Resources for Analyzing Drug Prescription Datasets

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Disclosure

OB, VH: No relationships with commercial interest

The views and opinions expressed do not necessarily state or reflect those of the U.S. Government, and they may not be used for advertising or product endorsement purposes.

CR: QuintilesIMS has many clients in the pharmaceutical industry, whose products are the subject of this Tutorial. However, all products are intended to only be mentioned for the purposes of this Tutorial and without any recommendation or judgment of their use.
Learning Objectives

• To become familiar with large prescription datasets
• To gain knowledge about tools available for analyzing prescription datasets
• To gain knowledge about clinical data models, such as OMOP
Overview

• Part 1 – Resources and use cases (OB)
  – Prescription datasets
  – RxNorm and NLM drug APIs; drug classification systems
  – Common use cases
• Part 2 – Drug data processing in practice (VH)
  – Implementing use cases with RxMix and R
• Part 3 – Experience with OHDSI (CR)
  – Clinical data models
  – Handling international drugs
Part 1 – Resources and use cases

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Part 1 overview

- Types of drug entities
  - Drugs
  - Drug classes
- Prescription datasets
  - Structure
  - Sources
- Drug data processing
  - Mapping drugs to standards
  - Aggregating drugs (by ingredient, by class)
- Resources for processing drug datasets
  - RxNorm
  - Drug classification systems
  - NLM drug APIs
- Common use cases
  - Pharmaco-epidemiology
  - Assess exposure to drugs by ingredient or class
  - Identify potentially inappropriate medications
Part 1 – Resources and use cases

TYPES OF DRUG ENTITIES
Types of drug entities (drugs I)

- **Ingredient**
  - Azithromycin

- **Drug form**
  - Ingredient + dose form
    - Azithromycin Oral Tablet

- **Clinical drug (unit of prescription)**
  - Ingredient + dose form + strength
    - Azithromycin 250 MG Oral Tablet

- **Pack (packaging level)**
  - Collection of clinical drugs (unit of dispensation)
    - Z-PAK \{6 (Azithromycin 250 MG Oral Tablet [Zithromax]) \}
  - Collection of clinical drugs (bulk)
    - Manufacturer: Apotex Corp.; pack size: 500 in 1 BOTTLE
Types of drug entities (drugs II)

• Generic vs. Brand
  • G: Azithromycin 250 MG Oral Tablet
  • B: Zithromax 250 MG Oral Tablet

• Single vs. multi-ingredient drug
  • S: Amoxicillin 250 MG Oral Capsule
  • M: Amoxicillin 250 MG / Clavulanate 125 MG Oral Tablet

• Systemic vs. topical drugs
  • S: Azithromycin 250 MG Oral Tablet
  • T: Azithromycin 10 MG/ML Ophthalmic Solution

• Base vs. salt/ester (as basis of strength substance)
  • B: Erythromycin 250 MG Oral Tablet
  • S: Erythromycin Ethylsuccinate 400 MG Oral Tablet
Types of drug entities (drug classes)

**Atorvastatin**

- Therapeutic class
  - *Anticholesteremic Agent*

- Chemical structure
  - n/a

- Mechanism of action
  - HMG-CoA Reductase Inhibitor

- Physiologic effect
  - Decreased Cholesterol Synthesis
Types of drug entities (drug classes)

ANTIINFECTIVES FOR SYSTEMIC USE

ANTIBACTERIALS FOR SYSTEMIC USE

MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS

Macrolides

azithromycin

Antibiotics

SENSORY ORGANS

OPHTHALMOLOGICALS

ANTIINFECTIVES
Part 1 – Resources and use cases

PRESCRIPTION DATASETS
Structure

- Transactions captured at dispensation time (pharmacy)
  - Pharmaceutical claims data sent to payers

- Common elements
  - Prescription ID 999999
  - Patient identifier 123456
  - Date (prescription) 20161112
  - Product ID (NDC) 00071015623
  - Total quantity dispensed 30
  - Days supply 30
  - Cost data --
  - Drug name LIPITOR
  - Strength 20
  - Generic name Atorvastatin
  - Prescriber ID 789

