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Leveraging RxNorm and drug classifications for analyzing prescription datasets



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Outline

◆ Drug ontologies

- RxNorm
- Drug classification systems

◆ Use cases

- Comparing prescribed vs. defined daily dose
- Identifying potentially inappropriate medications for elderly patients
- Identifying potential risk in drug prescriptions during pregnancy



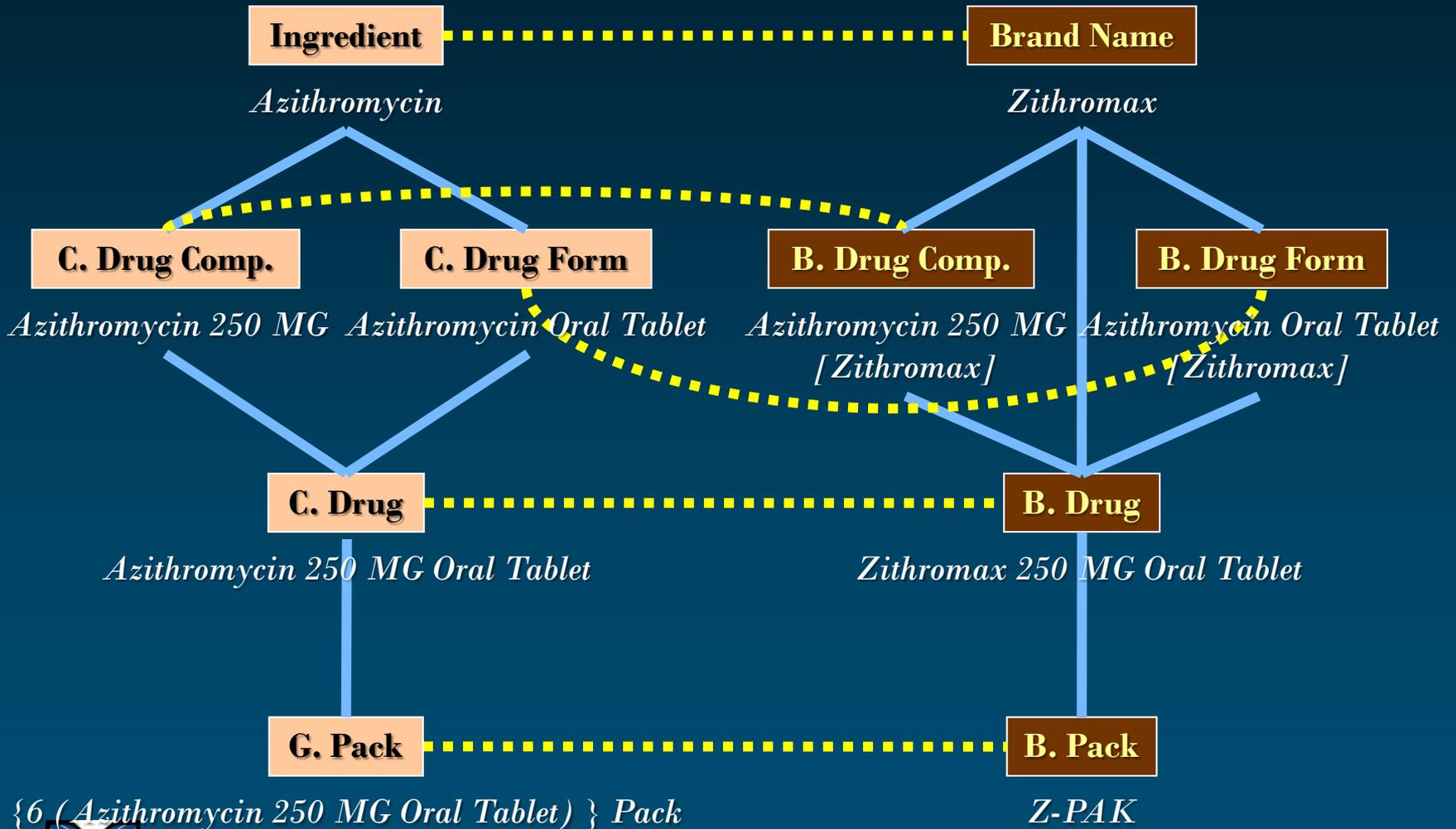
Drug ontologies

RxNorm

- ◆ Terminology integration system
 - Structured Product Labels, First DataBank, Micromedex, Multum, MeSH, SNOMED CT, NDF-RT, ATC, ...
- ◆ Scope
 - Drug names and codes
 - Drugs available on the U.S. market
- ◆ Developer: National Library of Medicine
- ◆ Publicly available*
- ◆ Monthly updates
- ◆ Size: > 10k ingredients; 19k clinical drugs
- ◆ Uses: e-prescription, information exchange, analytics



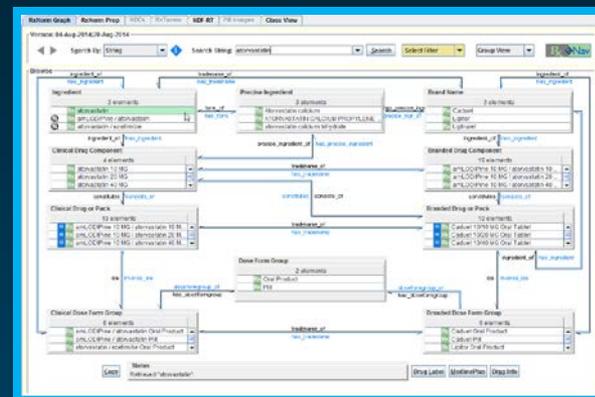
RxNorm Example



Applications

◆ RxNav

- Drug-centric browser
- Links among drug entities (graph)
- Links to other sources of information
 - Drug classes
 - Drug-drug interactions from DrugBank



◆ RxClass

- Drug class-centric browser
 - NDF-RT, MeSH and ATC
- All classes for a given drug
- All drug members for a given class
- Class-class similarity

