



# Phenotype evaluation

Gowtham Rao, MD, PhD

Myocardial Infarction

Angioedema



# Agenda – 50 minutes



## Success: students can

Know how to recognize the presence of misclassification errors in the phenotype

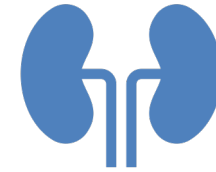
Errors and how they causes bias to the study results.

How would you fix them



## Theory (10 min)

What is measurement error  
Phenotype evaluation workflow



## Examples (40 min)

**See one:** Acute Myocardial Infarction  
(20 min)

**Do one:** Angioedema (20 min)



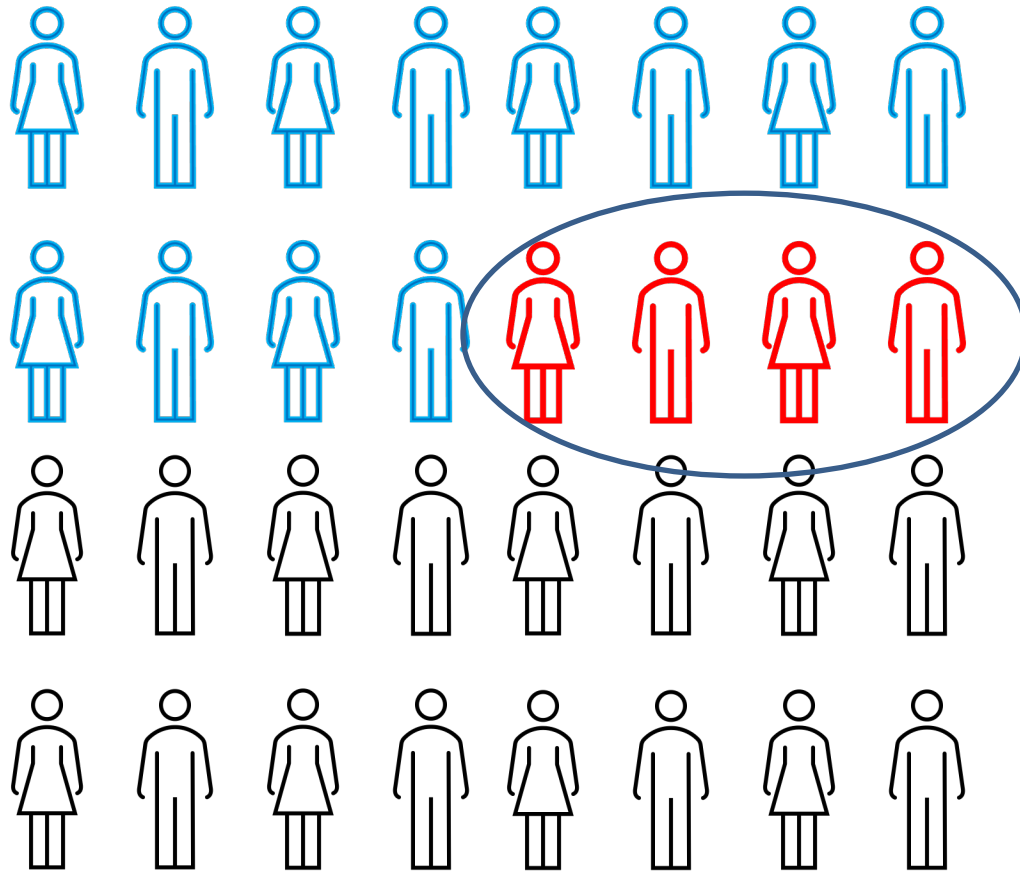
# Theory - Misclassification errors

## What are misclassification errors

- Sensitivity errors
- Specificity errors
- Index date misclassification errors



# Theory - Sensitivity Error



Persons in data source that have the phenotype of interest but were not identified

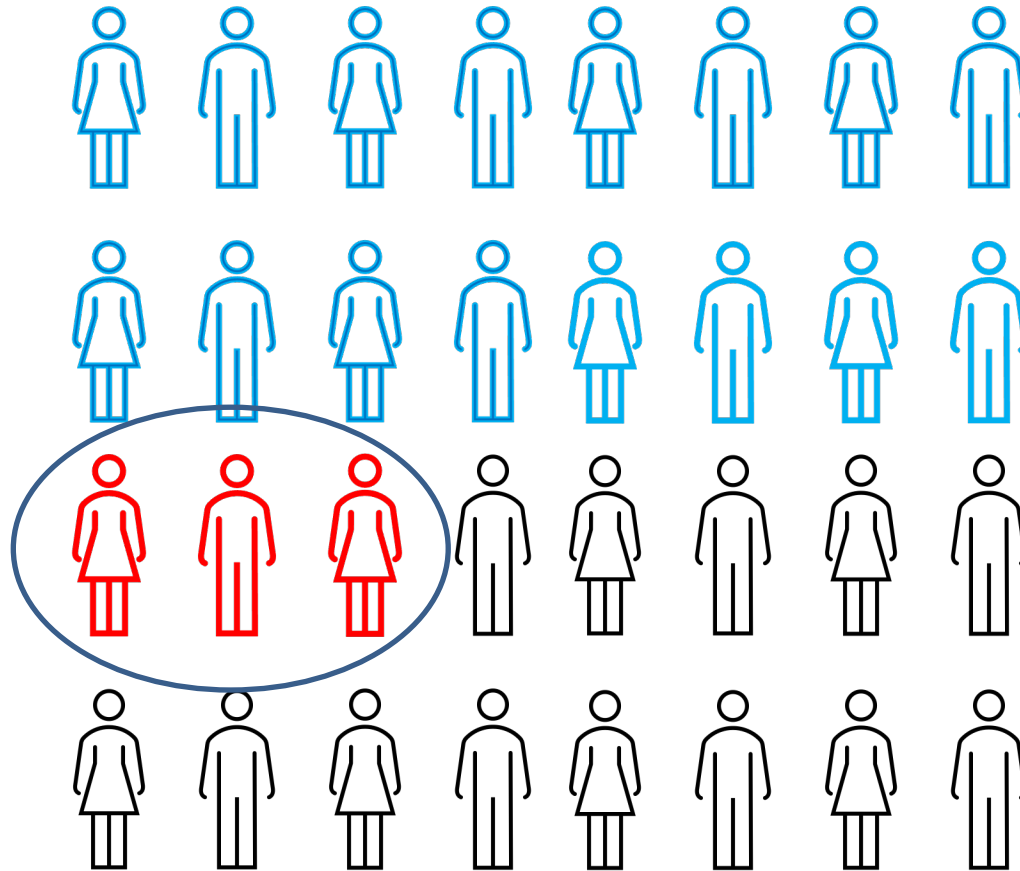


Persons in data source that were identified by the algorithm

We may say that a given cohort definition has **sensitivity errors**, if we *observe evidence* that there are persons in the data source who may have the phenotype of interest but are not in the cohort.