NDCs are not unique identifiers for clinical drugs

Drug names are not standardized
### Product Name from Medicaid Claims

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>COUMADIN</td>
<td>270</td>
</tr>
<tr>
<td>COUMADIN TAB</td>
<td>13</td>
</tr>
<tr>
<td>COUMADIN TABLET</td>
<td>215</td>
</tr>
<tr>
<td>JANTOVEN</td>
<td>130</td>
</tr>
<tr>
<td>JANTOVEN TAB</td>
<td>24</td>
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<tr>
<td>JANTOVEN TABLET</td>
<td>262</td>
</tr>
<tr>
<td>WARFARIN</td>
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</tr>
<tr>
<td>WARFARIN TAB</td>
<td>763</td>
</tr>
<tr>
<td>WARFARIN SODIUM</td>
<td>8,717</td>
</tr>
<tr>
<td>WARFARIN SODIUM TA</td>
<td>95</td>
</tr>
<tr>
<td>WARFARIN SODIUM TAB</td>
<td>516</td>
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<td>WARFARIN SODIUM TABL</td>
<td>587</td>
</tr>
<tr>
<td>WARFARIN SODIUM TABLET</td>
<td>8,555</td>
</tr>
</tbody>
</table>

Source: Dan Malone
Product Identification: NDCs

- National Drug Codes
  - Product identification system
  - Three components
    - Manufacturer
    - Product
    - Packaging
- Introduced in 1972 by FDA
  - Only format permitted by NCPDP
  - Mandated by HIPAA regulations for drug transactions

Source: Dan Malone
NDC Elements: 3 segments

XXXXX-XXXX-XX

Manufacturer  Product  Packaging
NDC Forms

Warfarin Sodium 1 MG Oral Tablet

XXXX-XXXX-XX (4-4-2) → 0XXXX XXXX XX
0555-0831-02 (Teva Pharmaceuticals USA, Inc.; 100 in 1 BOTTLE) → 00555083102

XXXXXX-XXXX-XX (5-3-2) → XXXXXX 0XXX XX
21695-672-30 (Rebel Distributors Corp; 30 in 1 BOTTLE) → 21695067230

XXXXXX-XXXXX-X (5-4-1) → XXXXXX XXXXX 0X
50090-1213-0 (A-S Medication Solutions; 30 in 1 BOTTLE) → 50090121300
NDC Characteristics

• 11 Digit code (leading zero for 4-4-2 format)
• Hyphens between segments are missing in claims transmission (Field 407 in NCPDP claim format)
• NDC codes set by the manufacturer/labeler
• High turnover compared to other drug IDs
• Product codes are unique to manufacturer – not to the chemical entity
• Package codes are unique to the manufacturer and product – there is no standardization for packaging codes

Source: Dan Malone
Source of prescription datasets

• Surescripts transactions
• Data from payers
  – Medicaid
  – Medicare Part D
• Commercial health analytics companies
  – Truven (120M patients)
  – PharMetrics Plus (100M patients)
  – Ambulatory EMR (35M patients)
  – Open Claims (250M patients)
• Reagan-Udall Foundation for the FDA
  – IMEDS Research Lab (temporarily suspended)
Part 1 – Resources and use cases

DRUG DATA PROCESSING
Mapping and aggregation

• Mapping to standard resources (e.g., RxNorm)
  – Standard names and codes
  – Standard set of relations among drug entities
  – Link to drug classification systems
  – E.g., NDC $\rightarrow$ clinical drug

• Aggregation
  – “roll up” to the appropriate level of granularity for analytics (use case-dependent)
  – E.g., branded drug $\rightarrow$ clinical drug $\rightarrow$ ingredient $\rightarrow$ drug class

