

Eliciting the intension of medication value sets

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Motivation

- **Meaningful Use** specifies criteria that must be met to be eligible for incentive payments under the American Reinvestment and Recovery Act (ARRA).
- **Clinical Quality Measures (CQMs)** are tools used to measure the quality of care provided.
 - Providers and hospitals must report CQMs to fulfill MU2 requirements.
- **Value Sets** are lists of standardized terms used in CQMs.
- **The Value Set Authority Center (VSAC)** is the part of the NLM that is responsible for validating and delivering the value sets.
- **Assist in Quality Assurance of value sets**
 - Some work have been done on disease value sets
 - We look specifically at the medication value sets

Investigating 183 medication value sets

- Examples of value set names:
 - Statin
 - Methylxanthines
 - IV Antibiotics Used For Prophylaxis for Colon Surgery
 - Antibiotic Medications for Pharyngitis
 - ACE Inhibitor or ARB
 - ADHD Medications
- Value sets contain lists of clinical drugs or ingredients
 - We normalize to RxNorm IN
 - Atenolol 100 MG Oral Tablet → Atenolol
 - Lipitor → Atorvastatin

Objective

Value set: Misc. Antidepressants

Bupropion

Isocarboxazid ----- Isocarboxazid

Phenelzine ----- Phenelzine

Selegiline ----- Selegiline

Tranylcypromine ----- Tranylcypromine

rasagukube

vilazodone

Monoamine Oxidase Inhibitors

Eliciting the intension for medication value sets to support quality assurance and curation task of clinical quality measures.

- Drug classes have an explicit, agreed-upon definition.
- Elicitation is performed by mapping the definition of the class onto the value set intension when the drug members are similar.

CQM for “Coronary Artery Disease: Beta-Blocker Therapy Prior Myocardial Infarction”

Coronary Artery Disease (C... x			
https://vsac.nlm.nih.gov/vsac/pc/measure/html/370			
Google			
eMeasure Title	Coronary Artery Disease (CAD): Beta-Blocker Therapy—Prior Myocardial Infarction (MI) or Left Ventricular Systolic Dysfunction (LVEF <40%)		
eMeasure Identifier (Measure Authoring Tool)	145	eMeasure Version number	3
NQF Number	0070	GUID	80744ae2-de81-4b16-a71d-69522eb865c5

Initial Patient Population	All patients aged 18 years and older with a diagnosis of coronary artery disease seen within a 12 month period
Denominator	Equals Initial Patient Population who also have prior MI or a current or prior LVEF <40%
Denominator Exclusions	None
Numerator	Patients who were prescribed beta-blocker therapy
Numerator Exclusions	Not Applicable
Denominator Exceptions	Documentation of medical reason(s) for not prescribing beta-blocker therapy (eg, allergy, intolerance, other medical reasons) Documentation of patient reason(s) for not prescribing beta-blocker therapy (eg, patient declined, other patient reasons) Documentation of system reason(s) for not prescribing beta-blocker therapy (eg, other reasons attributable to the health care system)

$$\text{Beta-Blocker Therapy} = \frac{\# \text{ Patients who recieved beta-blocker therapy}}{\# \text{ Patients diagnosed with Myocardial Infarction}}$$

• "Medication, Active: Beta Blocker Therapy" using "Beta Blocker Therapy Grouping Value Set (2.16.840.1.113883.3.526.3.1174)"

• "Diagnosis, Resolved: Myocardial Infarction" using "Myocardial Infarction Grouping Value Set (2.16.840.1.113883.3.526.3.403)"

Myocardial infarction in VSAC

Search Results

Value Set Details

Value Set Information

Available Updates: Approved By Steward Versions: MU2 EP Update 2014-07-01 [Export Value Set Results \(Excel\)](#)

Metadata

Measure

Grouping

Name:
Myocardial Infarction

Type:
Grouping

Steward:
American Medical Association-convened Physician Consortium for Performance Improvement(R)

OID:
2.16.840.1.113883.3.526.3.403

Definition ID:
20140501

Program:
CMS, MU2 EP Update 2014-07-01 using this value set

Value Set Members

Expansion ID: 20121025

Expanded Code List

View

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Code	Descriptor	Code System	Version	Code System OID
10273003	Acute infarction of papillary muscle (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
129574000	Postoperative myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
15990001	Acute myocardial infarction of posterolateral wall (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
161502000	History of - myocardial infarct at age less than 60 (situation)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
161503005	History of - myocardial infarct at age greater than 60 (situation)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
1755008	Old myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
194798004	Acute anteroapical infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
194802003	True posterior myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
194809007	Acute atrial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
194856005	Subsequent myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
22298006	Myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
233835003	Acute widespread myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
233838001	Acute posterior myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
233839009	Old anterior myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
233840006	Old inferior myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
233841005	Old lateral myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
233842003	Old posterior myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
233843008	Silent myocardial infarction (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
275905002	History of - myocardial problem (situation)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96
30277009	Acute myocardial infarction with rupture of ventricle (disorder)	SNOMEDCT	2013-09	2.16.840.1.113883.6.96