# Theory - Specificity Error



Persons in data source that do not have the phenotype of interest but were not identified



Persons in data source that were identified by the algorithm

We may say that a given cohort definition has **specificity errors**, if we *observe evidence* that subjects in the Cohort do not have the phenotype of interest.



# Theory - Index-date misclassification

We may say that a given cohort definition has index-date misclassification error, if we *observe evidence* that subjects identified in the cohort have incorrect designation of event start date.





# Theory - Different from PheValuator

- PheValuator – quantifies sensitivity, specificity, positive predictive value and negative predictive value.
- What is Missing
  - Insights to the origin of these errors
  - So that we may fix them



# Theory - Why is knowing errors important

- Imperfect data → We may end up studying the wrong subset
- Blind → Impact both internal and external validity
- Anticipate bias → critical decisions
- Good quality research → identify and reduce bias

Acute new event ✓



Follow-up visit







# Process - Phenotype development and evaluation

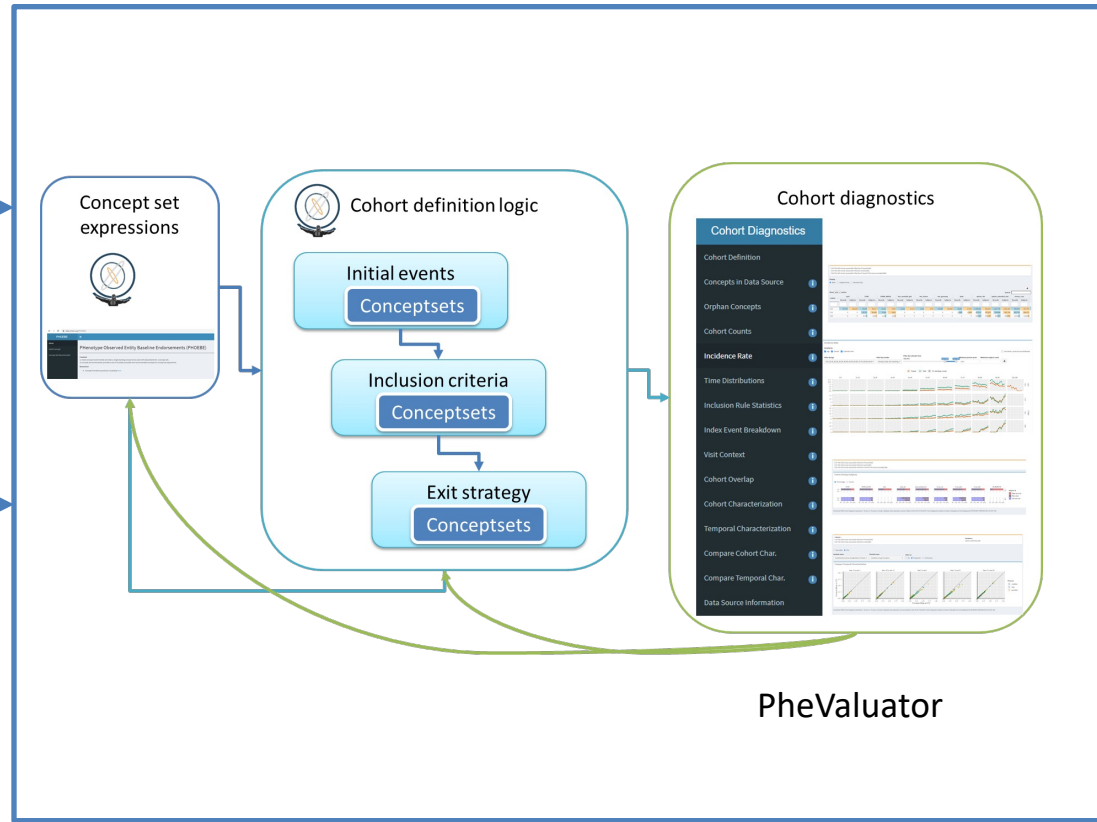
## Required Inputs:



Clinical description



Prior knowledge from  
literature or other  
sources



## Expected Outputs:

{Cohort definition(s)}



Evaluation report





# Acute Myocardial Infarction (20 min)

- Clinical Description - identify
  - Strengtheners: signs, symptoms, diagnostic evaluation, treatments
  - Disqualifiers: mutually exclusive/cannot be present at the same time

Acute new event ✓



Presentation: New onset severe angina (more than usual).

Diagnostic Evaluation: EKG changes

Therapy Plan: nitroglycerin, ASA, anticoagulants, beta blockers, Hospitalize, biomarkers (troponins).

Reperfusion therapy – PCI/CABG

Prognosis: variable – 1 to 3 days. May re-occur.