• Temporal aggregation
  – Aggregate individual prescriptions into longer spans (“drug eras” in OHDSI)
**ALIMENTARY TRACT AND METABOLISM**
**A02 DRUGS FOR ACID RELATED DISORDERS**
**A02B DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)**

**Proton pump inhibitors**

<table>
<thead>
<tr>
<th>ATC code</th>
<th>Name</th>
<th>DDD</th>
<th>U</th>
<th>Adm.R</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>A02BC05</td>
<td>esomeprazole</td>
<td>30</td>
<td>mg</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>mg</td>
<td>P</td>
<td></td>
</tr>
</tbody>
</table>

**Esomeprazole (283742)**

**Esomeprazole 40 MG Delayed Release Oral Capsule (606730)**

**Esomeprazole 40 MG Delayed Release Oral Capsule [Nexium] (606731)**

**00186504031**

**0186-5040-31**
Part 1 – Resources and use cases

RESOURCES FOR PROCESSING DRUG DATASETS – RXNORM
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

https://www.nlm.nih.gov/research/umls/rxnorm/
## Normalization Lexical level

<table>
<thead>
<tr>
<th>Name</th>
<th>Code</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>WARFARIN (COUMADIN) NA 1MG TAB</td>
<td>4005203</td>
<td>VANDF</td>
</tr>
<tr>
<td>warfarin 1 mg oral tablet</td>
<td>3617</td>
<td>MMSL</td>
</tr>
<tr>
<td>WARFARIN NA 1MG TAB,UD</td>
<td>4014039</td>
<td>VANDF</td>
</tr>
<tr>
<td>WARFARIN NA 1MG TAB,UD [VA Product]</td>
<td>N0000161787</td>
<td>NDFRT</td>
</tr>
<tr>
<td>WARFARIN SODIUM 1 mg ORAL TABLET</td>
<td>14198</td>
<td>NDDF</td>
</tr>
<tr>
<td>WARFARIN SODIUM 1 mg ORAL TABLET</td>
<td>60429-784</td>
<td>MTHSPL</td>
</tr>
<tr>
<td>Warfarin Sodium 1 MG Oral Tablet</td>
<td>104045</td>
<td>MMX</td>
</tr>
<tr>
<td>WARFARIN SODIUM 1 mg ORAL TABLET</td>
<td>63629-4017</td>
<td>MTHSPL</td>
</tr>
<tr>
<td>WARFARIN SODIUM 1 mg ORAL TABLET [Warfarin Sodium]</td>
<td>53808-0985</td>
<td>MTHSPL</td>
</tr>
<tr>
<td>Warfarin Sodium 1 MILLIGRAM In 1 TABLET ORAL TABLET</td>
<td>15330-100</td>
<td>MTHSPL</td>
</tr>
<tr>
<td>WARFARIN SODIUM 1.09 MG ORAL TABLET</td>
<td>281572</td>
<td>MTHFDA</td>
</tr>
<tr>
<td>Warfarin Sodium 1mg Oral tablet</td>
<td>933</td>
<td>GS</td>
</tr>
<tr>
<td>Warfarin sodium 1mg tablet (product)</td>
<td>319733000</td>
<td>SNOMEDCT_US</td>
</tr>
<tr>
<td>Warfarin Sodium Tab 1 MG</td>
<td>6749</td>
<td>MDDB</td>
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<tr>
<td>Warfarin Sodium, 1 mg oral tablet</td>
<td>3617</td>
<td>MMSL</td>
</tr>
<tr>
<td>WARFARIN SODIUM@1 mg@ORAL@TABLET</td>
<td>14198</td>
<td>NDDF</td>
</tr>
</tbody>
</table>

*Warfarin Sodium 1 MG Oral Tablet (855288)*
Normalized form

- Strength: 1 MG
- Ingredient: Warfarin Sodium
- Dose form: Oral Tablet

Warfarin Sodium 1 MG (855287)

Clinical drug component

- Ingredient: Warfarin Sodium
- Dose form: Oral Tablet
- Clinical drug form: Warfarin Oral Tablet (374319)

