



Application of Cohort Diagnostics to build the outcome phenotype

Anaphylaxis in relation to drug exposure

10-minute tutorial

June 8th, 2021



What is anaphylaxis?

Acute, potentially life-threatening, multisystem syndrome

Caused by the sudden release of mast cell mediators into the systemic circulation.

Immunoglobulin E (IgE)-mediated reactions

Foods

Drugs, and

Insect stings

Any agent capable of inciting a sudden, systemic degranulation of mast cells

US data: The lifetime prevalence of anaphylaxis in the general population based on cross-sectional survey is at least 1.6%.

Wood et.al.. Anaphylaxis in America: the prevalence and characteristics of anaphylaxis in the United States. J Allergy Clin Immunol. 2014 Feb;133(2):461-7



What is **NOT** anaphylaxis?

J ALLERGY CLIN IMMUNOL
VOLUME 125, NUMBER 2

TABLE V. Symptoms and signs of anaphylaxis

Cutaneous/subcutaneous/mucosal tissue
Flushing, pruritus, hives (urticaria), swelling, morbilliform rash, pilor erection
Periorbital pruritus, erythema and swelling, conjunctival erythema, tearing
Pruritus and swelling of lips, tongue, uvula/palate
Pruritus in the external auditory canals
Pruritus of genitalia, palms, soles
Respiratory
Nose: pruritus, congestion, rhinorrhea, sneezing
Larynx: pruritus and tightness in the throat, dysphonia and hoarseness, dry staccato cough, stridor, dysphagia
Lung: shortness of breath, chest tightness, deep cough, wheezing/bronchospasm (decreased peak expiratory flow)
Cyanosis
Gastrointestinal
Nausea, cramping abdominal pain, vomiting (stringy mucus), diarrhea
Cardiovascular
Chest pain, palpitations, tachycardia, bradycardia, or other dysrhythmia
Feeling faint, altered mental status, hypotension, loss of sphincter control, shock, cardiac arrest
CNS
Aura of impending doom, uneasiness, throbbing headache, dizziness, confusion, tunnel vision; in infants and children, sudden behavioral changes, such as irritability, cessation of play, and clinging to parent
Other
Metallic taste in the mouth
Dysphagia
Uterine contractions in postpubertal female patients

Adapted from references 24, 25, 93, and 94. Sudden onset of symptoms and signs is characteristic of anaphylaxis.

SIMONS S167

TABLE VI. Differential diagnosis of anaphylaxis

Common entities	Nonorganic disease
Acute generalized hives	Vocal cord dysfunction
Acute asthma	Munchausen syndrome
Syncope (faint, vasovagal episode)	
Panic attack	
Aspiration of a foreign body	Shock
Cardiovascular event (myocardial infarction, pulmonary embolus)	Hypovolemic
Neurologic event (seizure, stroke)	Cardiogenic
	Distributive (eg, spinal cord injury)
	Septic (might involve all of the above)
Postprandial syndromes	Other
Pollen-food syndrome*	Nonallergic angioedema
Scombroidosis†	Red Man syndrome (vancomycin)
Monosodium glutamate	Urticarial vasculitis
Sulfites	Hyper-IgE urticaria syndrome
	Progesterone anaphylaxis
	Pheochromocytoma
	Idiopathic systemic capillary leak syndrome
Excess endogenous histamine	
Mastocytosis/clonal mast cell disorders‡	
Basophilic leukemia	
Flush syndromes	
Perimenopause	
Carcinoid	
Autonomic epilepsy	
Medullary carcinoma thyroid	



Follow along on app if you like (link in chat)



<https://data.ohdsi.org/Ohdsi10MinuteTutorialCohortDiagnosticsAnaphylaxis/>

Slides are screenshots from this app because live demo is not feasible



Anaphylaxis due to vaccine



- Start with broad concept-set/code-set: “Anaphylaxis and descendant”

Vocabulary version choices:

