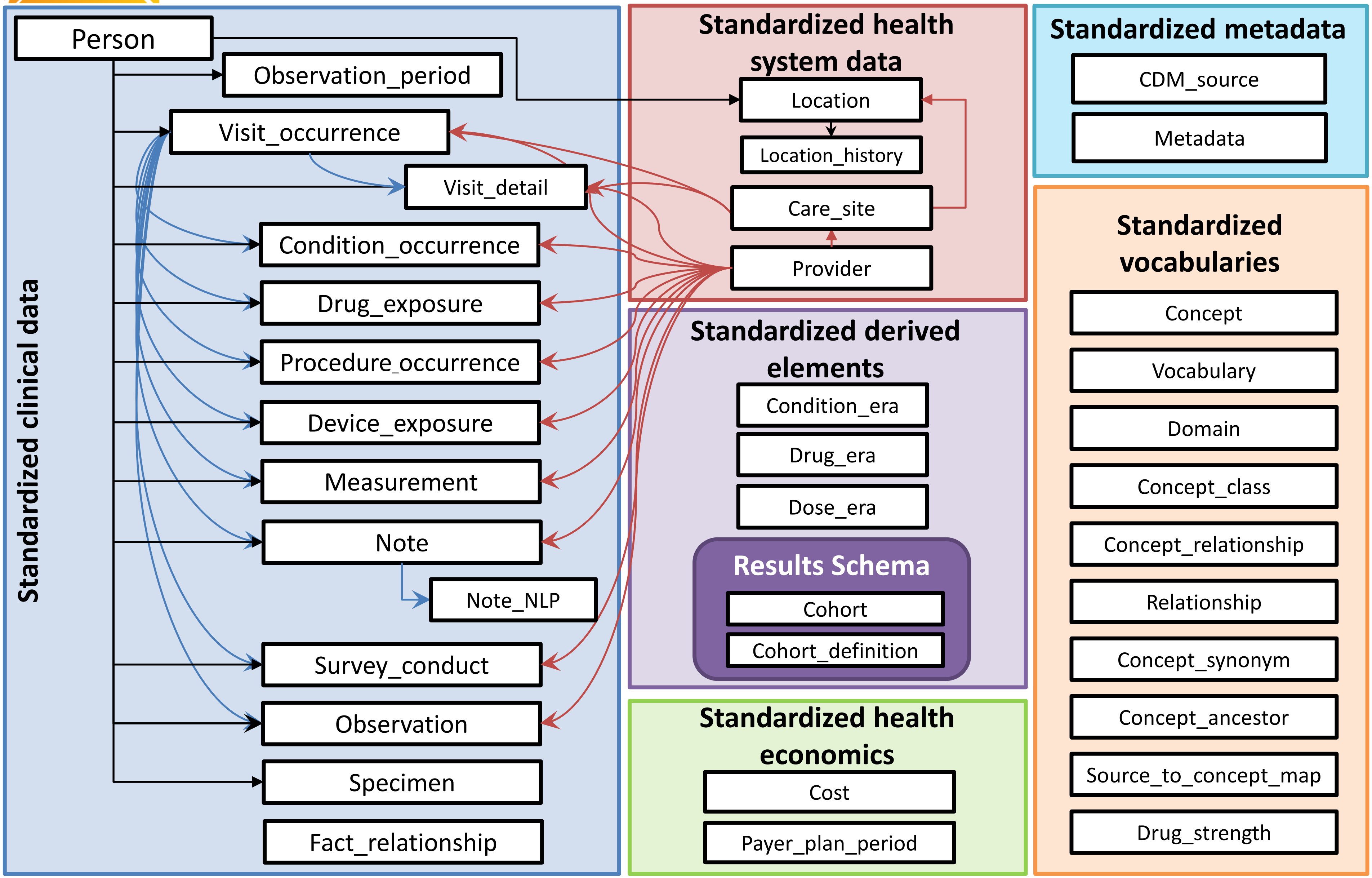
Id	Code	Name	Class	RC	DRC	Distance	Domain	Vocabulary
313217	49436004	Atrial fibrillation	Clinical Finding	32,938,949	38,400,483	1	Condition	SNOMED

Children

Id	Code	Name	Class	RC	DRC	Distance	Domain	Vocabulary
4154290	282825002	Paroxysmal atrial fibrillation	Clinical Finding	2,919,750	2,919,750	1	Condition	SNOMED

Data Sources

OMOP CDM Version 6



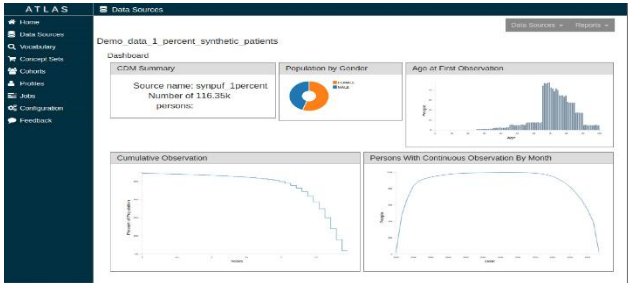
Purpose of Achilles

- ACHILLES is a platform which enables the characterization, quality assessment and visualization of observational health databases.

- ACHILLES provides users with an interactive, exploratory framework to assess patient demographics, the prevalence of conditions, drugs and procedures, and to evaluate the distribution of values for clinical observations.

Achilles – Under the Hood

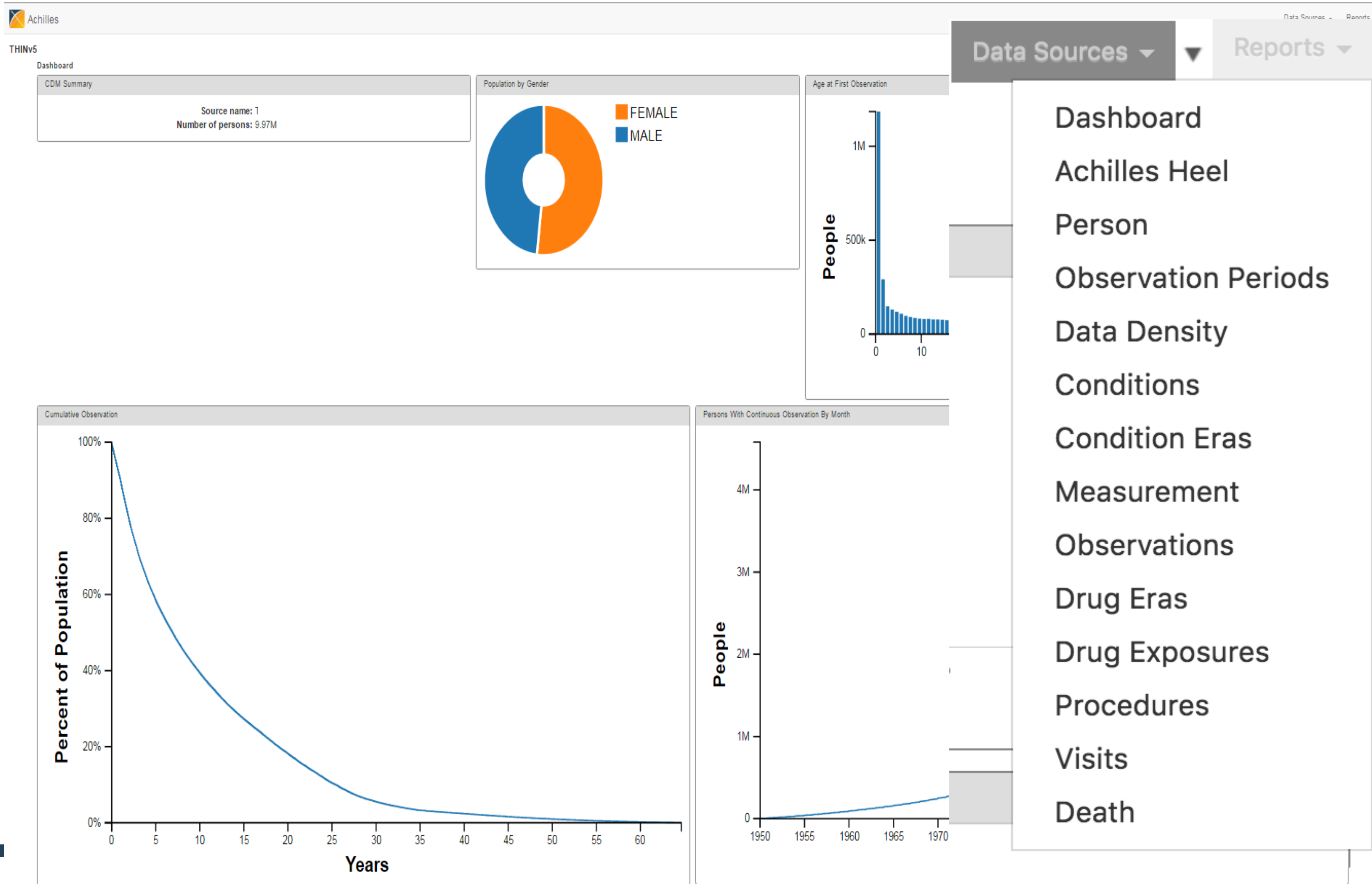
- Two step process
  - Step 1: R Routine running against the local CDM instance. This R routine calculates summary statistics which allow to describe the distribution of patient-level data as well as a generic view on the quality of the data. The output of this step is summarized (and hence de-identfied) set of data stored in results tables in the CDM.
  - Step 2: webapplication which can run standalone from a CDM instance. It requires the ACHILLES R results generated in step 1 as input. The webapplication allows interactive exploration for each of the entities (tables) in the OMOP scheme individually (not possible to query across multiple entities at the same time)



OMOP CDM

Basic Navigation

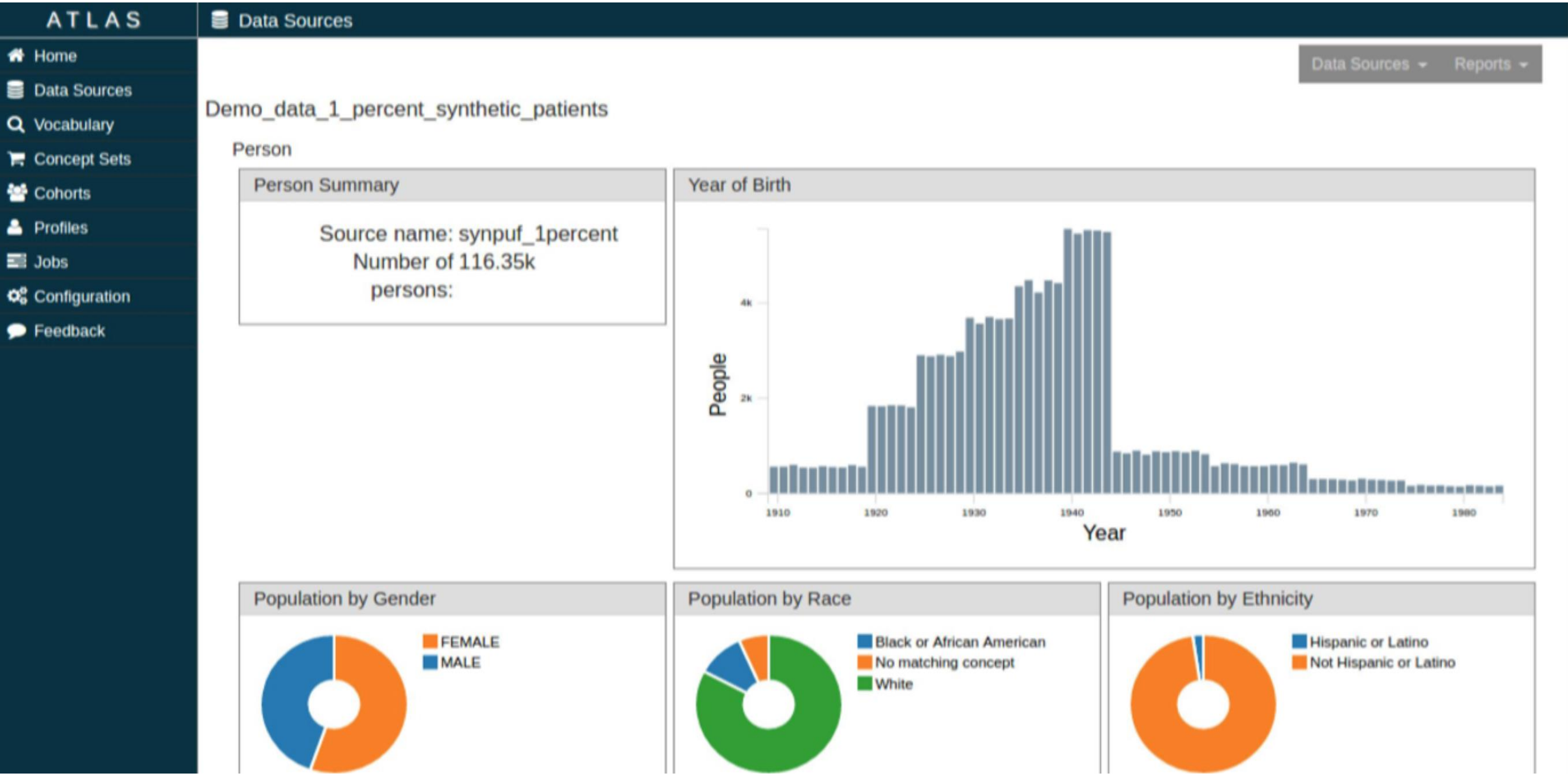
http://ohdsi.org/web/ACHILLES



Examples

http://ohdsi.org/web/ATLAS

Examples


ATLAS
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Concept Sets
Cohorts
Profiles
Jobs
Configuration
Feedback
Data Sources
Reports
Demo_data_1_percent_synthetic_patients
Person
Person Summary
Source name: synpuf_1percent
Number of 116.35k
persons:
Year of Birth
People
4k
2k
0
1910
1920
1930
1940
1950
1960
1970
1980
Year
Population by Gender
FEMALE
MALE
Population by Race
Black or African American
No matching concept
White
Population by Ethnicity
Hispanic or Latino
Not Hispanic or Latino

Examples


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Profiles
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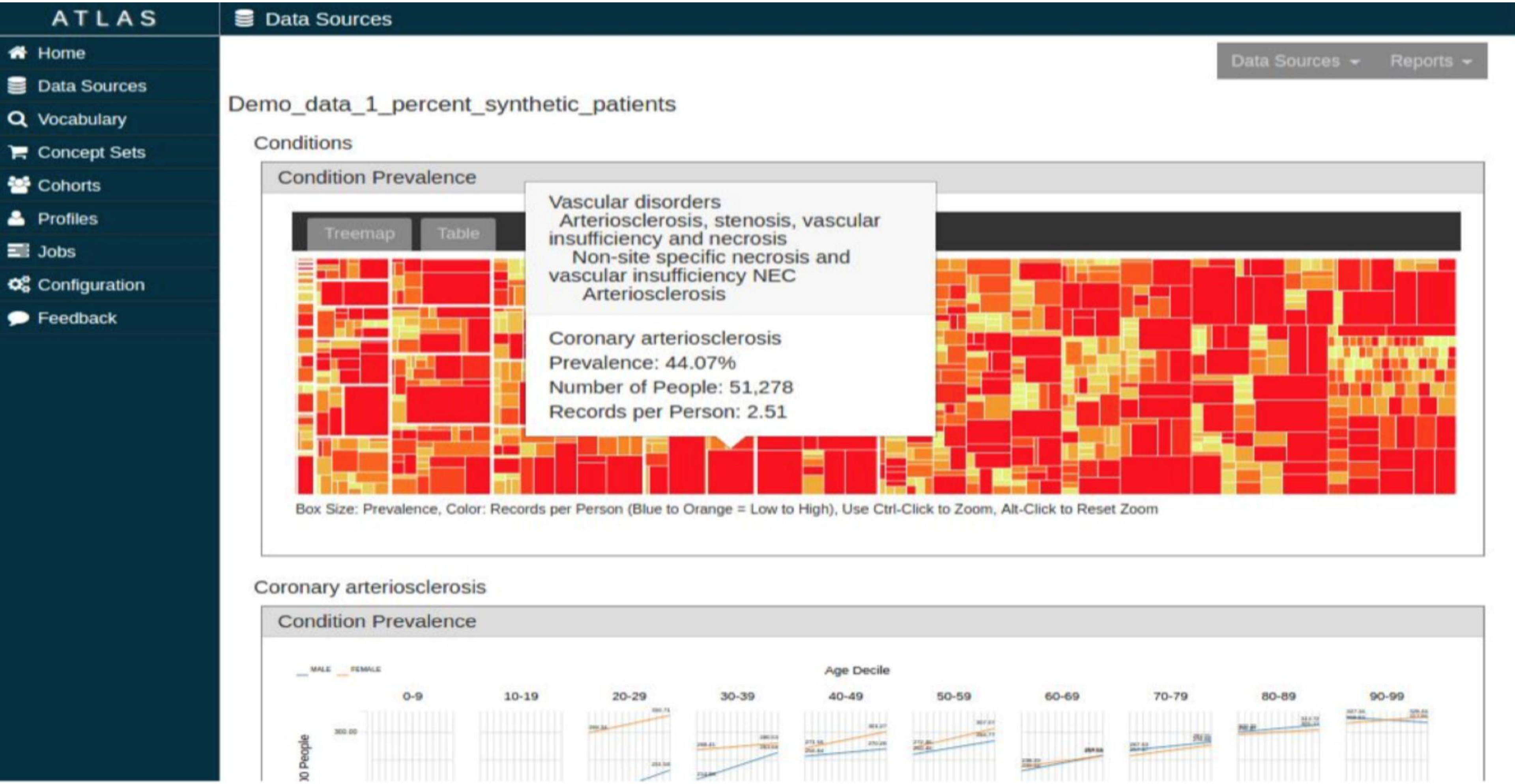
Feedback
Data Sources
Reports
Demo_data_1_percent_synthetic_patients
Conditions
Condition Prevalence
Treemap
Table
Box Size: Prevalence, Color: Records per Person (Blue to Orange = Low to High), Use Ctrl-Click to Zoom, Alt-Click to Reset Zoom
Dashboard
Achilles Heel
Person
Observation Periods
Data Density
Conditions
Condition Eras
Measurement
Observations
Drug Eras
Drug Exposures
Procedures
Visits
Death

Examples


ATLAS
Data Sources
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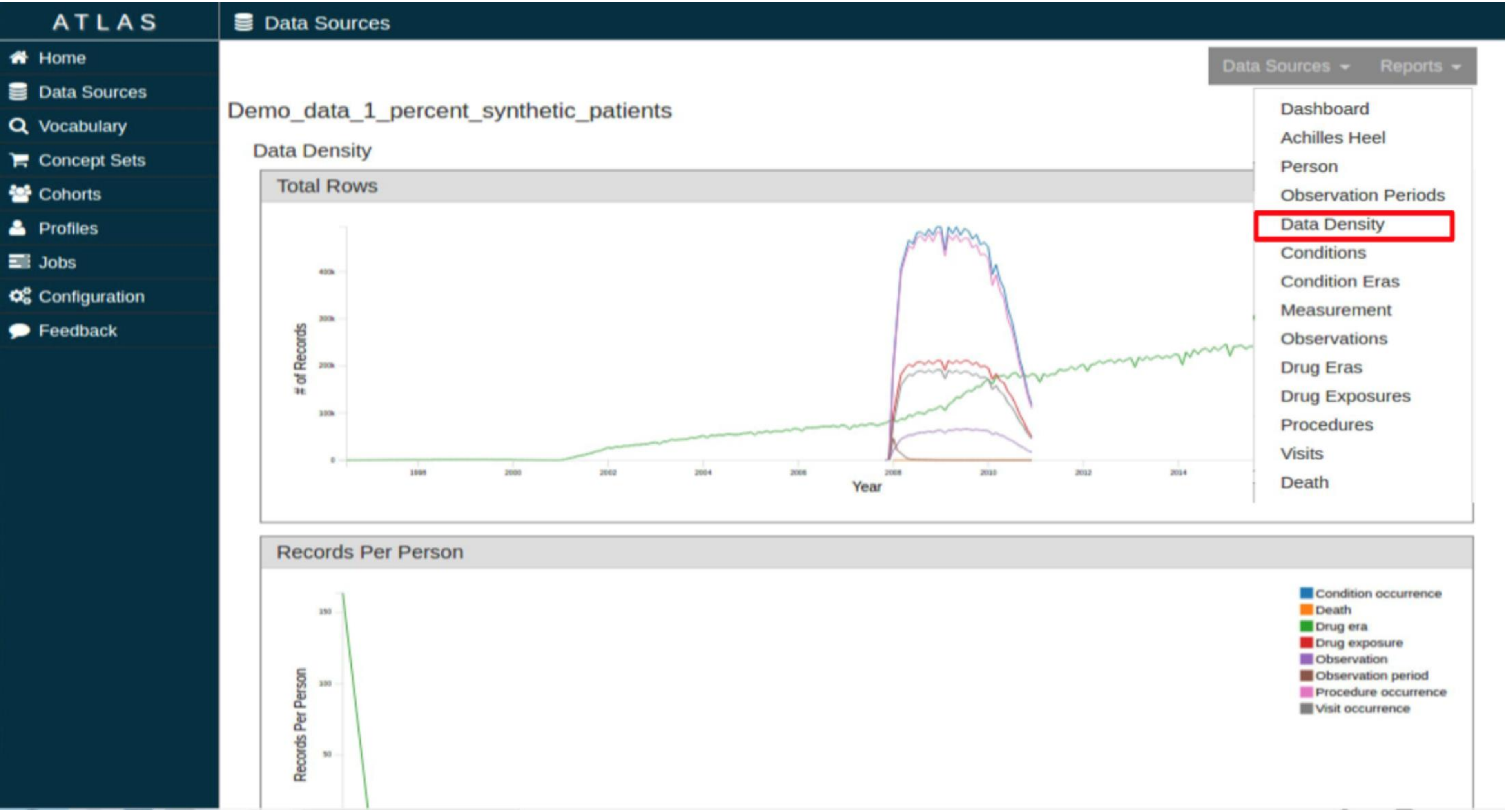
Data Sources
Vocabulary
Concept Sets
Cohorts
Profiles
Jobs
Configuration
Feedback
Data Sources
Reports
Demo_data_1_percent_synthetic_patients
Conditions
Condition Prevalence
Treemap
Table
Vascular disorders
Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Non-site specific necrosis and vascular insufficiency NEC
Arteriosclerosis
Coronary arteriosclerosis
Prevalence: 44.07%
Number of People: 51,278
Records per Person: 2.51
Box Size: Prevalence, Color: Records per Person (Blue to Orange = Low to High), Use Ctrl-Click to Zoom, Alt-Click to Reset Zoom
Coronary arteriosclerosis
Condition Prevalence
MALE
FEMALE
Age Decile
0-9
10-19
20-29
30-39
40-49
50-59
60-69
70-79
80-89
90-99

Examples



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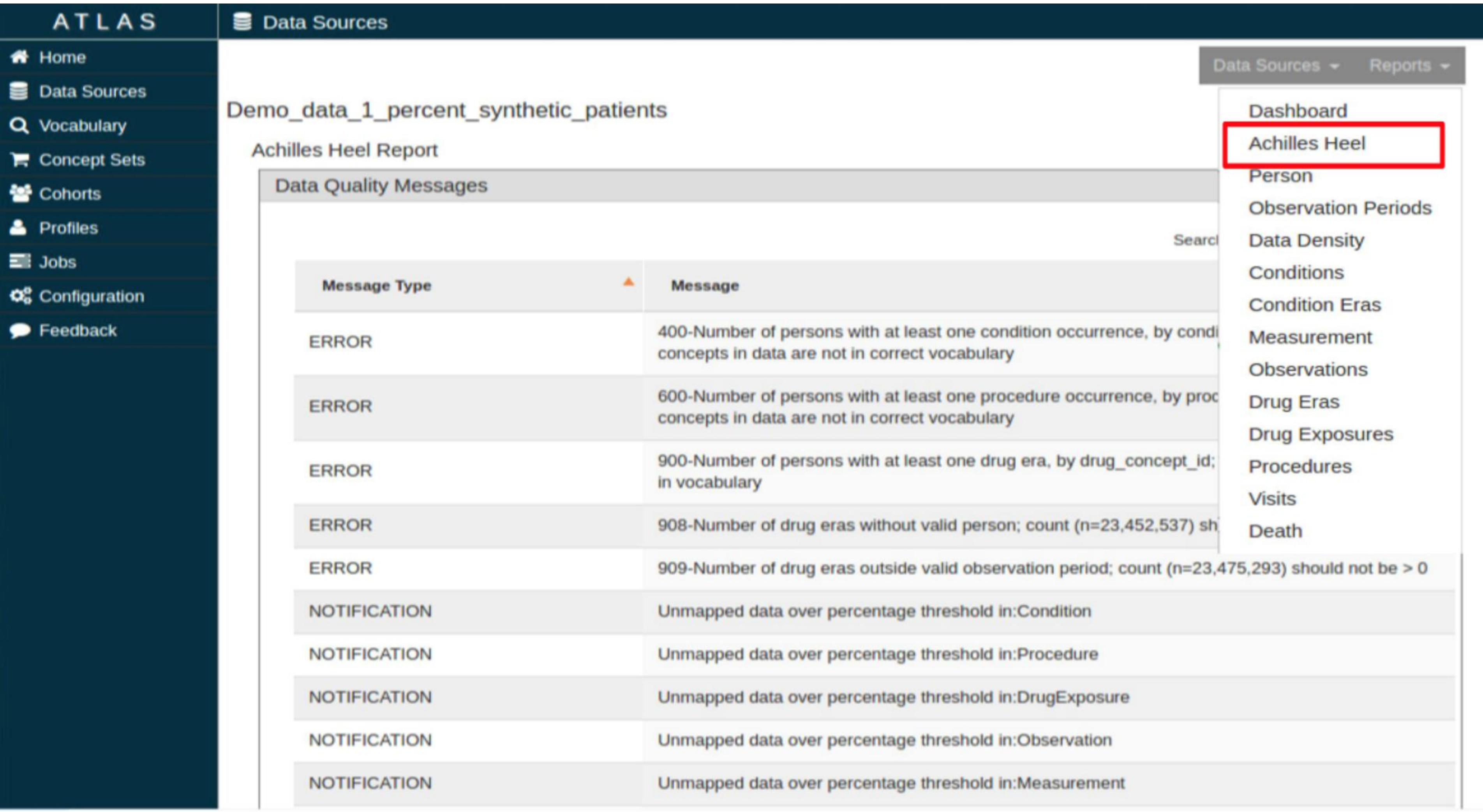
Drug Eras
Drug Exposures
Procedures
Visits
Death
of Records
Year
Records Per Person
Records Per Person
Condition occurrence
Death
Drug era
Drug exposure
Observation
Observation period
Procedure occurrence
Visit occurrence

Examples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Data Sources
Reports
Demo_data_1_percent_synthetic_patients
Achilles Heel Report
Data Quality Messages
Searc
Message Type
Message
ERROR
400-Number of persons with at least one condition occurrence, by condi
concepts in data are not in correct vocabulary
ERROR
600-Number of persons with at least one procedure occurrence, by proc
concepts in data are not in correct vocabulary
ERROR
900-Number of persons with at least one drug era, by drug_concept_id;
in vocabulary
ERROR
908-Number of drug eras without valid person; count (n=23,452,537) sh
ERROR
909-Number of drug eras outside valid observation period; count (n=23,475,293) should not be > 0
NOTIFICATION
Unmapped data over percentage threshold in:Condition
NOTIFICATION
Unmapped data over percentage threshold in:Procedure
NOTIFICATION
Unmapped data over percentage threshold in:DrugExposure
NOTIFICATION
Unmapped data over percentage threshold in:Observation
NOTIFICATION
Unmapped data over percentage threshold in:Measurement
Dashboard
Achilles Heel
Person
Observation Periods
Data Density
Conditions
Condition Eras
Measurement
Observations
Drug Eras
Drug Exposures
Procedures
Visits
Death

Cohort:
Definition and characterization

Construct of a 'Cohort'

Cohort

From Wikipedia, the free encyclopedia

Cohort may refer to:

Phenotype

- Cohort (statistics), a group of subjects with a common defining characteristic, for example age group
- Cohort study, a form of longitudinal study used in medicine and social science

Source: Disambiguation page, Wikipedia https://en.wikipedia.org/wiki/Cohort Retrieved September 30th 2018

Defining 'phenotype'

Journal of the American Medical Informatics Association, 0(0), 2017, 1–6
doi: 10.1093/jamia/ocx110
Perspective

Perspective

High-fidelity phenotyping: richness and freedom from bias

George Hripcsak[1] and David J Albers[1]

- A phenotype is a specification of an observable, potentially changing state of an organism (as distinguished from the genotype, derived from genetic makeup).
- The term phenotype can be applied to patient characteristics inferred from electronic health record (EHR) data.
- The goal is to draw conclusions about a target concept based on raw EHR data, claims data, or other clinically relevant data.
- Phenotype algorithms – ie, algorithms that identify or characterize phenotypes – may be generated by domain exerts and knowledge engineers, or through diverse forms of machine learning to generate novel representations of data.