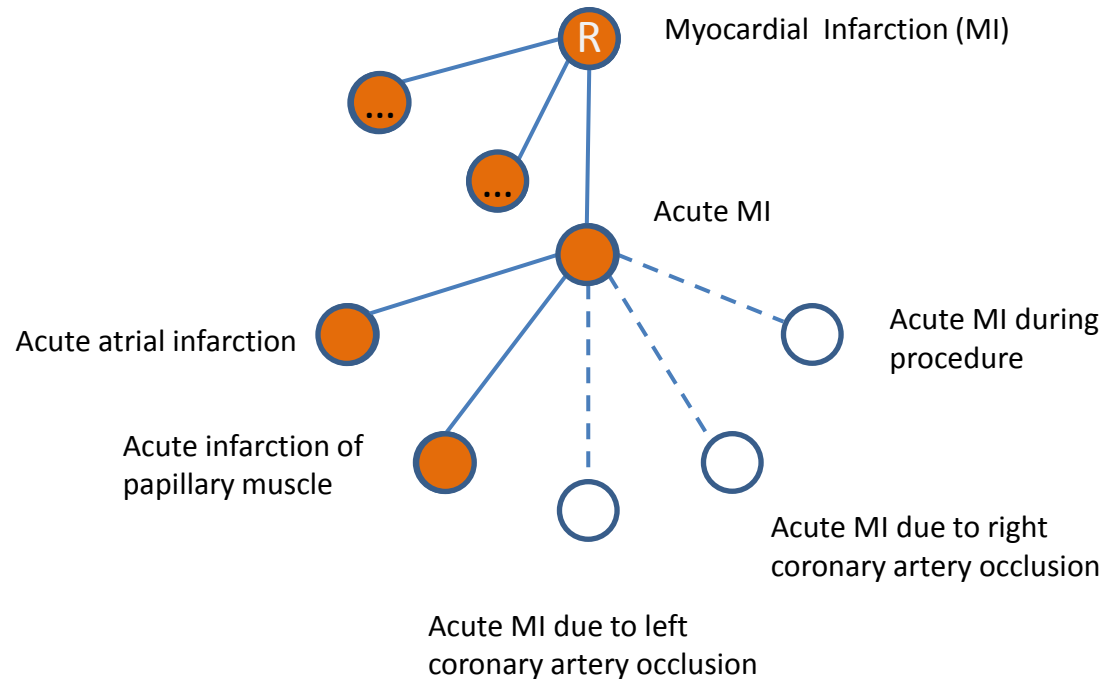
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Prior work assessing the completeness and correctness of diagnosis value sets



Winnenburg, R., Bodenreider, O., 2013. Metrics for assessing the quality of value sets in clinical quality measures, in: AMIA Annual Symposium Proceedings. American Medical Informatics Association, p. 1497-1505.

Beta-blockers in VSAC

Search Results

Value Set Details

Value Set Information

Available Updates: Approved By Steward Versions: MU2 EP Update 2014-07-01 [Export Value Set Results \(Excel\)](#)

Metadata

Member Of

Name:

Beta Blocker Therapy

Type:

Extensional

Steward:

American Medical Association-convened Physician Consortium for Performance Improvement(R)

OID:

2.16.840.1.113883.3.526.2.133

Definition ID:

20140501

Program:

CMS, MU2 EP Update 2014-07-01 using this value set

Value Set Members

Expansion ID: 20130614

Expanded Code List

View

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Code	Descriptor	Code System	Version	Code System OID
1297753	Betaxolol Hydrochloride 10 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
1297757	Betaxolol Hydrochloride 20 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
152916	Atenolol 50 MG / Chlorthalidone 12.5 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
197379	Atenolol 100 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
197380	Atenolol 25 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
197381	Atenolol 50 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
197382	Atenolol 100 MG / Chlorthalidone 25 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
197383	Atenolol 50 MG / Chlorthalidone 25 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
198000	Bendroflumethiazide 5 MG / Nadolol 40 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
198001	Bendroflumethiazide 5 MG / Nadolol 80 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
198005	Nadolol 160 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
198006	Nadolol 20 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
198007	Nadolol 40 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
198008	Nadolol 80 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
198104	Pindolol 10 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
198105	Pindolol 5 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
198284	Timolol 10 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
198285	Timolol 20 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
198286	Timolol 5 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8
199277	Pindolol 15 MG Oral Tablet	RXNORM	2014-01	2.16.840.1.113883.6.8

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Drugs are organized into classes according to their chemical and pharmacological properties

RxClass - exploring drug classes and their RxNorm drug members

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[FAQ](#)

[Tutorial](#)



- [Mitosis Modulators](#) (15)
- [Neurotransmitter Agents](#) (770)
 - [Adrenergic Agents](#) (259)
 - [Adrenergic Agonists](#) (114)
 - [Adrenergic Antagonists](#) (92)
 - [Adrenergic alpha-Antagonists](#) (41)
 - [Adrenergic beta-Antagonists](#) (49)
 - [Adrenergic beta-1 Receptor Antagonists](#) (16)
 - [Adrenergic beta-2 Receptor Antagonists](#) (0)
 - [Adrenergic beta-3 Receptor Antagonists](#) (0)
 - [Adrenergic Uptake Inhibitors](#) (41)
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 - [Histamine Agents](#) (126)
 - [Neurokinin-1 Receptor Antagonists](#) (2)
 - [Neurotransmitter Uptake Inhibitors](#) (81)
 - [Purinerbic Agents](#) (11)
 - [Serotonin Agents](#) (89)
 - [Nitric Oxide Donors](#) (5)

Source of drug-class relations

☒ ATC ☒ MeSH ☒ DailyMed ☐ NDFRT ☐ FDA SPL

Adrenergic beta-Antagonists

☐ by class name/id ☒ by RxNorm drug name/id

Adrenergic beta-Antagonists

class: **Adrenergic beta-Antagonists** / id: **D000319** / class type: **MESHPA** / [show context](#)

49 RxNorm generic drugs in MeSH

Type	RXCUI	RxNorm Name	Source Id	Source Name	Relation	All classes
IN	149	Acebutolol	D000070	Acebutolol	INDIRECT	Show
PIN	142130	Acebutolol Hydrochloride	D000070	Acebutolol	INDIRECT	Show
IN	597	Alprenolol	D000526	Alprenolol	DIRECT	Show
PIN	81947	Alprenolol Hydrochloride	D000526	Alprenolol	DIRECT	Show
IN	1202	Atenolol	D001262	Atenolol	INDIRECT	Show
IN	1520	Betaxolol	D015784	Betaxolol	INDIRECT	Show

Measuring the equivalence between drug classes

ATC: Beta Blocking Agents

Acebutolol	Nadolol
Alprenolol	nebivolol
Atenolol	mepindolol
Betaxolol	Oxprenolol
Bisoprolol	Practolol
bopindolol	Sotalol
Bupranolol	talinolol
Carteolol	tertatolol
carvedilol	Timolol
Celiprolol	Penbutolol
esmolol	Pindolol
Labetalol	Propranolol
Metoprolol	