Warfarin Sodium 1 MG Oral Tablet (855288)

Clinical drug
Relations among drug entities

Ingredient: Azithromycin

C. Drug Comp.: Azithromycin 250 MG
C. Drug Form: Azithromycin Oral Tablet
C. Drug: Azithromycin 250 MG Oral Tablet

B. Drug Comp.: Azithromycin 250 MG [Zithromax]
B. Drug Form: Azithromycin Oral Tablet [Zithromax]
B. Drug: Zithromax 250 MG Oral Tablet

G. Pack: {6 (Azithromycin 250 MG Oral Tablet) } Pack
B. Pack: Z-PAK

Brand Name: Zithromax
RxNav – RxNorm browser

https://mor.nlm.nih.gov/RxNav/
Part 1 – Resources and use cases

RESOURCES FOR PROCESSING DRUG DATASETS – DRUG CLASSIFICATION SYSTEMS

DMMI Saturday [Kury]
ATC/DDD Index

- **Origin**
  - World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology (Norway)

- **Purpose**
  - For drug utilization research / pharmaco-epidemiology

- **1257 classes (1-4)**

- **Organization**
  - Drug classification on 4 levels
    - Anatomical
    - Therapeutic
    - Chemical
  - Drugs (5th level)

---

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

<table>
<thead>
<tr>
<th>ATC code</th>
<th>Name</th>
<th>DDD</th>
<th>U</th>
<th>Adm.R</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>J01CA04</td>
<td>amoxicillin</td>
<td>1 g</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 g</td>
<td>P</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Established Pharmacologic Classes (EPCs)

• **Origin**
  – Veterans Health Administration’s National Drug File-Reference Terminology (NDF-RT)
  • For use by the U.S. Food and Drug Administration (FDA)

• **Purpose**
  – For drug classification in the Structured Product Labels

• **595 classes**

• **No hierarchical organization**

• **Examples**
  – **Macrolide antibacterial** (e.g., Azithromycin)
Mechanism of action (MoA)  
Physiologic effect (PE)  
Chemical structure (Chem)  

- Origin  
  - Veterans Administration’s National Drug File-Reference Terminology (NDF-RT)  

- Purpose  
  - For drug classification in the Structured Product Labels  
  - For drug classification at the VA  

- Number of classes  
  - MoA: 608; PE: 1866; Chem: 10,000  

- Hierarchical organization  

- Examples  
  - MoA: HMG-CoA Reductase Inhibitor (e.g., atorvastatin)  
  - PE: Decreased Blood Pressure (e.g., enalapril)  
  - Chem: Penicillins (e.g., amoxicillin)
VA Classes

• Origin
  – Veterans Administration’s National Drug File-Reference Terminology (NDF-RT)

• Purpose
  – For drug classification in the VA formulary

• 486 classes

• Shallow hierarchical organization (3 levels)

• Examples
  – L1: ANTIMICROBIALS
  – L2: PENICILLINS AND BETA-LACTAM ANTIMICROBIALS
  – L3: QUINOLONES (e.g., Ofloxacin 200 MG Oral Tablet)

• NB: links to clinical drugs rather than ingredients
RxClass – Drug class browser

Class Browser
- Anatomical Therapeutic Chemical (ATC1-4)
- Established Pharmacologic Classes (EPC) [from DailyMed]
  - Names from 4-H - alp
  - Names from alp - Ant
  - Names from Ant - Asp
  - Names from Aty - Blo
  - Names from Blo - CD1
  - Names from CD2 - Col
  - Names from Com - Dih
  - Names from Dih - Ery
  - Names from Esl - Gon
  - Names from Gro - Hum
  - Names from Hum - Ina
  - Names from Ina - Int
  - Names from Int - Lin
  - Names from Lip - Low
  - Names from Lym - Mus
    - Lymphocyte Growth Factor (1)
    - Macrolide (1)
    - Macrolide Antibacterial (1)
    - Macrolide Antimicrobial (3)
    - Mast Cell Stabilizer (3)
    - Megakaryocyte Growth Factor (1)
    - Melanin Synthesis Inhibitor (1)
    - Melatonin Receptor Agonist (2)
    - Metabolic Alkaliminer (0)
    - Metal Chelator (2)
    - Methylated Sulphonamide
      - Antibacterial (1)
      - Methylating Agent (2)
      - Methyprprimerene (2)
      - Microsomal Triglyceride Transfer Protein Inhibitor (1)