Combining billing codes, clinical notes, and medications from electronic health records provides superior phenotyping performance

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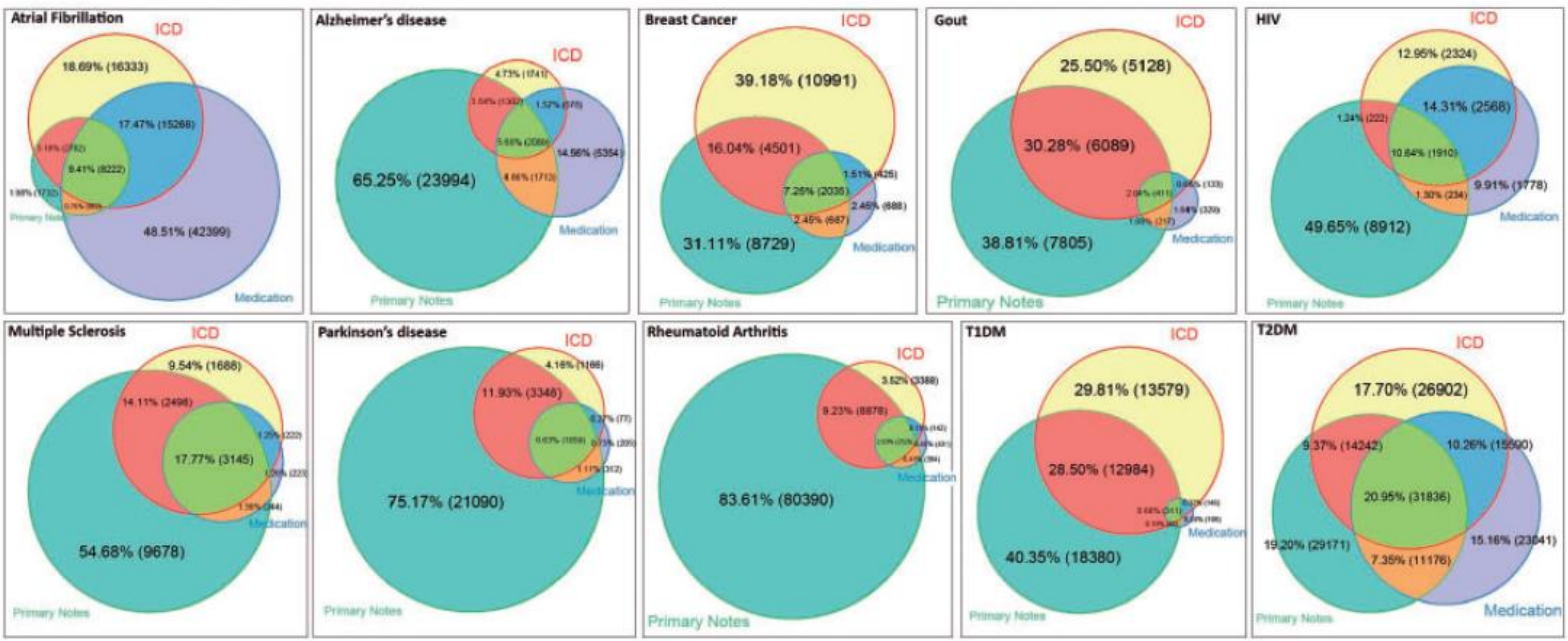
ACCEPTED 15 July 2015
PUBLISHED ONLINE FIRST 2 September 2015

AMIA
INFORMATICS PROFESSIONALS. LEADING THE WAY.

OXFORD
UNIVERSITY PRESS

Wei-Qi Wei[1], Pedro L Teixeira[1], Huan Mo[1], Robert M Cronin[1,2], Jeremy L Warner[1,2], Joshua C Denny[1,2]

Figure 1: Weighted Venn diagrams of the distributions of patients with ICD-9, primary notes, and specific medications. Each color represents a resource. Different area colors represent the number of patients that were found within intersecting resources.



Two Approaches to Phenotyping

Rule-Based Phenotyping

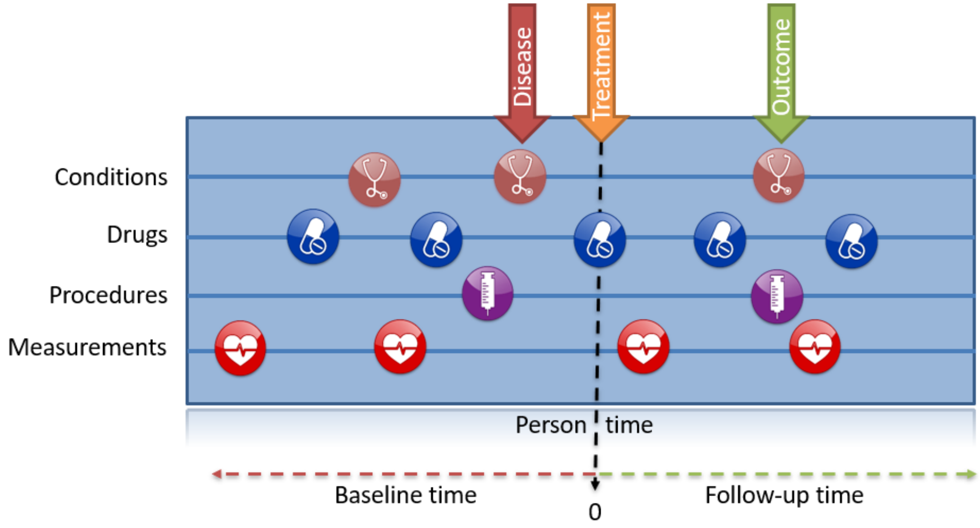
Probabilistic Phenotyping

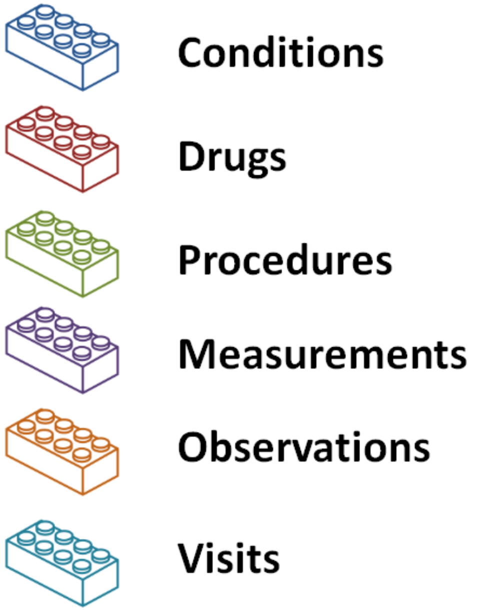
Data are the building blocks for Phenotyping

Person level dataset

With time-stamped events

Events organized in domains





Data are the building blocks for Phenotyping

Conditions

Drugs

Procedures

Measurements

Observations

Visits

Sponsor

Benefit Plan

Cost

OHDSI's definition of 'cohort'

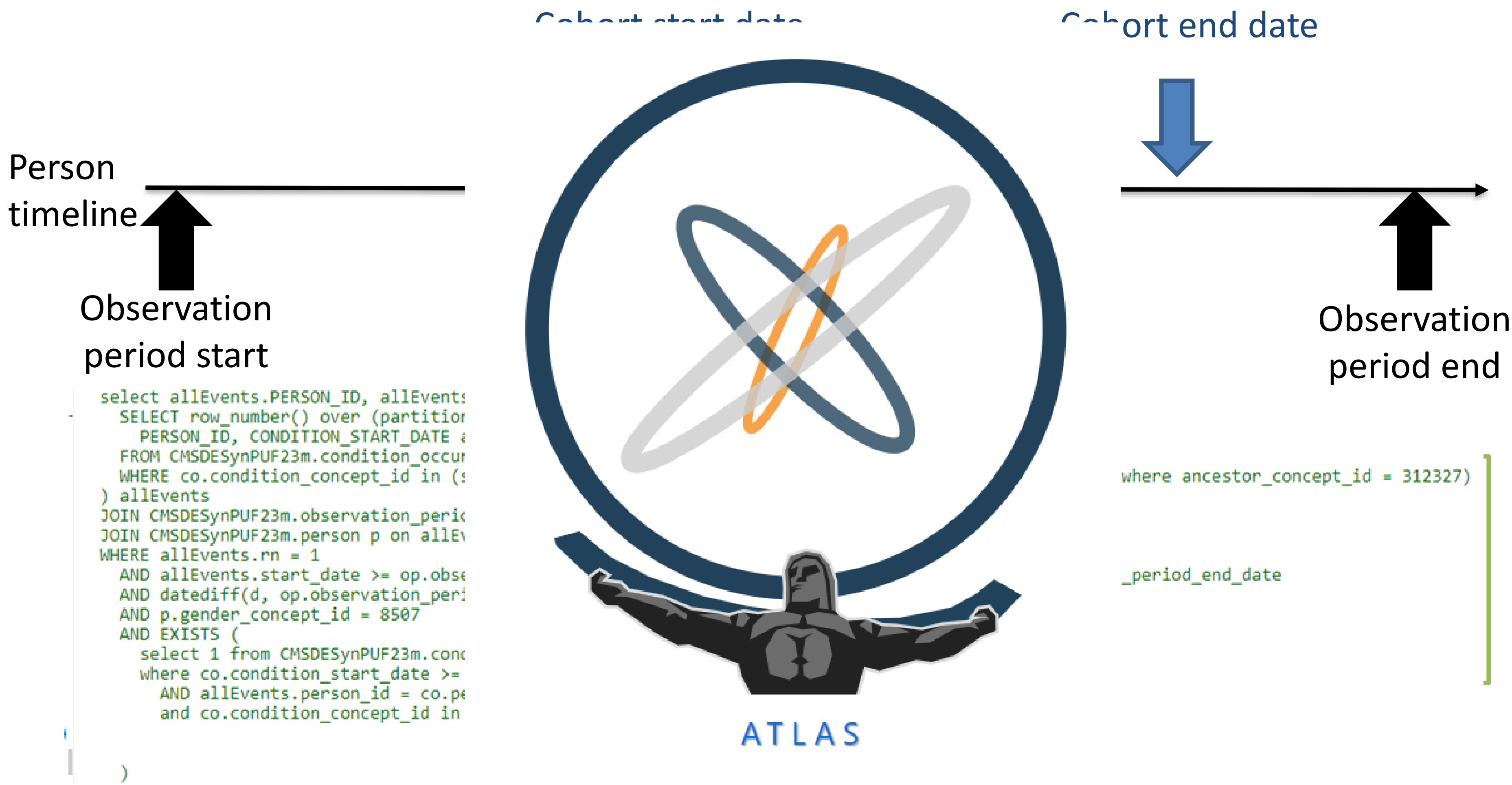
Cohort = a set of persons who satisfy one or more inclusion criteria for a <u>duration of time</u>

- One person may belong to multiple cohorts
- One person may belong to the same cohort at multiple different time periods
- One person may not belong to the same cohort multiple times during the same period of time
- One cohort may have zero or more members
- A codeset is NOT a cohort…

  …logic for how to use the codeset in a criteria is required

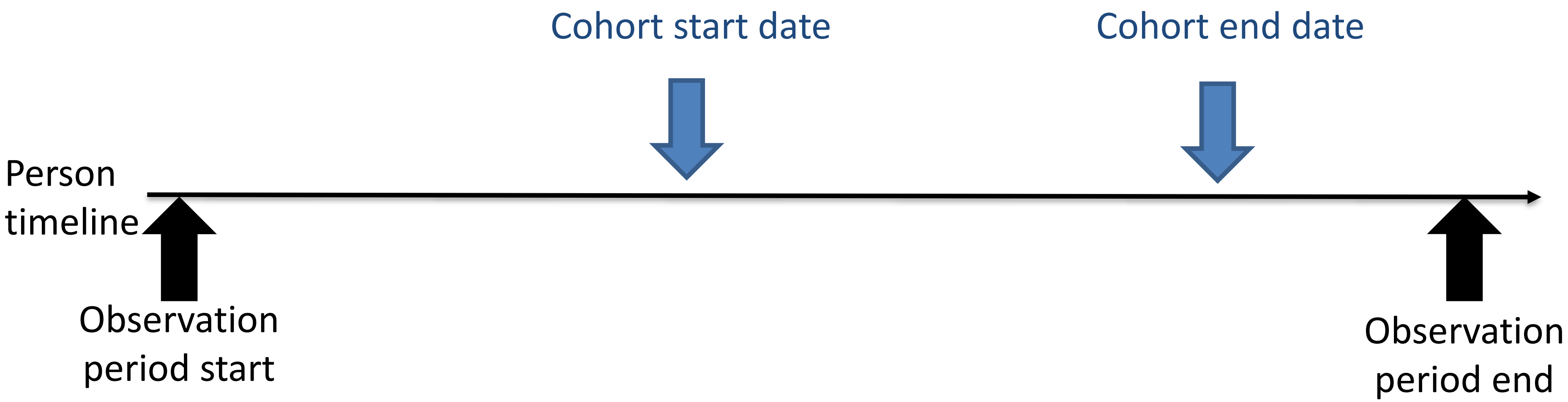
Cohort = Phenotype for a duration of time

OHDSI's definition of 'cohort'



*simulated data

Anatomy of rule based cohort definition



Criteria: rules, specific to a CDM, that is used to identify records (events) from patient data

Criteria Types:

1. Cohort entry events
2. Inclusion criteria
3. Cohort exit
4. Cohort eras

Rule based cohort definition in Atlas

Cohort Entry Events

Cohort Entry Events: CDM records selected from patient data that qualify the person for presence in a cohort.

+ Add Initial Event

Restrict initial events

Inclusion Criteria

New inclusion criteria

Inclusion Criteria: Use other patient data relative to the initial event to qualify the initial event as valid for inclusion. "Attrition study diagram."

Limit qualifying events to: earliest event per person.

Cohort Exit

Event Persistence:

Event will persist until: end of continuous ob

Censoring Events:

Exit Cohort based on the following criteria:

No censoring events selected.

Cohort Exit: Modify how long each event persists the patient's presence in the cohort, or identify records that censor the event.

- End of observation period
- Fixed time relative to event start date
- Censoring observations, e.g. procedure, or end of therapy

Cohort Eras

- Specify era collapse gap size: 0 days
- *add trimming options...*

Cohort Eras: Chain remaining event dates with an allowable gap with optional left- and/or right-censor the final eras (trimming).

Cardiovascular, Bleeding, and Mortality Risks in Elderly Medicare Patients Treated With Dabigatran or Warfarin for Nonvalvular Atrial Fibrillation

David J. Graham, MD, MPH; Marsha E. Reichman, PhD; Michael Wernecke, BA; Rongmei Zhang, PhD; Mary Ross Southworth, PharmD; Mark Levenson, PhD; Ting-Chang Sheu, MPH; Katrina Mott, MHS; Margie R. Goulding, PhD; Monika Houstoun, PharmD, MPH; Thomas E. MaCurdy, PhD; Chris Worrall, BS; Jeffrey A. Kelman, MD, MMSc

Background—The comparative safety of dabigatran versus warfarin for treatment of nonvalvular atrial fibrillation in general practice settings has not been established.

Methods and Results—We formed new-user cohorts of propensity score–matched elderly patients enrolled in Medicare who initiated dabigatran or warfarin for treatment of nonvalvular atrial fibrillation between October 2010 and December 2012. Among 134 414 patients with 37 587 person-years of follow-up, there were 2715 primary outcome events. The hazard ratios (95% confidence intervals) comparing dabigatran with warfarin (reference) were as follows: ischemic stroke, 0.80 (0.67–0.96); intracranial hemorrhage, 0.34 (0.26–0.46); major gastrointestinal bleeding, 1.28 (1.14–1.44); acute myocardial infarction, 0.92 (0.78–1.08); and death, 0.86 (0.77–0.96). In the subgroup treated with dabigatran 75 mg twice daily, there was no difference in risk compared with warfarin for any outcome except intracranial hemorrhage, in which case dabigatran risk was reduced. Most patients treated with dabigatran 75 mg twice daily appeared not to have severe renal impairment, the intended population for this dose. In the dabigatran 150-mg twice daily subgroup, the magnitude of effect for each outcome was greater than in the combined-dose analysis.

Conclusions—In general practice settings, dabigatran was associated with reduced risk of ischemic stroke, intracranial hemorrhage, and death and increased risk of major gastrointestinal hemorrhage compared with warfarin in elderly patients with nonvalvular atrial fibrillation. These associations were most pronounced in patients treated with dabigatran 150 mg twice daily, whereas the association of 75 mg twice daily with study outcomes was indistinguishable from warfarin except for a lower risk of intracranial hemorrhage with dabigatran. (*Circulation*. **2015;131:157-164. DOI: 10.1161/CIRCULATIONAHA.114.012061.**)

Key Words: anticoagulant ■ pharmacoepidemiology ■ safety ■ thrombin inhibitor ■ warfarin

Graham et al. description of the outcomes

Study Outcomes

The primary outcomes were ischemic stroke, major bleeding with specific focus on intracranial and gastrointestinal bleeding, and AMI. Secondary outcomes were all hospitalized bleeding events and mortality. The *International Classification of Diseases, Ninth Revision, Clinical Modification* codes used to define these outcomes are listed in Table II in the online-only Data Supplement. The codes defining ischemic stroke have a positive predictive value (PPV) of 88% to 95%.[18–20] Major bleeding was defined as

Table 2. International Classification of Disease, 9th edition, Clinical Modification (ICD 9-CM) codes used to define study outcomes.

Outcome	ICD-9 Codes	Position	Setting
AMI	410 (all)	1st or 2nd	IP only
Ischemic stroke	433.x1, 434.x (except subcode: x0), 436	1st	IP only

Rule based cohort definition in Atlas

Cohort Entry Events

Cohort Entry Events: CDM records selected from patient data that qualify the person for presence in a cohort.

+ Add Initial Event

Restrict initial events

Inclusion Criteria

New inclusion criteria

Inclusion Criteria: Use other patient data relative to the initial event to qualify the initial event as valid for inclusion. "Attrition study diagram."

Limit qualifying events to: earliest event per person.

Cohort Exit

Event Persistence:

Event will persist until: end of continuous ob

Censoring Events:

Exit Cohort based on the following criteria:

No censoring events selected.

Cohort Exit: Modify how long each event persists the patient's presence in the cohort, or identify records that censor the event.

- End of observation period
- Fixed time relative to event start date
- Censoring observations, e.g. procedure, or end of therapy

Cohort Eras

- Specify era collapse gap size: 0 days
- *add trimming options...*

Cohort Eras: Chain remaining event dates with an allowable gap with optional left- and/or right-censor the final eras (trimming).

Graham et al. description of the cohort(s)

A new-user retrospective cohort design was used to compare patients initiating dabigatran or warfarin for the treatment of nonvalvular AF.[10] We identified all patients with any inpatient or outpatient diagnoses of AF or atrial flutter based on *International Classification of Diseases, Ninth Revision* coding who also filled at least 1 prescription for either drug from October 19, 2010 (US dabigatran approval date) through December 31, 2012, the study end date. Patients were excluded if they had <6 months of enrollment in Medicare before their index dispensing, were aged <65 years, received prior treatment with a study medication or rivaroxaban or apixaban (anticoagulants approved during the study), were in a skilled nursing facility or nursing home, or were receiving hospice care on the date of their cohort-qualifying prescription. Patients were also excluded if they had a hospitalization that extended beyond the index dispensing date. Patients discharged from the hospital on the same day as their index dispensing were included. Patients undergoing dialysis and kidney transplant recipients were also excluded. Additionally, because warfarin is approved for indications other than AF, we excluded patients with diagnoses indicating the presence of mitral valve disease, heart valve repair or replacement, deep vein thrombosis, pulmonary embolism, or joint replacement surgery in the preceding 6 months.

Demo: Implementing cohorts in ATLAS

Follow along at:

(during training)

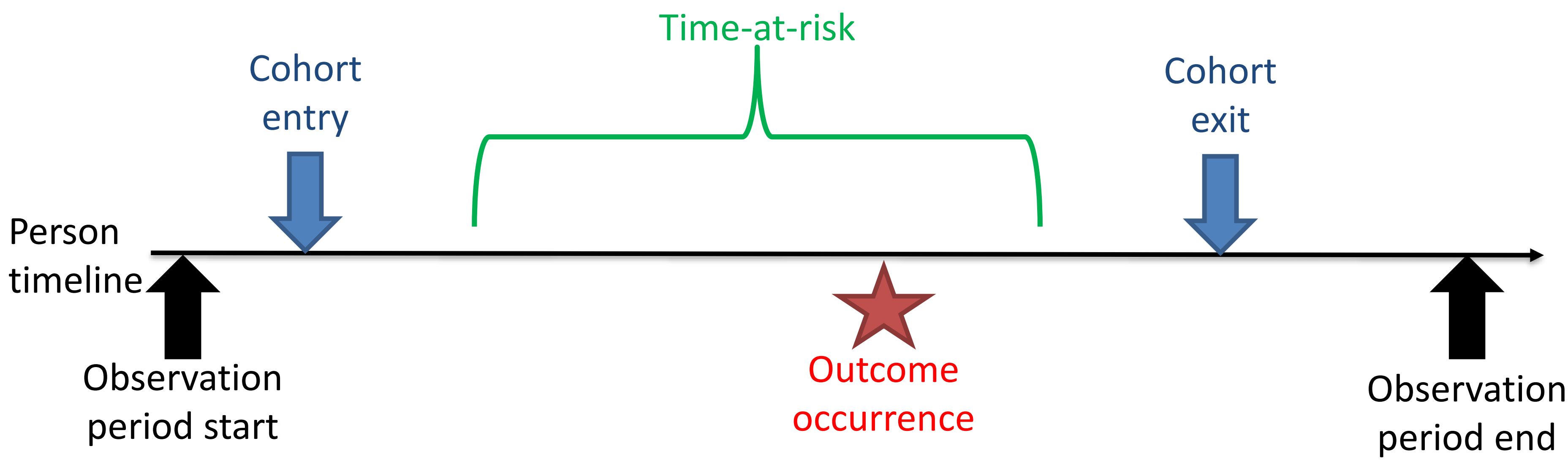
https://overview.ohdsi.amazingawsdemos.com

(public demo environment)

http://ohdsi.org/web/ATLAS

Incidence rate

Dissecting the anatomy of incidence



Incidence metrics:

$$\text{Incidence proportion} = \frac{\text{\# persons in the target cohort who have new outcome occurrence during the time-at-risk}}{\text{\# persons in the target cohort with time-at-risk*}}$$

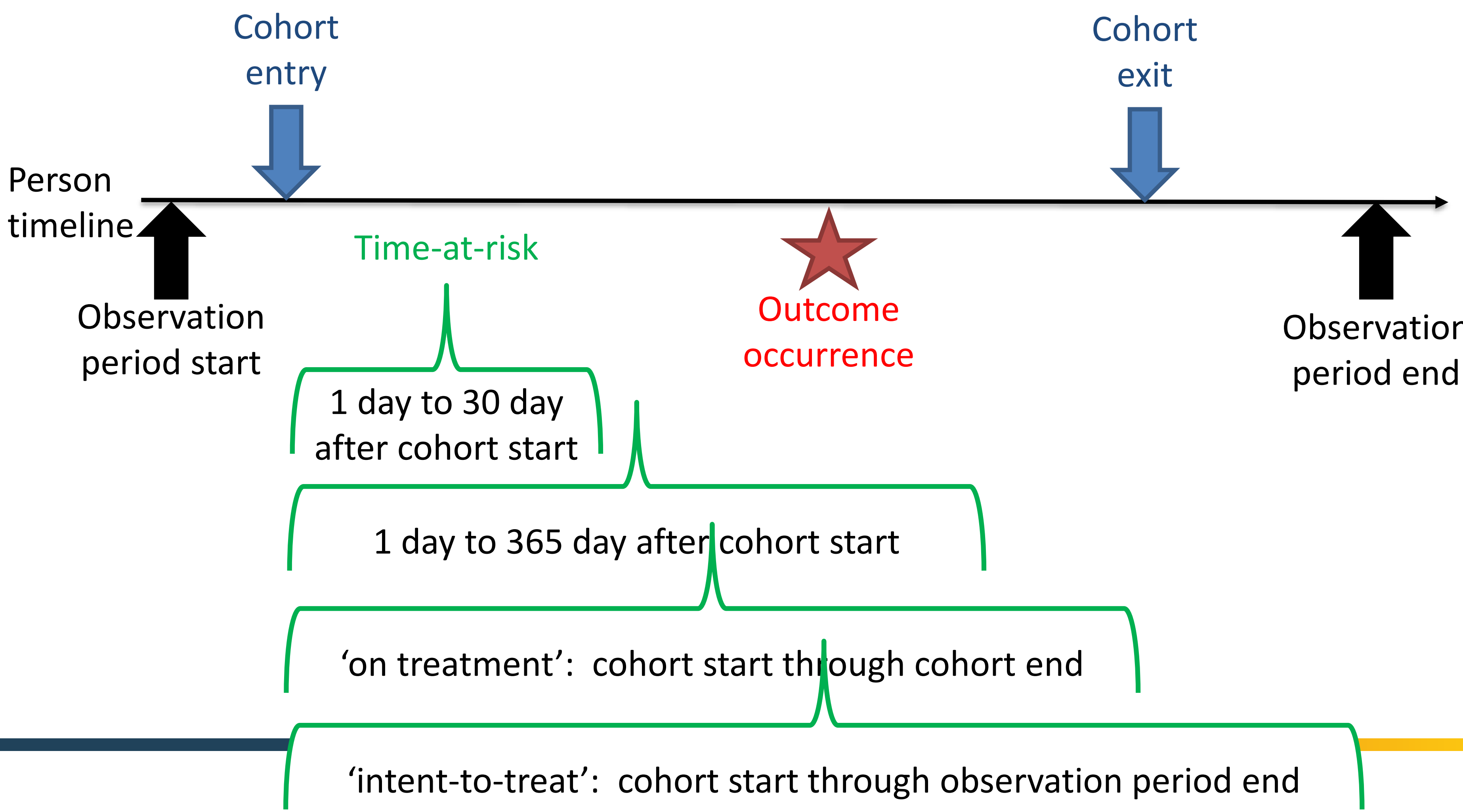
$$\text{Incidence rate} = \frac{\text{\# persons in the target cohort who have new outcome occurrence during the time-at-risk}}{\text{person-time at-risk for persons in the target cohort with time-at-risk*}}$$

Myriad difficult choices that researchers have to make to produce a 'simple answer'

- How should the target cohort be defined?
- How should the outcome be defined?
- How should the time-at-risk be defined?
- How to account for patients with incomplete time-at-risk?
- Which statistical metrics should be reported?
- Which data should be used?

Myriad difficult choices that researchers have to make to produce a 'simple answer'

- **How should the time-at-risk be defined?**



Decisions for incidence rate estimations in the OHDSI framework

- What's your **T**arget cohort(s)?
- What's your **O**utcome cohort(s)?
- What's your time-at-risk?
- What's your stratification criteria?