☒ Concept Set Expression ☐ Resolved ☐ Mapped ☐ Orphan concepts ☐ Json Subjects: 241,823 Records: 241,823

Show entries

Search:

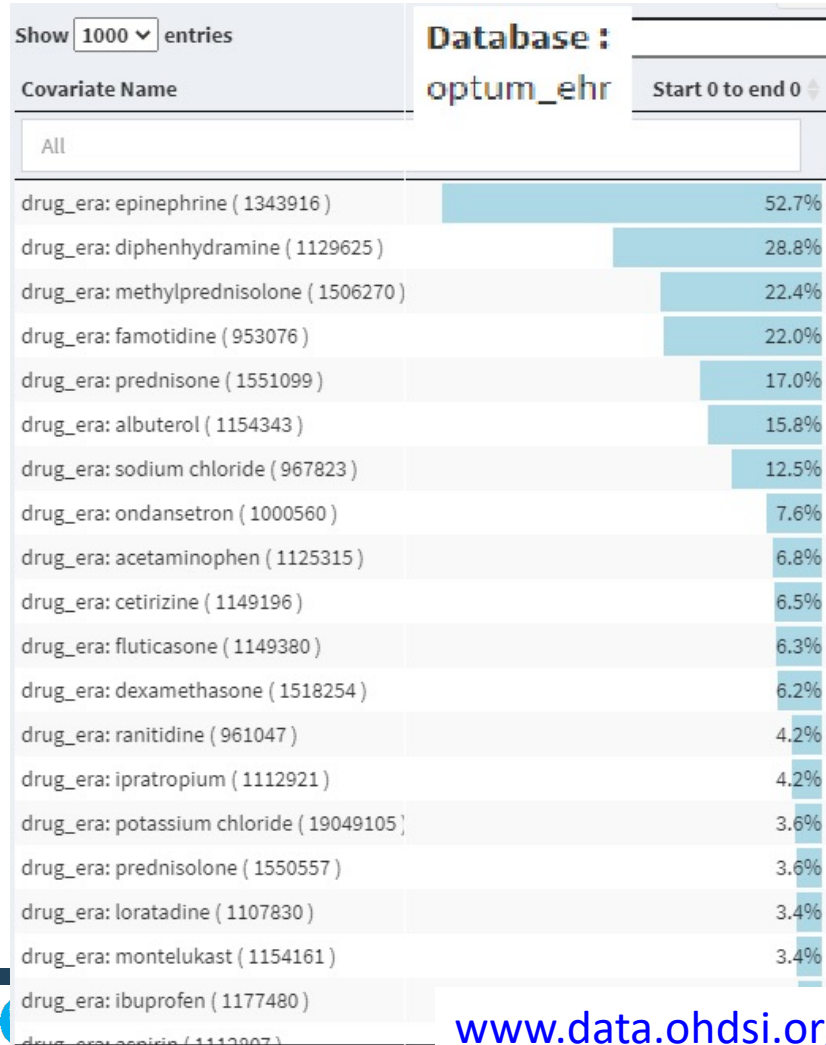
Concept Id	Concept Name	Exclude	Descendants	Mapped	Standard Concept	Invalid	Concept Code	Domain Id	Vocabulary Id	Concept Class Id
All	All	All	All	All	All	All	All	All	All	All
441202	Anaphylaxis		✓		S		39579001	Condition	SNOMED	Clinical Finding

Optum_ehr	Optum_extended_dod	Truven_ccae	Truven_mdcd	Truven_mdcr
All	All	All	All	All
142,150	241,823	431,953	92,695	16,655