PhenotypeLibrary 3.2.0

Reference

Articles ▾

Changelog

Guidelines on writing clinical description for Condition Phenotypes

Gowtham A. Rao

Overview, Presentation, Diagnostic Evaluation,  
Therapy Plan, Prognosis

2022-09-06

Source: vignettes/GuidelinesOnClinicalDescriptionForConditionPhenotypes.Rmd

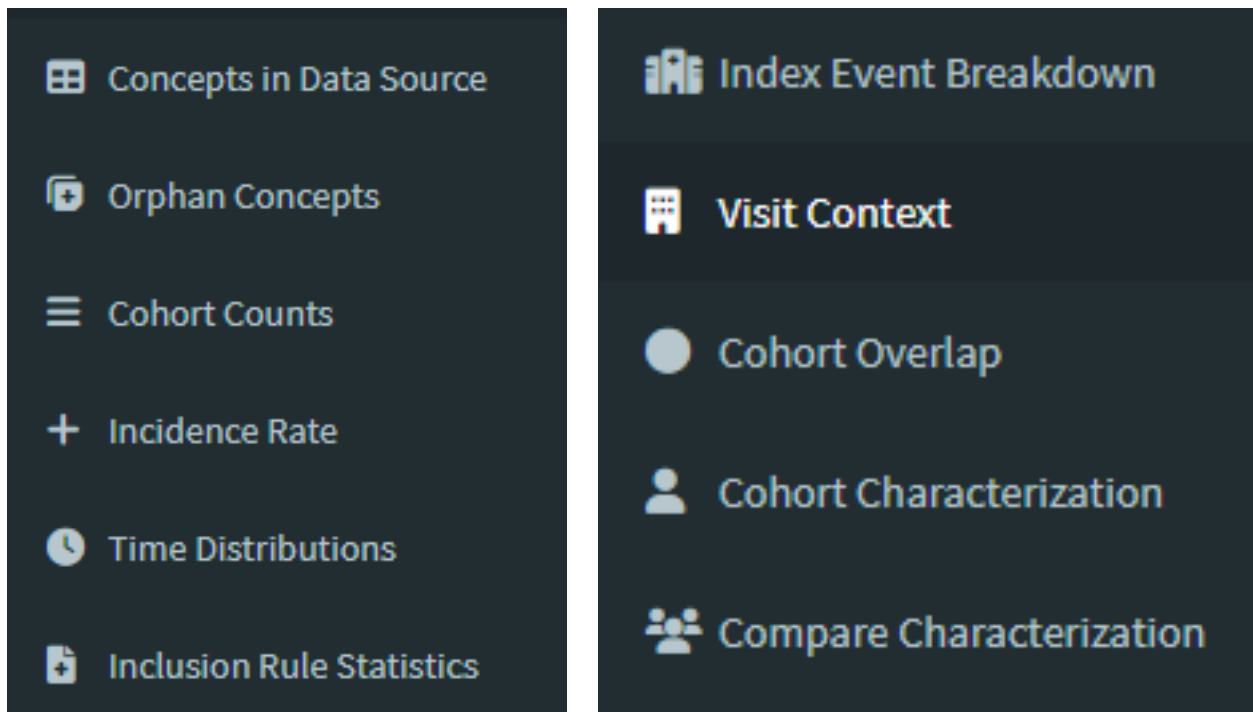
<https://ohdsi.github.io/PhenotypeLibrary/articles/GuidelinesOnClinicalDescriptionForConditionPhenotypes.html>



# Tool – Cohort Diagnostics

<https://data.ohdsi.org/Ohdsi22CdTutorialMyocardialInfarction/>

- Explore descriptive statistics on the cohort from data source
- Set of diagnostics (We'll use a subset in this workshop)





# Cohort Diagnostics – Cohort Count

**Cohort Diagnostics**

- </> Cohort Definition
- 📊 Concepts in Data Source
- 🗑️ Orphan Concepts
- ☰ Cohort Counts**
- + Incidence Rate
- 🕒 Time Distributions
- 📁 Index Event Breakdown
- 🗂️ Visit Context
- 🔍 Cohort Overlap
- 👤 Cohort Characterization
- 👥 Compare Characterization
- ⚙️ Meta data

**Database(s)**

PharMetrics Plus 5 pct samp ▼

**Cohorts**

C25: [OHDSI2022] Acute myo ▼

## Cohort Counts

C25: [OHDSI2022] Acute myocardial infarction events

**Display**

☒ Both ☐ Persons ☐ Records

Search

			PharMetrics Plus 5 pct sample	
	Cohort Id ↕	Cohort Name ↕	Persons ↕	Records ↕
<input type="radio"/>	25	[OHDSI2022] Acute myocardial infarction events	38,626	40,395

1–1 of 1 rows   Show 20 ▼

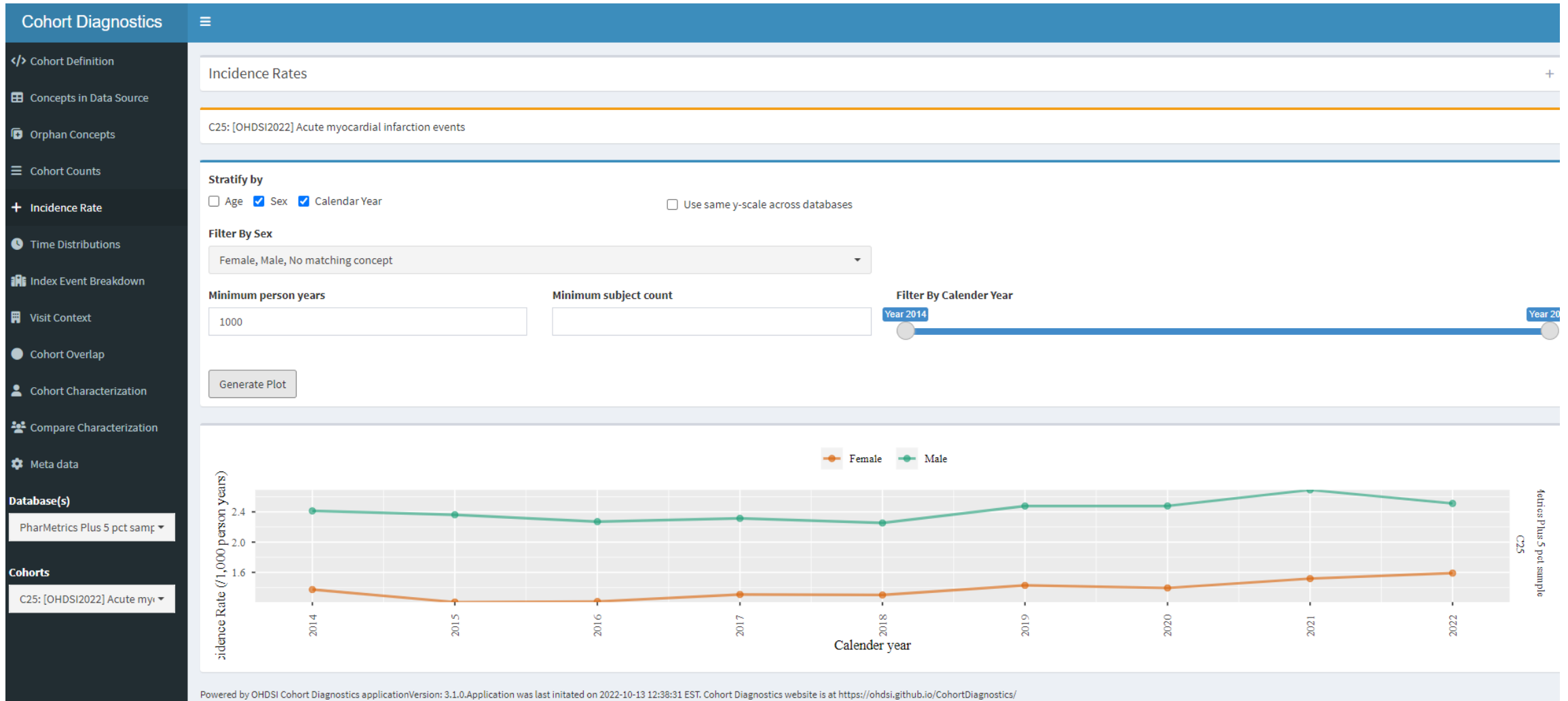
Download CSV (filtered)