Demo: Implementing incidence rates in ATLAS

Follow along at:

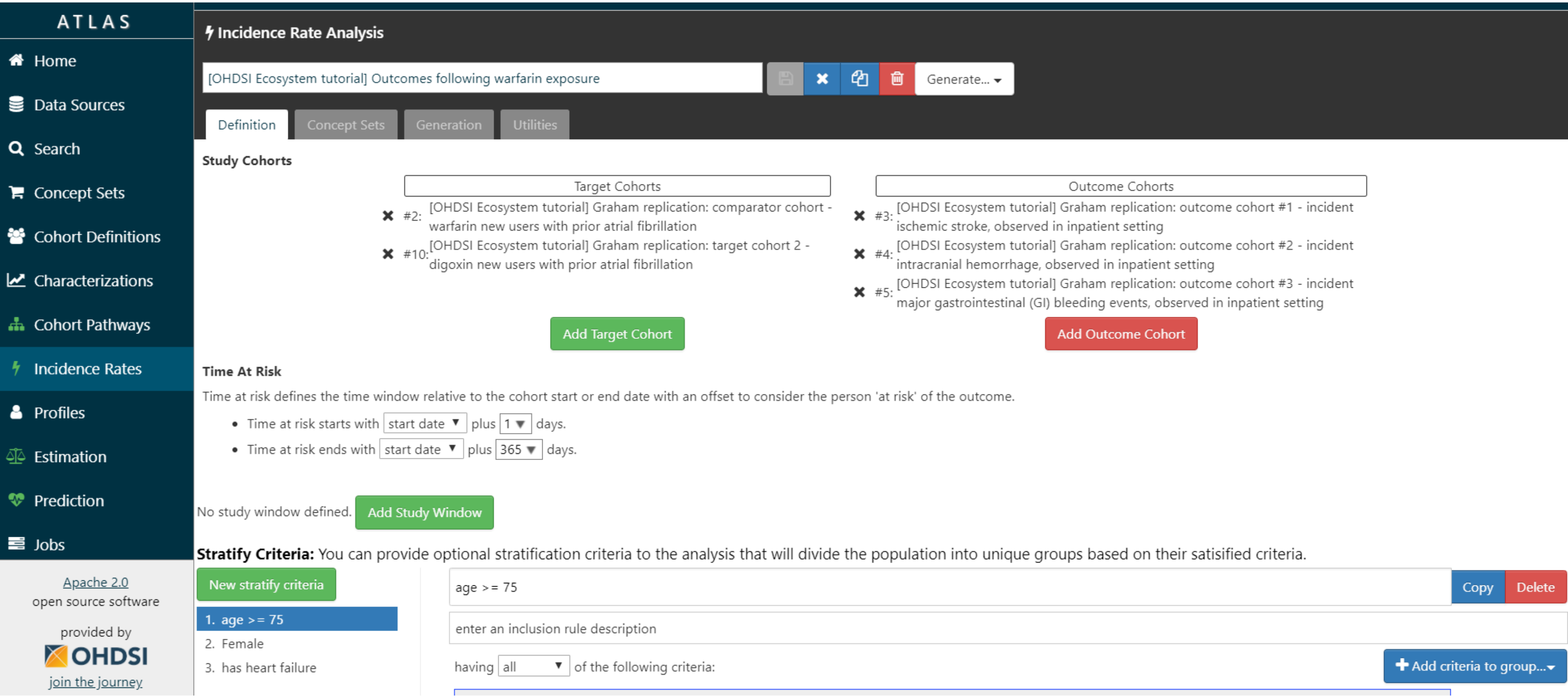
(during training)

https://overview.ohdsi.amazingawsdemos.com

(public demo environment)

http://ohdsi.org/web/ATLAS

Demo: incidence rate specification



Demo: incidence rate generation

Incidence Rate Analysis

[OHDSI Europe tutorial] Cardiovascular and Bleeding Risks in Elderly Medicare Patients Treate

Generate...

Definition | Concept Sets | Generation | Utilities

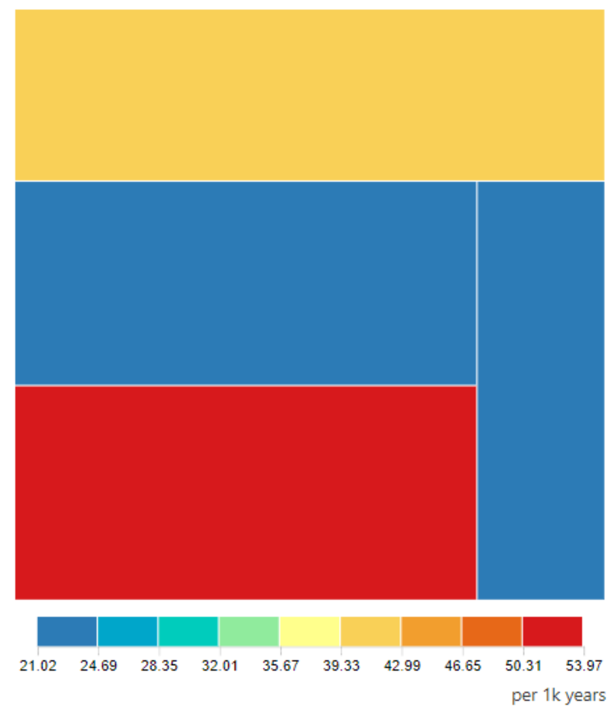
Export Analysis to CSV

Source	Name		Persons	Cases	Proportion [+|-] per 1k persons	Time At Risk (years)	Rate [+|-] per 1k years	Started	Duration	
TRUVENMDCR_V698	Truven MDCR	Execute	19,288	201	10.42	5,606	35.85	2018-03-21, 15:20	00:01:12	Remove

Showing target cohort: [OHDSI Europe tutorial] Graham replicatio and outcome cohort: [OHDSI Europe tutorial] Graham replicatic

	Persons	Cases	Proportion [+|-] per 1k persons	Time At Risk (years)	Rate [+|-] per 1k years
Summary Statistics:	19,288	201	10.42	5,606	35.85

Stratify Rule	N	Cases	Proportion [+|-] per 1k persons	Time At Risk (years)	Rate [+|-] per 1k years
1. Gender = MALE	10,839	99	9.13	3,223	30.72
2. Age >= 75	11,101	150	13.51	3,239	46.31



Estimation:
Population-level effect estimation using the comparative cohort design

Full-day tutorial in 30 minutes

- Will focus on key concepts here
- View video of full day here: https://www.ohdsi.org/past-events/2017-tutorials-population-level-estimation/

Two types of questions

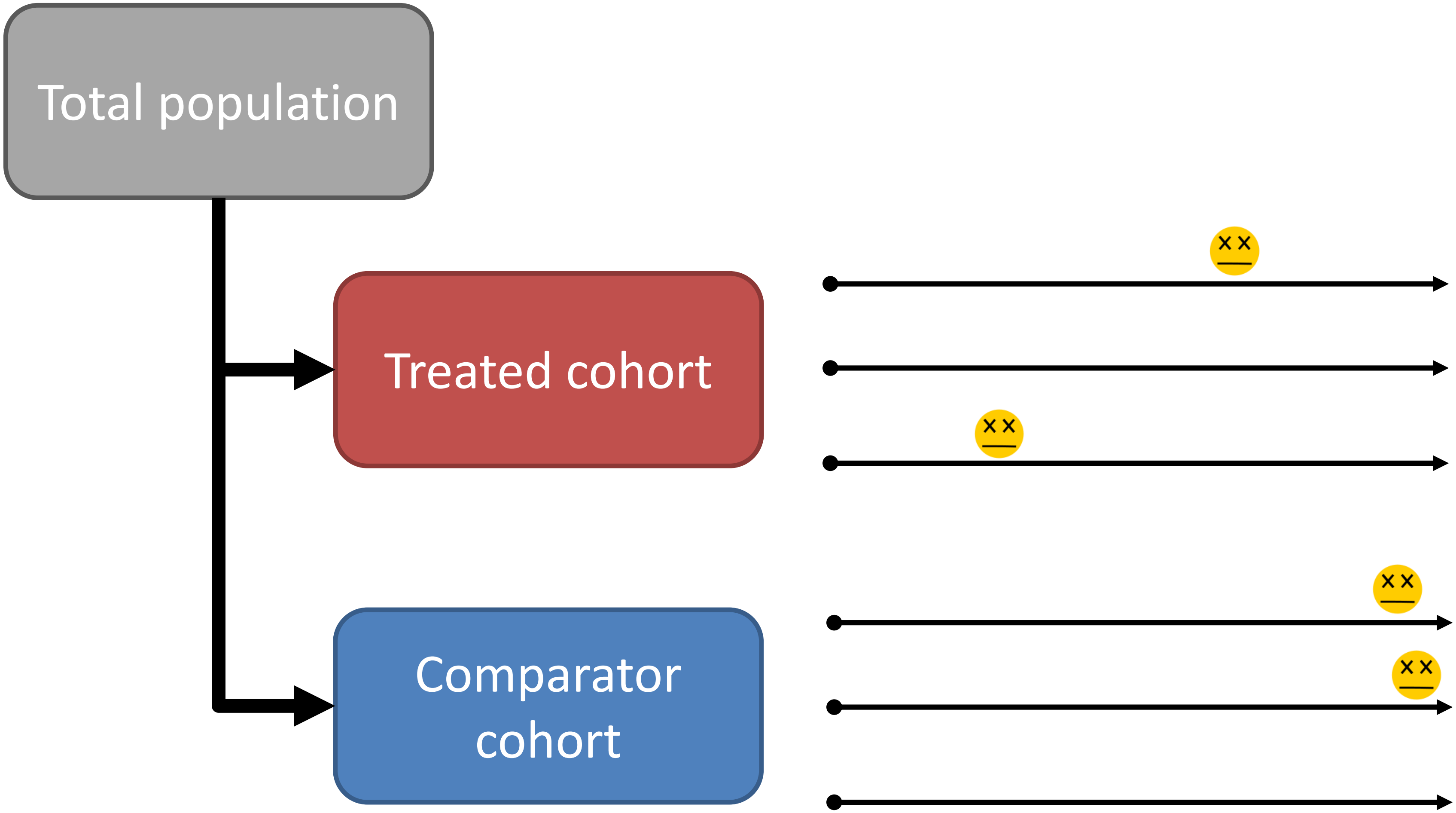
- Does exposure T cause outcome O?

  Effect estimation

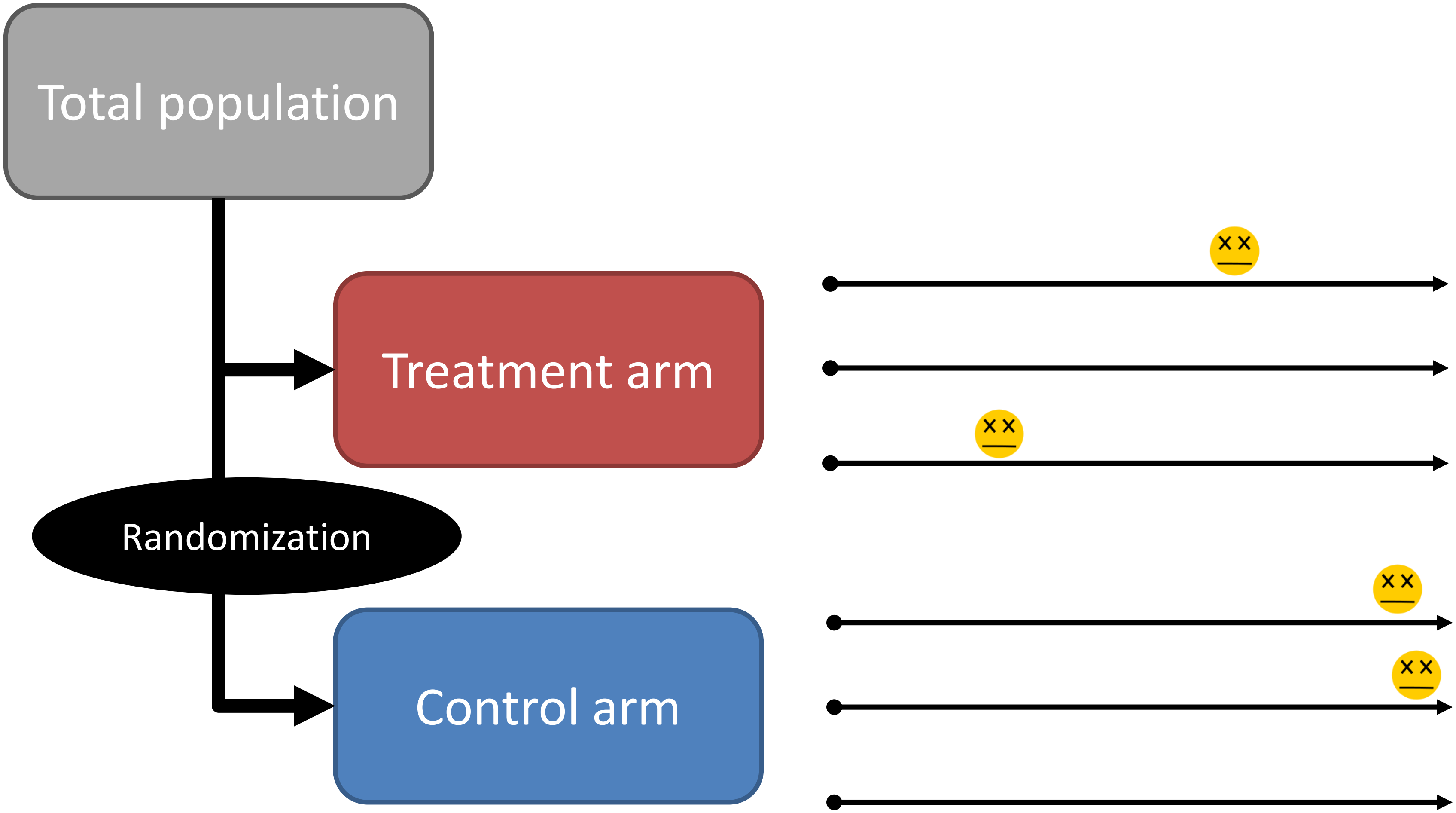
- Does exposure T cause outcome O compared to exposure C?

  Comparative effect estimation

New-user cohort design



Randomized controlled trial



New-user cohort design

Treatment assignment is not random!

Doctors have reasons why they prescribe a drug to some patients and not to others

Propensity score (PS)

The propensity score is the probability of receiving the treatment, conditional on a set of baseline characteristics

$$P(\, treatment \mid X) = f(\, \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \dots \,)$$

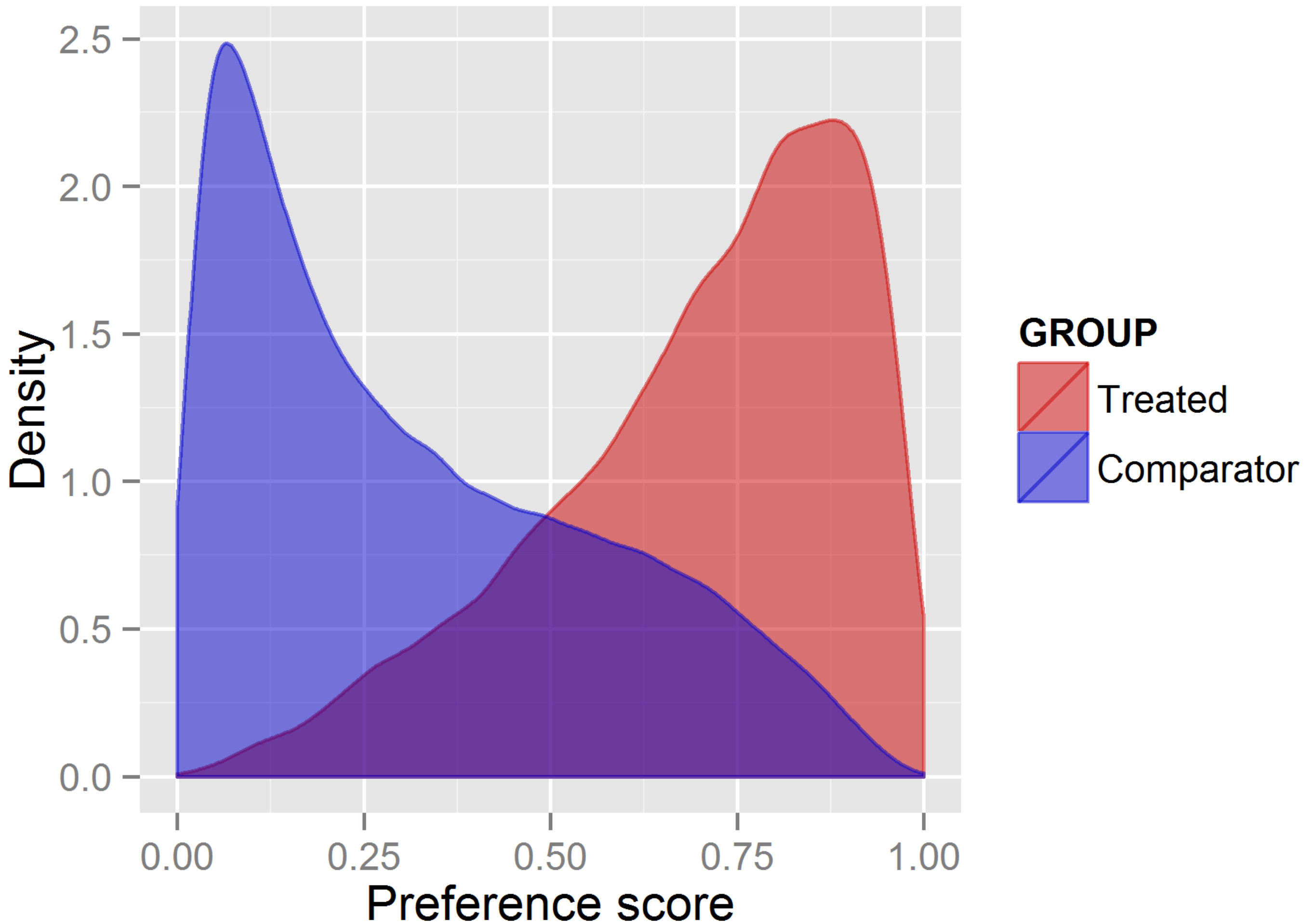
Intercept

Charlson Comorbidity Index

Gender

Age

PS score distribution



Using the PS

- **Trimming**

  if P(treatment) is around 50%, treatment assignment 'must be random'

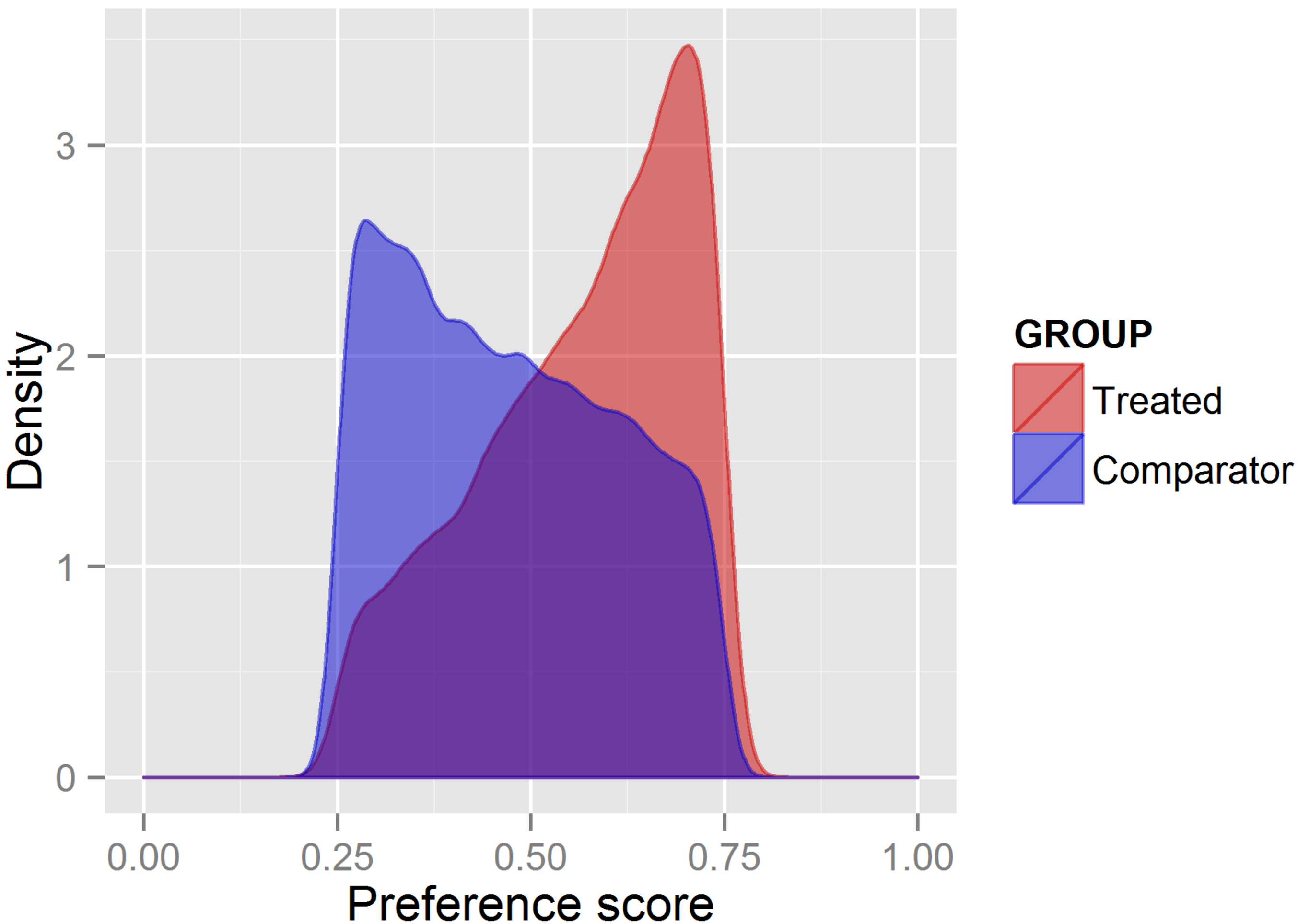
- **Stratification or matching**

  only compare subjects to subjects with a similar PS

- **Inverse probability weighting**
- **Adding to the outcome model**

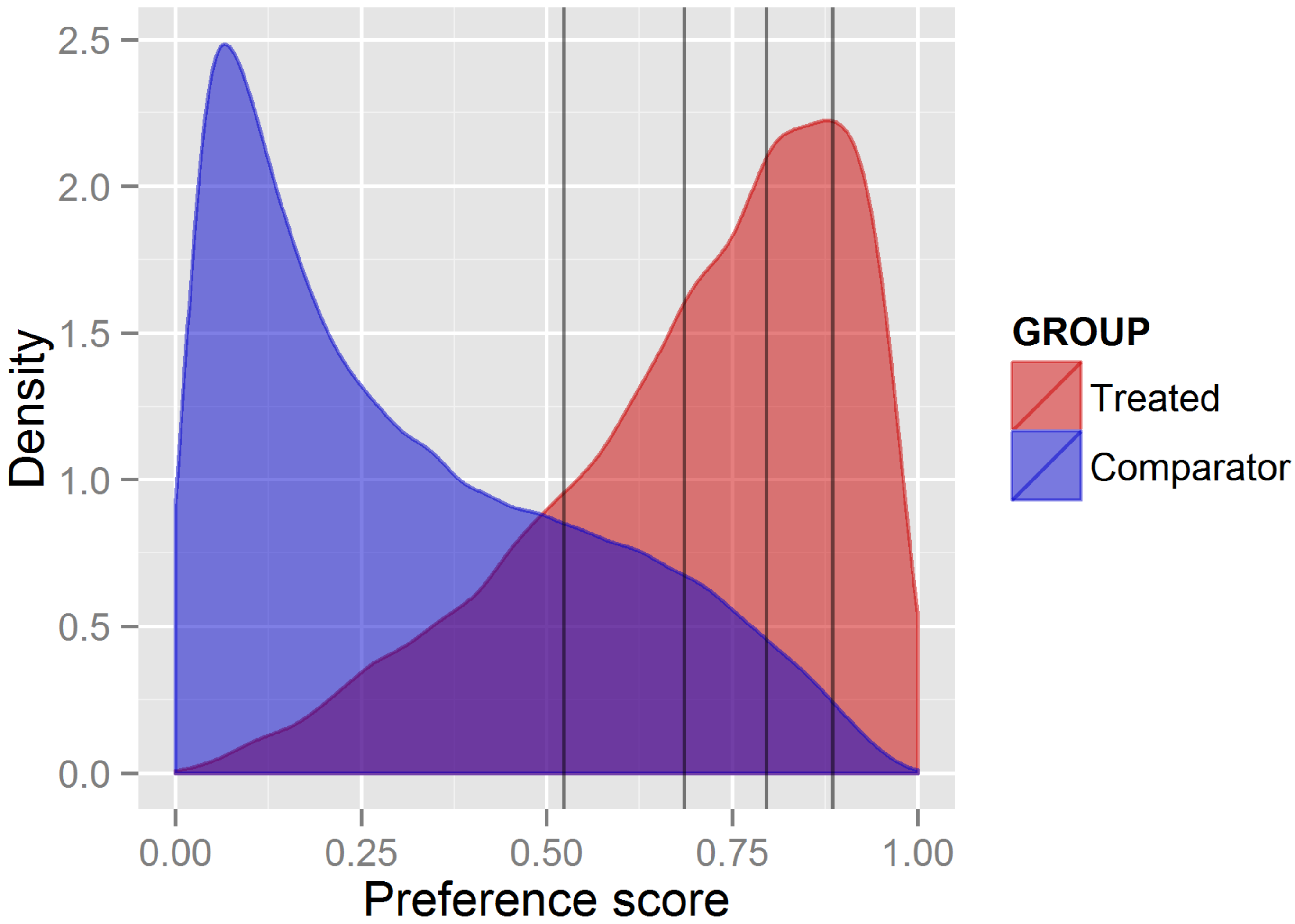
  correct for the PS in the model used to predict the outcome

Trimming

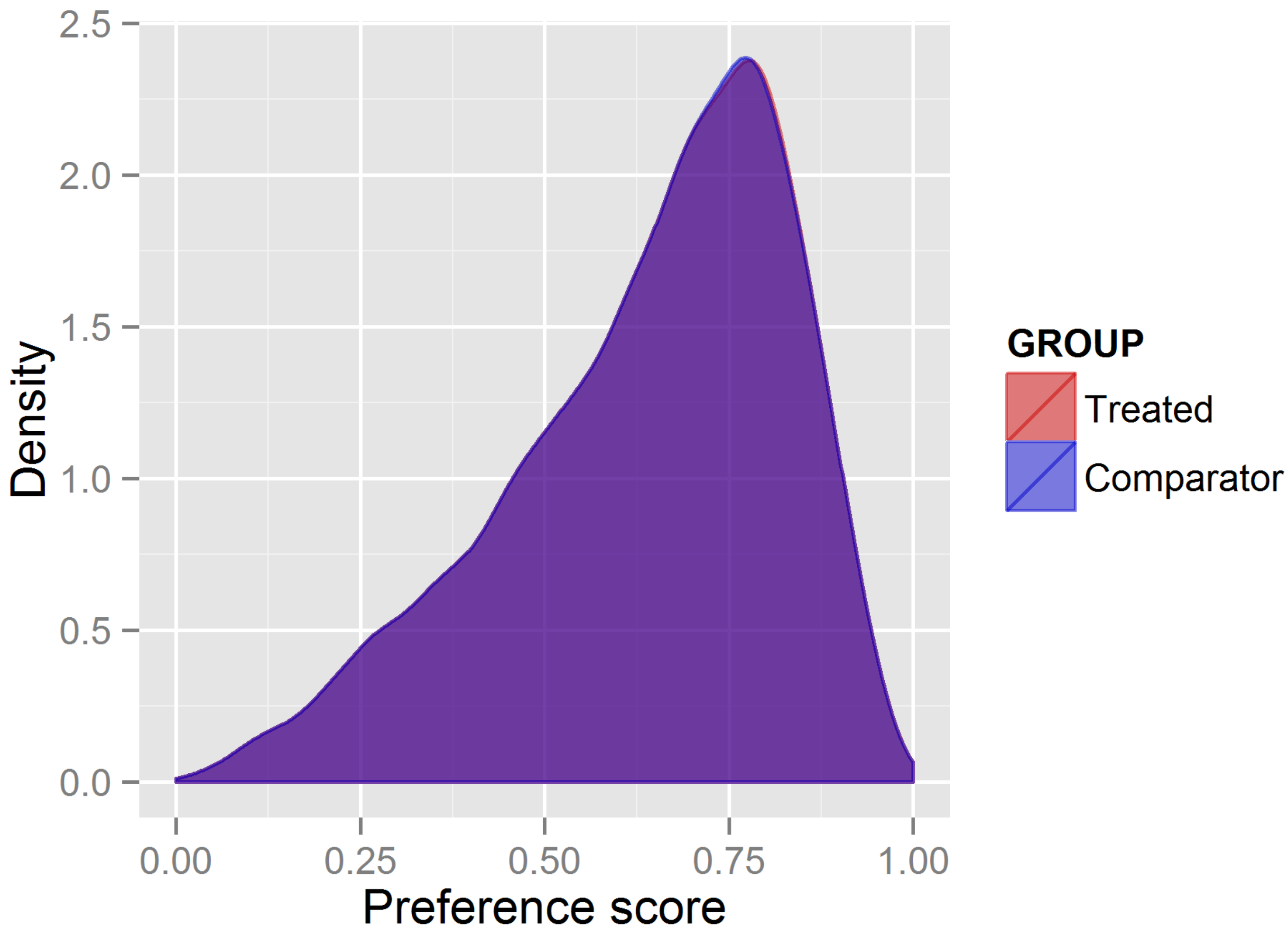


3
2
1
0
Density
0.00
0.25
0.50
0.75
1.00
Preference score
GROUP
Treated
Comparator

Stratifying



Matching



2.5
2.0
1.5
1.0
0.5
0.0
Density
0.00
0.25
0.50
0.75
1.00
Preference score
GROUP
Treated
Comparator

Which variables go into the PS model?