Diagnostics: what's happening on index date

✓ Drugs



Domain name

Drug

Covariate Name

Start 0 to end 0

Database : optum_extended_dod

drug_era: epinephrine (1343916)	19.0%
drug_era: methylprednisolone (1506270)	8.9%
drug_era: diphenhydramine (1129625)	7.9%
drug_era: prednisone (1551099)	5.8%
drug_era: sodium chloride (967823)	3.4%
drug_era: albuterol (1154343)	3.1%
drug_era: dexamethasone (1518254)	2.4%
drug_era: fluticasone (1149380)	1.8%
drug_era: famotidine (953076)	1.7%
drug_era: prednisolone (1550557)	1.6%
drug_era: ondansetron (1000560)	1.5%
drug_era: montelukast (1154161)	1.5%
drug_era: triamcinolone (903963)	1.1%
drug_era: hydroxyzine (777221)	1.0%
drug_era: ranitidine (961047)	1.0%
drug_era: mometasone (905233)	0.8%
drug_era: amoxicillin (1713332)	0.6%

Database

optum_extended_dod

Temporal Choice

Start 0 to end 0

Cohort

C3: [CD] Anaphylaxis all type



Diagnostics: what's happening on index date



Conditions

Covariate Name	Start 0 to end 0
All	Optum EHR
condition_occurrence: Anaphylaxis (441202)	62.5%
condition_occurrence: Food anaphylaxis (434219)	22.9%
condition_occurrence: Allergic rhinitis (257007)	12.3%
condition_occurrence: Allergic disposition (43530807)	11.8%
condition_occurrence: Peanut-induced anaphylaxis (435987)	9.4%
condition_occurrence: Essential hypertension (320128)	8.6%
condition_occurrence: Asthma (317009)	7.5%
condition_occurrence: Urticaria (139900)	6.0%
condition_occurrence: Dyspnea (312437)	5.5%
condition_occurrence: Allergic rhinitis due to pollen (256439)	5.3%
condition_occurrence: Uncomplicated asthma (45768910)	5.1%
condition_occurrence: Accidental poisoning (436581)	4.8%
condition_occurrence: Hyperlipidemia (432867)	4.7%
condition_occurrence: Eruption (140214)	4.3%
condition_occurrence: Angioedema (432791)	4.3%
condition_occurrence: Seafood-induced anaphylaxis (442010)	3.9%
condition_occurrence: Drug-induced anaphylaxis (4084168)	3.5%
condition_occurrence: Toxic effect of venom (440905)	3.4%
condition_occurrence: Swelling / lump finding (443257)	3.4%

Domain name	Database	Temporal Choice
Condition	optum_extended_dod	
Covariate Name	Start 0 to end 0	0 to end 0
All	Optum DOD	
condition_occurrence: Anaphylaxis (441202)	46.9%	
condition_occurrence: Food anaphylaxis (434219)	34.5%	
condition_occurrence: Allergic rhinitis (257007)	19.9%	
condition_occurrence: Allergic rhinitis due to pollen (256439)	18.3%	
condition_occurrence: Peanut-induced anaphylaxis (435987)	13.9%	
condition_occurrence: Allergic disposition (43530807)	10.8%	
condition_occurrence: Atopic dermatitis (133834)	6.9%	
condition_occurrence: Dyspnea (312437)	6.3%	
condition_occurrence: Essential hypertension (320128)	5.9%	
condition_occurrence: Ingestion dermatitis due to food (4066820)	5.8%	
condition_occurrence: Angioedema (432791)	5.5%	
condition_occurrence: Urticaria (139900)	5.3%	
condition_occurrence: Seafood-induced anaphylaxis (442010)	5.2%	
condition_occurrence: Allergic urticaria (139902)	5.1%	
condition_occurrence: IgE-mediated allergic asthma (312950)	4.7%	
condition_occurrence: Asthma (317009)	4.7%	
condition_occurrence: Eruption (140214)	4.4%	
condition_occurrence: Cough (254761)	4.0%	
condition_occurrence: Allergic rhinitis due to animal dander (443558)	3.4%	