The screenshot shows the RxClass interface with a search bar and a list of drug classes. The selected class is 'HMG CoA reductase inhibitors / ATC10AA / class type: ATC1.4 / show context'. Below the class name, there is a table listing 7 RxNorm generic drugs in ATC.

Type	NCID	Belongs Term	Source ID	Source Term	Relation	ATC codes
R	83267	atorvastatin	CT0405	atorvastatin	DIRECT	
R	47127	rosuvastatin	CT0404	rosuvastatin	DIRECT	
R	6272	lovastatin	CT0402	lovastatin	DIRECT	
R	86134	pitavastatin	CT0406	pitavastatin	DIRECT	
R	42463	pravastatin	CT0403	pravastatin	DIRECT	
R	301642	rosuvastatin	CT0407	rosuvastatin	DIRECT	
R	36057	simvastatin	CT0401	simvastatin	DIRECT	



Application Programming Interfaces (APIs)

◆ RxNorm

- Map drug names and codes to RxNorm
 - Including approximate matches and spelling suggestions
- Navigate among drug entities (e.g., brand to generic)

◆ RxClass

- Map drug class names and codes to classification systems
- Link between drug classes and their drug members
- Similarity between drug classes

◆ Usage

- 30,000 unique users per month
- 1B calls in 2015

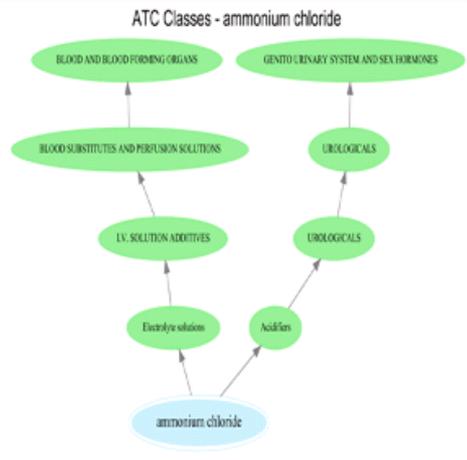


RxNav

RxNav is a browser for several drug information sources, including RxNorm, RxTerms and NDF-RT. RxNav finds drugs in RxNorm from the names and codes in its constituent vocabularies.