- Traditional: hard thinking by expert
- High-Dimensional PS: rank many variables (e.g. all
  dru … re
  (ar
  (H

Important: make sure not to put the exposures themselves in the model!

- Our approach: put everything (demographics, all drugs, all drug classes, all conditions, all disease classes, all procedures, all observations, all severity indexes) in a regularized regression

Types of outcome models

- Logistic

  Did the outcome occur yes/no?
- Poisson

  How many times did the outcome occur?
- Cox

  What was the time to the first outcome or end of observation?
- Conditional or non-conditional (Logistic, Poisson, Cox)

  stratify by PS strata or matched sets

Cardiovascular, Bleeding, and Mortality Risks in Elderly Medicare Patients Treated With Dabigatran or Warfarin for Nonvalvular Atrial Fibrillation

David J. Graham, MD, MPH; Marsha E. Reichman, PhD; Michael Wernecke, BA;
Rongmei Zhang, PhD; Mary Ross Southworth, PharmD; Mark Levenson, PhD;
Ting-Chang Sheu, MPH; Katrina Mott, MHS; Margie R. Goulding, PhD;
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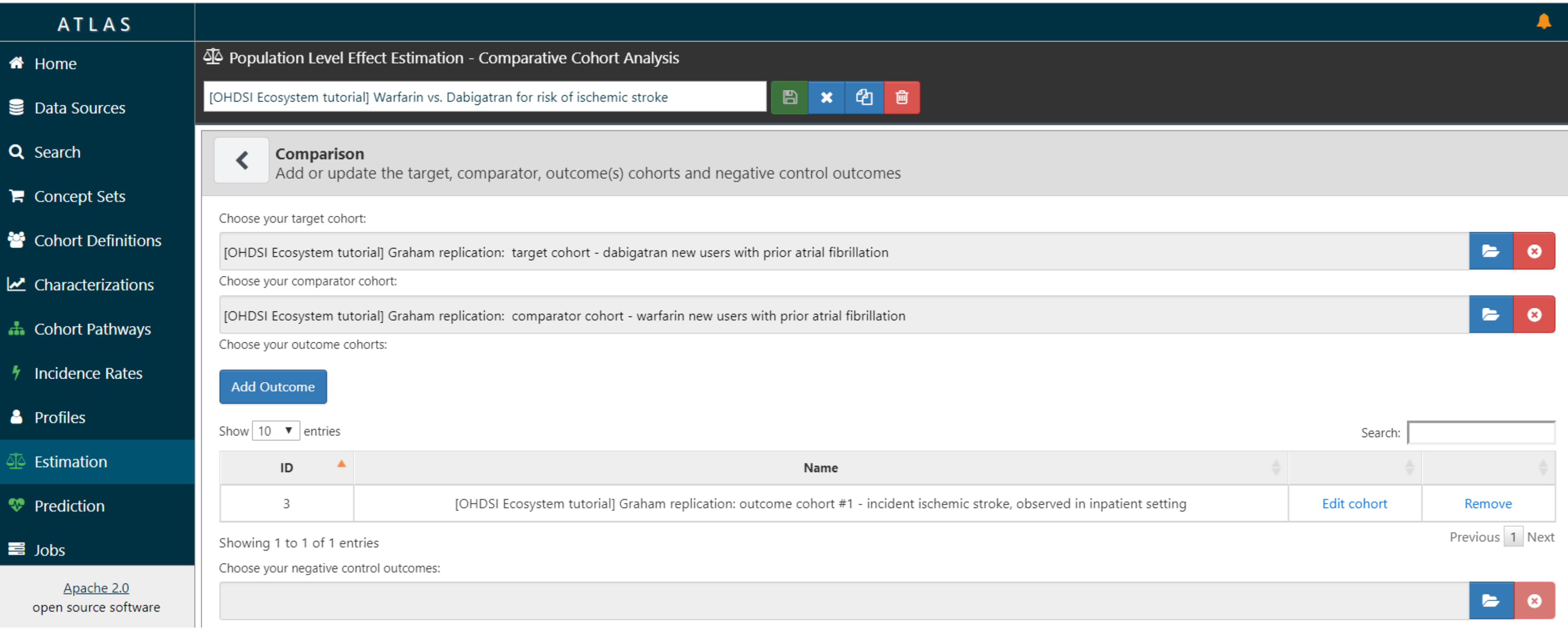
Key Words: anticoagulant ■ pharmacoepidemiology ■ safety ■ thrombin inhibitor ■ warfarin

What is the design used by Graham et al?

Input parameter	Design choice
Target cohort (T)	dabigatran new users with prior atrial fibrillation
Comparator cohort (C)	warfarin new users with prior atrial fibrillation
Outcome cohort (O)	Ischemic stroke
Time-at-risk	1 day after cohort start → cohort end
Model specification	1:1 propensity score-matched univariable conditional Cox proportional hazards

Graham et al. description of the cohort selection strategy

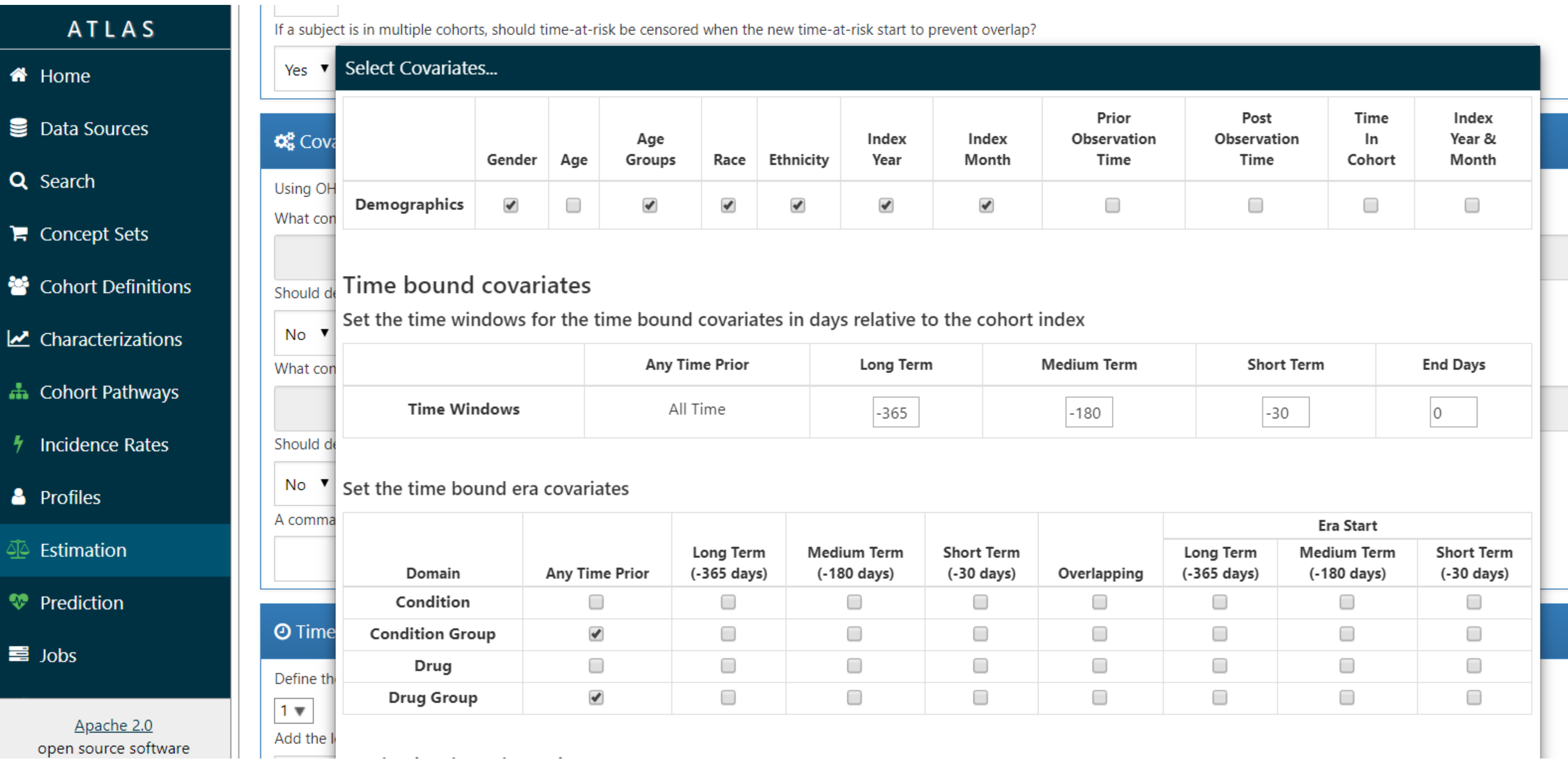


Graham et al. description of the covariate adjustment strategy

To reduce confounding due to imbalance in study covariates, propensity score matching was used.[14–16] Unconditional logistic regression was used to estimate the predicted probability of patients initiating dabigatran therapy given their sociodemographic characteristics, baseline medical comorbidities, medications used during the preceding 6 months, prescriber characteristics, and other potentially relevant variables (Table 1 and

Table I in the online-only Data Supplement). Dabigatran users were propensity score matched to warfarin users in a 1:1 ratio with the use of a greedy matching algorithm. The balance of measured covariates between the matched cohorts was assessed with the standardized mean difference, a measure not influenced by sample size and thus useful for comparing cohorts in large observational studies.[17] A standardized mean difference of ≤0.1 indicates a negligible difference in the measured variables between groups.[17]

Graham et al. replication: Designing the covariate adjustment strategy in ATLAS



Graham et al. replication: Designing the covariate adjustment strategy in ATLAS

What concepts do you want to include in baseline covariates in the propensity score model? (Leave blank if you want to include everything)

OHDSI estimation tutorial - Graham replication: covariates to include in PS model

What concepts do you want to exclude from baseline covariates in the propensity score model? (Leave blank if you want to include everything)

OHDSI estimation tutorial - Graham replication: covariates to exclude in PS model

How do you want to restrict your cohorts based on the propensity score distribution?

None

Do you want to perform matching or stratification?

Matching

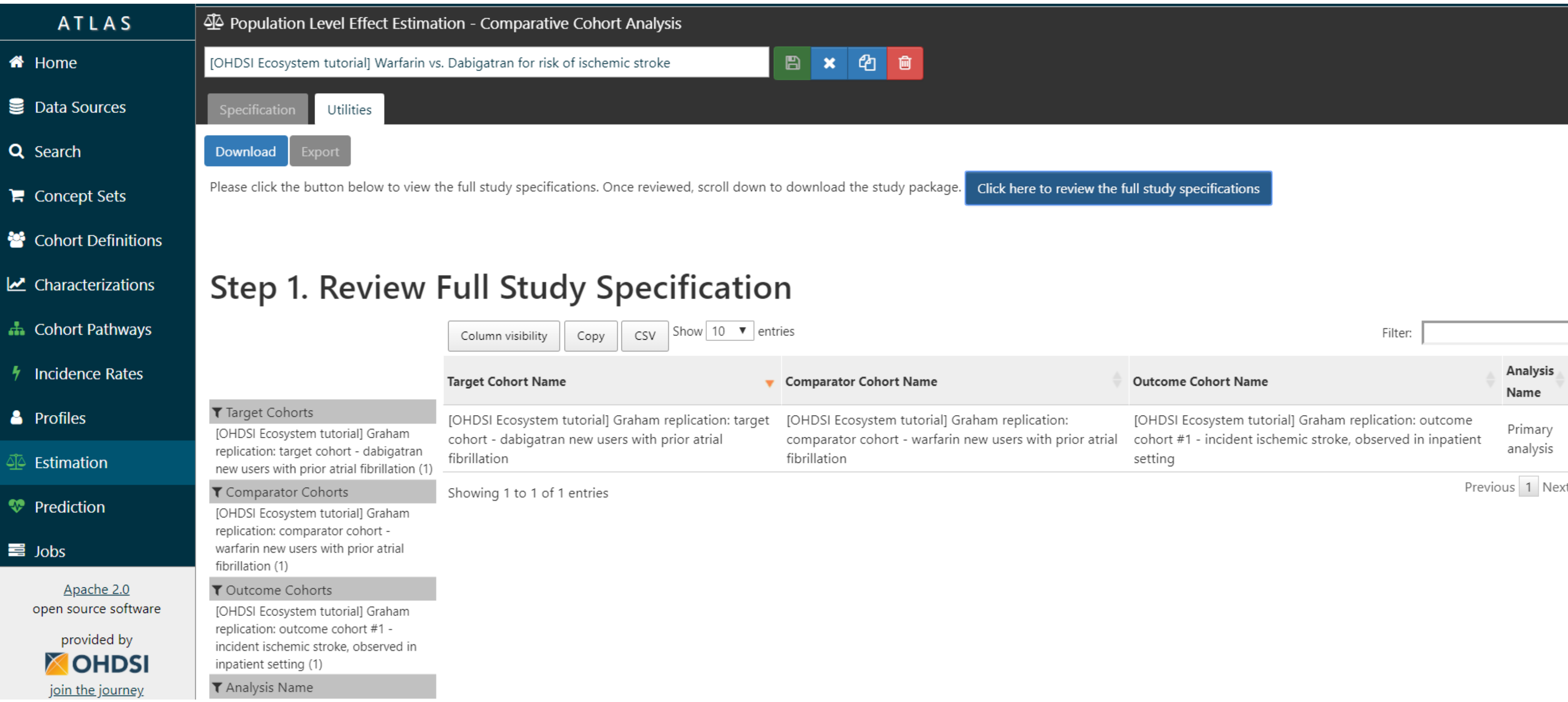
How many comparator patients do you want to select for each target patient (within a defined caliper)?

1

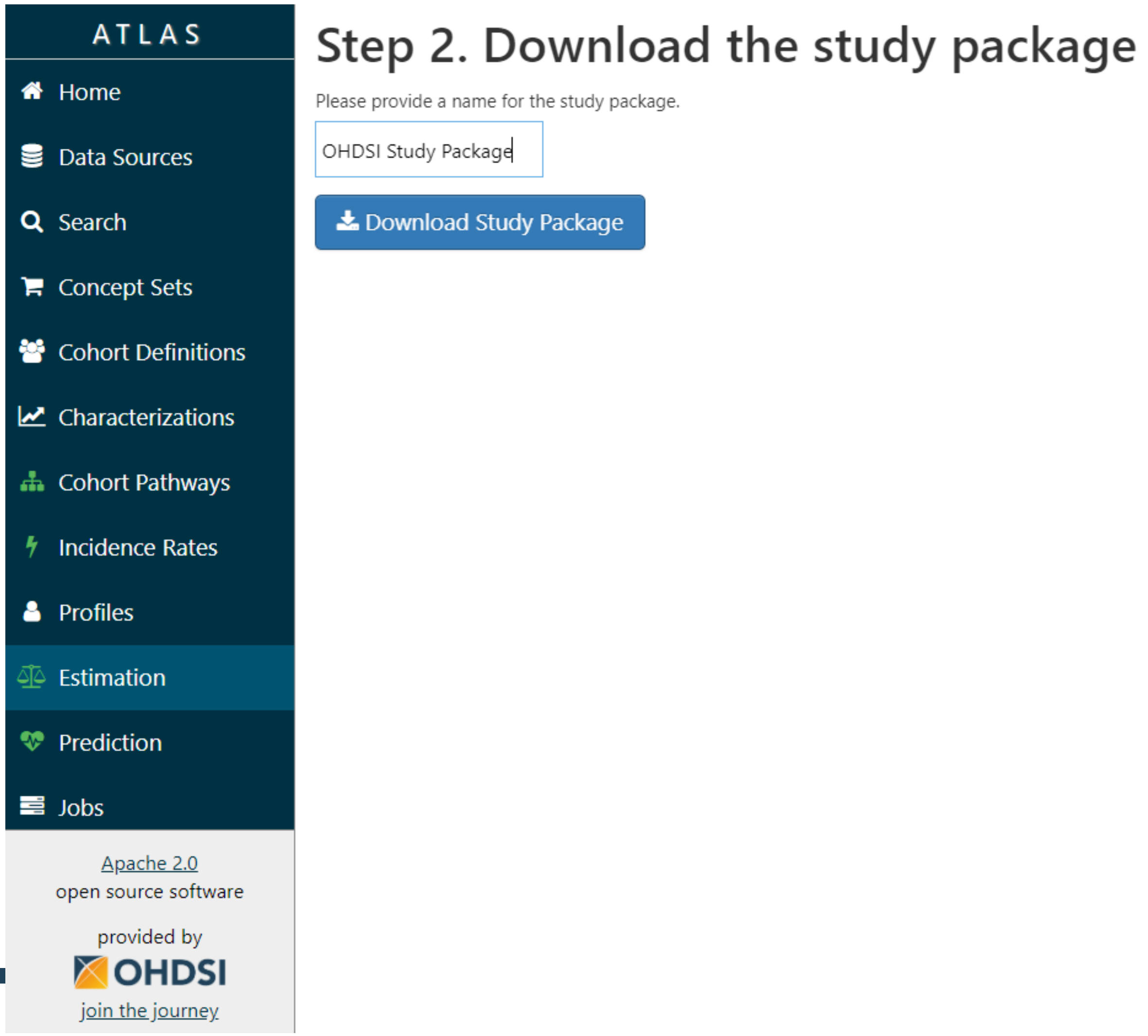
Do you want to adjust for baseline covariates in the outcome model?