Diagnostics: what's happening on index date



• Procedure

Covariate Name	Start 0 to end 0
All	optum EHR
procedure_occurrence: Therapeutic, prophylactic, or diagnostic injection (specif...	19.2%
procedure_occurrence: Therapeutic, prophylactic, or diagnostic injection (specif...	18.6%
procedure_occurrence: Therapeutic, prophylactic, or diagnostic injection (specif...	18.5%
procedure_occurrence: Collection of venous blood by venipuncture (2108115)	16.4%
procedure_occurrence: Emergency department visit for the evaluation and manage	14.3%
procedure_occurrence: Emergency department visit for the evaluation and manage	10.3%
procedure_occurrence: Office or other outpatient visit for the evaluation and ma...	9.9%
procedure_occurrence: Intravenous infusion, hydration; each additional hour (Lis...	8.5%
procedure_occurrence: Electrocardiogram, routine ECG with at least 12 leads; tra...	7.8%
procedure_occurrence: Emergency department visit for the evaluation and manage	7.8%
procedure_occurrence: Office or other outpatient visit for the evaluation and ma...	7.4%
procedure_occurrence: Critical care, evaluation and management of the critically...	7.2%
procedure_occurrence: Pressurized or nonpressurized inhalation treatment for acu	6.9%
procedure_occurrence: Office or other outpatient visit for the evaluation and ma...	6.0%
procedure_occurrence: Electrocardiogram, routine ECG with at least 12 leads; int...	3.8%
procedure_occurrence: Office or other outpatient visit for the evaluation and ma...	3.3%
procedure_occurrence: Radiologic examination, chest; single view, frontal (2211...	3.3%
procedure_occurrence: General examination of patient (4036803)	3.3%
procedure_occurrence: Intravenous infusion, for therapy, prophylaxis, or diagnos...	3.1%

Covariate Name	Start 0 to end 0
All	
procedure_occurrence: Office or other outpatient visit for the evaluation and ma...	17.5%
procedure_occurrence: Office or other outpatient visit for the evaluation and ma...	15.2%
procedure_occurrence: Collection of venous blood by venipuncture (2108115)	14.4%
procedure_occurrence: Office or other outpatient visit for the evaluation and ma...	12.3%
procedure_occurrence: Emergency department visit for the evaluation and manage	10.8%
procedure_occurrence: Office consultation for a new or established patient, whic...	8.8%
procedure_occurrence: Therapeutic, prophylactic, or diagnostic injection (specif...	8.4%
procedure_occurrence: Therapeutic, prophylactic, or diagnostic injection (specif...	7.8%
procedure_occurrence: Spirometry, including graphic record, total and timed vita...	7.3%
procedure_occurrence: Therapeutic, prophylactic, or diagnostic injection (specif...	7.1%
procedure_occurrence: Emergency department visit for the evaluation and manage	6.9%
procedure_occurrence: Emergency department visit for the evaluation and manage	6.9%
procedure_occurrence: Office or other outpatient visit for the evaluation and ma...	6.1%
procedure_occurrence: Critical care, evaluation and management of the critically...	5.1%
procedure_occurrence: Electrocardiogram, routine ECG with at least 12 leads; int...	5.0%
procedure_occurrence: Pressurized or nonpressurized inhalation treatment for acu	3.6%
procedure_occurrence: Radiologic examination, chest; single view, frontal (2211...	3.5%
procedure_occurrence: Electrocardiogram, routine ECG with at least 12 leads; tra...	3.5%
procedure_occurrence: Bronchodilation responsiveness, spirometry as in 94010, pr	3.5%
procedure_occurrence: Office consultation for a new or established patient, whic	2.4%