MeSH: Adrenergic beta Antagonists

Acebutolol	Nadolol	
Alprenolol	nebivolol	
Atenolol	mepindolol	
Betaxolol	Oxprenolol	carazolol
Bisoprolol	Practolol	icatibant
bopindolol	Sotalol	Levobunolol
Bupranolol	talinolol	Metipranolol
Carteolol	tertatolol	
carvedilol	Timolol	
Celiprolol	Penbutolol	
esmolol	Pindolol	
Labetalol	Propranolol	
Metoprolol		

$$JC(A, M) = \frac{A \cap M}{A \cup M} = \frac{25}{29} (86\%)$$

Measuring the equivalence between value sets and drug classes

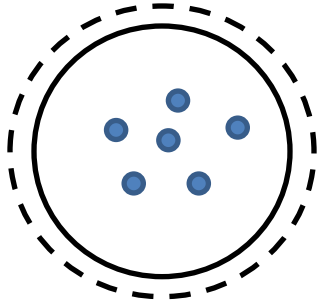
Value Set: Beta Blocker therapy

Acebutolol
Atenolol
Betaxolol
Bisoprolol
Carteolol
Labetalol
Metoprolol
Nadolol
Pindolol
Propranolol
Timolol

ATC: Adrenergic beta-Antagonists

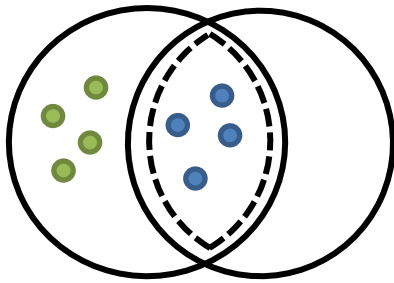
Acebutolol	Alprenolol
Atenolol	bopindolol
Betaxolol	Bupranolol
Bisoprolol	Celiprolol
Carteolol	esmolol
Labetalol	mepindolol
Metoprolol	nebivolol
Nadolol	Oxprenolol
Pindolol	Penbutolol
Propranolol	Practolol
Timolol	Sotalol
	talinalol
	tertatalol

Strategies for mapping value sets onto drug classes

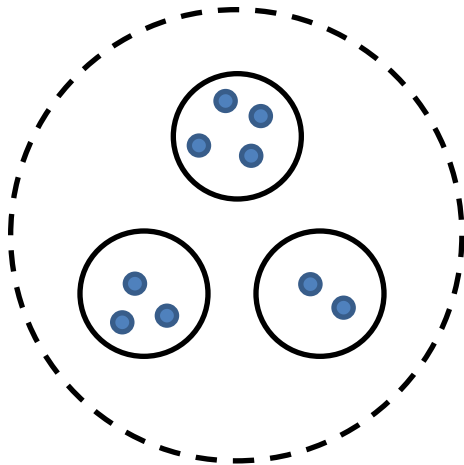


1. Value set maps onto a single class

-- value set
— drug class
● members in the value set
● members in the drug class



2. Value set maps onto an intersection of classes



3. Value set maps onto a union of classes

Materials

- Medication value sets (9/01/2014 release)
 - 98 value sets contained only 1 ingredient and were excluded
 - 5 value sets contained only multi-ingredient drugs and were excluded.
- RxClass and RxNorm API
 - ATC, MeSH, DailyMed, NDF-RT
 - Located at <http://rxnav.nlm.nih.gov>

Source Terminology	# Classes
ATC	882
DailyMed Chemical Structure	467
DailyMed Established Pharm. Class	431
DailyMed Mechanism of Action	348
DailyMed Physiological Effect	239
MeSH Pharm. Action	350
NDF-RT Disease	1434
Total	~4,000

Strategy 1: Value set maps onto a single class

Statin

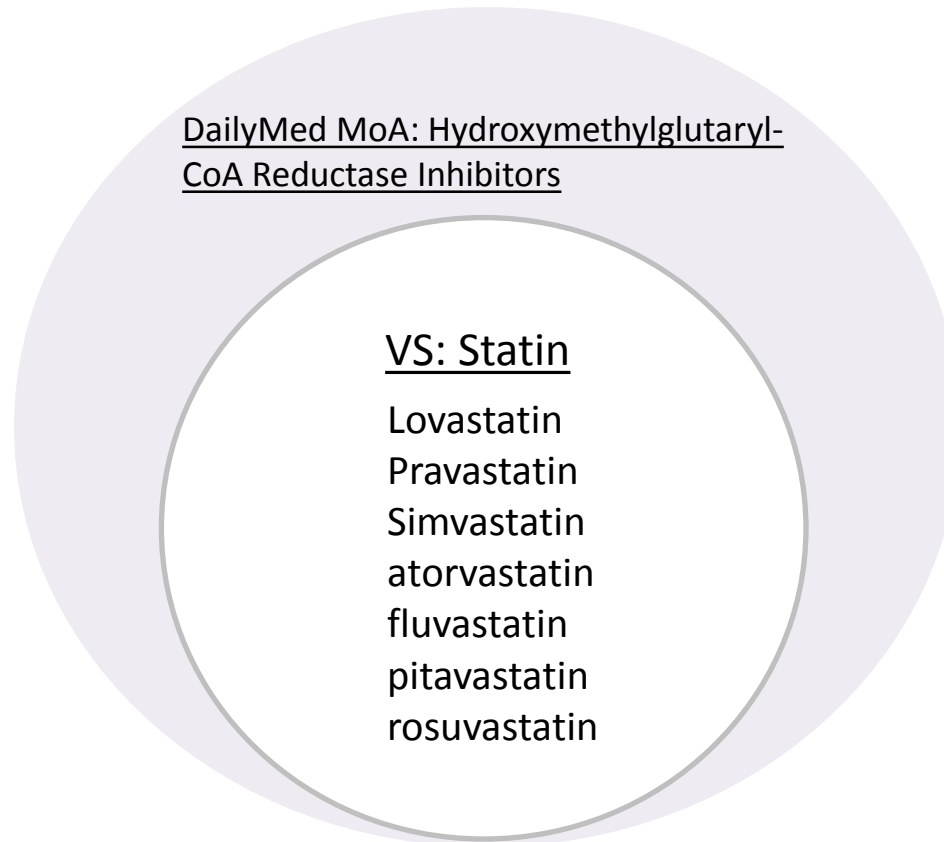
24 HR Lovastatin 10 MG Extended Release Oral Tablet
24 HR Lovastatin 20 MG / Niacin 1000 MG Extended Release Oral Tablet
24 HR Niacin 1000 MG / Simvastatin 20 MG Extended Release Oral Tablet
24 HR fluvastatin 80 MG Extended Release Oral Tablet
Amlodipine 10 MG / atorvastatin 10 MG Oral Tablet
Amlodipine 5 MG / atorvastatin 80 MG Oral Tablet
Fenofibrate 145 MG / Simvastatin 20 MG Oral Tablet
Fenofibrate 145 MG / Simvastatin 40 MG Oral Tablet
Lovastatin 10 MG Oral Tablet
Pravastatin Sodium 10 MG Oral Tablet
Rosuvastatin calcium 5 MG Oral Tablet
Simvastatin 10 MG / sitagliptin 100 MG Oral Tablet
MG Oral Tablet
atorvastatin 10 MG Oral Tablet
atorvastatin 20 MG / ezetimibe 10 MG Oral Tablet
atorvastatin 20 MG Oral Tablet
ezetimibe 10 MG / Simvastatin 10 MG Oral Tablet
fluvastatin 20 MG Oral Capsule
pitavastatin 1 MG Oral Tablet