No

Graham et al. replication: Designing a protocol in ATLAS

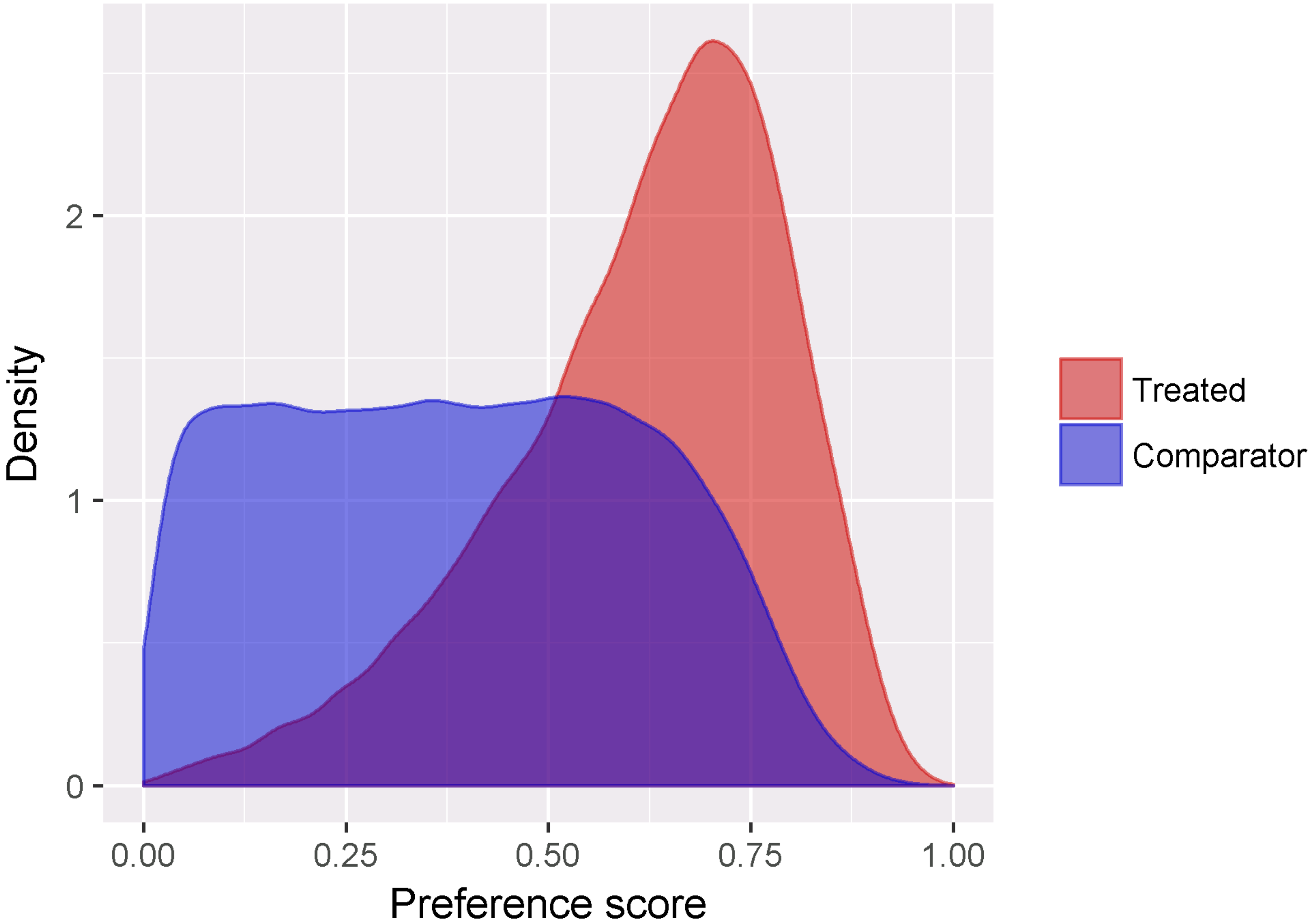


Graham et al. replication: Designing the source code in ATLAS

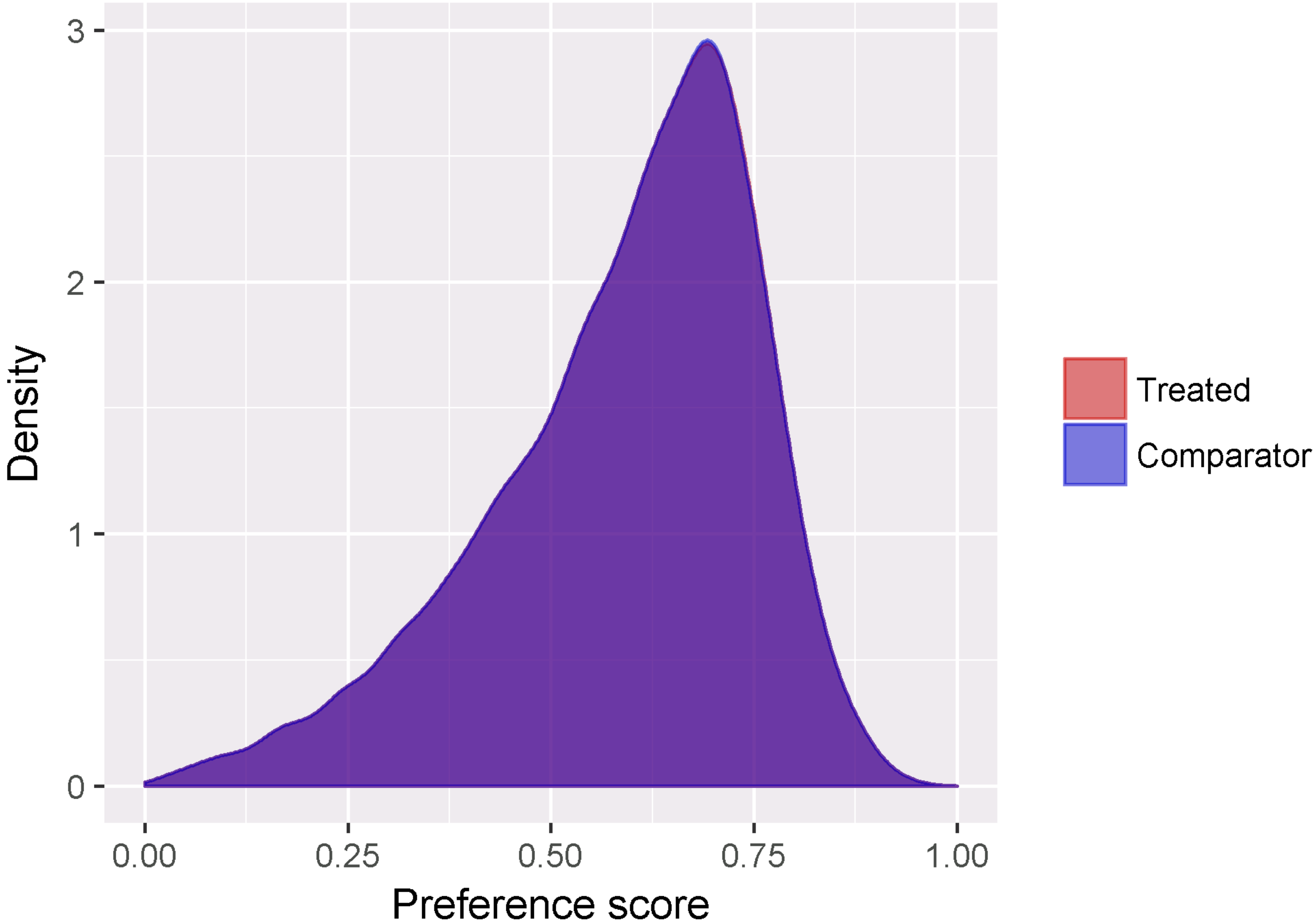


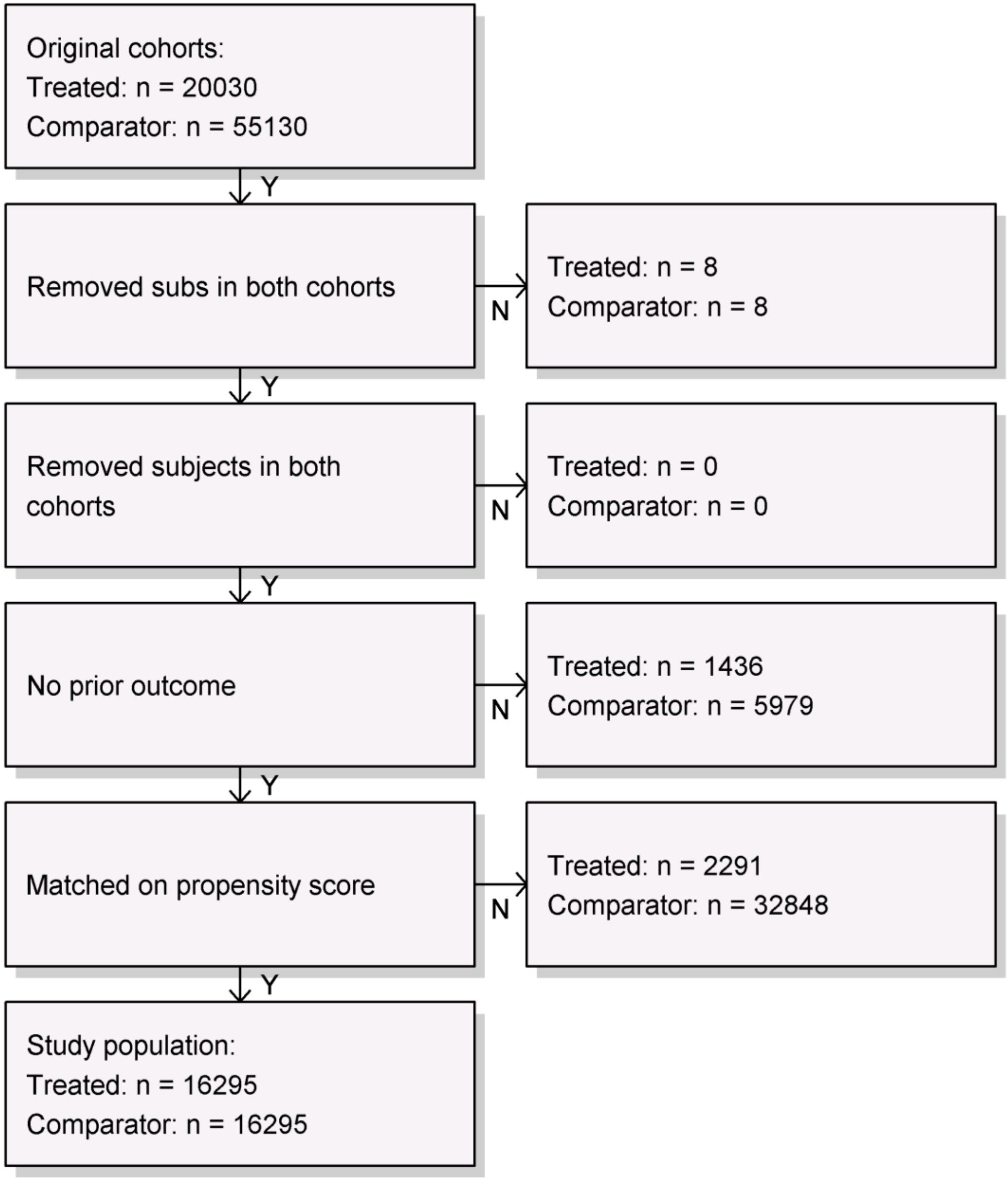
Interpreting results

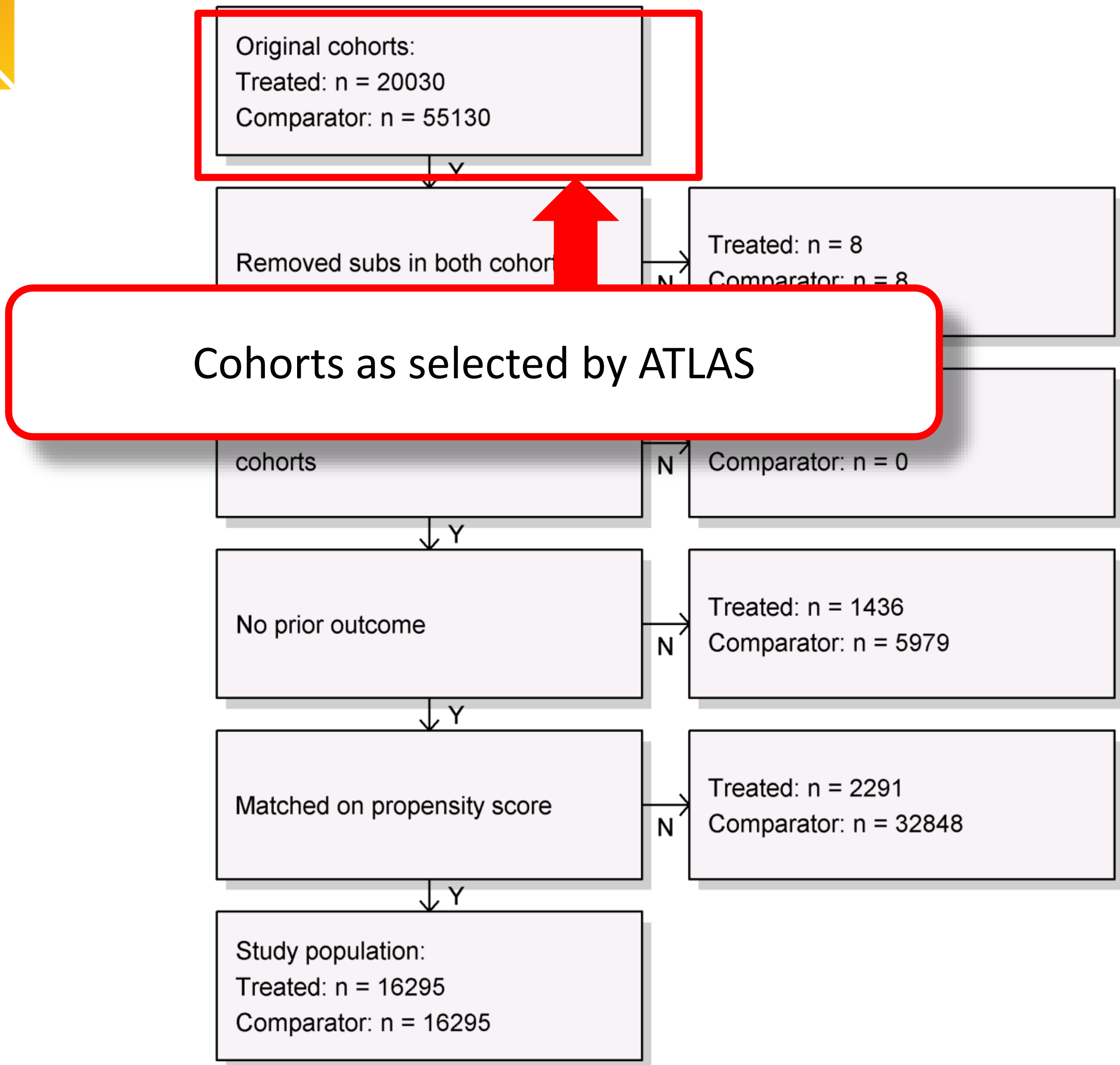
Plot propensity score distribution



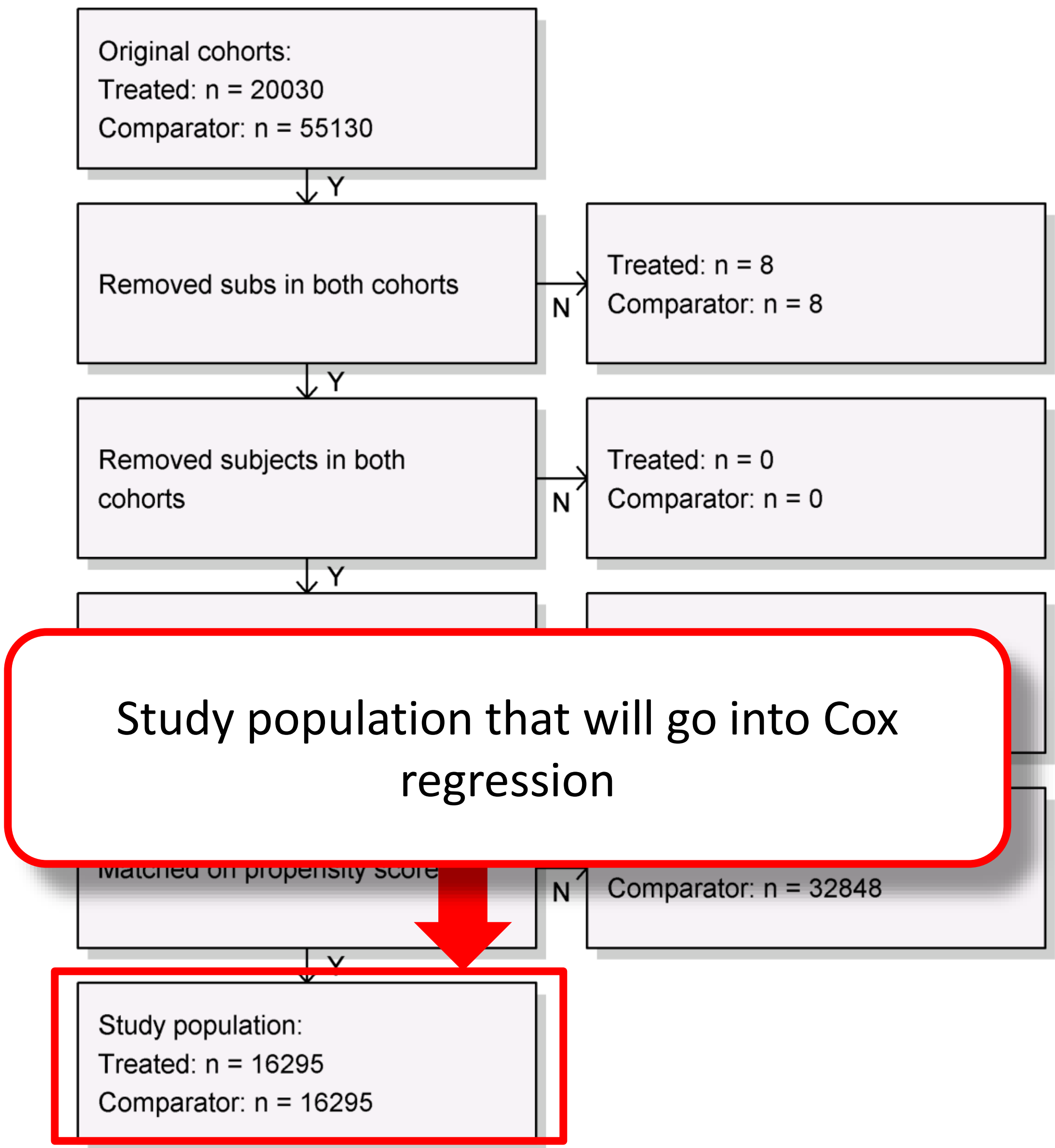
After matching



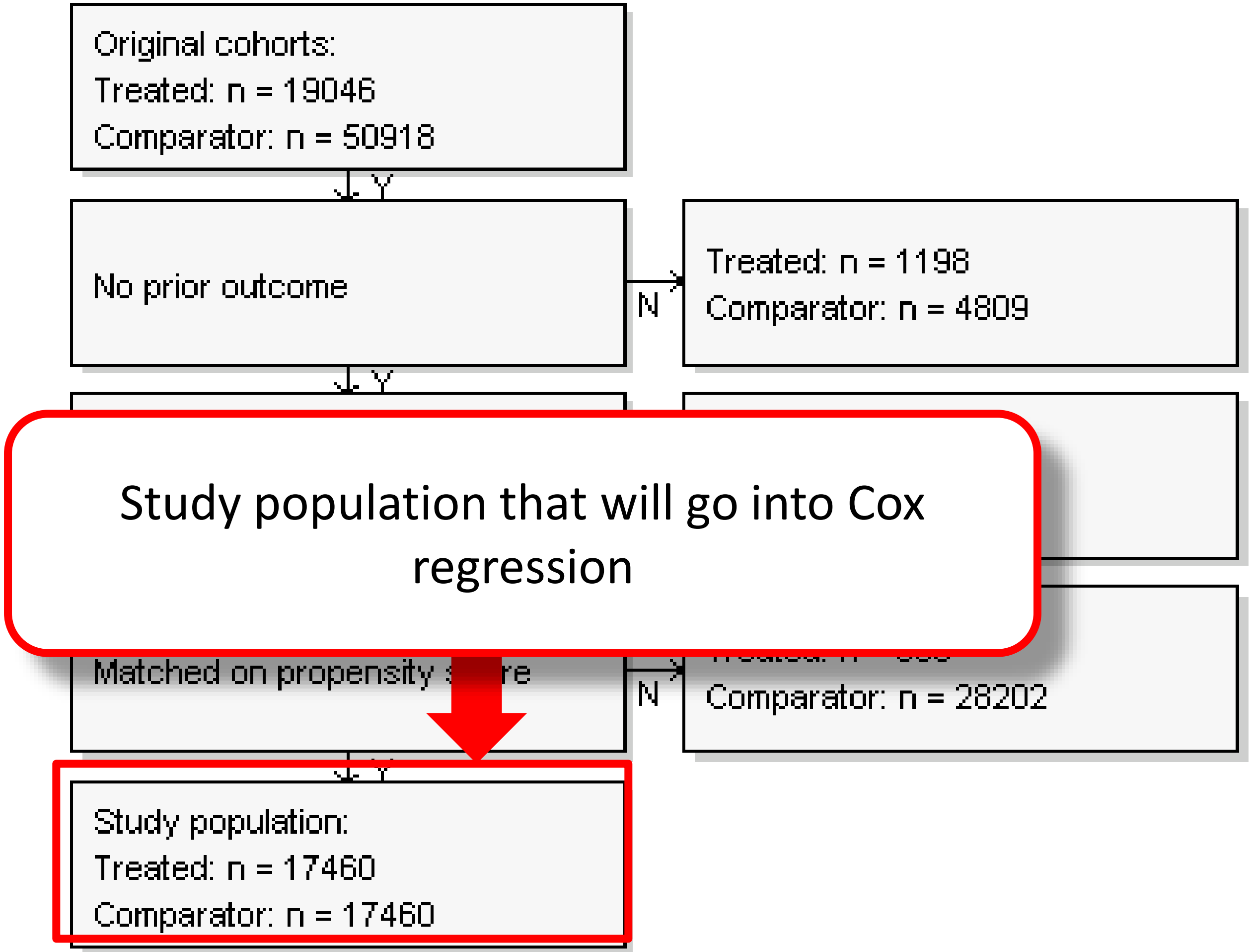

Original cohorts:
Treated: n = 20030
Comparator: n = 55130
Y
Removed subs in both cohorts
N
Treated: n = 8
Comparator: n = 8
Y
Removed subjects in both cohorts
N
Treated: n = 0
Comparator: n = 0
Y
No prior outcome
N
Treated: n = 1436
Comparator: n = 5979
Y
Matched on propensity score
N
Treated: n = 2291
Comparator: n = 32848
Y
Study population:
Treated: n = 16295
Comparator: n = 16295



Original cohorts:
Treated: n = 20030
Comparator: n = 55130
Y
Cohorts as selected by ATLAS
Treated: n = 8
N
cohorts
Comparator: n = 0
N
Y
No prior outcome
Treated: n = 1436
Comparator: n = 5979
N
Y
Matched on propensity score
Treated: n = 2291
Comparator: n = 32848
N
Y
Study population:
Treated: n = 16295
Comparator: n = 16295

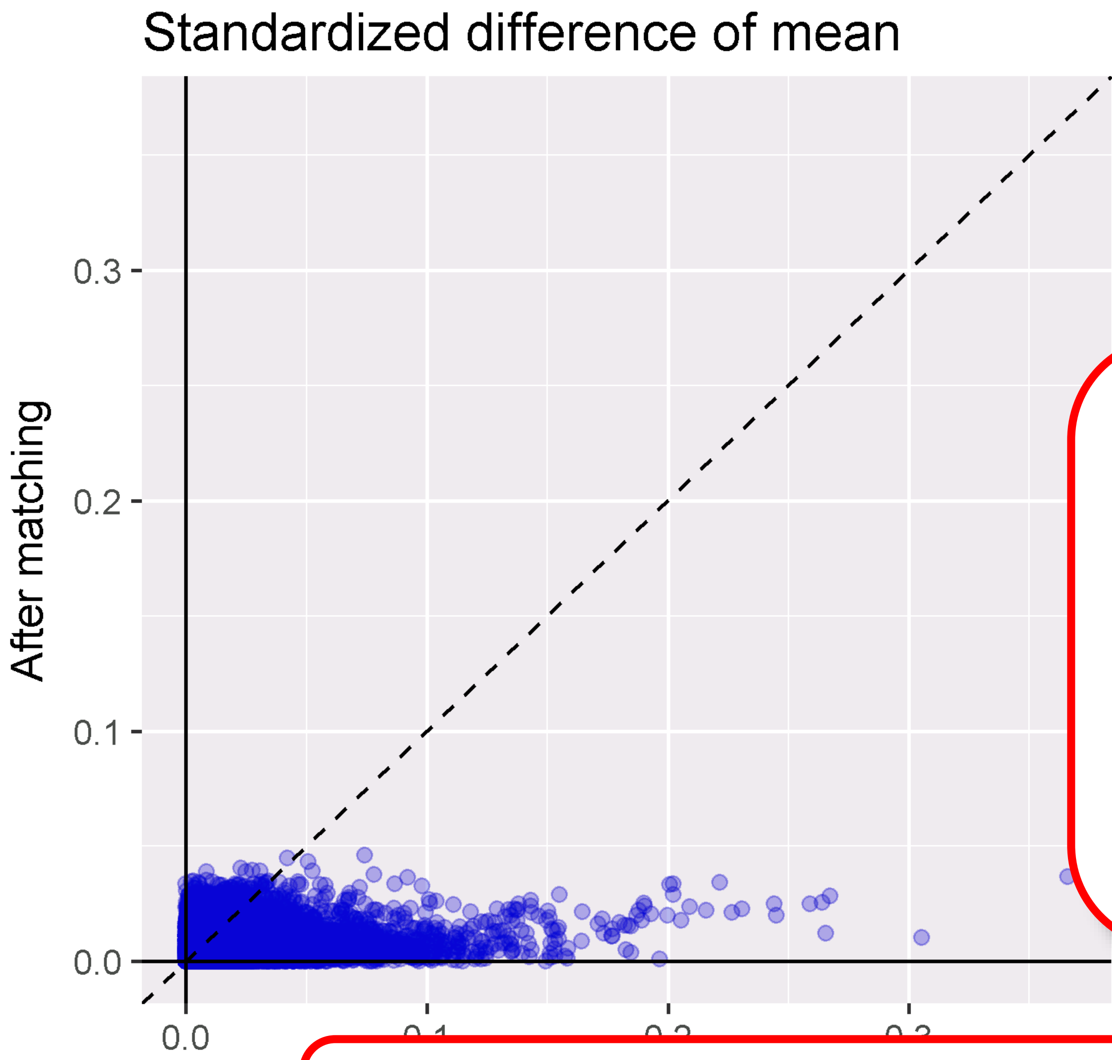

Original cohorts:
Treated: n = 20030
Comparator: n = 55130
Y
Removed subs in both cohorts
N
Treated: n = 8
Comparator: n = 8
Y
Removed subjects in both cohorts
N
Treated: n = 0
Comparator: n = 0
Y
Study population that will go into Cox regression
N
Comparator: n = 32848
Y
Study population:
Treated: n = 16295
Comparator: n = 16295

Attrition



Original cohorts:
Treated: n = 19046
Comparator: n = 50918
Y
No prior outcome
N
Treated: n = 1198
Comparator: n = 4809
Y
Study population that will go into Cox regression
Matched on propensity s re
N
Comparator: n = 28202
Y
Study population:
Treated: n = 17460
Comparator: n = 17460

Covariate balance



Most covariates are binary:

$$\frac{abs(P_{\text{target group}} - P_{\text{comparator group}})}{\text{standard deviation}}$$

Graham: "A standardized mean difference of ≤0.1 indicates a negligible difference."

Inspect the outcome model

Model type: cox
Stratified: TRUE
Use covariates: FALSE
Use inverse probability of treatment weighting: FALSE
Status: OK

	Estimate	lower .95	upper .95	logRr	seLogRr
treatment	0.78000	0.51050	1.18316	-0.24846	0.2144

Population counts

	treatedPersons	comparatorPersons	treatedExposures	comparatorExposures
Count	16295	16295	16295	16295

Outcome counts

	treatedPersons	comparatorPersons	treatedExposures	comparatorExposures
Count	81	73	81	73

Time at risk

	treatedDays	comparatorDays
Days	1682365	1515233

Inspect the outcome model

Model type: cox
Stratified: TRUE
Use covariates: FALSE
Use inverse probability of treatment weighting: FALSE
Status: OK

	Estimate	lower .95	upper .95	logRr	seLogRr
treatment	0.78000	0.51050	1.18316	-0.24846	0.2144

Point estimate and 95% confidence interval

Population counts

	treatedPersons	comparatorPersons	treatedExposures	comparatorExposures
C				16295

C

			edExposures	comparatorExposures
Count	81	73	81	73

Time at risk

	treatedDays	comparatorDays
Days	1682365	1515233

Inspect the outcome model

Model type: cox
Stratified: TRUE
Use covariates: FALSE
Use inverse probability of treatment weighting: FALSE
Status: OK

	Estimate	lower .95	upper .95	logRr	seLogRr
treatment	0.78000	0.51050	1.18		

Population counts

	treatedPersons	com	es
Count	16295	1629	

Outcome counts

	treatedPersons	comparatorPersons	treat Exposures	comparatorExposures
Count	81	73	81	73

Time at risk

	treatedDays	comparatorDays
Days	1682365	1515233

Target group (dabigatran) has more outcomes, but also more time at risk

Inspect the outcome model

Model type: cox
Stratified: TRUE
Use covariates: FALSE
Use inverse probability of treatment weighting: F
Status: OK

	Estimate	lower .95	upper .95	logRr
treatment	0.78000	0.51050	1.18316	

Population counts

	treatedPersons	comparatorPers		
Count	16295	16295		

Outcome counts

	treatedPersons	comparatorPersons	treat Exposures	comparatorExposures
Count	81	73	81	73

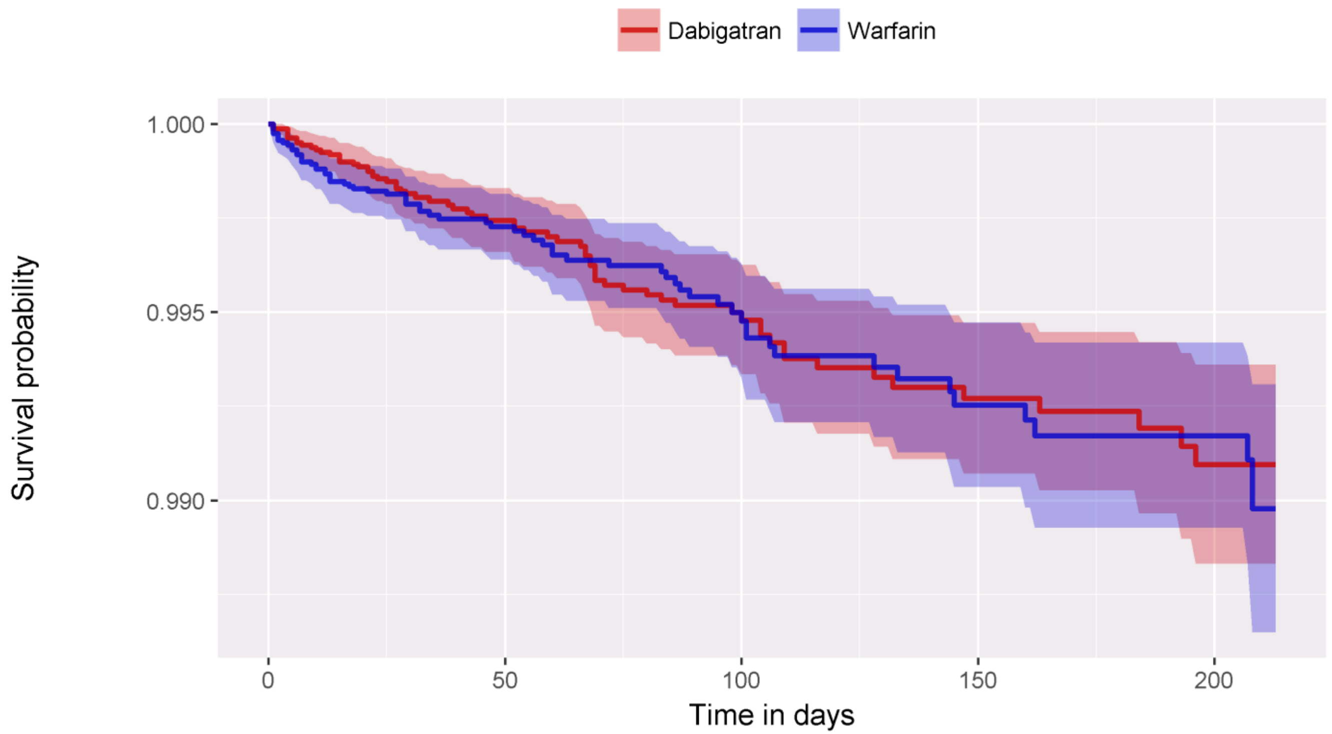
Time at risk

	treatedDays	comparatorDays
Days	1682365	1515233

Graham:
$IR_{dabigatran}$ = 11.3
$IR_{warfarin}$ = 13.9
$HR_{adjusted}$ = 0.80 (0.67–0.96)

$IR_{dabigatran}$ = 17.6
$IR_{warfarin}$ = 17.6
$HR_{adjusted}$ = 0.78 (0.51 – 1.18)

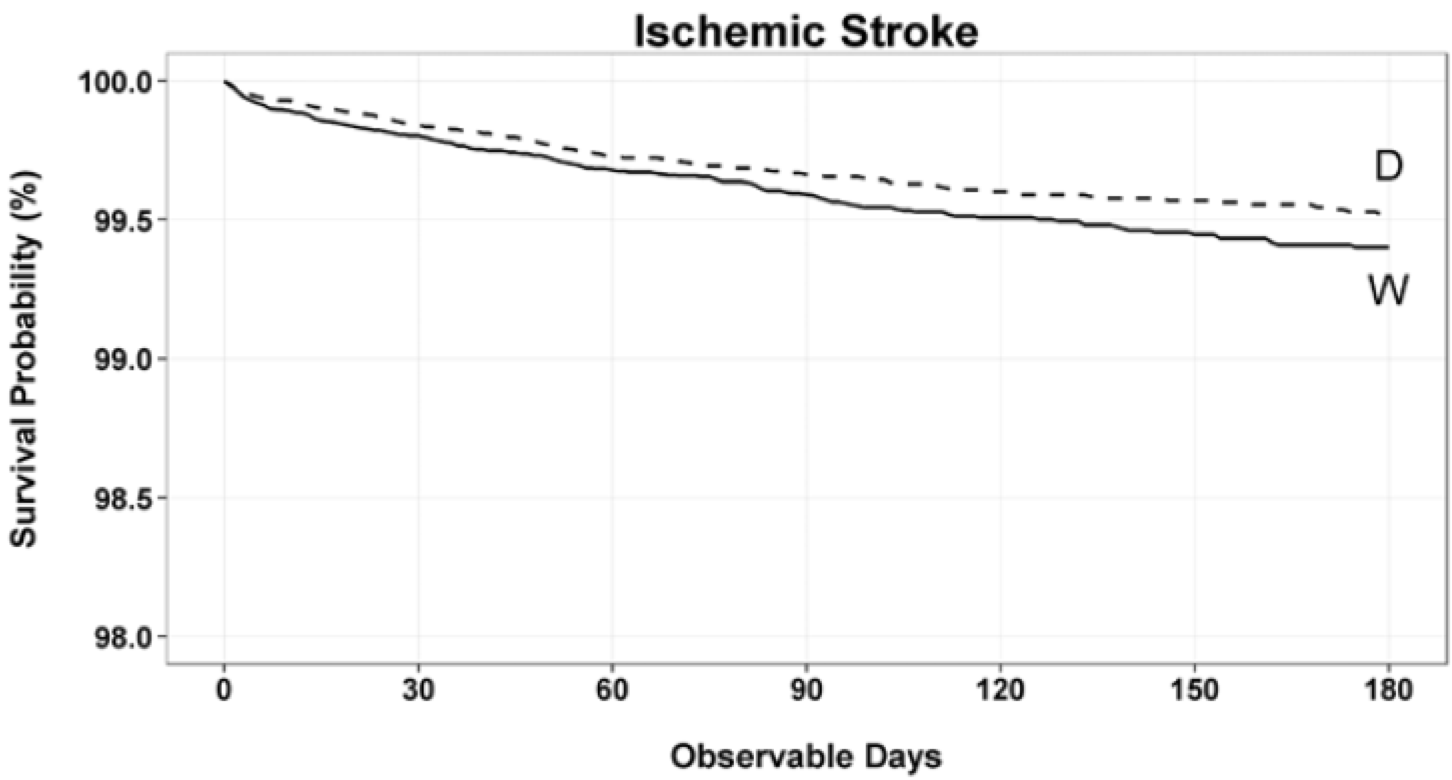
Kaplan Meier plot



Number at risk					
Dabigatran	16,295	9,664	5,019	3,303	1,980
Warfarin	16,295	9,087	4,494	2,717	1,637

Kaplan Meier plot

Graham:



In conclusion

- ATLAS can
  - Write protocol
  - Generate R code to do a study
- Not shown:
  - Include negative controls & calibrate P-value
  - Synthesize positive controls & calibrate CI
  - Multiple T, C, O
  - Multiple analyses
- Other study designs available in R
  - Self-controlled case series
  - Case-crossover & case-time-control
  - Case-control
  - Self-controlled cohort

Prediction:
Patient-level predictive modeling and evaluation

Installing the R Package

Instructions found on the github: https://github.com/OHDSI/PatientLevelPrediction

1. On Windows, make sure RTools is installed.
2. The DatabaseConnector and SqlRender packages require Java. Java can be downloaded from http://www.java.com.
3. Random forest, Naive Bayes and MLP require python 3.6. Python 3.6 can be downloaded from: https://www.continuum.io/downloads.
4. In R, use the following commands to download and install PatientLevelPrediction:

```
install.packages("drat")
drat::addRepo("OHDSI")
install.packages("PatientLevelPrediction")
```