Diagnostics: what's happening on index date

characteristic	optum_ehr (n = 142,150)	optum_extended_dod (n = 241,823)	truven_ccae (n = 431,953)	truven_mdcd (n = 92,695)	truven_mdcr (n = 16,655)
All	All	All	All	All	All
Age group					
0 - 4	10.4%	15.7%	17.7%	22.4%	
5 - 9	8.9%	11.9%	14.3%	18.5%	
10 - 14	8.2%	8.6%	10.6%	14.7%	
15 - 19	8.5%	6.6%	8.4%	11.4%	
20 - 24	7.0%	4.8%	5.8%	3.5%	
25 - 29	6.6%	5.5%	5.1%	4.1%	<0.0%
30 - 34	6.4%	6.0%	5.4%	4.0%	<0.0%
35 - 39	6.4%	6.3%	5.8%	3.9%	<0.0%
40 - 44	6.2%	6.1%	5.9%	3.5%	0.0%
45 - 49	6.4%	5.7%	5.8%	3.1%	0.1%
50 - 54	6.2%	5.2%	5.5%	3.0%	0.3%
55 - 59	5.8%	4.5%	5.0%	2.8%	0.9%
60 - 64	4.5%	3.6%	4.2%	2.1%	1.6%
65 - 69	3.5%	3.6%	0.4%	1.1%	34.2%
70 - 74	2.3%	2.6%		0.7%	25.5%
75 - 79	1.5%	1.7%		0.5%	17.5%
80 - 84	0.9%	1.0%		0.4%	11.2%
85 - 89	0.3%	0.6%		0.3%	5.8%
90 - 94		0.1%		0.0%	2.3%
95 - 99					0.5%
100 - 104					0.1%
Gender: female					
Gender = female	56.1%	55.0%	54.2%	54.7%	62.0%



Anaphylaxis due to vaccine

- Modify concept-set/code-set: “Anaphylaxis exclude environmental”

All	All	All	All	All
Optum_ehr	Optum_extended_dod	Truven_ccae	Truven_mdcd	Truven_mdcr
All	All	All	All	All
142,150	241,823	431,953	92,695	16,655
95,609	123,886	194,498	50,242	12,937