Comments

Powered by OHDSI Cohort Diagnostics applicationVersion: 3.1.0.Application was last initiated on 2022-10-13 12:38:31 EST. Cohort Diagnostics website is at <https://ohdsi.github.io/CohortDiagnostics/>

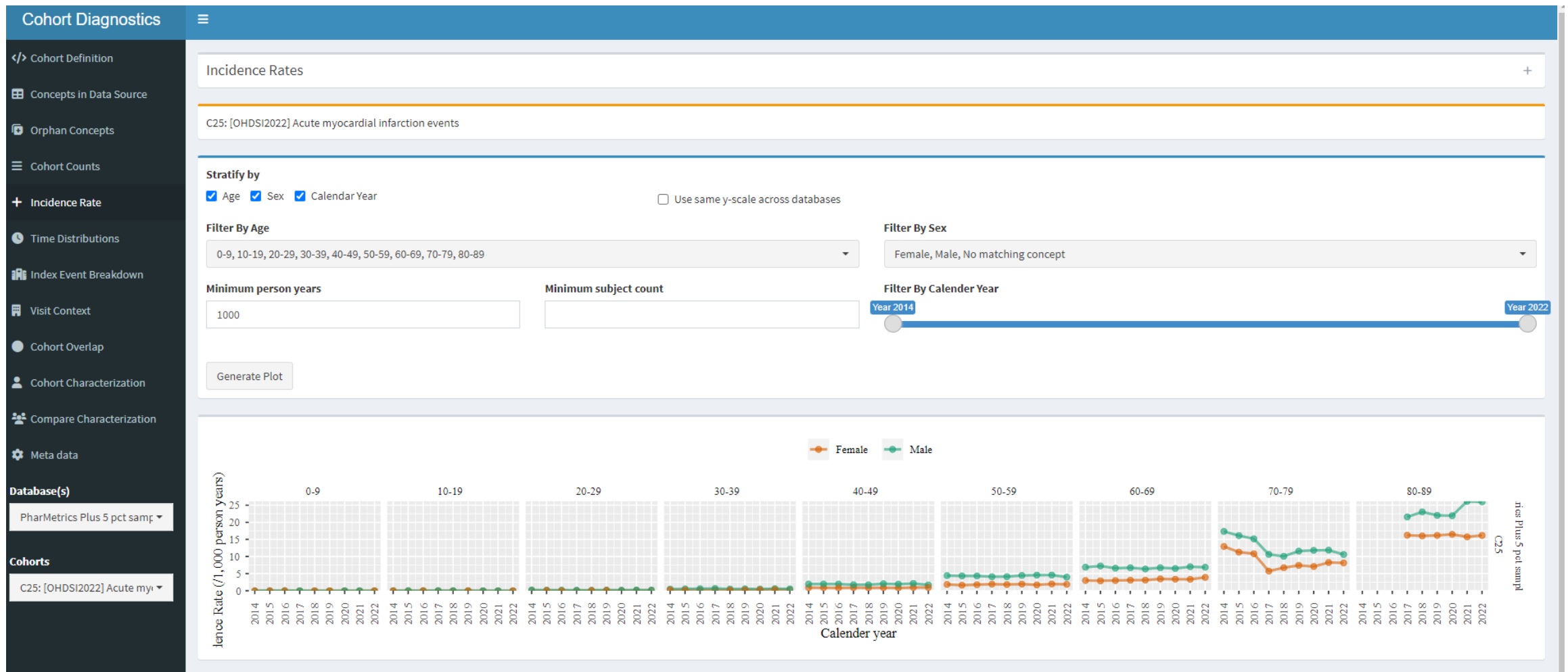


# Cohort Diagnostics – Incidence Rate





# Cohort Diagnostics – Incidence Rate





# Cohort Diagnostics – Index Event Breakdown

Cohort Diagnostics

</> Cohort Definition

Concepts in Data Source

Orphan Concepts

Cohort Counts

+ Incidence Rate

Time Distributions

**Index Event Breakdown**

Visit Context

Cohort Overlap

Cohort Characterization

Compare Characterization

Meta data

Database(s)

PharMetrics Plus 5 pct sampl...

Cohort

C25: [OHDSI2022] Acute myo...