Launch RxNav



RxNav

APIs

RxMix

RxClass

<http://rxnav.nlm.nih.gov/>

News

Statistics

RxNav brand names

Recent brand names added

Alecensa	Aspercreme with Lidocaine
Bendeka	Bridion
Broncovac Sore Throat	Canker Cover
Clear Eyes Pure Relief	Empliciti
FLUAD 2015-2016	Hydase
Hypertet	Kanuma

DailyMed API in RxMix

Functionality of the [DailyMed API](#) has been added to RxMix. Included are functions to retrieve drug classes, manufacturer drug names, National Drug Codes (NDCs), packaging information and drug class members. See RxMix for more details including runnable examples.

Video Tutorials

RxMix

[Using RxMix to Retrieve NDCs for an](#)

NDC Properties Function

A new function to retrieve National Drug Code (NDC) properties for an NDC, a Structured Product Label (SPL) or an RxNorm concept is now available. See [getNDCProperties](#) (SOAP) or [/ndcproperties](#) (REST).

NDC History Function

A function to retrieve National Drug Code (NDC) history for any RxNorm concept is now available. The function provides past

Use case #1

Comparing prescribed vs. defined daily dose

[Bodenreider, AMIA, 2014]

Prescribed vs. defined daily dose

◆ Dataset

- Surescripts feed
- All prescriptions to ER patients
- For 3 months in 2011 in a Bethesda hospital

◆ Reference for defined daily dose: ATC

◆ Methods

- RxNorm clinical drug \rightarrow RxNorm ingredient \leftrightarrow ATC ingredient \rightarrow ATC defined daily dose \leftrightarrow prescribed daily dose
- Restricted to systemic drugs (based on dose form)

◆ Findings

- Confirmed feasibility
- 25% of the prescriptions exactly match the ATC DDD
- 50% of the prescriptions within 66-150% of the ATC DDD
- 75% of the prescriptions within 50-200% of the ATC DDD



ATC/DDD Index

◆ Origin

- World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology (Norway)
- For drug utilization research / pharmaco-epidemiology
 - Not for clinical purposes

◆ Organization

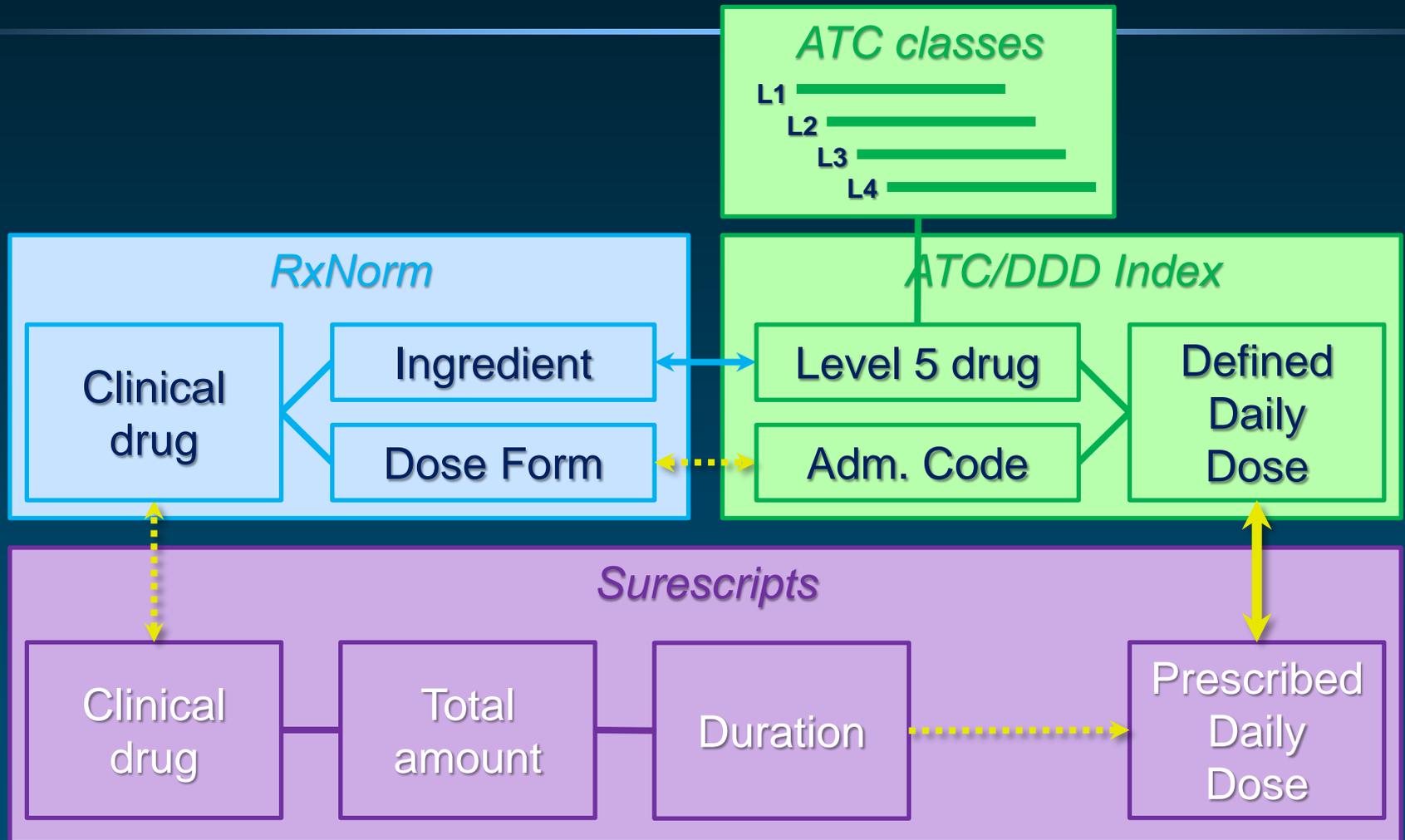
- Drug classification on 4 levels
 - Anatomical
 - Therapeutic
 - Chemical