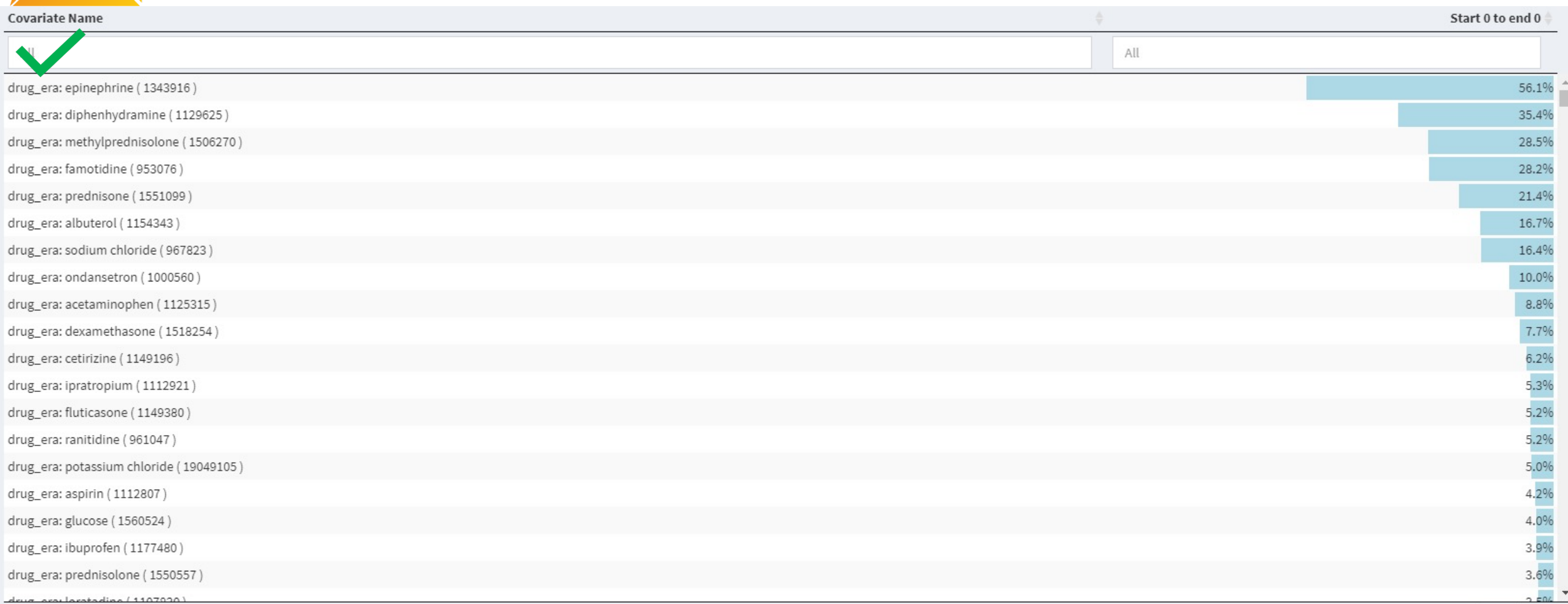
Show 100 entries

Concept Id	Concept Name	Exclude	Descendants	Mapped	Standard Concept	Invalid	Concept Cod
All	All	All	All	All	All	All	All
441202	Anaphylaxis		✓		S		39579001
434219	Food anaphylaxis	✓	✓		S		91941002
4083866	Anaphylaxis caused by venom	✓	✓		S		241930003
4221182	Anaphylaxis due to substance	✓			S		417516000
3661863	Anaphylaxis caused by insect bite and/or insect sting	✓	✓		S		871926004
42538690	Anaphylaxis caused by low temperature	✓	✓		S		762455001
44178658	Anaphylaxis due to latex	✓	✓		S		44178658