Index Events

C25: [OHDSI2022] Acute myocardial infarction events

All

Standard concepts

Non Standard Concepts

Display

Both

Records

Persons

Search

Concept Id	Concept Name	Concept Code	Domain Field	Vocabulary Id	PharMetrics Plus 5 pct sampl...
					Persons
4270024	Acute non-ST segment elevation myocardial infarction	401314000	condition_concept_id	SNOMED	21,113
4296653	Acute ST segment elevation myocardial infarction	401303003	condition_concept_id	SNOMED	8,151
444406	Acute subendocardial infarction	70422006	condition_concept_id	SNOMED	5,198
37309626	Myocardial infarction due to demand ischemia	16837681000119104	condition_concept_id	SNOMED	3,882
312327	Acute myocardial infarction	57054005	condition_concept_id	SNOMED	3,720
43020460	Acute ST segment elevation myocardial infarction involving left anterior descending coronary artery	285981000119103	condition_concept_id	SNOMED	1,579
46270163	Acute ST segment elevation myocardial infarction due to right coronary artery occlusion	15713121000119105	condition_concept_id	SNOMED	1,549
438170	Acute myocardial infarction of inferior wall	73795002	condition_concept_id	SNOMED	855
434376	Acute myocardial infarction of anterior wall	54329005	condition_concept_id	SNOMED	680
438438	Acute myocardial infarction of anterolateral wall	70211005	condition_concept_id	SNOMED	353
438447	Acute myocardial infarction of inferolateral wall	65547006	condition_concept_id	SNOMED	188
45766241	Subsequent non-ST segment elevation myocardial infarction	703360004	condition_concept_id	SNOMED	136



# Cohort Diagnostics – Visit Context

Cohort Diagnostics

</> Cohort Definition

Concepts in Data Source

Orphan Concepts

Cohort Counts

Incidence Rate

Time Distributions

Index Event Breakdown

Visit Context

Cohort Overlap

Cohort Characterization

Compare Characterization

Meta data

Database(s)

PharMetrics Plus 5 pct sam

Cohort

C25: [OHDSI2022] Acute my

Visit Context

C25: [OHDSI2022] Acute myocardial infarction events

Display

☒ All ☐ Before ☐ During ☐ Simultaneous ☐ After

Display

☒ Persons ☐ Records

	PharMetrics Plus 5 pct sample (38,626)			
Visit Concept Name ↓	Before ↓	During ↓	Simultaneous ↓	After ↓
Inpatient Visit	2,548	2,384	28,810	7,969
Emergency Room - Hospital	6,217	39	7,555	5,665
Outpatient Hospital	10,925	90	6,909	16,640
Inpatient Hospital	3,543	75	5,275	15,338
Ambulance - Land	2,544	<5	2,688	2,304
Observation Room	1,377	<5	2,310	3,193
Ambulatory Surgical Center	5,332	10	1,878	6,692
Pharmacy visit	17,175	<5	1,481	22,022
Office Visit	18,191	21	876	26,122
Outpatient Visit	6,147	351	786	9,115
Outpatient Critical Care Facility	162	<5	319	71
Urgent Care Facility	580		114	228





# Cohort Diagnostics – Cohort Characterization

What to look for	Time frame	Variable (for MI)	Type of error
Do we observe concepts (events) that reflect known <b>risk factors</b> or <b>co-existing conditions</b> of the outcome	-365 to -1 -365 to 0	Hypertension, Diabetes mellitus, Hyperlipidemia, tobacco/nicotine, Coronary atherosclerosis	Sensitivity (Strengtheners)
Do you observe concepts (events) that reflect <b>expected</b> symptoms, signs, diagnostic workup, therapeutic/treatments or complications for the outcome (e.g., proportions of common treatments, known diagnostic procedures)	-30 to +30	Chest pain, critical care, ambulance, EKG, cardiac enzymes/troponin, catheterization, echo Aspirin, clopidogrel, nitroglycerin, Shock, cardiac failure, arrhythmia	Specificity (Strengtheners)
Do you observe concepts (events) that shouldn't be seen but are, concepts that may suggest presence of disease that may <b>invalidate</b> the phenotype? (e.g., mutually exclusive condition, differential diagnosis)	-30 to +30	Pleuritic pneumonia, aortic rupture, Cardiac transplant Historical Myocardial Infarction	Specificity (disqualifiers)
Do you observe concepts in the time prior that suggest outcome <b>started earlier</b> (e.g., Specific treatment, cooccurring conditions, specific diagnostic work, a complication or an exacerbation of the condition)?	-365 to -30	Like above	Index-Date Misclassification
Are cohort characteristics for the same PAs when observed over multiple data source similar or different?	-30 to +30		Specificity Sensitivity



# Risk factors

Group by Database

Group by Time ID

Search

Covariate Name ↕	Analysis Name ↕	Concept Id ↕	Database Name ↕	T (-365d to 0d) ↓	T (-365d to -1d) ↕	T (0d to 0d) ↕
	conditionocc					
Essential hypertension	ConditionOccurrence	320128	PharMetrics Plus 5 pct sample	0.7	0.5	0.5
Hyperlipidemia	ConditionOccurrence	432867	PharMetrics Plus 5 pct sample	0.5	0.3	0.4
Acute non-st segment elevation myocardial infarction	ConditionOccurrence	4270024	PharMetrics Plus 5 pct sample	0.5		0.5
Chest pain	ConditionOccurrence	77670	PharMetrics Plus 5 pct sample	0.4	0.2	0.3
Atherosclerosis of coronary artery without angina p...	ConditionOccurrence	764123	PharMetrics Plus 5 pct sample	0.4	0.2	0.3
Type 2 diabetes mellitus without complication	ConditionOccurrence	4193704	PharMetrics Plus 5 pct sample	0.3	0.2	0.2
Dyspnea	ConditionOccurrence	312437	PharMetrics Plus 5 pct sample	0.3	0.2	0.1
Congestive heart failure	ConditionOccurrence	319835	PharMetrics Plus 5 pct sample	0.2	0.1	0.2
Acute renal failure syndrome	ConditionOccurrence	197320	PharMetrics Plus 5 pct sample	0.2	0.1	0.2
Acute st segment elevation myocardial infarction	ConditionOccurrence	4296653	PharMetrics Plus 5 pct sample	0.2		0.2
Type 2 diabetes mellitus	ConditionOccurrence	201826	PharMetrics Plus 5 pct sample	0.2	0.1	0.1
Nicotine dependence	ConditionOccurrence	4209423	PharMetrics Plus 5 pct sample	0.2	0.1	0.1
Gastroesophageal reflux disease without esophagitis	ConditionOccurrence	4144111	PharMetrics Plus 5 pct sample	0.2	0.1	0.1
Pure hypercholesterolemia	ConditionOccurrence	437827	PharMetrics Plus 5 pct sample	0.2	0.1	0.1
Obesity	ConditionOccurrence	433736	PharMetrics Plus 5 pct sample	0.2	0.1	0.1
Mixed hyperlipidemia	ConditionOccurrence	438720	PharMetrics Plus 5 pct sample	0.2	0.1	0.0
Atrial fibrillation	ConditionOccurrence	313217	PharMetrics Plus 5 pct sample	0.1	0.1	0.1
Anemia	ConditionOccurrence	439777	PharMetrics Plus 5 pct sample	0.1	0.1	0.1
Blood chemistry abnormal	ConditionOccurrence	436230	PharMetrics Plus 5 pct sample	0.1	0.1	0.1
Chronic obstructive lung disease	ConditionOccurrence	255573	PharMetrics Plus 5 pct sample	0.1	0.1	0.1
Acute hypoxemic respiratory failure	ConditionOccurrence	46271075	PharMetrics Plus 5 pct sample	0.1	0.0	0.1
Heart failure	ConditionOccurrence	316139	PharMetrics Plus 5 pct sample	0.1	0.1	0.1