RxClass
Exploring drug classes and their RxNorm drug members

azithromycin
- by class name/id
- by RxNorm drug name/id
- ingredient drug only
- Edit Drug Sources

Macrolide Antimicrobial

class: Macrolide Antimicrobial / id: N0000175935 / class type: EPC / show context

3 RxNorm generic drugs for has_EPC in DailyMed / similar classes

<table>
<thead>
<tr>
<th>Type</th>
<th>RXCUI</th>
<th>RxNorm Name</th>
<th>Relation</th>
<th>All classes</th>
</tr>
</thead>
<tbody>
<tr>
<td>IN</td>
<td>10631</td>
<td>Azithromycin</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>21212</td>
<td>Clarithromycin</td>
<td>DIRECT</td>
<td></td>
</tr>
<tr>
<td>IN</td>
<td>4053</td>
<td>Erythromycin</td>
<td>DIRECT</td>
<td></td>
</tr>
</tbody>
</table>

Print
Part 1 – Resources and use cases

RESOURCES FOR PROCESSING DRUG DATASETS – NLM DRUG APIS
NLM drug APIs

- Expose the content of RxNorm, RxTerms and NDF-RT (and other resources)
  - Logical structure, not storage format
  - Up-to-date information (monthly updates of RxNorm)
  - Additional features
    - Normalized and approximate matching; spelling correction
    - Drug-drug interactions checking (from DrugBank)
    - Link to drug classes (from ATC, DailyMed, MeSH, NDF-RT)
    - Archive of NDCs since 2007
  - Optimized graph traversal (pre-computed)

- For use in applications
  - Web services
  - SOAP, REST (XML, JSON)
  - Independent of any programming language
API documentation and examples

RxNorm API

The RxNorm API is a web service for accessing the current RxNorm data set. With one exception, no license is needed to use the RxNorm API. This is because the data returned from the API is from the RxNorm vocabulary, a non-proprietary vocabulary developed by the National Library of Medicine.

The API can be accessed by clients in two different ways:
- RxNorm RESTful web services
- RxNorm SOAP web services

Please check RxNorm API changes for the current updates.

Functions and Resources

In the table, the base URI (https://rxnav.nlm.nih.gov/REST/) for the REST resources has been omitted to improve readability.

<table>
<thead>
<tr>
<th>SOAP Function</th>
<th>REST resource</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>filterByProperty</td>
<td>/rcui/{rcui}/filter</td>
<td>Filter by property</td>
</tr>
<tr>
<td>findRxciByld</td>
<td>/rcui?ldtype</td>
<td>Search by identifier to find RxNorm concepts</td>
</tr>
<tr>
<td>findRxciByString</td>
<td>/rcui?name</td>
<td>Search by name to find RxNorm concepts</td>
</tr>
<tr>
<td>getAllClasses</td>
<td>/classes</td>
<td><strong>TO BE DEPRECATED</strong>. Use the RxClass API functions to return the drug class concepts for the specified drug vocabulary</td>
</tr>
<tr>
<td>getAllConceptsByTTY</td>
<td>/allconcepts</td>
<td>Return the RxNorm concepts for the specified term types</td>
</tr>
<tr>
<td>getAllHistoricalNDCs</td>
<td>/rcui/{rcui}/allhistoricalndcs</td>
<td>Return all National Drug Codes (NDC) for a concept</td>
</tr>
<tr>
<td>getAllNDCs</td>
<td>/rcui/{rcui}/allndcs</td>
<td><strong>TO BE DEPRECATED</strong>. Use getAllHistoricalNDCs or /rcui/{rcui}/allhistoricalndcs instead.</td>
</tr>
<tr>
<td>getAllProperties</td>
<td>/rcui/{rcui}/allProperties</td>
<td>Return all properties for a concept</td>
</tr>
<tr>
<td>getAllRelatedInfo</td>
<td>/rcui/{rcui}/allrelated</td>
<td>Return all related concept information</td>
</tr>
</tbody>
</table>
### ATC code Name DDD U Adm.R Note
A02BC05 esomeprazole 30 mg O
30 mg P