- Drugs (5th level)
- Daily dose
 - For a given route

J **ANTIINFECTIVES FOR SYSTEMIC USE**
J01 **ANTIBACTERIALS FOR SYSTEMIC USE**
J01C **BETA-LACTAM ANTIBACTERIALS, PENICILLINS**
J01CA **Penicillins with extended spectrum**

ATC code	Name	DDD	U	Adm.R	Note
J01CA04	<u>amoxicillin</u>	1	g	O	
		1	g	P	

Methods Overview



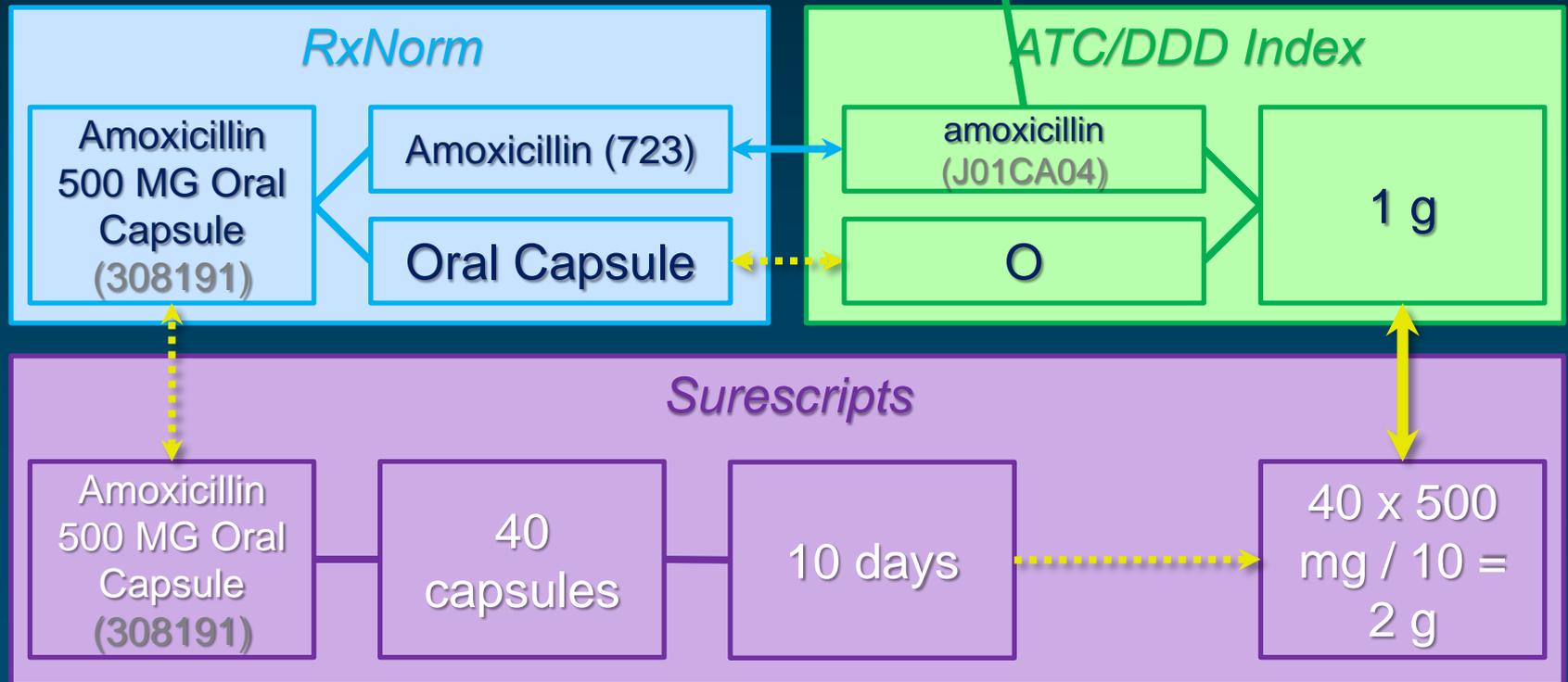
Methods Example

J **ANTIINFECTIVES FOR SYSTEMIC USE**

J01 **ANTIBACTERIALS FOR SYSTEMIC USE**

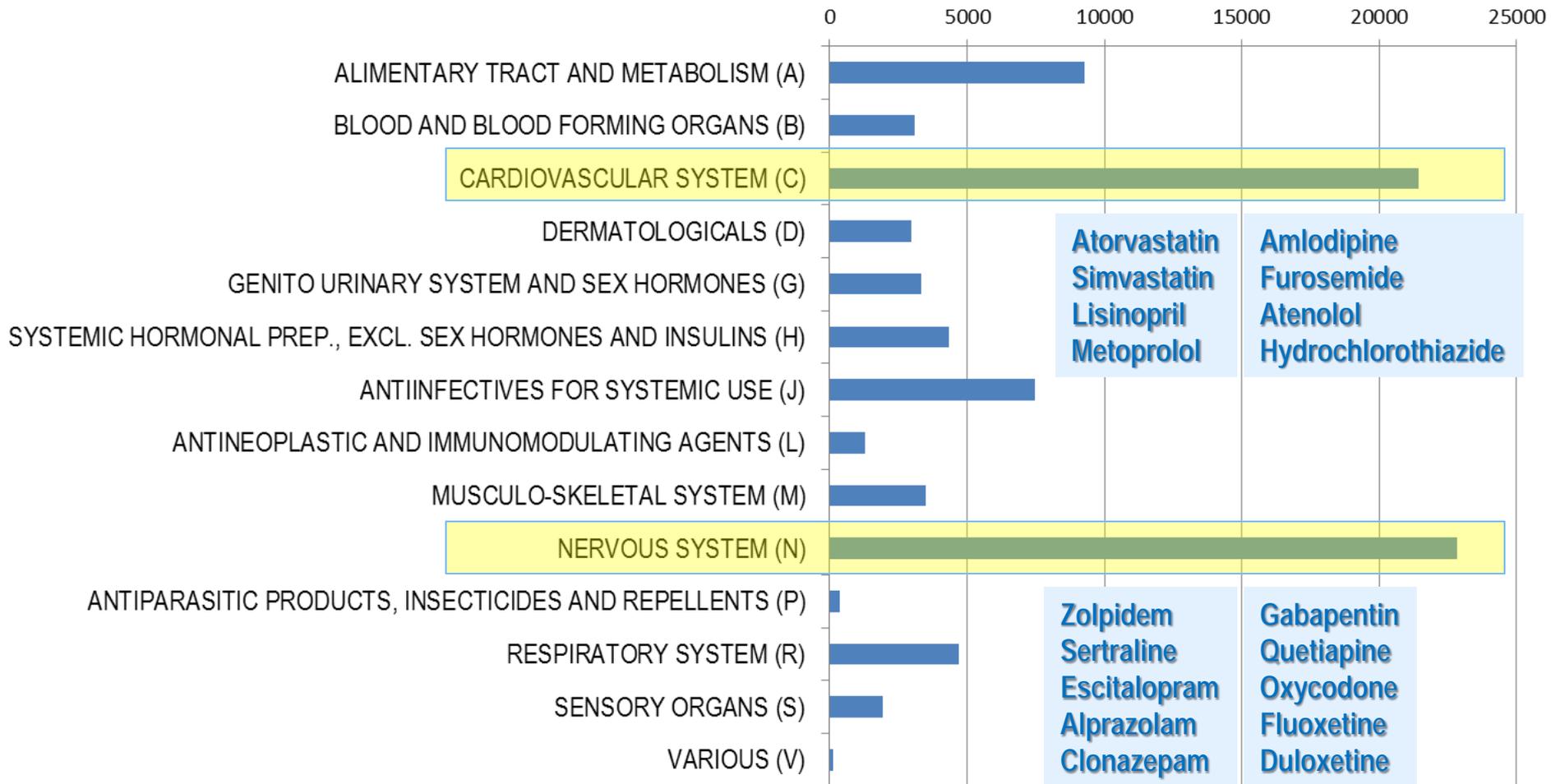
J01C **BETA-LACTAM ANTIBACTERIALS, PENICILLINS**

J01CA **Penicillins with extended spectrum**

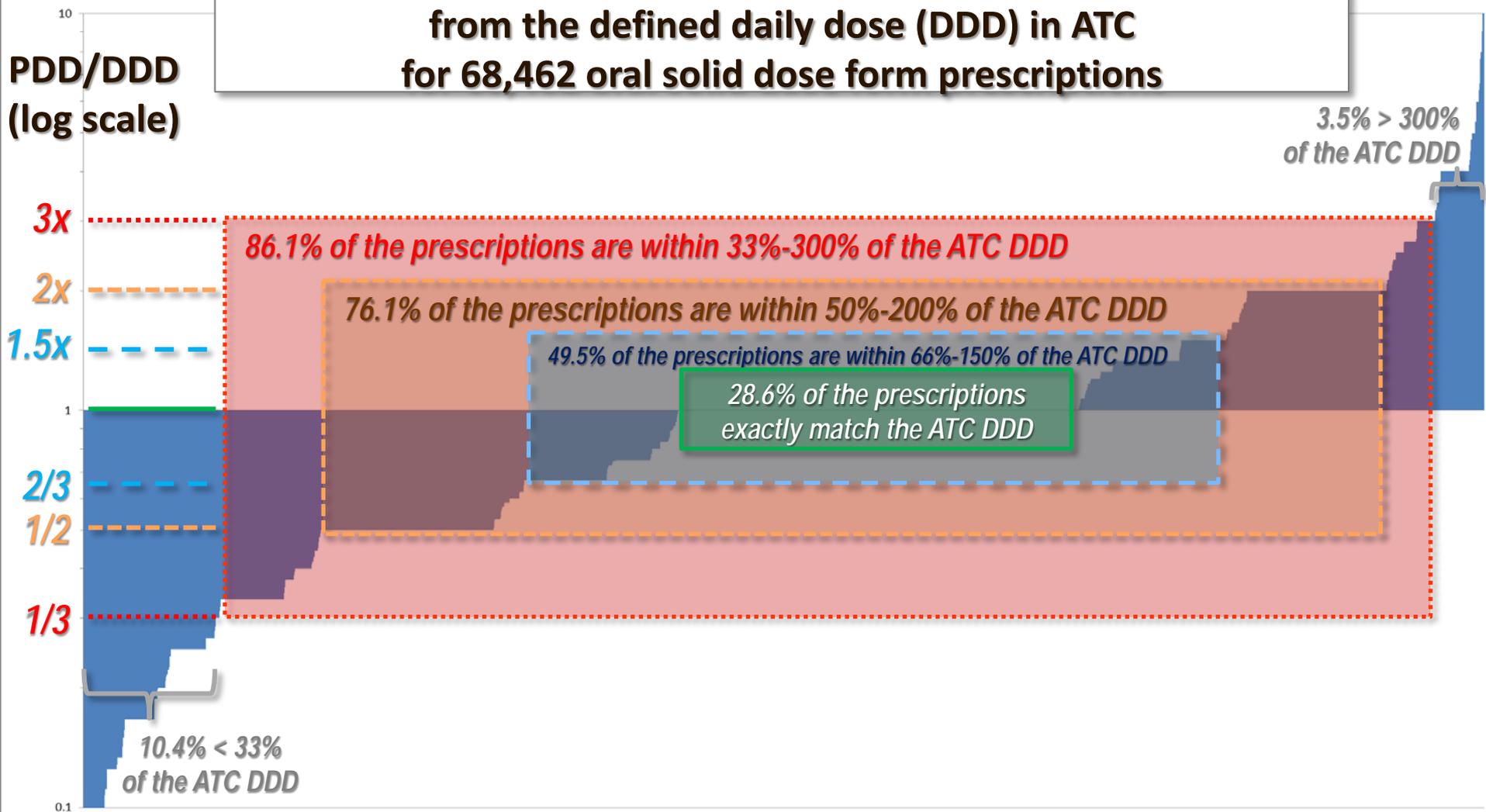