# Signs and symptoms

Covariate Name ↕	Analysis Name ↕	Concept Id ↕	Database Name ↕	T (0d to 0d) ↕
<input type="text" value="chest"/>	<input type="text" value="condition"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Chest pain	ConditionEraGroupOverlap	77670	PharMetrics Plus 5 pct sample	0.5

Covariate Name ↕	Analysis Name ↕	Concept Id ↕	Database Name ↕	T (0d to 0d) ↕
<input type="text" value="Dyspnea"/>	<input type="text" value="condition"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Dyspnea	ConditionEraGroupOverlap	312437	PharMetrics Plus 5 pct sample	0.1

Covariate Name ↕	Analysis Name ↕	Concept Id ↕	Database Name ↕	T (0d to 0d) ↕
<input type="text" value="crit"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Critical care, evaluation and management of the critically ill or critically injured patient; first 3...	ProcedureOccurrence	2514441	PharMetrics Plus 5 pct sample	0.4

Covariate Name ↕	Analysis Name ↕	Concept Id ↕	Database Name ↕	T (0d to 0d) ↕
<input type="text" value="ambula"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Ambulance service, advanced life support, emergency transport, level 1 (als 1 - emergency)	Observation	2614668	PharMetrics Plus 5 pct sample	0.3

Covariate Name ↕	Analysis Name ↕	Concept Id ↕	Database Name ↕	T (0d to 0d) ↕
<input type="text" value="ele"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Electrocardiogram, routine ecg with at least 12 leads; interpretation and report only	ProcedureOccurrence	2313816	PharMetrics Plus 5 pct sample	0.6



# Procedures

Covariate Name ↑	Analysis Name ↑	Concept Id ↑	Database Name ↑	T (0d to 0d) ↑
	procedure			
Electrocardiogram, routine ecg with at least 12 leads; interpretation and report only	ProcedureOccurrence	2313816	PharMetrics Plus 5 pct sample	0.6
A comprehensive history; a comprehensi	ProcedureOccurrence	2514437	PharMetrics Plus 5 pct sample	0.5
A comprehensive history; a comprehensive examination; and medical decision making of high complexity. Counseling a...	ProcedureOccurrence	2514406	PharMetrics Plus 5 pct sample	0.5
Radiographic procedure of chest	ProcedureOccurrence	4190759	PharMetrics Plus 5 pct sample	0.4
Critical care, evaluation and management of the critically ill or critically injured patient; first 30-74 minutes	ProcedureOccurrence	2514441	PharMetrics Plus 5 pct sample	0.4
Echocardiography	ProcedureOccurrence	4230911	PharMetrics Plus 5 pct sample	0.3
Radiologic examination, chest; single view	ProcedureOccurrence	725068	PharMetrics Plus 5 pct sample	0.3
Measurement of cardiac sampling and pressure, left heart, percutaneous approach	ProcedureOccurrence	2786548	PharMetrics Plus 5 pct sample	0.3
Fluoroscopy of multiple coronary arteries using low osmolar contrast	ProcedureOccurrence	2789604	PharMetrics Plus 5 pct sample	0.3
Radiologic examination, chest; single view, frontal	ProcedureOccurrence	2211359	PharMetrics Plus 5 pct sample	0.3
Catheter placement in coronary artery(s) for coronary angiography, including intraprocedural injection(s) for coronary ...	ProcedureOccurrence	40756950	PharMetrics Plus 5 pct sample	0.2
Radiographic imaging procedure	ProcedureOccurrence	4178367	PharMetrics Plus 5 pct sample	0.2
Respiratory therapy	ProcedureOccurrence	4203780	PharMetrics Plus 5 pct sample	0.2
Administration of anesthesia	ProcedureOccurrence	4160439	PharMetrics Plus 5 pct sample	0.2
Echocardiography, transthoracic, real-time with image documentation (2d), includes m-mode recording, when perform...	ProcedureOccurrence	2313869	PharMetrics Plus 5 pct sample	0.2
Electrocardiogram, routine ecg with at least 12 leads; tracing only, without interpretation and report	ProcedureOccurrence	2313815	PharMetrics Plus 5 pct sample	0.2
Fluoroscopy of left heart using low osmolar contrast	ProcedureOccurrence	2785799	PharMetrics Plus 5 pct sample	0.2
A comprehensive history; a comprehensive examination; and medical decision making of moderate complexity. Counse...	ProcedureOccurrence	2514405	PharMetrics Plus 5 pct sample	0.1
Cat scan - whole body	ProcedureOccurrence	4060500	PharMetrics Plus 5 pct sample	0.1
Dilation of coronary artery, one artery with drug-eluting intraluminal device, percutaneous approach	ProcedureOccurrence	2725905	PharMetrics Plus 5 pct sample	0.1



# Search Echocardiogram

Covariate Name ↑	Analysis Name ↑	Concept Id ↑	Database Name ↑	T (0d to 0d) ↑
<input type="text" value="echo"/>	<input type="text" value="procedure"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Echocardiography	ProcedureOccurrence	4230911	PharMetrics Plus 5 pct sample	0.3
Echocardiography, transthoracic, real-time with image documentation (2d), includes m-mode recording, when perform...	ProcedureOccurrence	2313869	PharMetrics Plus 5 pct sample	0.2
Echocardiography, transthoracic, real-time with image documentation (2d), includes m-mode recording, when perform...	ProcedureOccurrence	2313871	PharMetrics Plus 5 pct sample	0.0