Multi-ingredient &
non-prescribable drugs

Lovastatin
Pravastatin
Simvastatin
atorvastatin
fluvastatin
pitavastatin
rosuvastatin

Strategy 1: Value set maps onto a single class



$$JC(A, M) = \frac{7}{7} (100\%)$$

Strategy 2: Value set maps onto an intersection of classes

Beta Blocker Therapy

24 HR Propranolol Hydrochloride 120 MG Extended Release Capsule
24 HR carvedilol phosphate 10 MG Extended Release Capsule
24 HR metoprolol succinate 100 MG Extended Release Tablet
Acebutolol Hydrochloride 100 MG Oral Capsule
Acebutolol Hydrochloride 200 MG / Hydrochlorothiazide 12.5 MG Oral Tablet
Atenolol 100 MG / Chlorthalidone 25 MG Oral Tablet
Atenolol 100 MG Oral Tablet
Atenolol 25 MG Oral Tablet
Bendroflumethiazide 5 MG / Nadolol 40 MG Oral Tablet
Bendroflumethiazide 5 MG / Nadolol 80 MG Oral Tablet
Betaxolol Hydrochloride 10 MG Oral Tablet
Betaxolol Hydrochloride 20 MG Oral Tablet
Bisoprolol Fumarate 10 MG / Hydrochlorothiazide 6.25 MG Oral Tablet
Bisoprolol Fumarate 10 MG Oral Tablet
Bisoprolol Fumarate 2.5 MG / Hydrochlorothiazide 6.25 MG Oral Tablet
Bisoprolol Fumarate 5 MG / Hydrochlorothiazide 6.25 MG Oral Tablet
Bisoprolol Fumarate 5 MG Oral Tablet
Carteolol Hydrochloride 2.5 MG Oral Tablet
Carteolol Hydrochloride 5 MG Oral Tablet
Clopamide 5 MG / Pindolol 10 MG Oral Tablet
Hydrochlorothiazide 25 MG / Labetalol hydrochloride 100 MG Oral Tablet
Hydrochlorothiazide 50 MG / Metoprolol Tartrate 100 MG Oral Tablet
Hydrochlorothiazide 50 MG / Pindolol 10 MG Oral Tablet
Labetalol hydrochloride 100 MG Oral Tablet
Labetalol hydrochloride 50 MG Oral Tablet
Metoprolol Tartrate 100 MG Oral Tablet
Nadolol 160 MG Oral Tablet
Pindolol 5 MG Oral Tablet
Propranolol Hydrochloride 10 MG Oral Tablet
Propranolol Hydrochloride 160 MG Oral Tablet
Timolol 10 MG Oral Tablet
carvedilol 12.5 MG Oral Tablet