---

**Esomeprazole (283742)**

- Esomeprazole 40 MG Delayed Release Oral Capsule (606730)
- Esomeprazole 40 MG Delayed Release Oral Capsule [Nexium] (606731)

---

```java
rxnorm:findRxcuiById("NDC", "0186-5040-31", 0) → 606731
```

---

**A ALIMENTARY TRACT AND METABOLISM**
**A02 DRUGS FOR ACID RELATED DISORDERS**
**A02B DRUGS FOR PEPTIC ULCER AND GASTRO-oesophageal reflux disease (GORD)**
**A02BC Proton pump inhibitors**
Esomeprazole (283742)

Esomeprazole 40 MG Delayed Release Oral Capsule (606730)

Esomeprazole 40 MG Delayed Release Oral Capsule [Nexium] (606731)

rxnorm:getRelatedByType("606731", "IN") → 283742
### Proton pump inhibitors

<table>
<thead>
<tr>
<th>ATC code</th>
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<th>Adm.R</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>A02BC05</td>
<td>esomeprazole</td>
<td>30</td>
<td>mg</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>mg</td>
<td>P</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Esomeprazole (283742)**
- **Esomeprazole (A02BC05)**
- **Esomeprazole 40 MG Delayed Release Oral Capsule (606730)**
- **Esomeprazole 40 MG Delayed Release Oral Capsule [Nexium] (606731)**

\[\text{rxclass}:\text{getClassByRxNormDrugId}(\text{"283742"}, \text{"ATC"}, \text{"ALL"}) \rightarrow \text{A02BC, Proton pump inhibitors}\]
rxclass:getClassGraph("A02BC")

→ A02B, DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD);
A02, DRUGS FOR ACID RELATED DISORDERS;
A, ALIMENTARY TRACT AND METABOLISM
RxMix

• Graphical interface to the drug APIs
  – RxNorm, NDF-RT, RxTerms, RxImageAccess, Interactions, RxClass, MedEx, DailyMed
• Handles interoperability between functions
• Helps users compose complex queries
  – Find all the NDC codes for a given allergy class (e.g., barbiturates)
• Supports batch execution
Part 1 – Resources and use cases

COMMON USE CASES
Common use cases

• Pharmaco-epidemiology
  – Assess exposure to drugs (by ingredient or class)
  – Assess prescribed daily dose

• Identify potentially inappropriate medications
  – Elderly (Beers)
  – Pregnant women (Briggs)
Use case #1

Pharmaco-epidemiology

[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
Methods Example

RxNorm

Amoxicillin 500 MG Oral Capsule (308191) → Amoxicillin (723) → Oral Capsule

ATC/DDD Index

Amoxicillin (J01CA04) → amoxicillin (J01CA04) → 1 g

Surescripts

Amoxicillin 500 MG Oral Capsule (308191) → 40 capsules → 10 days → 40 x 500 mg / 10 = 2 g

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

- ALIMENTARY TRACT AND METABOLISM (A)
- BLOOD AND BLOOD FORMING ORGANS (B)
- CARDIOVASCULAR SYSTEM (C)
- DERMATOLOGICALS (D)
- GENITO URINARY SYSTEM AND SEX HORMONES (G)
- SYSTEMIC HORMONAL PREP., EXCL. SEX HORMONES AND INSULINS (H)
- ANTIINFECTIVES FOR SYSTEMIC USE (J)
- ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS (L)
- MUSCULO-SKELETAL SYSTEM (M)
- NERVOUS SYSTEM (N)
- ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS (P)
- RESPIRATORY SYSTEM (R)
- SENSORY ORGANS (S)
- VARIOUS (V)