Showing 1 to 9 of 9 entries

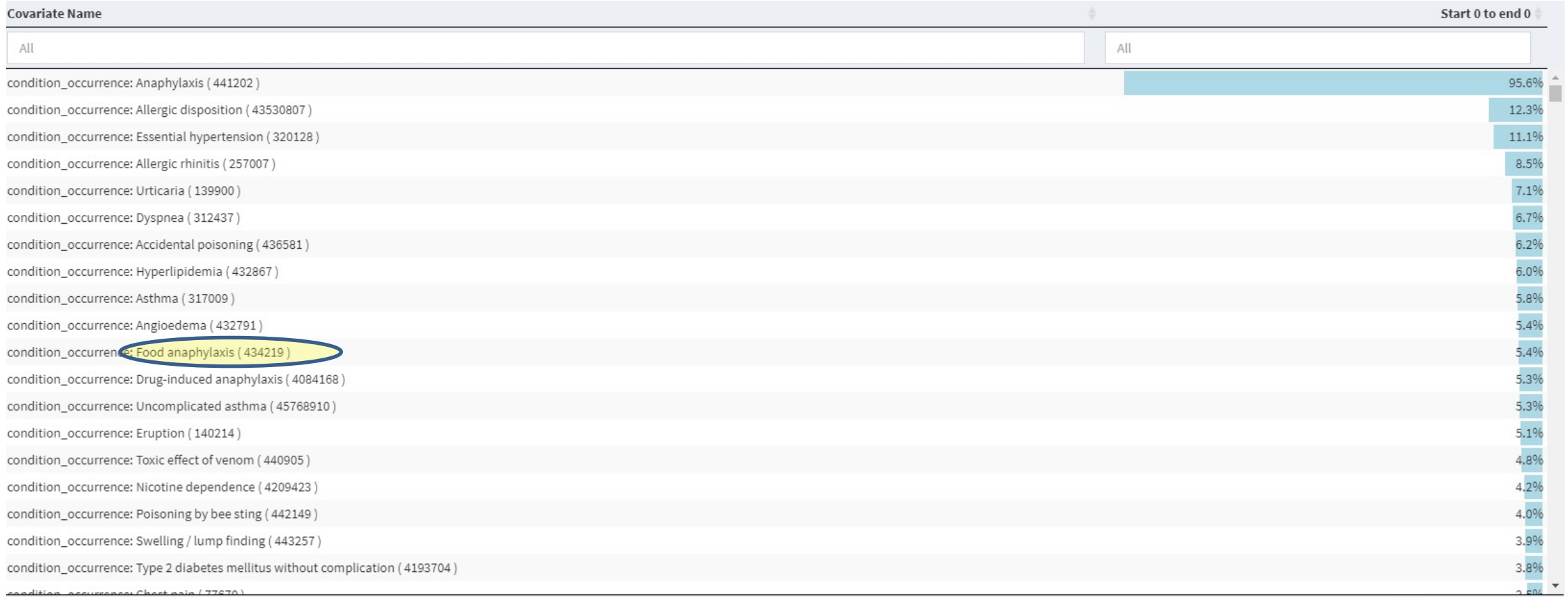


Diagnostics: what's happening on index date





Diagnostics: what's happening on index date





Diagnostics: what's happening on index date



characteristic	optum_ehr (n = 95,609)	optum_extended_dod (n = 123,886)	truven_ccae (n = 194,498)	truven_mdcd (n = 50,242)	truven_mdcr (n = 12,937)
All	All	All	All	All	All
Age group					
0 - 4	6.0%	7.6%	8.4%	13.5%	
5 - 9	6.0%	6.7%	8.0%	13.6%	
10 - 14	6.4%	5.9%	7.4%	12.9%	
15 - 19	8.1%	6.3%	8.6%	12.5%	
20 - 24	7.1%	5.0%	6.6%	4.4%	
25 - 29	7.0%	6.0%	6.2%	5.3%	
30 - 34	6.9%	6.9%	6.8%	5.6%	
35 - 39	7.1%	7.5%	7.8%	5.5%	
40 - 44	7.1%	7.7%	8.3%	5.0%	<0.0%
45 - 49	7.5%	7.5%	8.4%	4.6%	0.1%
50 - 54	7.4%	7.2%	8.3%	4.7%	0.3%
55 - 59	7.1%	6.4%	7.8%	4.4%	0.9%
60 - 64	5.6%	5.3%	6.8%	3.3%	1.7%
65 - 69	4.4%	5.1%	0.6%	1.8%	32.3%
70 - 74	2.9%	3.8%		1.1%	25.1%
75 - 79	1.9%	2.5%		0.7%	18.2%
80 - 84	1.3%	1.6%		0.5%	11.9%
85 - 89	0.3%	0.9%		0.5%	6.3%
90 - 94		0.1%		0.1%	2.5%
95 - 99					0.5%
100 - 104					0.1%
Gender: female					
Gender = female	57.9%	58.3%	58.6%	58.7%	61.0%

CohortDiagnostics&nanhulavic/#chiru-tah-timeDistribution

Index date misclassification



Study name: ConditionOccurrence, DrugEraStart, Procedure
Domain name: Drug
☐ All ☒ Proportion ☐ Continuous

Show 1000 entries

Search:

Start -30 to end -1

Covariate Name	
All	All
drug_era: epinephrine (1343916)	8.9%
drug_era: prednisone (1551099)	7.5%
drug_era: methylprednisolone (1506270)	6.8%
drug_era: diphenhydramine (1129625)	4.2%
drug_era: albuterol (1154343)	3.5%
drug_era: amoxicillin (1713332)	3.5%
drug_era: acetaminophen (1125315)	3.4%
drug_era: dexamethasone (1518254)	2.7%
drug_era: sodium chloride (967823)	2.5%
drug_era: azithromycin (1734104)	2.5%
drug_era: hydrocodone (1174888)	2.3%
drug_era: ondansetron (1000560)	2.2%
drug_era: fluticasone (1149380)	2.2%
drug_era: triamcinolone (903963)	1.6%
drug_era: prednisolone (1550557)	1.6%
drug_era: hydroxyzine (777221)	1.6%
drug_era: clavulanate (1759842)	1.6%
drug_era: trimethoprim (1705674)	1.5%
drug_era: sulfamethoxazole (1836430)	1.4%
drug_era: montelukast (1154161)	1.4%

Showing 1 to 659 of 659 entries

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