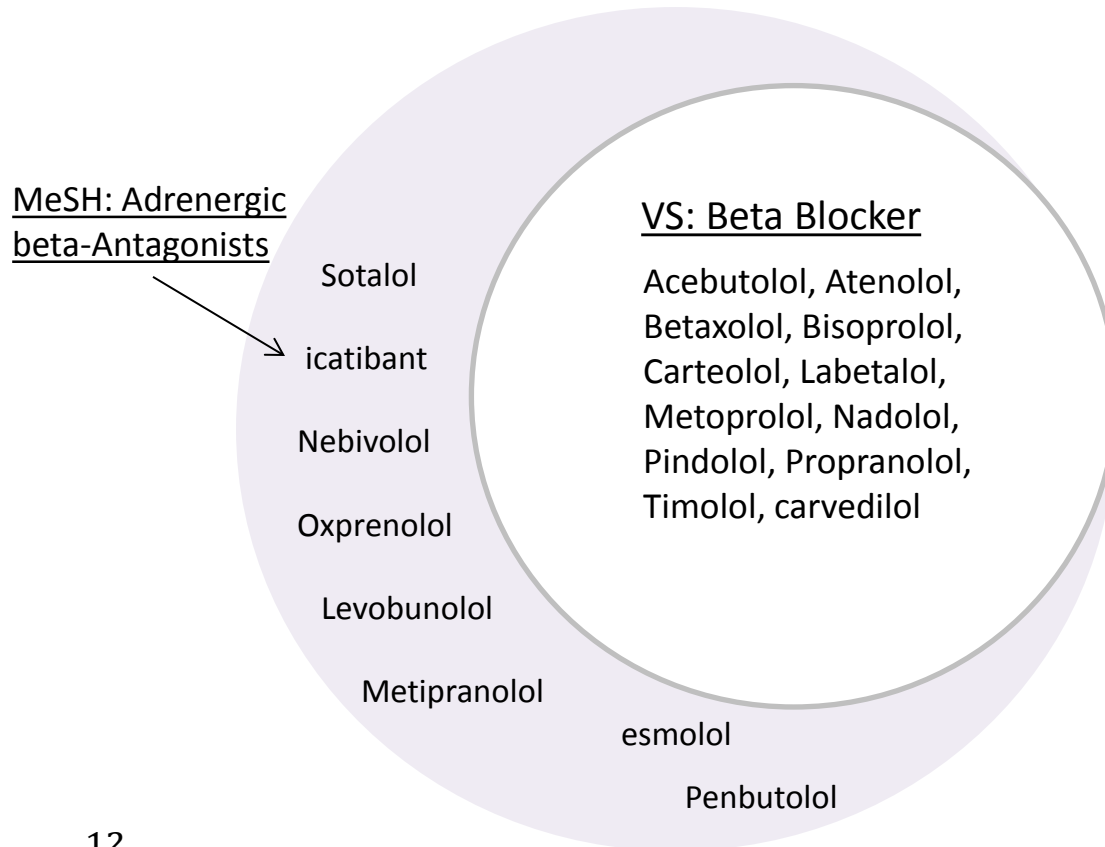
RxNorm IN



Multi-ingredient &
non-prescribable drugs

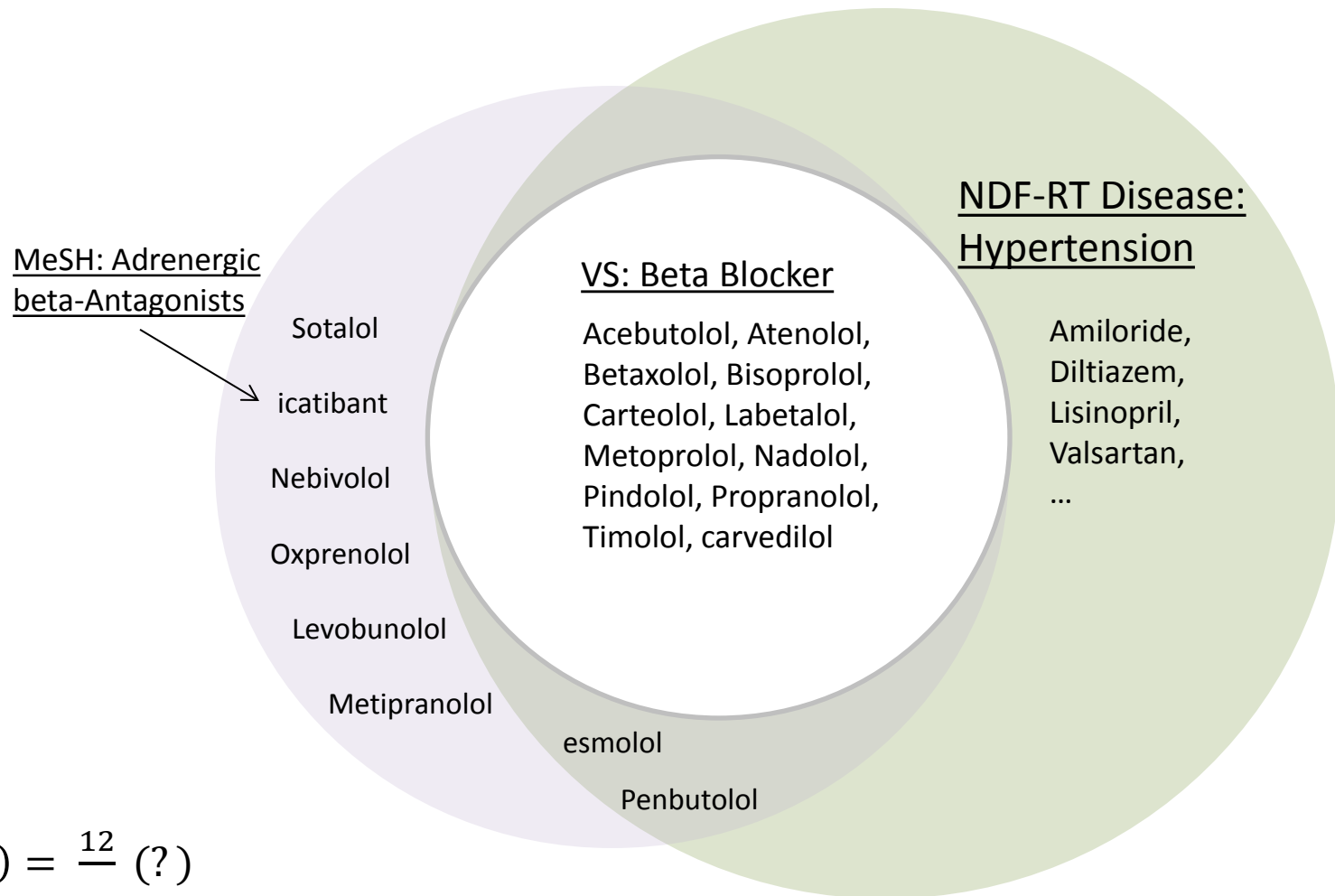
Acebutolol
Atenolol
Betaxolol
Bisoprolol
Carteolol
Labetalol
Metoprolol
Nadolol
Pindolol
Propranolol
Timolol
carvedilol