5. We recommend testing your instalation by running:

```
PatientLevelPrediction::checkPlpInstallation()
```

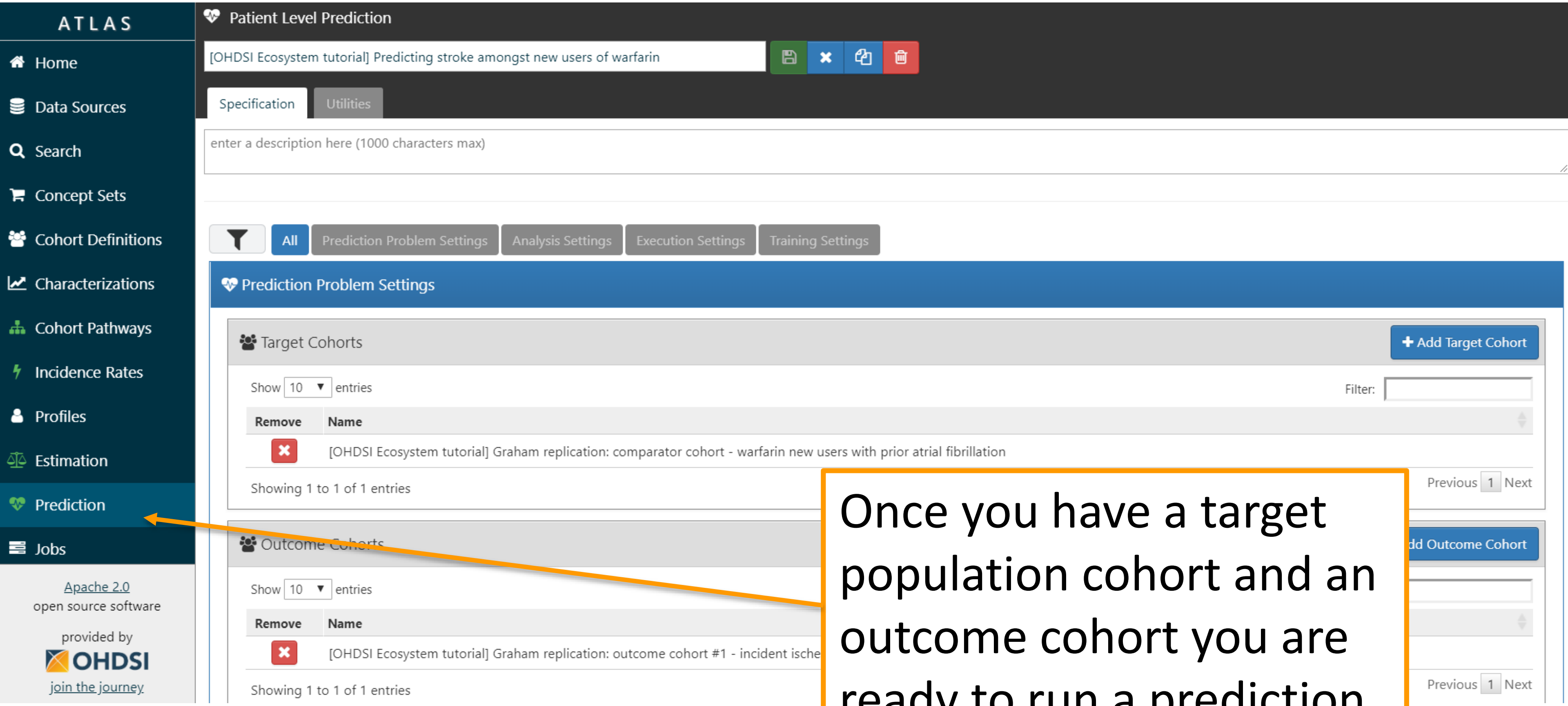
There is a function: checkPlpInstallation() that makes sure you have everything correctly set up

If you have a response other than 1 (indicating everything works), enter the response number in:

```
PatientLevelPrediction::interpretInstallCode()
```

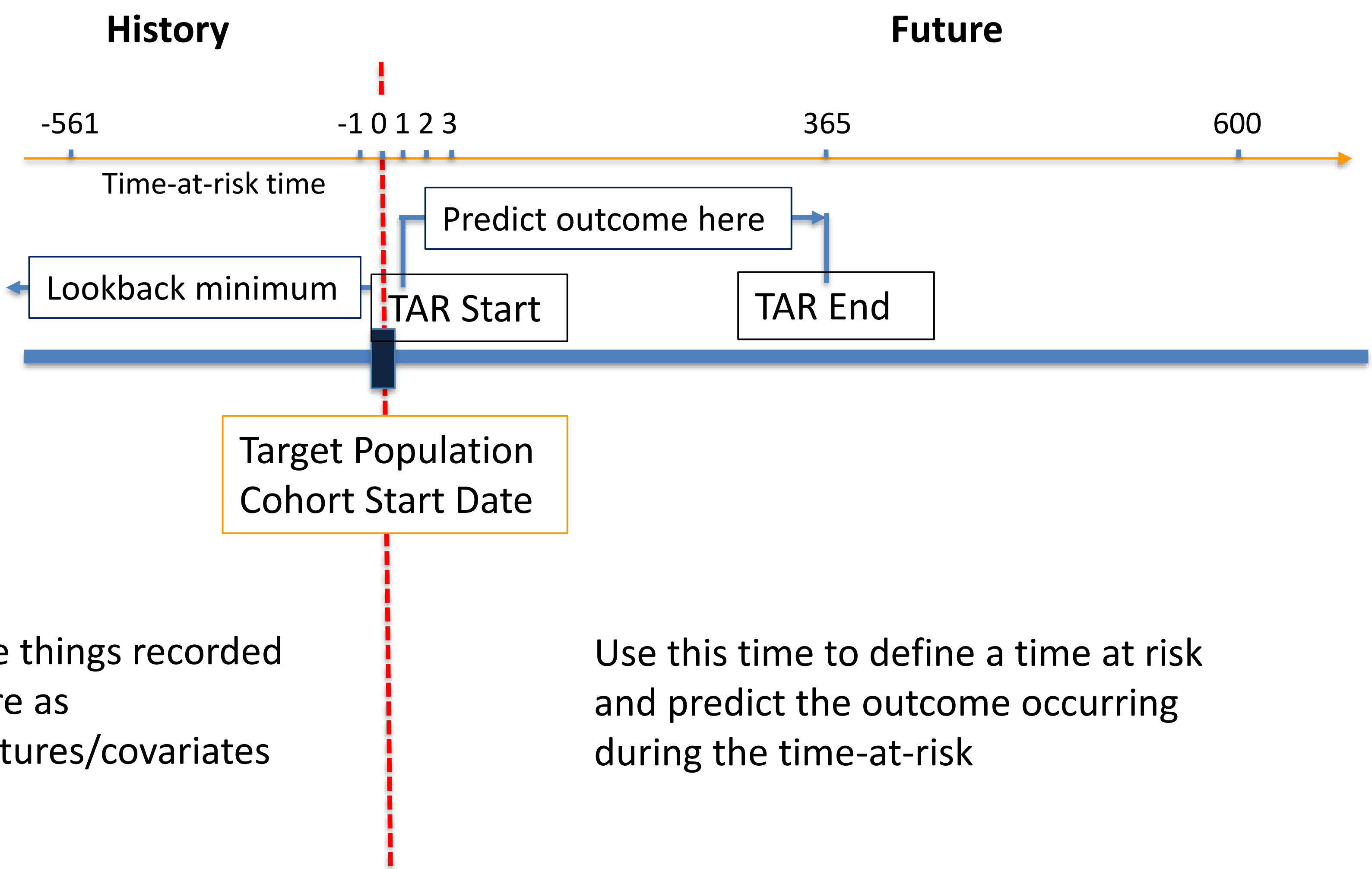
Non-windows users: Please note that the package uses python to implement some of the classifiers. The package pythonInR is used as the interface, and in Linux or Mac OS it uses the same python specified in path (the python that loads when you type the command python). Please make sure the anaconda python is specified in your path rather than any default python (unless it is set up with the following packages), as the packages: numpy, scikit-learn and tensorFlow are required to run the patient level prediciton python code.

Generating R Code With Atlas



Once you have a target population cohort and an outcome cohort you are ready to run a prediction

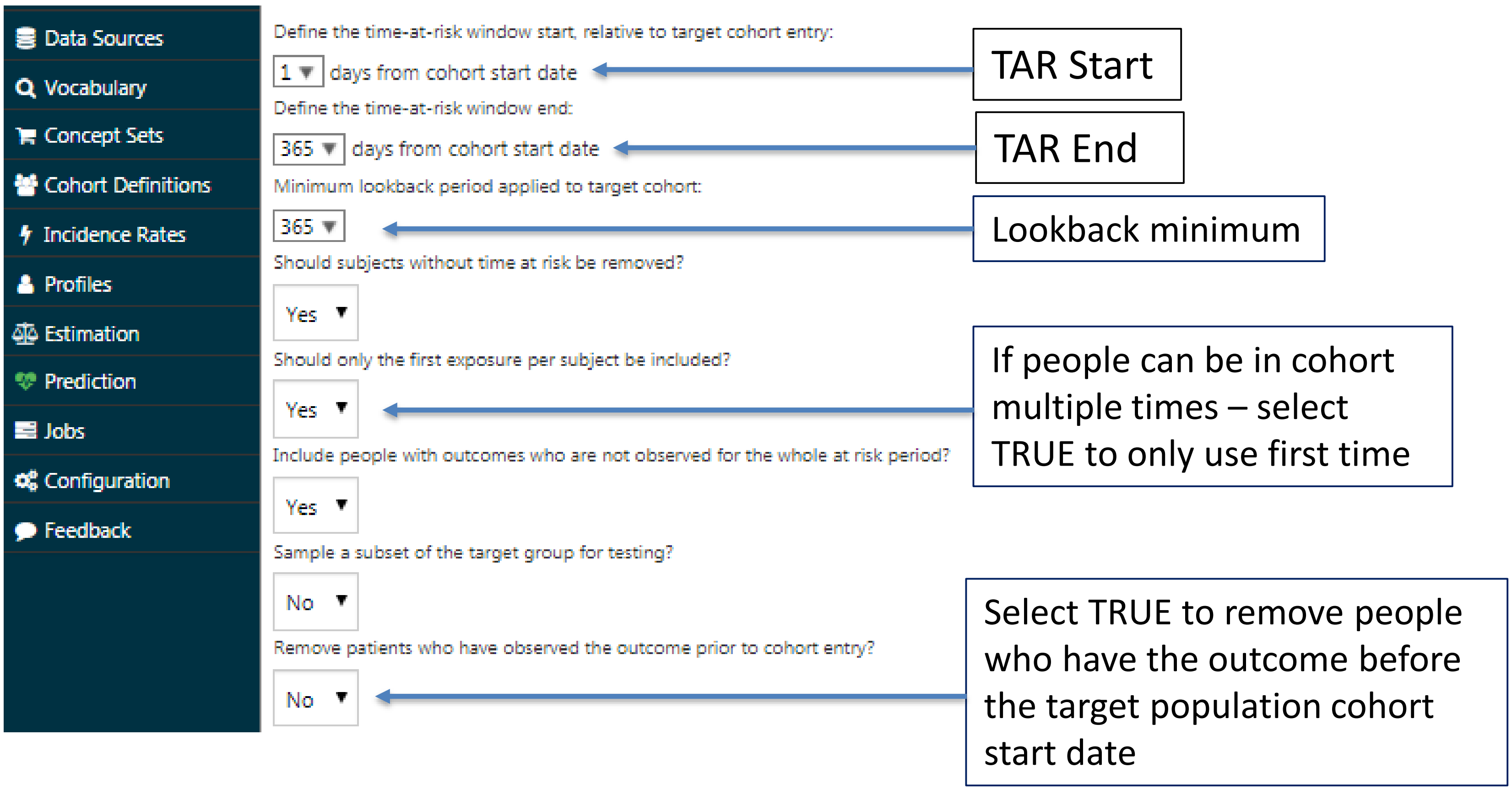
Prediction Parameters



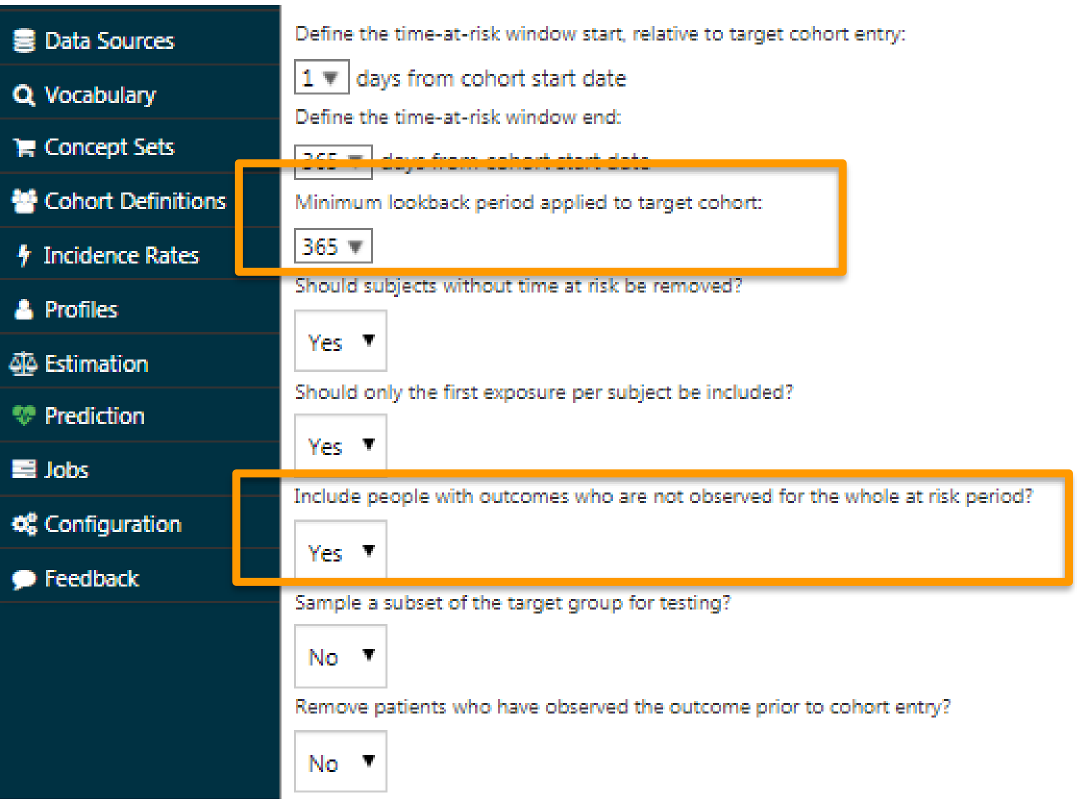
Use things recorded here as features/covariates

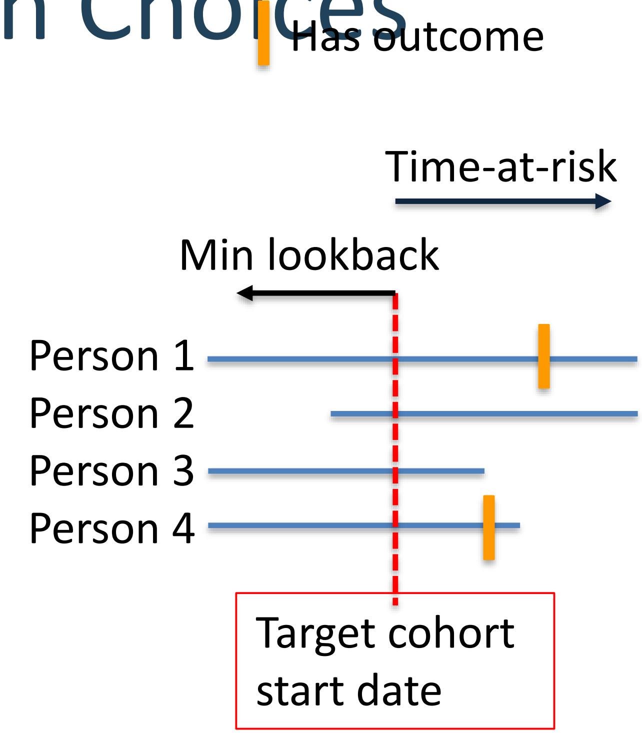
Use this time to define a time at risk and predict the outcome occurring during the time-at-risk

Prediction Design Choices



Prediction Design Choices

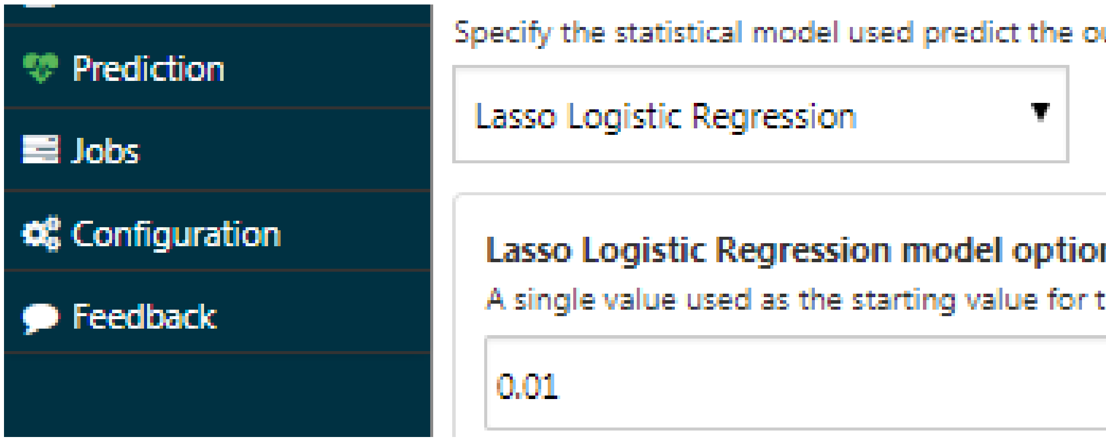




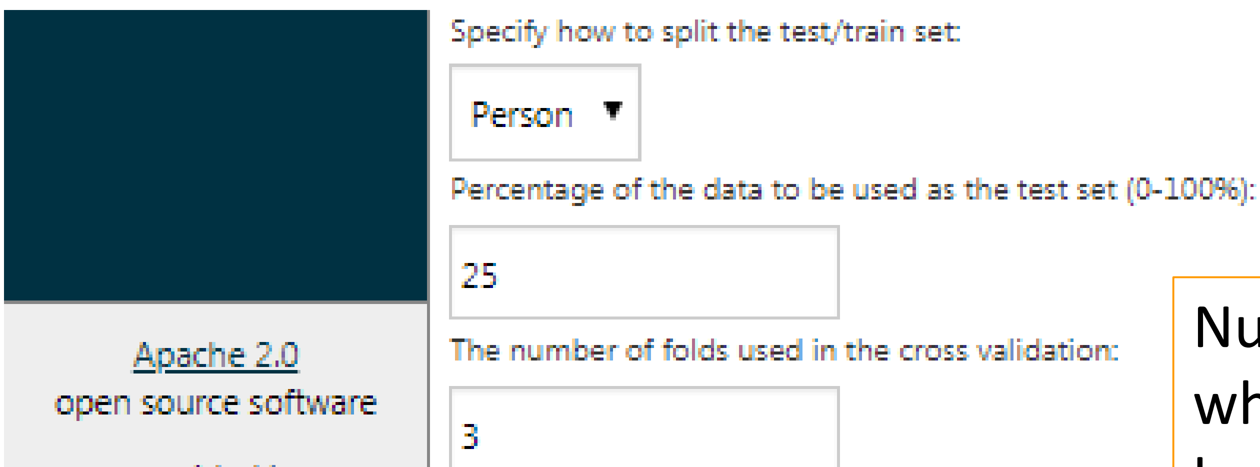
Person 2 doesn’t have min lookback so excluded

Persons 3&4 don’t have full time-at-risk

Training Choices



We do a automatic search for lasso logistic regression but a grid search for other model's hyperparameters



Test/train type and %

Number of folds to use when picking optimal hyper-parameters

Feature/Covariate Choices

Standardised Features:

- Demographics (e.g., age, gender, ethnicity)
- Conditions (+ condition groups using SNOMED/MEDRA vocabs)
- Drug (+ drug groups)
- Procedures
- Measurements
- Observations
- Counts
- Some existing risk models

(Flexible times before cohort start date (e.g., -365 to -1 days relative to cohort start date)

Custom Features:

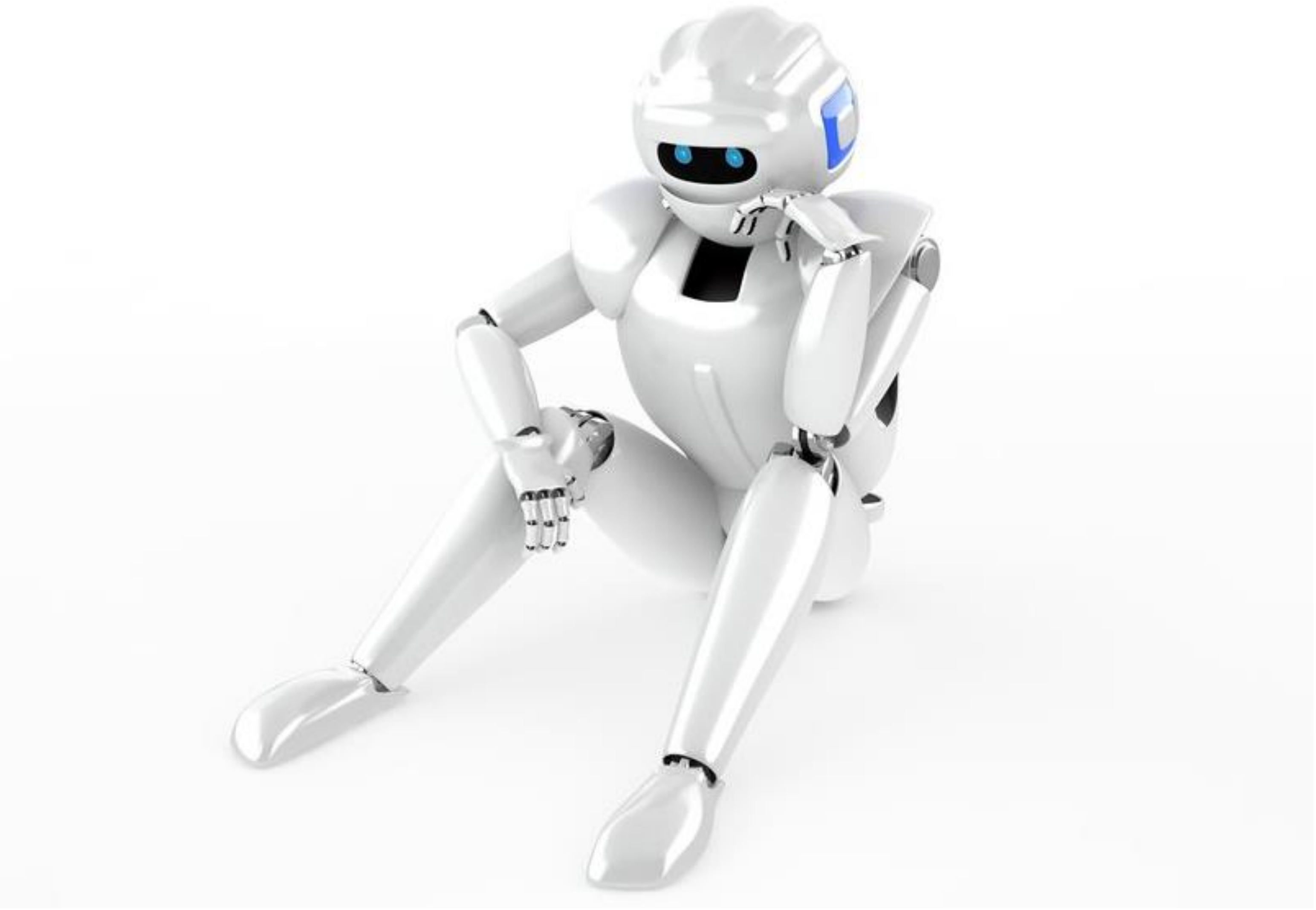
- Can also make any feature you want using R and SQL

Atlas Demo

I will show how to create the R code to predict bleeding within 1 to 365 days after first time wa

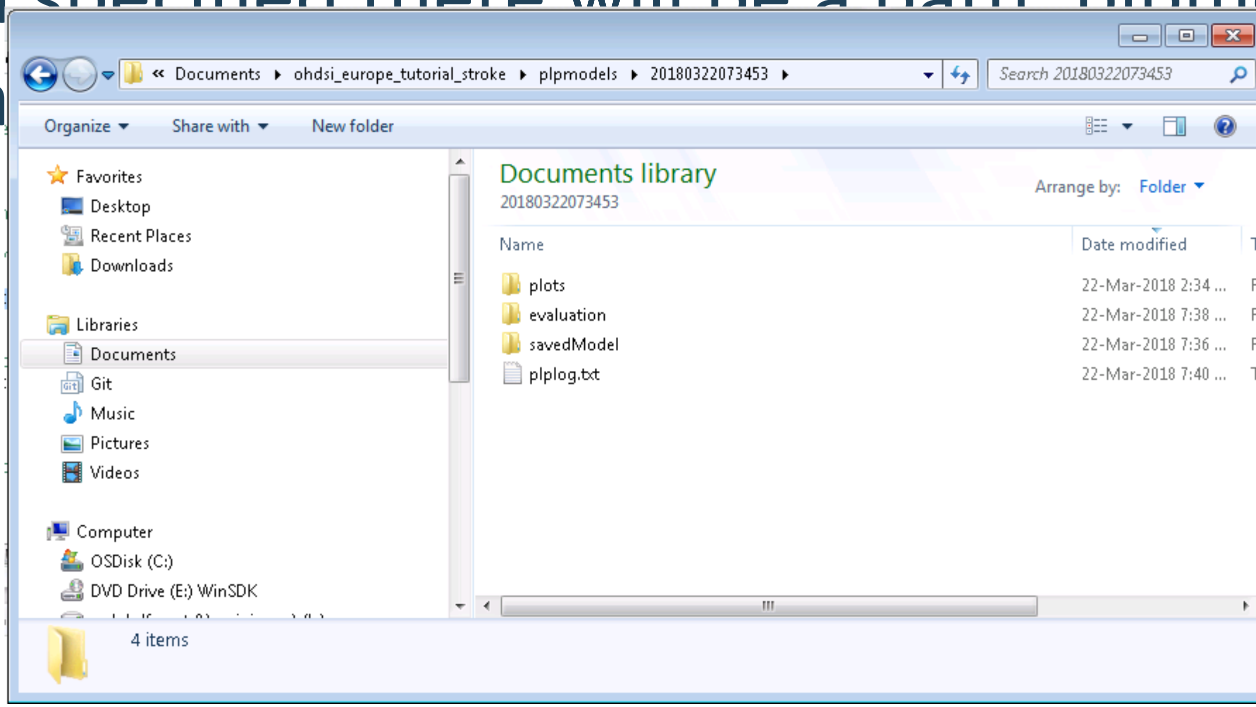
	Option	Choice
Prediction Design Choices	Time at risk start	1
	Time at risk end	365
	Remove prior outcomes	TRUE
	Require time-at-risk	TRUE
	Use all outcomes	TRUE
Training choices	Classifier	Lasso LR
	N-folds	3
	Test %	25
	Split type	Person
Feature Choices	All demo, conditions (+groups), drugs (+groups), measurements, observations, procedures 365 days prior	

PatientLevelPrediction Output



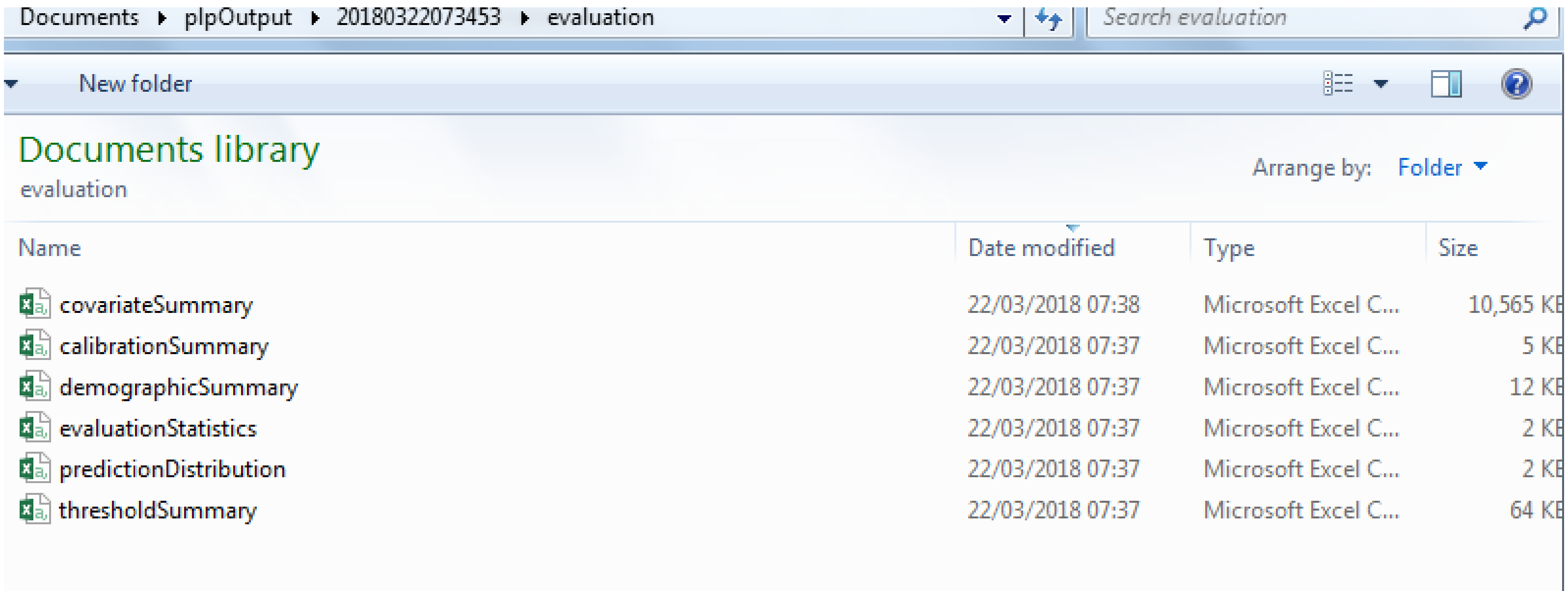
PatientLevelPrediction Output

- When you run the atlas code, in the directory you specified there will be a path: plpmodels-> ana