Results Prescription classification

Frequency of drugs by level-1 ATC group in the Surescripts prescription dataset **N=86,578**



Deviation of the prescribed daily dose (PDD) in Surescripts from the defined daily dose (DDD) in ATC for 68,462 oral solid dose form prescriptions



Use case #2

Identifying potentially inappropriate medications for elderly patients

PIMs for elderly patients

◆ Dataset

- Medicare Part D
- 1M beneficiaries ≥ 65
- All prescriptions for one year (2009)

◆ Reference list of PIMs: Beers list

◆ Methods

- NDC \rightarrow RxNorm clinical drug \rightarrow ingredient \leftrightarrow Beers
- Restricted to systemic drugs (based on dose form)

◆ Findings

- 47% of all beneficiaries were prescribed at least 1 PIM
- Top PIMs: *zolpidem* (6.3%), *nitrofurantoin* (4.5%)



Use case #3

*Identifying potential risk in drug prescriptions
during pregnancy*

Potential risk during pregnancy

◆ Dataset

- Large prescription dataset from private insurer (150M patients)
- 3.7M pregnant women; 19M prescriptions (2003-2014)
- OMOP clinical data model

◆ Reference list for risk during pregnancy: Briggs textbook

◆ Methods

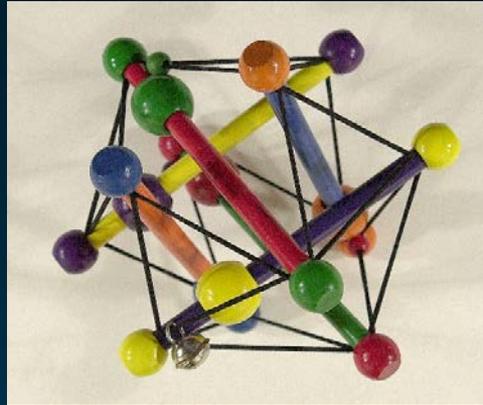
- RxNorm clinical drug → ingredient ↔ Briggs drug → fetal risk
- Restricted to systemic drugs (based on dose form)

◆ Findings

- 41.2% compatible with pregnancy or probably compatible
- 55.6% potential risk
- 3.29% high risk or contraindicated

Challenges

- ◆ Obsolete identifiers
 - Needed for analytics
- ◆ Reuse of identifiers
 - NDCs (time-indexed)
- ◆ Insufficient coverage in ontologies
 - International drugs
 - Over-the-counter drugs
- ◆ Granularity of knowledge
 - Ingredient-class vs. clinical drug-class
- ◆ Heterogeneity of drug classification
 - Different use cases



Medical Ontology Research

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