Strategy 2: Value set maps onto an intersection of classes



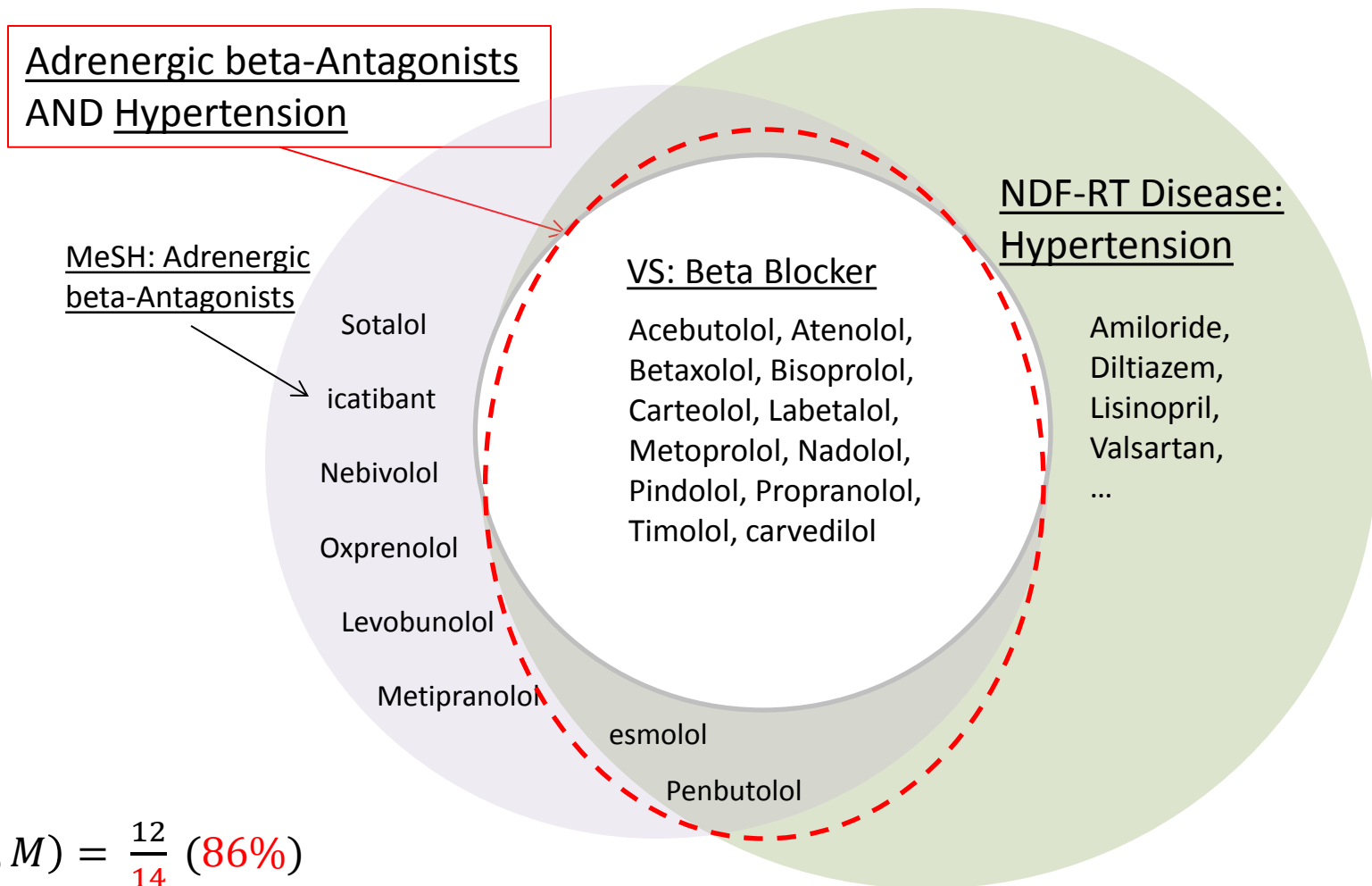
$$JC(A, M) = \frac{12}{20} (60\%)$$

Strategy 2: Value set maps onto an intersection of classes



$$JC(A, M) = \frac{12}{?} (?)$$

Strategy 2: Value set maps onto an intersection of classes



$$JC(A, M) = \frac{12}{14} \text{ (86\%)}$$

Strategy 3: Value set maps onto a union of classes

Anticoagulant Therapy

0.4 ML Dalteparin Sodium 25000 UNT/ML Prefilled Syringe
0.4 ML Enoxaparin sodium 100 MG/ML Prefilled Syringe
0.4 ML Fondaparinux sodium 12.5 MG/ML Prefilled Syringe
0.5 ML heparin sodium, porcine 10000 UNT/ML Prefilled Syringe
0.8 ML Fondaparinux sodium 12.5 MG/ML Prefilled Syringe
1 ML Dalteparin Sodium 10000 UNT/ML Prefilled Syringe
3 ML heparin sodium, porcine 1 UNT/ML Prefilled Syringe
Dalteparin Sodium 10000 UNT/ML Injectable Solution
Enoxaparin sodium 100 MG/ML Injectable Solution
Fondaparinux sodium 12.5 MG/ML Injectable Solution
Warfarin Sodium 1 MG Oral Tablet
apixaban 2.5 MG Oral Tablet
apixaban 5 MG Oral Tablet
argatroban 100 MG/ML Injectable Solution
dabigatran etexilate 150 MG Oral Capsule
dabigatran etexilate 75 MG Oral Capsule
fondaparinux 5 MG/ML Injectable Solution
heparin sodium, porcine 0.2 UNT/ML Injectable Solution
heparin sodium, porcine 0.25 UNT/ML Injectable Solution
lepirudin 50 MG/ML Injectable Solution
rivaroxaban 10 MG Oral Table