You maybe seeing:

- Verbatim concept id
- Not clinical id



# Measurements

Covariate Name ↕	Analysis Name ↕	Concept Id ↕	Database Name ↕	T (0d to 0d) ↓
<input type="text"/>	<input type="text" value="measu"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Troponin, quantitative	Measurement	2212605	PharMetrics Plus 5 pct sample	0.2
Blood count; complete (cbc), automated (hgb, hct, rbc, wbc and platelet count) and automated differential wbc count	Measurement	2212648	PharMetrics Plus 5 pct sample	0.2
Albumin (82040) bilirubin, total (82247) calcium, total (82310) carbon dioxide (bicarbonate) (82374) chloride (82435) cr...	Measurement	2212093	PharMetrics Plus 5 pct sample	0.2
Prothrombin time	Measurement	2212731	PharMetrics Plus 5 pct sample	0.1
Thromboplastin time, partial (ptt); plasma or whole blood	Measurement	2212742	PharMetrics Plus 5 pct sample	0.1
Natriuretic peptide	Measurement	2212470	PharMetrics Plus 5 pct sample	0.1
Magnesium	Measurement	2212453	PharMetrics Plus 5 pct sample	0.1
Calcium, total (82310) carbon dioxide (bicarbonate) (82374) chloride (82435) creatinine (82565) glucose (82947) potassi...	Measurement	2212090	PharMetrics Plus 5 pct sample	0.1
Creatine kinase (ck), (cpk); total	Measurement	2212290	PharMetrics Plus 5 pct sample	0.1
Creatine kinase (ck), (cpk); mb fraction only	Measurement	2212292	PharMetrics Plus 5 pct sample	0.1
Enzyme measurement	Measurement	4046263	PharMetrics Plus 5 pct sample	0.1
Blood count; complete (cbc), automated (hgb, hct, rbc, wbc and platelet count)	Measurement	2212649	PharMetrics Plus 5 pct sample	0.0
Fibrin degradation products, d-dimer; quantitative	Measurement	2212699	PharMetrics Plus 5 pct sample	0.0
Lipase	Measurement	2212441	PharMetrics Plus 5 pct sample	0.0
Cholesterol, serum, total (82465) lipoprotein, direct measurement, high density cholesterol (hdl cholesterol) (83718) tri...	Measurement	2212095	PharMetrics Plus 5 pct sample	0.0
Serum/plasma protein test	Measurement	4055657	PharMetrics Plus 5 pct sample	0.0
Urinalysis, by dip stick or tablet reagent for bilirubin, glucose, hemoglobin, ketones, leukocytes, nitrite, ph, protein, sp...	Measurement	2212166	PharMetrics Plus 5 pct sample	0.0
Lactate (lactic acid)	Measurement	2212427	PharMetrics Plus 5 pct sample	0.0



# Treatments

Covariate Name ↕	Analysis Name ↕	Concept Id ↕	Database Name ↕	T (-30d to -1d) ↕	T (1d to 30d) ↕	T (0d to 0d) ↕
catheter						
Catheter placement in coronary artery(s) for coronary angiograph...	ProcedureOccurrence	40756950	PharMetrics Plus 5 pct sample	0.0	0.2	0.2
Percutaneous transcatheter placement of intracoronary stent(s), ...	ProcedureOccurrence	43527998	PharMetrics Plus 5 pct sample	0.0	0.1	0.1
Catheterization of left heart	ProcedureOccurrence	4195852	PharMetrics Plus 5 pct sample	0.0		0.1
Coronary arteriography using two catheters	ProcedureOccurrence	4171675	PharMetrics Plus 5 pct sample			0.0
Catheter placement in coronary artery(s) for coronary angiograph...	ProcedureOccurrence	40756852	PharMetrics Plus 5 pct sample		0.1	0.0
Insertion of non-tunneled centrally inserted central venous cathet...	ProcedureOccurrence	2108190	PharMetrics Plus 5 pct sample	0.0	0.1	0.0
Arterial catheterization or cannulation for sampling, monitoring o...	ProcedureOccurrence	2108261	PharMetrics Plus 5 pct sample	0.0	0.1	0.0
Catheter placement in coronary artery(s) for coronary angiograph...	ProcedureOccurrence	40756979	PharMetrics Plus 5 pct sample		0.0	0.0
Catheter, guiding (may include infusion/perfusion capability)	DeviceExposure	2615865	PharMetrics Plus 5 pct sample		0.0	0.0
Insertion and placement of flow directed catheter (eg, swan-ganz)...	ProcedureOccurrence	2313886	PharMetrics Plus 5 pct sample		0.0	
Pharmaceuticals, cardiovascular system	ProcedureOccurrence	2241707	PharMetrics Plus 5 pct sample		0.0	