PatientLevelPrediction Output

- Evaluation folder:



PatientLevelPrediction Output

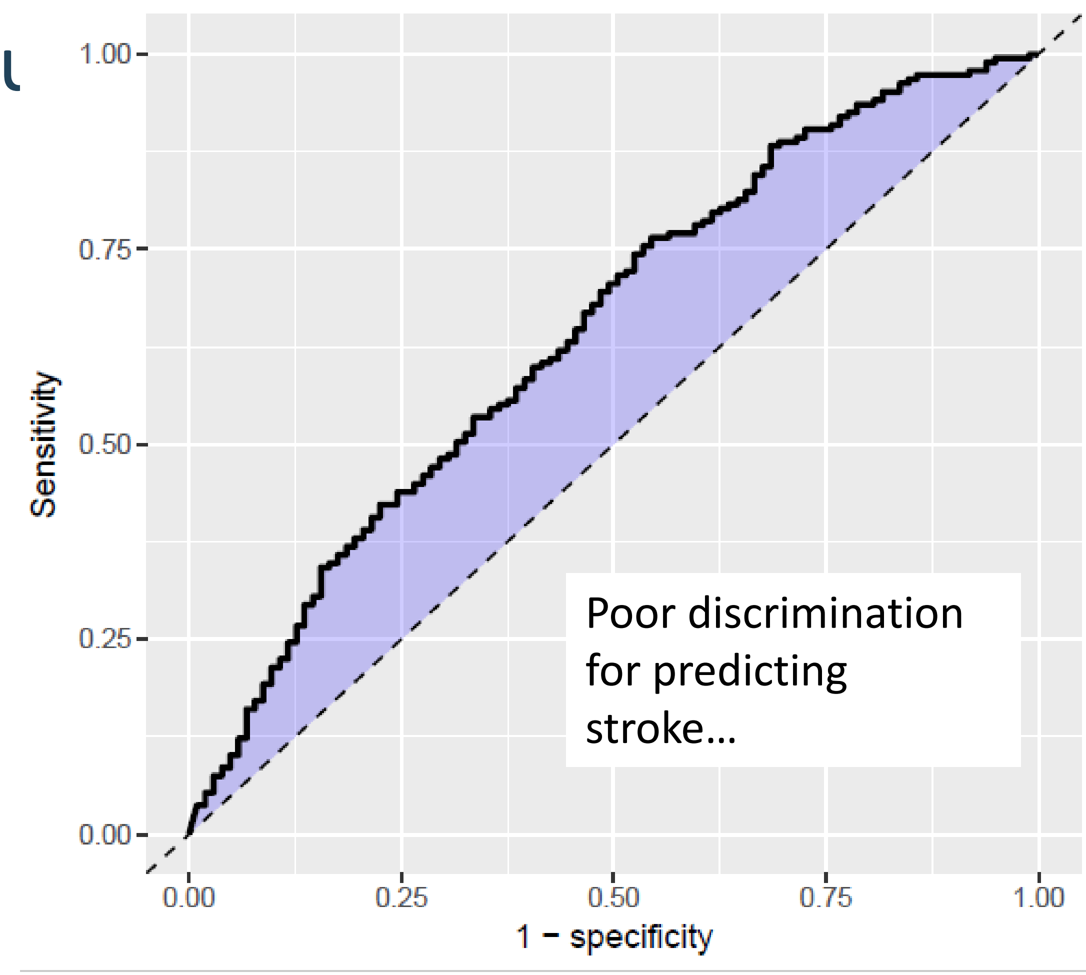
- EvaluationStatistics

populationSize	7134
outcomeCount	187
AUC.auc	0.649988
AUC.auc_lb95ci	0.611923
AUC.auc_ub95ci	0.688053
BrierScore	0.025352
BrierScaled	0.010316
CalibrationIntercept.Intercept	-0.01395
CalibrationSlope.Gradient	1.526665

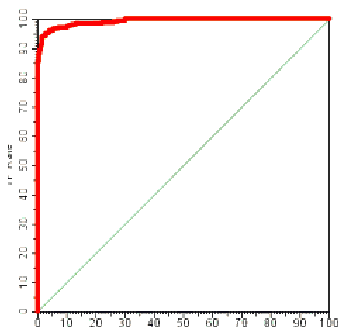
2.6% of population have outcome

PatientLevelPrediction Output

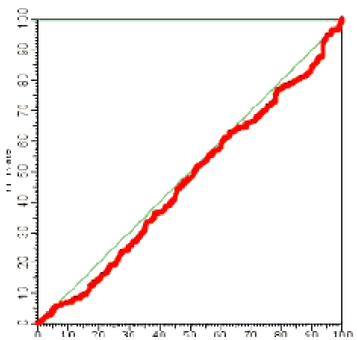
- ROC Plot: Measu discrimination



Near Perfect discrimination:

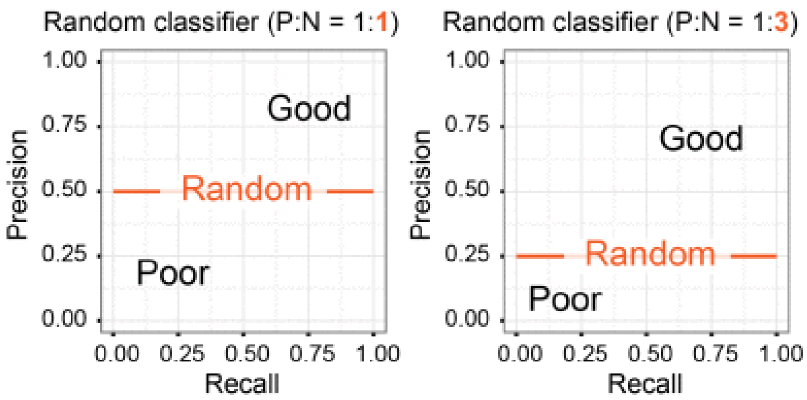


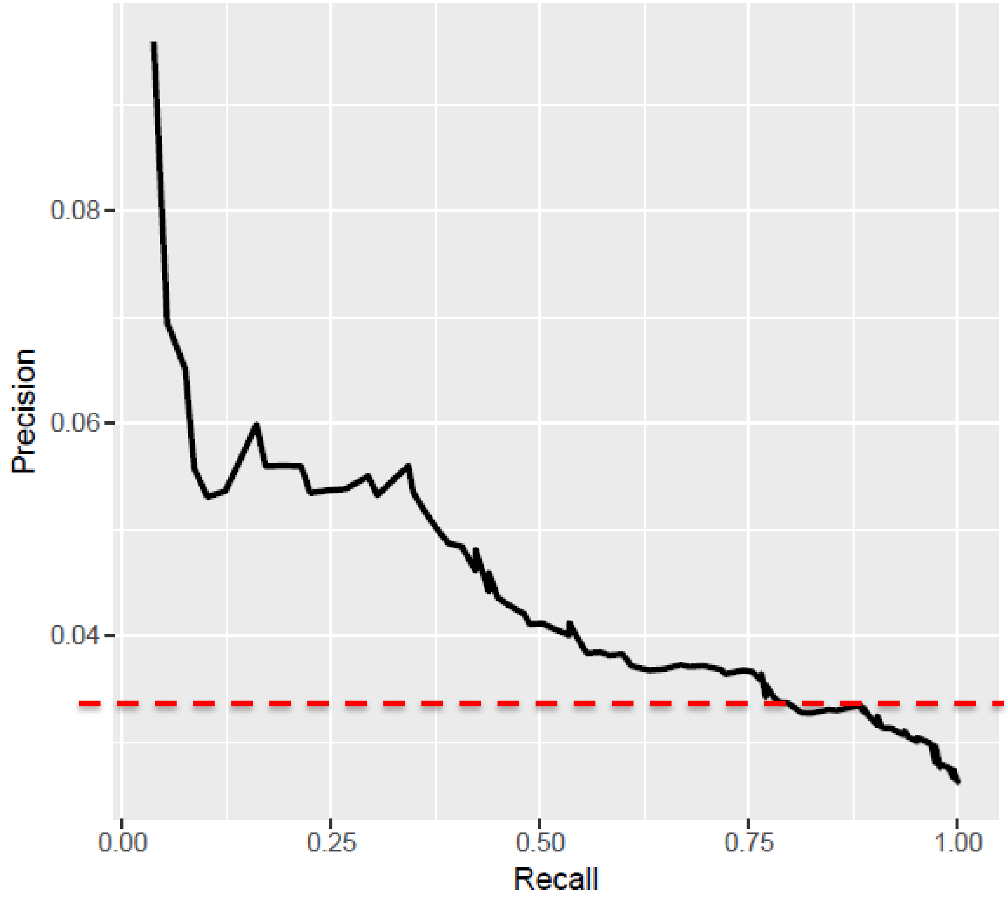
Worse discrimination:



PatientLevelPrediction Output

- Precision recall plot: Good to use when the outcome is rare to

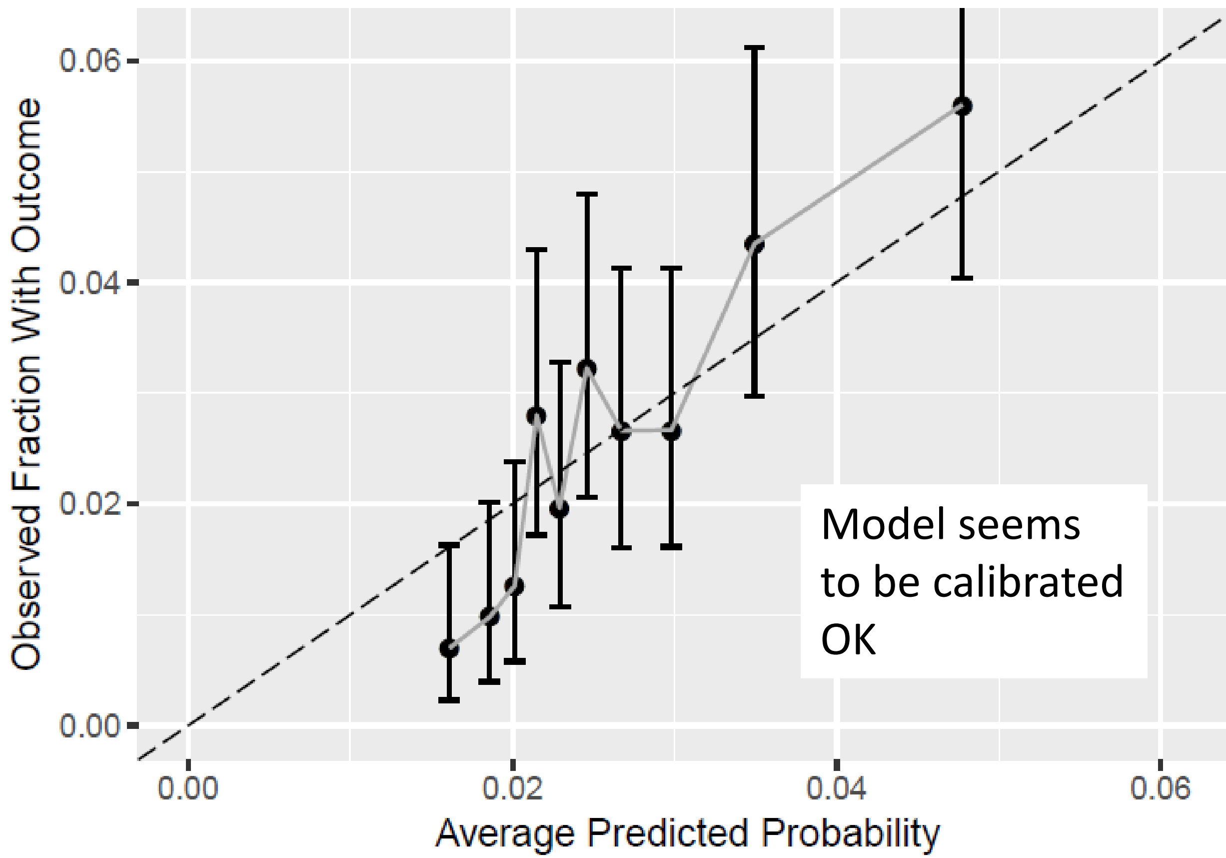




PatientLevelPrediction Output

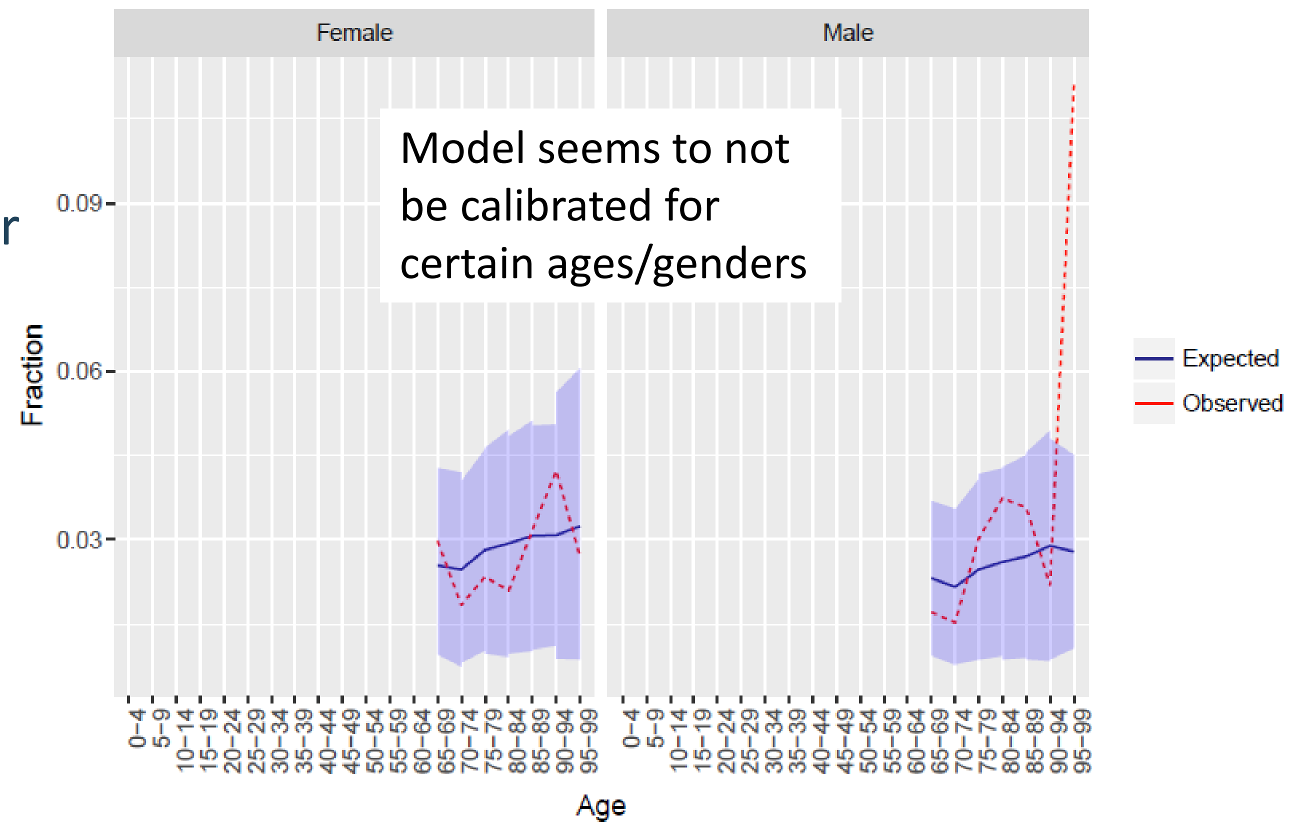
- Calibration Plot

- Good calibration means dots around x=y line



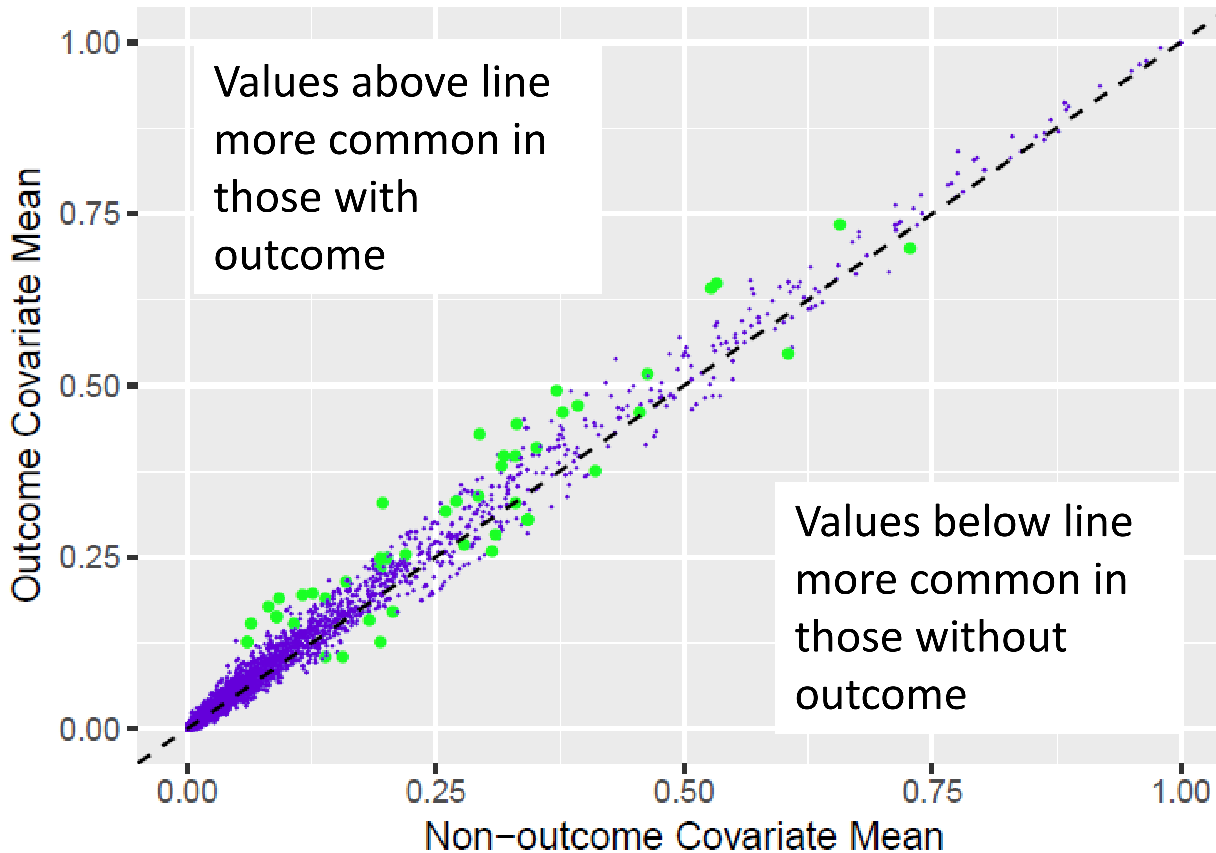
PatientLevelPrediction Output

- Demographic Calibration:
- What expected and observed to be similar across age/gender
- If observed/expected differ than maybe need to treat that strata differently



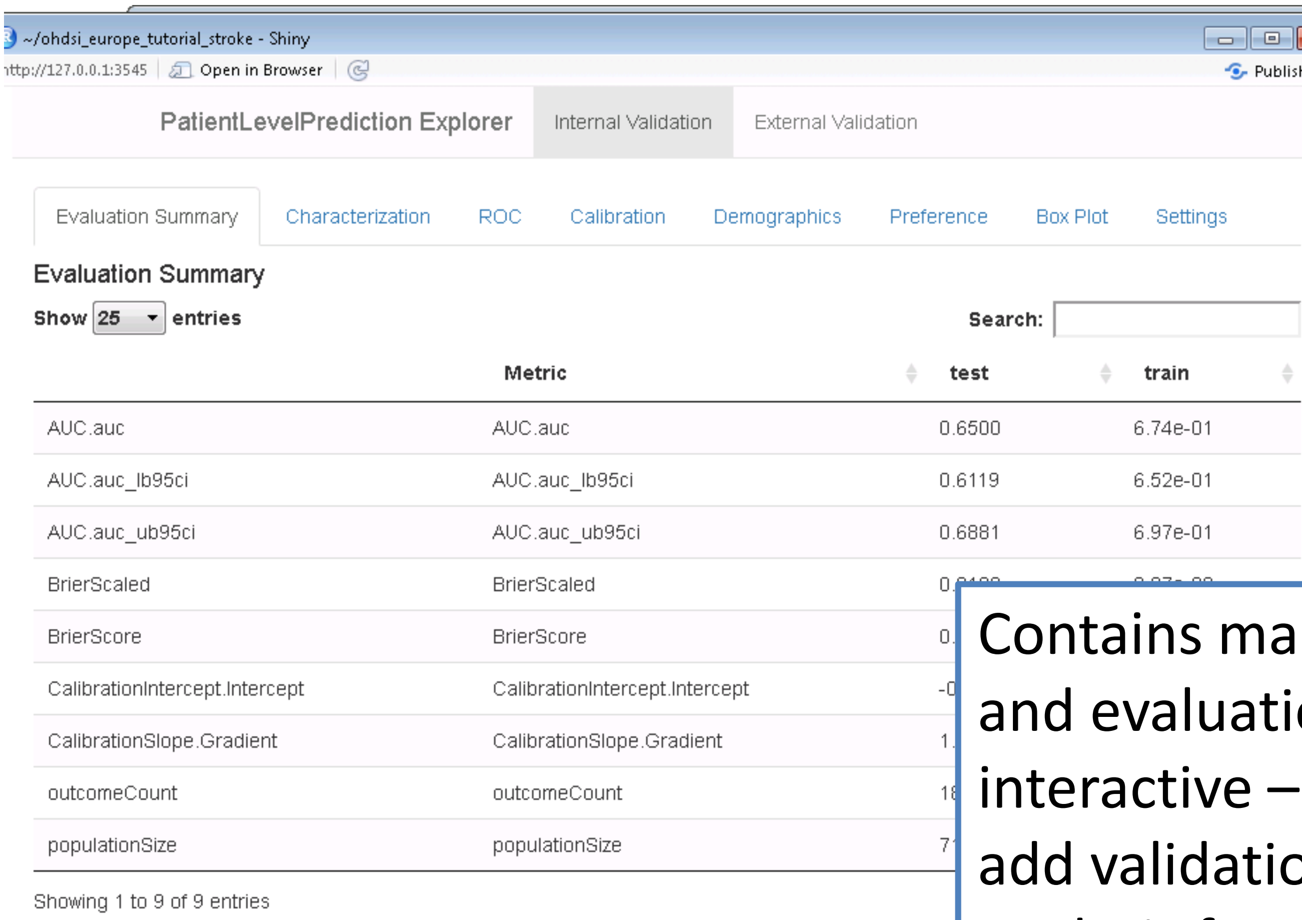
PatientLevelPrediction Output

- Variable scatterplot: shows differences between people with outcome and without outcome



PatientLevelPrediction Shiny View

- PatientLevelPrediction::viewPlp(runPlp = results, validatePlp = externalVal)



	Metric	test	train
AUC.auc	AUC.auc	0.6500	6.74e-01
AUC.auc_lb95ci	AUC.auc_lb95ci	0.6119	6.52e-01
AUC.auc_ub95ci	AUC.auc_ub95ci	0.6881	6.97e-01
BrierScaled	BrierScaled	0.	
BrierScore	BrierScore	0.	
CalibrationIntercept.Intercept	CalibrationIntercept.Intercept	-0	
CalibrationSlope.Gradient	CalibrationSlope.Gradient	1.	
outcomeCount	outcomeCount	18	
populationSize	populationSize	7	

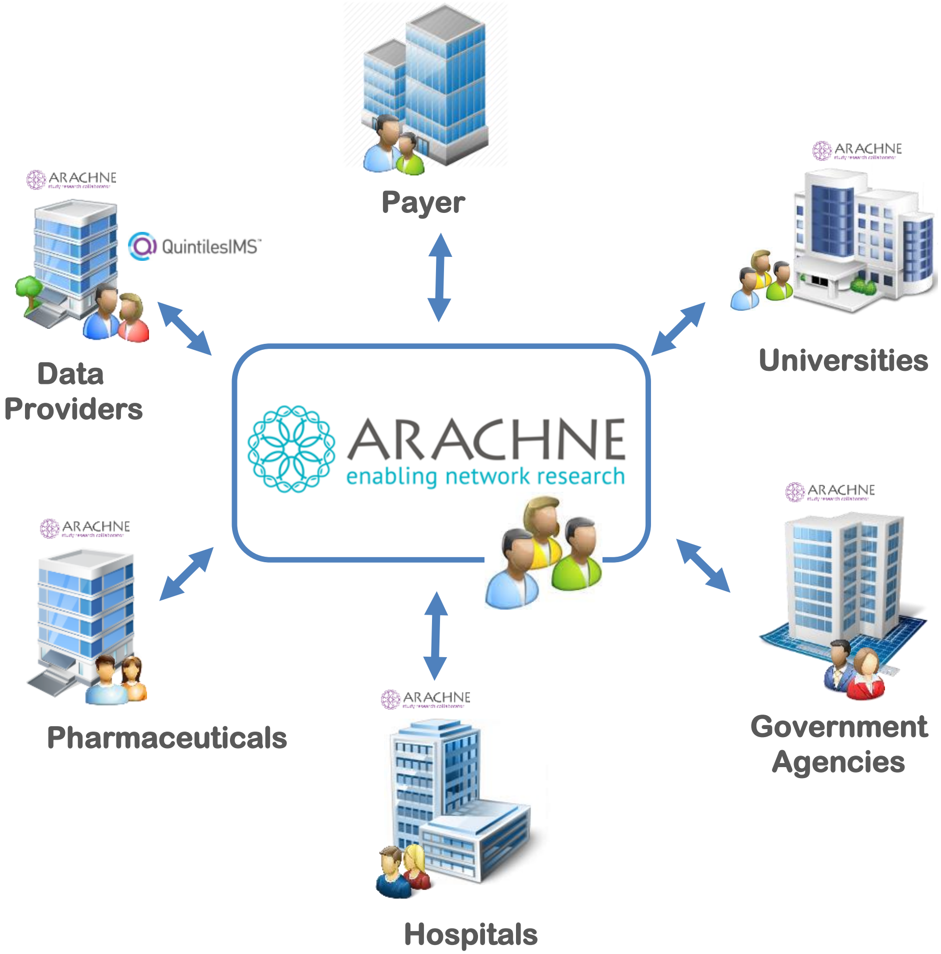
Contains main plots and evaluation but is interactive – can also add validation analysis for comparison

Network analyses using ARACHNE

ARACHNE Research Network

An open-source platform to enable federated studies across the OHDSI network

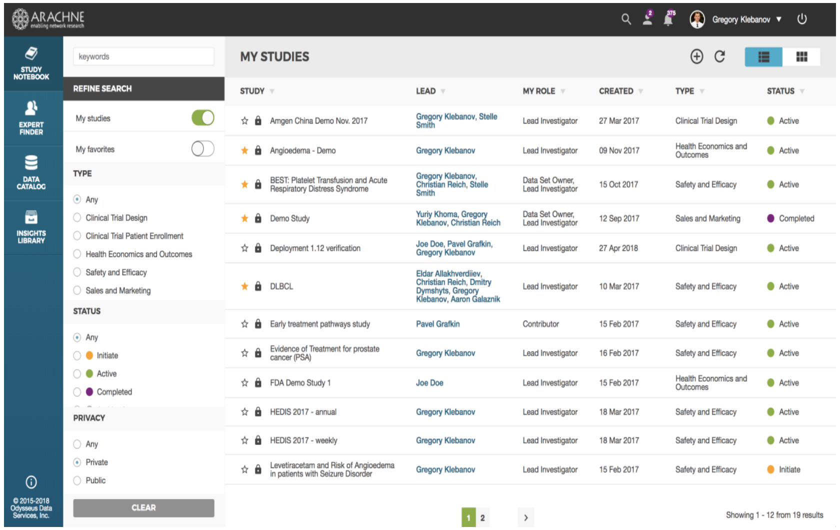
- Collaborative study lifecycle management
- Network Data catalog
- Secure, compliant and trusted data access
- Execute analysis across organizations
- Store analysis aggregate results
- Integration with OHDSI Tools (ATLAS, ACHILLES)
- Support for OHDSI standards and tools