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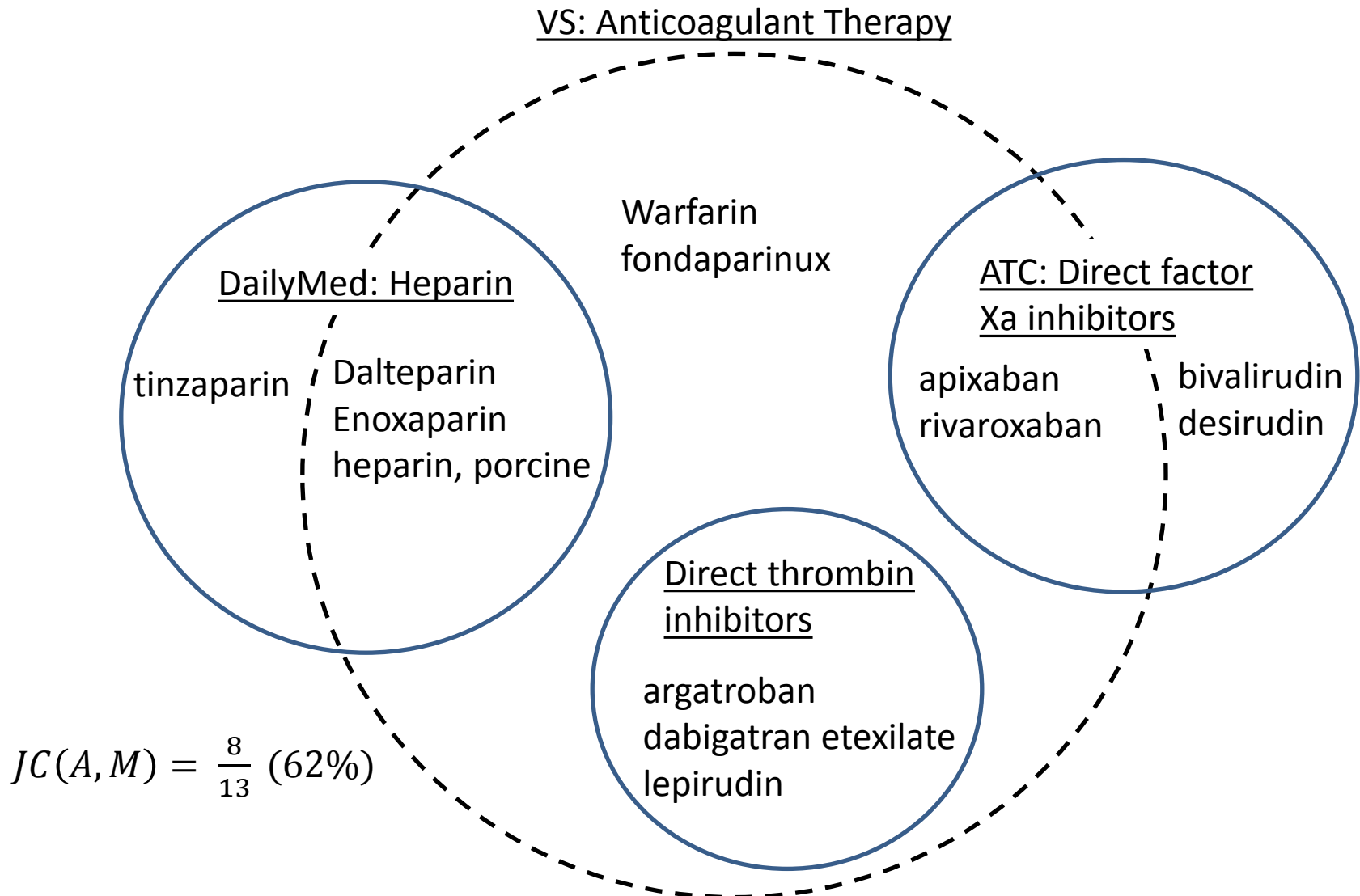
RxNorm IN



Multi-ingredient &
non-prescribable drugs

Dalteparin
Enoxaparin
Warfarin
apixaban
argatroban
dabigatran etexilate
fondaparinux
heparin, porcine
lepirudin
rivaroxaban

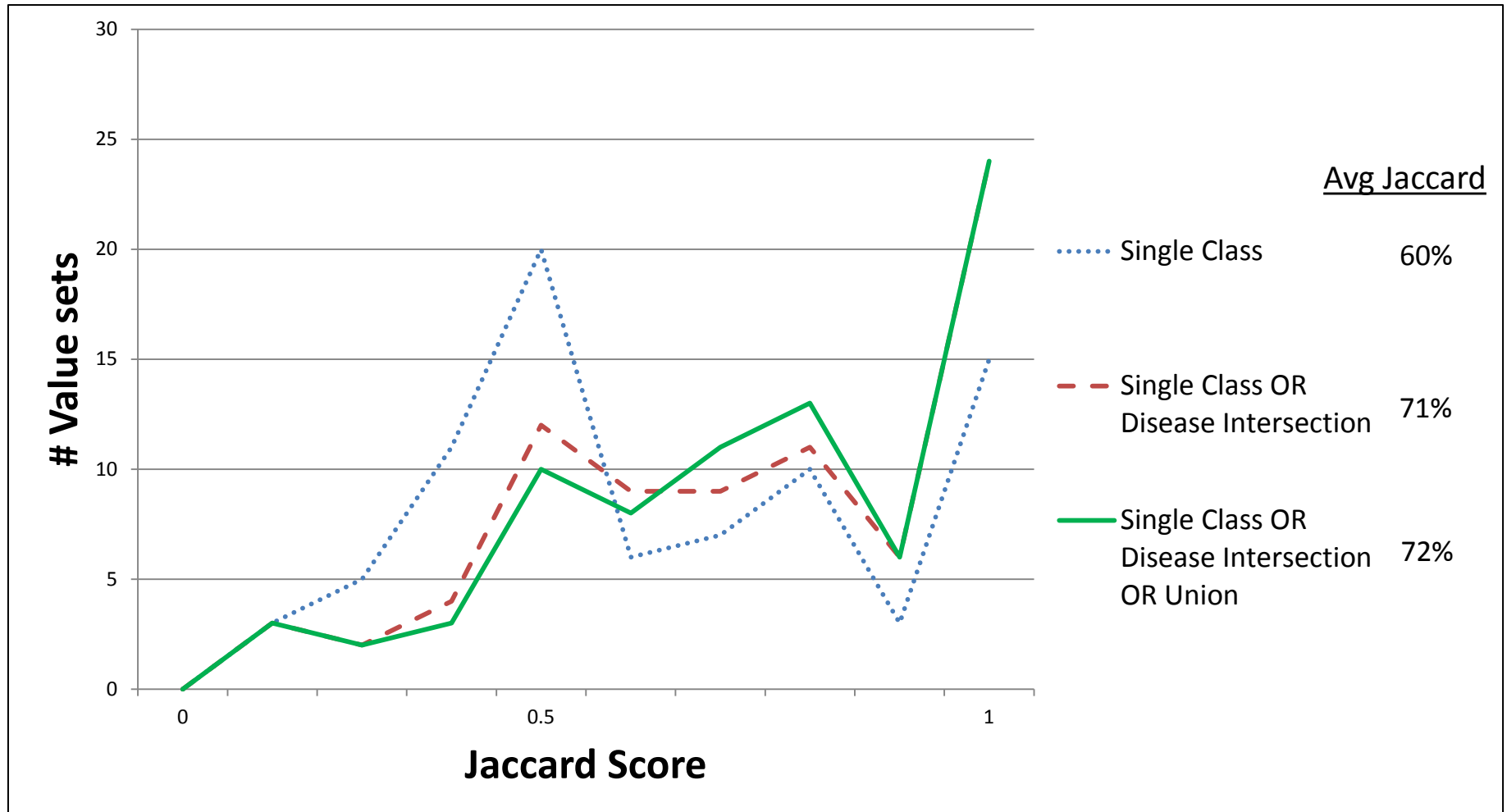
Strategy 3: Value set maps onto a union of classes