Notable drugs:
- Atorvastatin
- Simvastatin
- Lisinopril
- Metoprolol
- Amlodipine
- Furosemide
- Hydrochlorothiazide
- Zolpidem
- Sertraline
- Escitalopram
- Alprazolam
- Clonazepam
- Gabapentin
- Quetiapine
- Oxycodone
- Fluoxetine
- Duloxetine
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

- 86.1% of the prescriptions are within 33%-300% of the ATC DDD
- 76.1% of the prescriptions are within 50%-200% of the ATC DDD
- 49.5% of the prescriptions are within 66%-150% of the ATC DDD
- 28.6% of the prescriptions exactly match the ATC DDD
- 10.4% < 33% of the ATC DDD
- 3.5% > 300% of the ATC DDD
Use case #2

Identifying potentially inappropriate medications for elderly patients

[Mundkur, AMIA, 2016]
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 → RxNorm clinical drug → ingredient ↔ 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%)
**Methods Example**

**RxNorm**
- 55111047901
  - Zolpidem tartrate 10 MG Oral Tablet (854873)
  - Oral Tablet

**Beers**
- zolpidem
  - Oral Pill
  - DFG filter

**Medicare**
- 55111047901
  - Demographic data
  - 470,523 prescriptions
Use case #3

Identifying potential risk in drug prescriptions during pregnancy

[Dhombres, AMIA, 2016]
Potential risk during pregnancy

• Dataset
  – Large prescription dataset from private insurer (150M patients)
  – 3.7M pregnant women; 19M prescriptions (2003-2014)
  – OMOP common 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
Specific challenge

• Obsolete identifiers
  – NDC = drug + manufacturer + packaging information
  • 200,000 active NDCs
  • 400,000 obsolete NDCs in the past 10 years
• Obsolete NDCs
  • Removed from RxNorm (e-prescribing use case)
  • Needed for analytics (longitudinal datasets)
• RxNorm API provides access to obsolete NDCs
  • Mapping obsolete NDCs to active drugs
    – rxnorm:getNDCStatus( ndc, startDate, endDate, option )
  • List of all NDCs – active or obsolete – for a given drug
    – rxnorm:getAllHistoricalNDCs( rxcui, history )
Other challenges

- Reuse of identifiers
  - NDCs (time-indexed)
- Insufficient coverage in RxNorm
  - International drugs
  - Over-the-counter drugs
- Granularity of knowledge
  - Ingredient-class vs. clinical drug-class
- Heterogeneity of drug classification
  - Different use cases
Impact assessment

• 1B prescriptions from Medicare analyzed
  – Over a 10-year period (2005-2014)
• Vast majority of NDCs can be resolved with the RxNorm API functions
  – Minor issues
    • Start/End date do not match prescription date
    • Ambiguous mapping (multiple RxCUIs; often clinically insignificant – generic vs. brand)
  – <5% unmapped NDCs (mostly supplies; OTCs)
Part 2 – Drug data processing in practice

Olivier Bodenreider, MD, PhD, NLM
Vojtech Huser, MD, PhD, NLM
Christian Reich, MD, PhD, QuintilesIMS
Part 2 overview

• Detailed look at the API

• Try it yourself (web part)
  – and get help (if you hit a problem)
  – 5-10 min

• R code examples
Part 2 – Drug data processing in practice

DETAILED LOOK AT THE API
API and RxMix web-tool

Functions and Resources

In the table, the base URI (https://rxnav.nlm.nih.gov/REST/) for the REST resources has been omitted to improve readability.