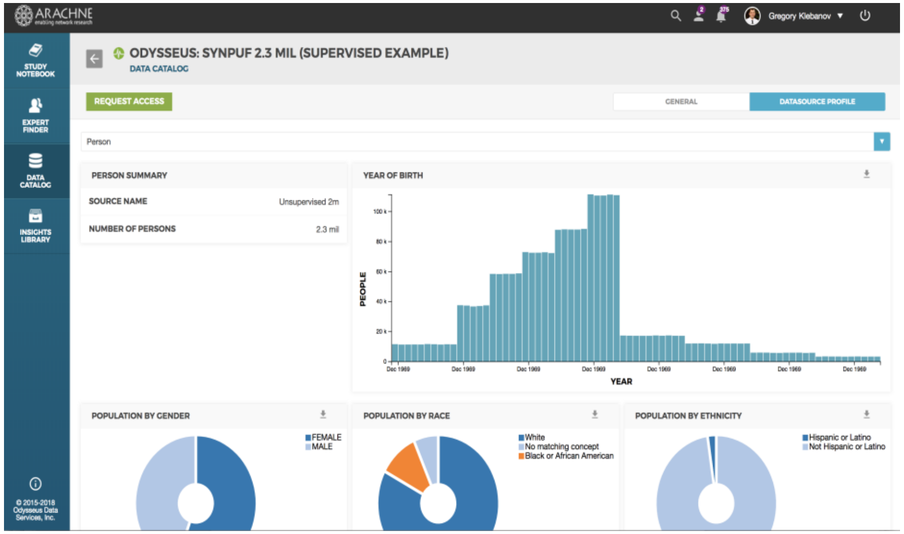


ARACHNE UI

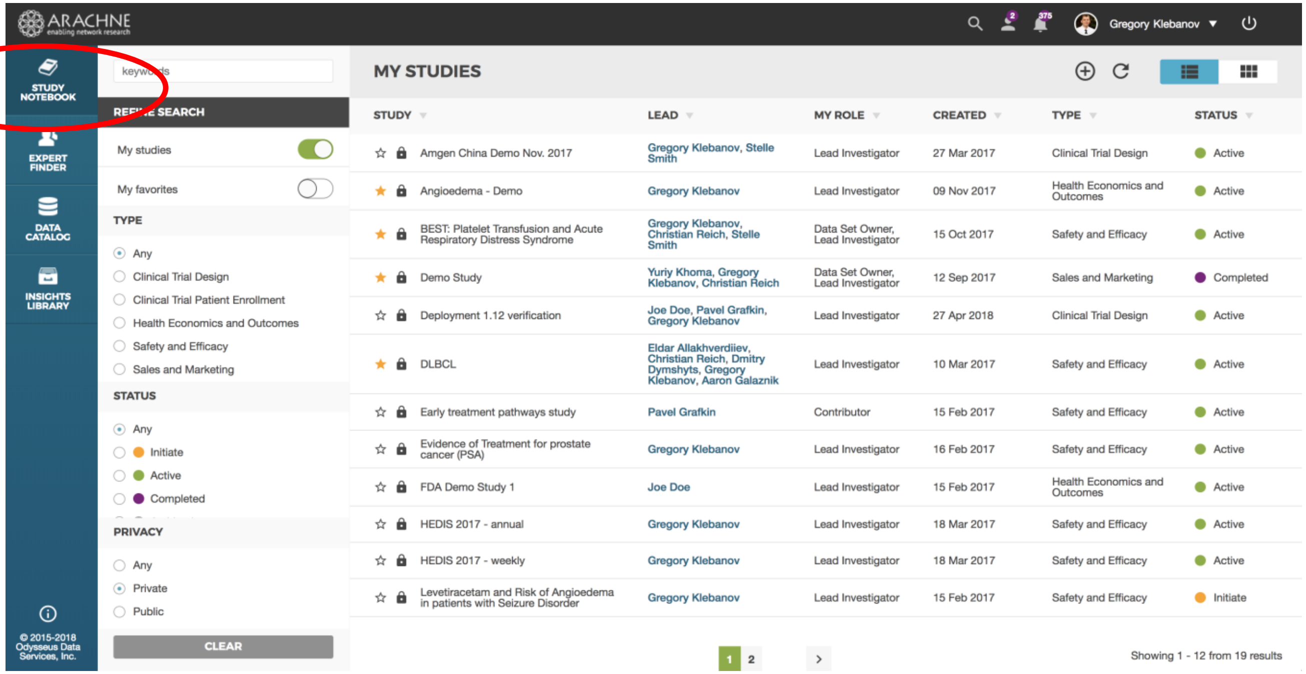
The ARACHNE UI allows access to the following:

- Network Studies
- OHDSI Participants (White pages)
- Network Data Catalog
- Insights Library





Study Workbook



Lists all participant’s studies, including those marked as “public” (viewed by anyone) and “private” (viewed by study collaborators only)

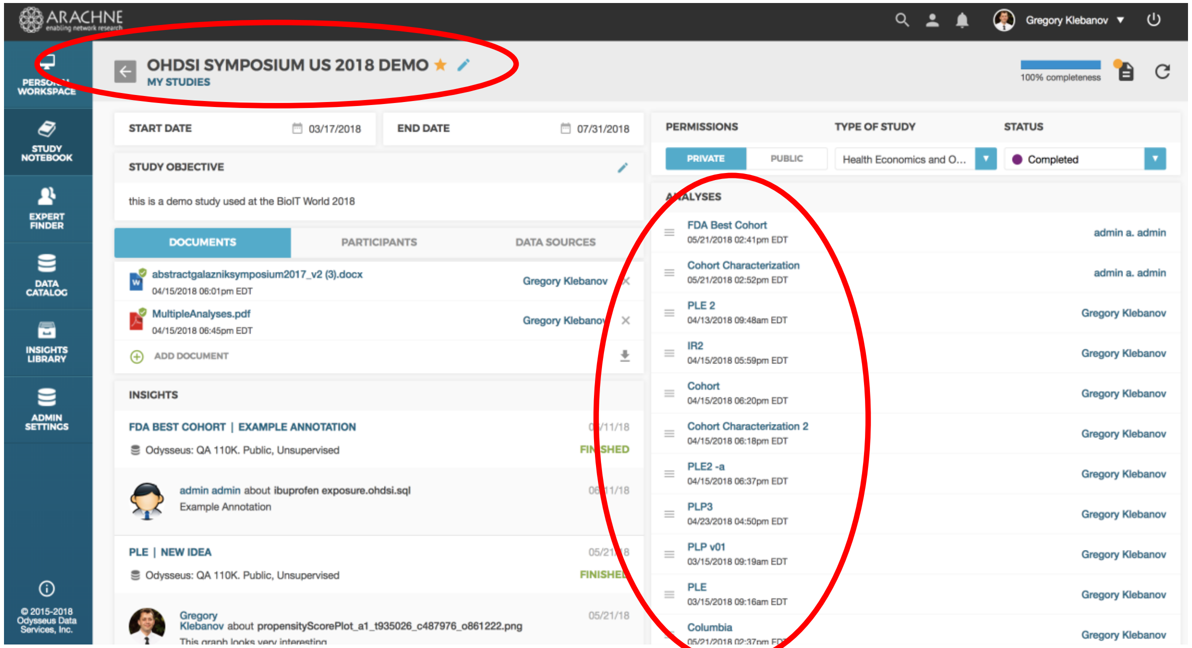
Network Study

The ARACHNE Network study is a collaborative workspace for all study documents, design artifacts, analysis code, execution activities as well as results repository

The ARACHNE Network study allows defining and setting a number of attributes, including name, objectives, lifecycle status, visibility (private or public), type of a study

The ARACHNE Network Study allows study members to create and manage a various study-related analyses:

- Simple cohort counts
- Cohort characterization
- Incidence rates
- PLP
- PLE
- Complex custom code



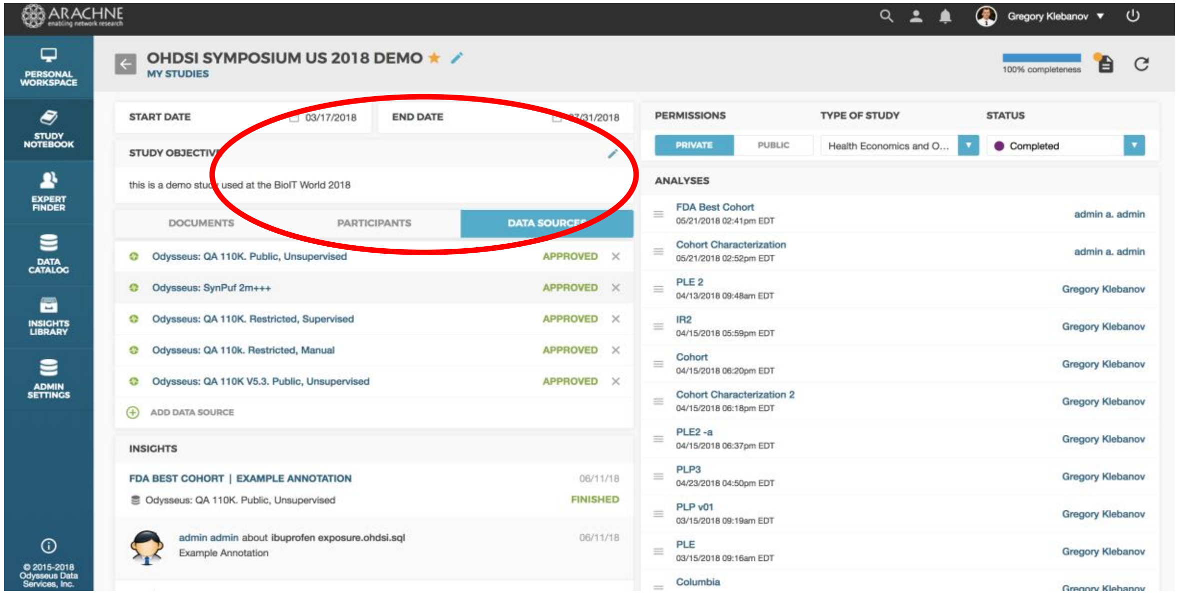
Study Data Sources and Collaborators

Study Lead Investigator can add data sets by requesting data set access. Data set becomes available for study analysis when approved by the data set owner

Study Lead Investigator can invite other OHDSI collaborators, including granting them the Lead Investigator role

Study Lead Investigators can modify study attributes, manage data access, collaborators

Study collaborators can create new analyses, execute them and review and annotate results



Simple Cohort Count Analysis

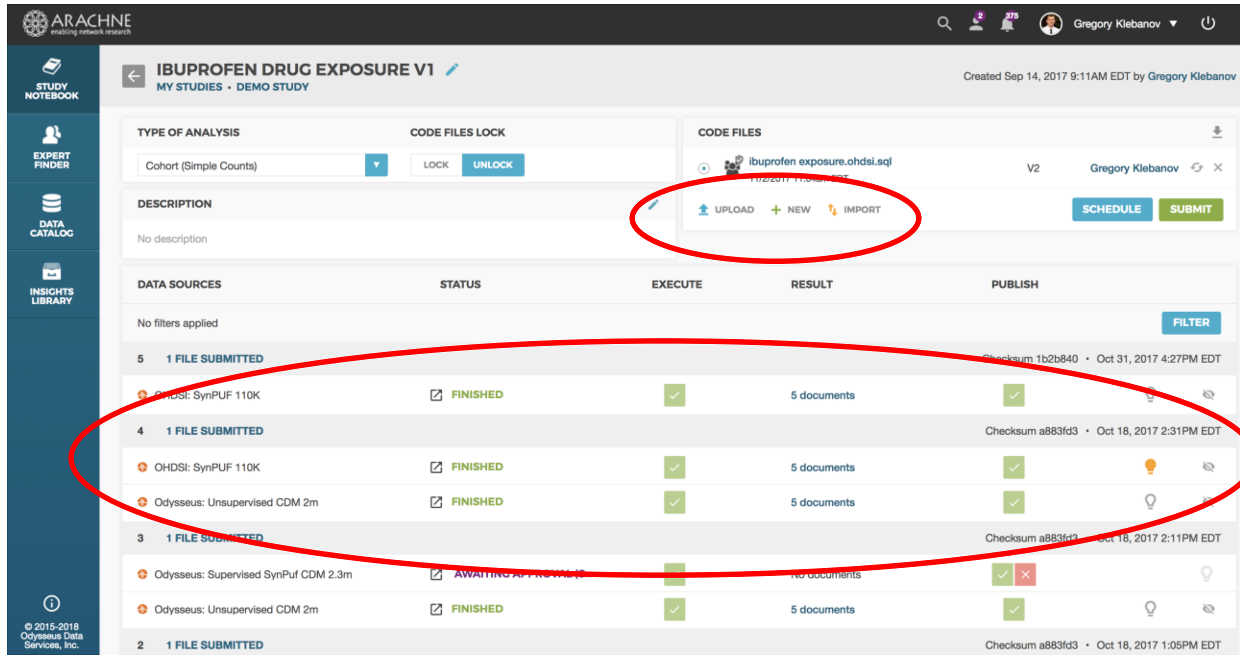
Allows performing simple counts

Cohorts definitions can be added by:

- Importing from ATLAS instances connected
- Uploading files
- Creating new file

An existing ATLAS defined cohort can be used:

- JSON
- OHDSI.SQL



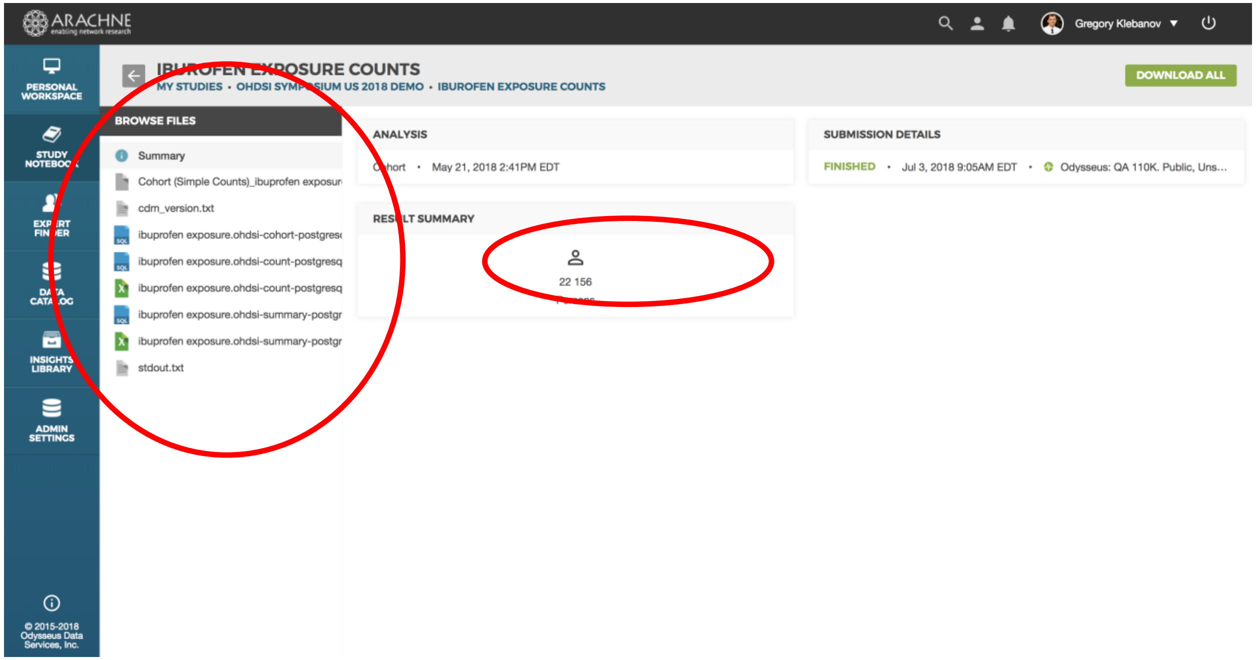
ARACHNE allows simultaneous analysis analysis execution against multiple data sets across the network.

Job submissions can be pre-scheduled

Simple Cohort Count Analysis

- ARACHNE will save a history of jobs executions, including:
  - Submitted Code
  - Execution and approval log
  - Analysis results

- The analysis submissions can be viewed and annotated

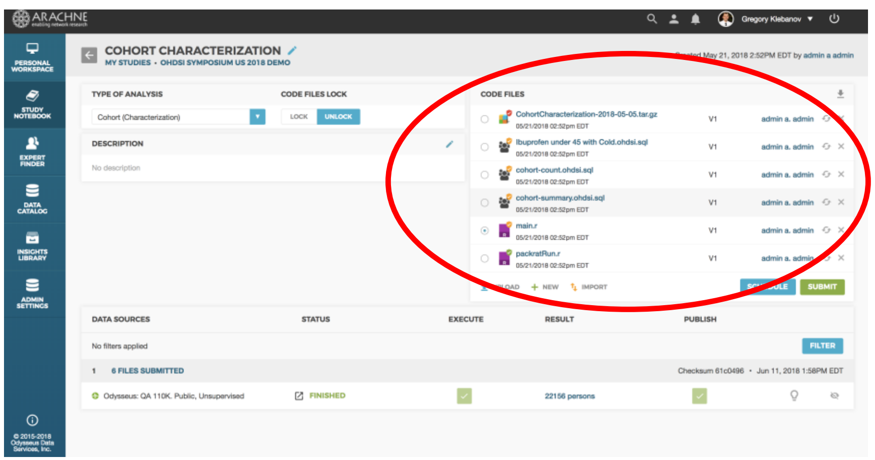


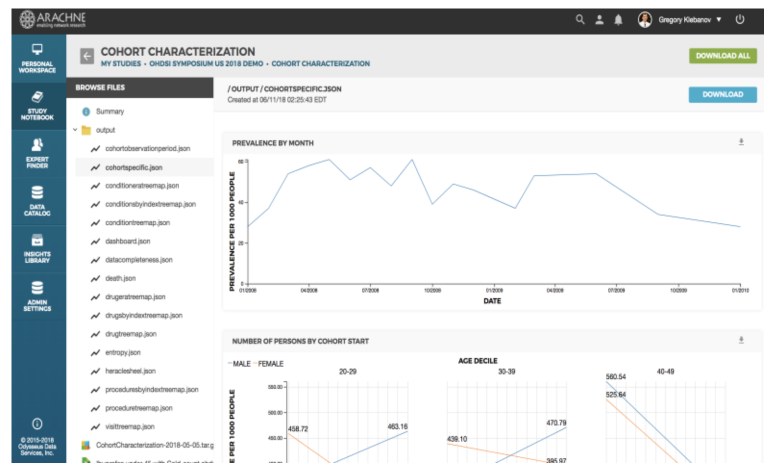
Cohort Characterization Analysis

The Cohort Characterization analysis allows performing Heracles against remote data

ARACHNE will automatically package analyses imported from ATLAS into a self-contained packrat R package

The Heracles execution parameters can be set by modifying the execution R module shell

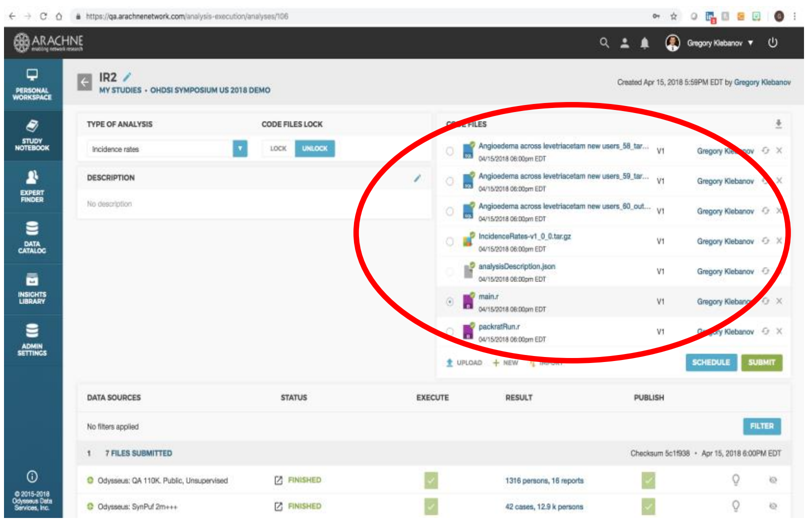


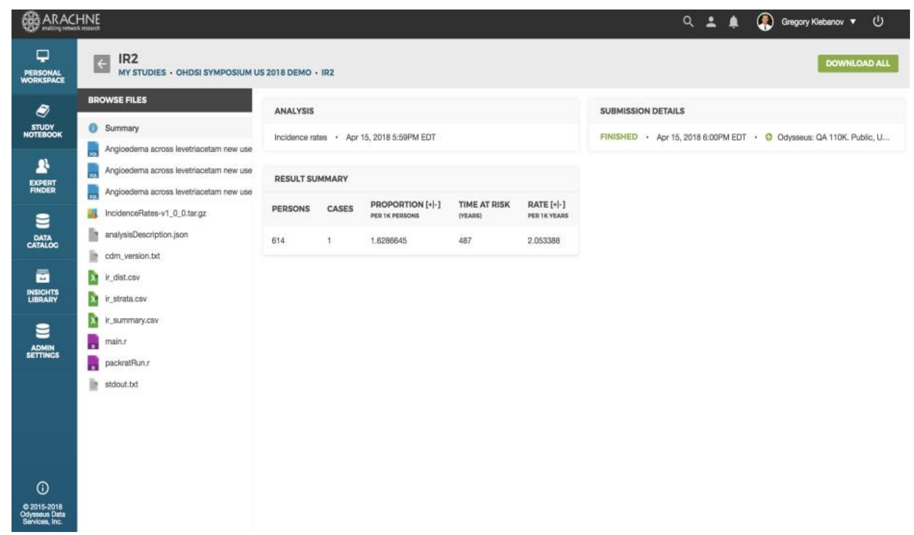


Incidence Rates

The Incidence Rate analysis allows performing calculating incidence rates against remote data

ARACHNE will automatically package analyses imported from ATLAS into a self-contained packrat R package

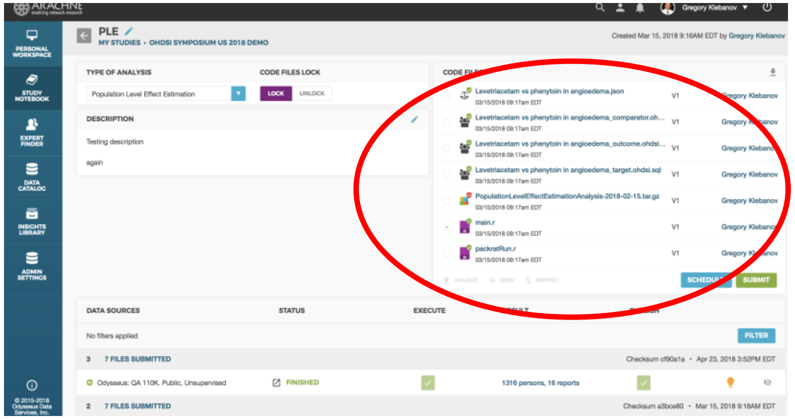


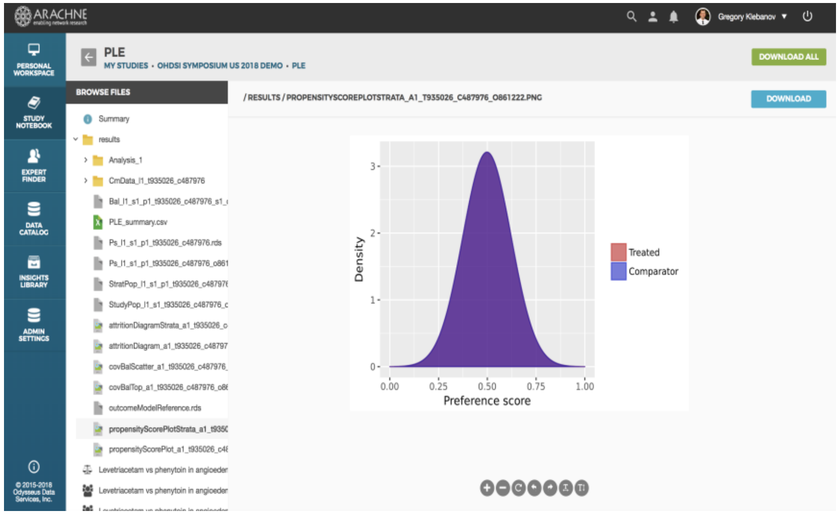


PLE and PLE methods

ARACHNE support both Population-Effect Estimation and Patient-Level Prediction methods

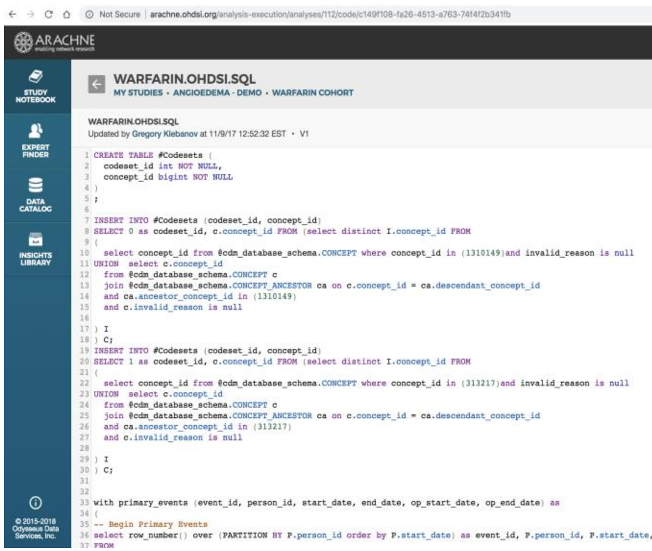
ARACHNE will automatically package analyses imported from ATLAS into a self-contained packrat R package

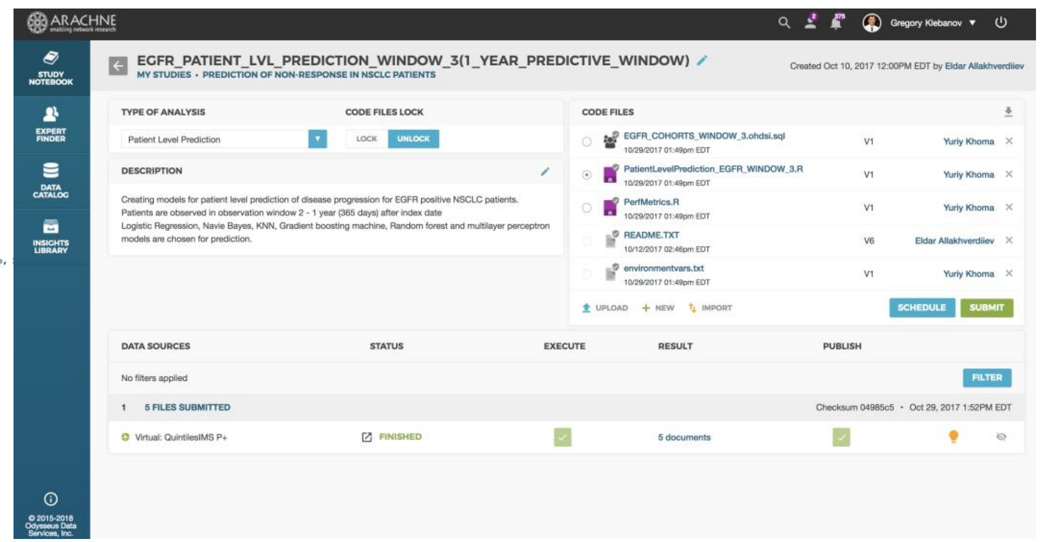




Custom Code

ARACHNE support the execution of the custom SQL or R code





Demo: Utilizing ARACHNE

Follow along at:
http://arachne.ohdsi.org/

Design and implement your own study!

Questions?

Thanks for joining
the journey!