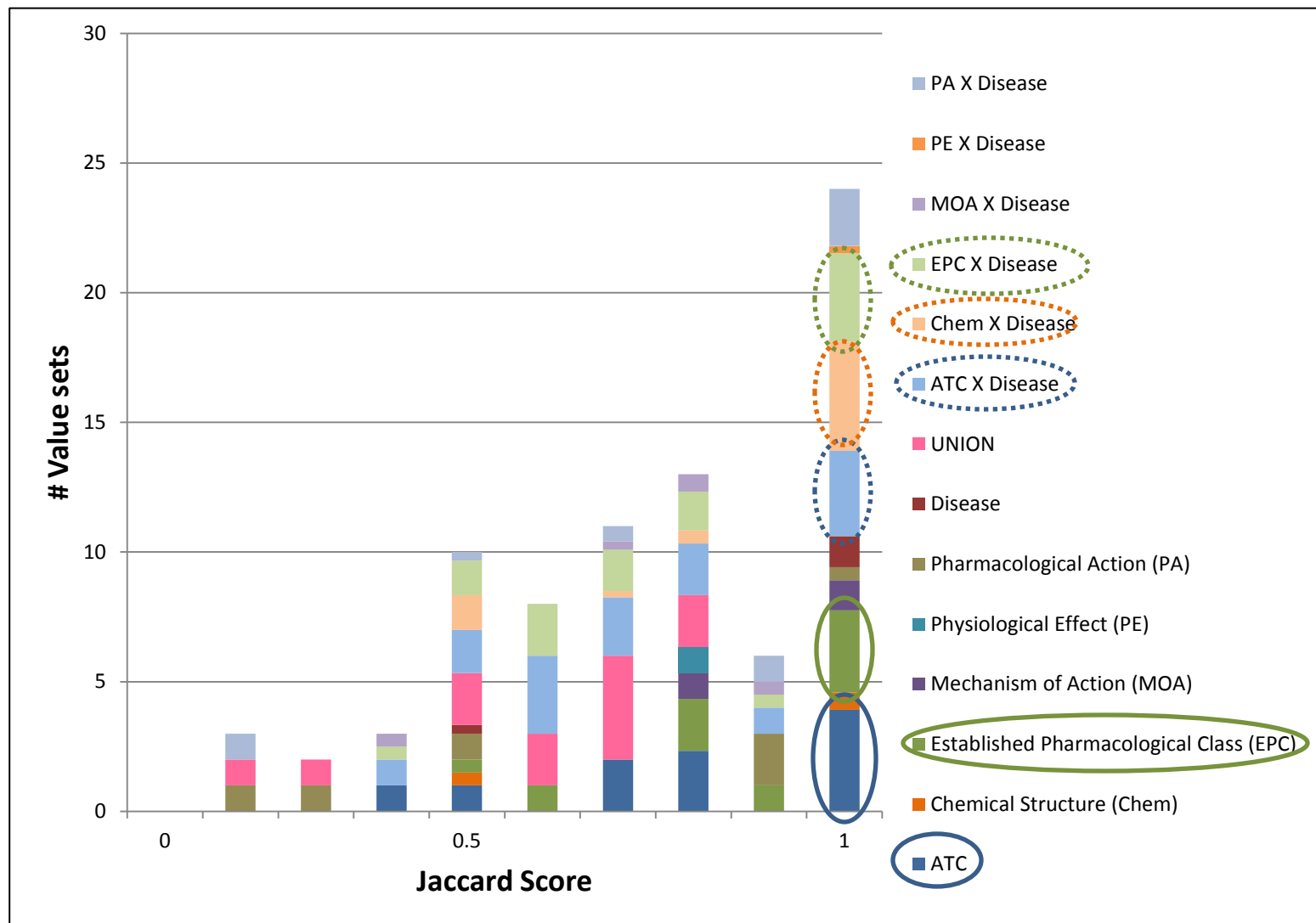
Results Summary

- We performed ~320M comparisons
 - 80 value sets * 4000 classes = 320K
 - **80 value sets * 4M intersections = 320M**
 - 80 value sets * ~100 union candidates = 8k
- We incrementally augmented the single class comparisons with the intersections and unions
 - The **intersection** offered the largest improvement
- **We elicited the intension with >70% equivalence for 54% (43/80) value sets.**

Contribution of methods



Contribution of sources



Discussion

- Are we able to elicit the intension of the value sets?
 - 30% (24/80) of the value sets mapped to classes with high equivalence scores (100% Jaccard score)
 - We can infer the intension of the value set from the class
 - 23% (18/80) of the value sets mapped to classes with low equivalence scores (<50% Jaccard score)
 - We have not elicited the intension of the value set and further investigation is required

Limitations and future work

- There is an opportunity for Quality Assurance.
 - E.g. Should esmolol and Penbutolol be part of the beta-blocker value set?
 - Qualitative evaluation by an expert is needed.
 - We are working with a pharmacist to address this.
- There are different classification systems built for different purposes, which may result in different elicited intensions.

Acknowledgements

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Fellows

Kalpa Gunaratna

Wei Wei

Raymonde Uy

Eliciting the intension of medication value sets

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