# Bad signs

Covariate Name ↑	Analysis Name ↑	Concept Id ↑	Database Name ↑	T (0d to 0d) ↓
Electrocardiogram, routine ecg with at least 12 leads; interpretation and report only	ProcedureOccurrence	2313816	PharMetrics Plus 5 pct sample	0.6
A comprehensive history; a comprehensi	ProcedureOccurrence	2514437	PharMetrics Plus 5 pct sample	0.4
A comprehensive history; a comprehensive examination; and medical decision making of high complexity. Counseling ...	ProcedureOccurrence	2514406	PharMetrics Plus 5 pct sample	0.4
Radiographic procedure of chest	ProcedureOccurrence	4190759	PharMetrics Plus 5 pct sample	0.4
Critical care, evaluation and management of the critically ill or critically injured patient; first 30-74 minutes	ProcedureOccurrence	2514441	PharMetrics Plus 5 pct sample	0.4
Echocardiography	ProcedureOccurrence	4230911	PharMetrics Plus 5 pct sample	0.3
Radiologic examination, chest; single view	ProcedureOccurrence	725068	PharMetrics Plus 5 pct sample	0.3
Measurement of cardiac sampling and pressure, left heart, percutaneous approach	ProcedureOccurrence	2786548	PharMetrics Plus 5 pct sample	0.3
Fluoroscopy of multiple coronary arteries using low osmolar contrast	ProcedureOccurrence	2789604	PharMetrics Plus 5 pct sample	0.3
Radiologic examination, chest; single view, frontal	ProcedureOccurrence	2211359	PharMetrics Plus 5 pct sample	0.3
Catheter placement in coronary artery(s) for coronary angiography, including intraprocedural injection(s) for coronary ...	ProcedureOccurrence	40756950	PharMetrics Plus 5 pct sample	0.2
Radiographic imaging procedure	ProcedureOccurrence	4178367	PharMetrics Plus 5 pct sample	0.2
Respiratory therapy	ProcedureOccurrence	4203780	PharMetrics Plus 5 pct sample	0.2
Administration of anesthesia	ProcedureOccurrence	4160439	PharMetrics Plus 5 pct sample	0.2
Physical therapy procedure	Observation	4238738	PharMetrics Plus 5 pct sample	0.2
Echocardiography, transthoracic, real-time with image documentation (2d), includes m-mode recording, when perfor...	ProcedureOccurrence	2313869	PharMetrics Plus 5 pct sample	0.2
Electrocardiogram, routine ecg with at least 12 leads; tracing only, without interpretation and report	ProcedureOccurrence	2313815	PharMetrics Plus 5 pct sample	0.2





# Index Event Misclassification

Covariate Name ↑	Analysis Name ↓	Concept Id ↑	Database Name ↓	T (-30d to -1d) ↓	T (0d to 0d) ↓
	procedure				
Electrocardiogram, routine ecg with at least 12 leads; interpretation and report only	ProcedureOccurrence	2313816	PharMetrics Plus 5 pct sample	0.2	0.6
A comprehensive history; a comprehensi	ProcedureOccurrence	2514437	PharMetrics Plus 5 pct sample	0.2	0.4
A comprehensive history; a comprehensive examination; and medical decision maki...	ProcedureOccurrence	2514406	PharMetrics Plus 5 pct sample	0.1	0.4
Radiographic procedure of chest	ProcedureOccurrence	4190759	PharMetrics Plus 5 pct sample	0.1	0.4
Critical care, evaluation and management of the critically ill or critically injured patie...	ProcedureOccurrence	2514441	PharMetrics Plus 5 pct sample	0.1	0.4
Echocardiography	ProcedureOccurrence	4230911	PharMetrics Plus 5 pct sample	0.1	0.3
Radiologic examination, chest; single view	ProcedureOccurrence	725068	PharMetrics Plus 5 pct sample	0.1	0.3
Measurement of cardiac sampling and pressure, left heart, percutaneous approach	ProcedureOccurrence	2786548	PharMetrics Plus 5 pct sample	0.0	0.3
Fluoroscopy of multiple coronary arteries using low osmolar contrast	ProcedureOccurrence	2789604	PharMetrics Plus 5 pct sample	0.0	0.3
Radiologic examination, chest; single view, frontal	ProcedureOccurrence	2211359	PharMetrics Plus 5 pct sample	0.1	0.3
Catheter placement in coronary artery(s) for coronary angiography, including intrapr...	ProcedureOccurrence	40756950	PharMetrics Plus 5 pct sample	0.0	0.2
Radiographic imaging procedure	ProcedureOccurrence	4178367	PharMetrics Plus 5 pct sample	0.1	0.2
Respiratory therapy	ProcedureOccurrence	4203780	PharMetrics Plus 5 pct sample	0.1	0.2
Administration of anesthesia	ProcedureOccurrence	4160439	PharMetrics Plus 5 pct sample	0.1	0.2



# Angioedema

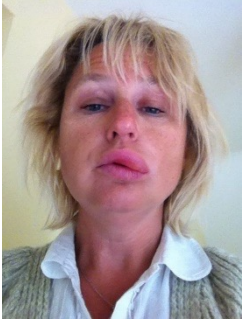
**Overview:** Angioedema is self-limited, localized subcutaneous (or submucosal) swelling, which results from extravasation of fluid into interstitial tissues.

**Presentation:** Angioedema may occur in isolation, accompanied by urticaria, or as a component of anaphylaxis. Angioedema typically affects areas with loose connective tissue, such as the face, lips, mouth, and throat, larynx, uvula, extremities, and genitalia. Maybe rapid or slow in onset, may be life threatening if involves the larynx, airways, Bowel wall angioedema presents as colicky abdominal pain.

**Assessment:** Clinical diagnosis, testing is of limited use. ACE inhibitor exposure, hereditary or acquired C1 inhibitor deficiency. May have no identifiable cause. May re occur. If airway involved and life threatening, may need intubation. Else observation. Manage anaphylaxis if present.

**Plan:** Monitor, find and eliminate the etiology. Maintain airway – need for intubation

**Disqualifiers:** Cardiac edema (within 7 days), cellulitis (within 7 days), erysipelas (within 7 days), dermatitis (within 7 days), lymphedema (within 7 days), preceding insect sting (within 24 hours), preceding allergic reaction to food (within 24 hours)





# Cohort Diagnostics – Cohort Characterization

What to look for	Time frame	Variable (for Angioedema)	Type of error
Do we observe concepts (events) that reflect known <b>risk factors</b> or <b>co-existing conditions</b> of the outcome	-365 to -1 -365 to 0	Allergies	Sensitivity (Strengtheners)
Do you observe concepts (events) that reflect <b>expected</b> symptoms, signs, diagnostic workup, therapeutic/treatments or complications for the outcome (e.g., proportions of common treatments, known diagnostic procedures)	-30 to +30	Swelling, itching, edema	Specificity (Strengtheners)
Do you observe concepts (events) that shouldn't be seen but are, concepts that may suggest presence of disease that may <b>invalidate</b> the phenotype? (e.g., mutually exclusive condition, differential diagnosis)	-30 to +30		Specificity (disqualifiers)
Do you observe concepts in the time prior that suggest outcome <b>started earlier</b> (e.g., Specific treatment, cooccurring conditions, specific diagnostic work, a complication or an exacerbation of the condition)?	-365 to -30	Epienphrine	Index-Date Misclassification
Are cohort characteristics for the same PAs when observed over multiple data source similar or different?	-30 to +30		Specificity Sensitivity