<table>
<thead>
<tr>
<th>SOAP Function</th>
<th>REST resource</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>filterByProperty</td>
<td>/rxcui/{rxcui}/filter</td>
<td>Filter by property</td>
</tr>
<tr>
<td>findRxcuiById</td>
<td>/rxcui?idtype</td>
<td>Search by identifier to find RxNorm concepts</td>
</tr>
<tr>
<td>findRxcuiByName</td>
<td>/rxcui?name</td>
<td>Search by name to find RxNorm concepts</td>
</tr>
<tr>
<td>getAllClasses</td>
<td>/classes</td>
<td>TO BE DEPRECATED. Use the RxClass API functions to return the drug class concepts for the specified drug vocabulary</td>
</tr>
<tr>
<td>getAllConceptsByTTY</td>
<td>/allconcepts</td>
<td>Return the RxNorm concepts for the specified term types</td>
</tr>
<tr>
<td>getAllINDCs</td>
<td>/rxcui/{rxcui}/allIndcs</td>
<td>Return all National Drug Codes (NDC) for a concept</td>
</tr>
</tbody>
</table>

https://rxnav.nlm.nih.gov/

https://mor.nlm.nih.gov/RxMix/
Esomeprazole (283742)

- Esomeprazole 40 MG Delayed Release Oral Capsule (606730)
- Esomeprazole 40 MG Delayed Release Oral Capsule [Nexium] (606731)

ATC code | Name          | DDD | U | Adm. R | Note
---------|---------------|-----|---|--------|-----
A02BC05  | esomeprazole  | 30  | mg| O      |     
          |               | 30  | mg| P      |     

00186504031

0186-5040-31
Functions

• rxnorm:findRxcuiById
  – Parameters
    • id_string: NDC
    • AllSourcesFlag: 0
  – Input: 00186504031 or 0186-5040-31
  – Output: 606731

• rxnorm:getRelatedByType
  – Parameters:
    • term_type: IN
  – Input: 606731
  – Output: Esomeprazole  283742
RxMix Demo
Output options - JSON

```json
{
  "function": {
    "input": "raloxifene",
    "level": 0,
    "name": "findRxcuiByString",
    "outputs": {
      "output": {
        "RXCUI": 72143
      }
    }
  },
  "function": {
    "input": 72143,
    "level": 1,
    "name": "getRelatedByType",
    "outputs": {
      "output_type": "BN",
      "output": {
        "RXCUI": 217010,
        "name": "Evista",
        "term_type": "BN"
      }
    }
  }
}
```
RxMix
Create applications from RxNorm, RxTerms, NDF-RT, and RxImageAccess APIs

Select Function
No function selected

LOAD
Combining functions
Saving your workflow
NDCs via RxNav
NDCs via RxNav

Raloxifene Hydrochloride 60 MG Oral Tablet [RxCUI = 1490065]

<table>
<thead>
<tr>
<th>NDC9</th>
<th>NDC11</th>
<th>NDC10</th>
<th>SPL_SET_ID</th>
<th>LABELER</th>
<th>PACKAGING</th>
<th>NDC9 PROPERTIES</th>
<th>PILL IMAGE</th>
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<td>Teva Pharmaceuticals USA, Inc.</td>
<td>100 in 1 BOTTLE</td>
<td>Show</td>
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<tr>
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</tbody>
</table>
Part 2 – Drug data processing in practice

TRY IT YOURSELF!
Try it!

- Find what these numbers have in common
  - Hint: find the RxCUI using the NDC identifier
## Solution

<table>
<thead>
<tr>
<th>ndc</th>
<th>rxn_drug_id</th>
<th>rxn_drug_label</th>
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<tr>
<td>00002416530</td>
<td>1490065</td>
<td>Raloxifene Hydrochloride 60 MG Oral Tablet</td>
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<td>Raloxifene Hydrochloride 60 MG Oral Tablet</td>
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<td>Raloxifene Hydrochloride 60 MG Oral Tablet</td>
</tr>
</tbody>
</table>
Part 2 – Drug data processing in practice

R CODE EXAMPLES
Resources

• Using API in R
  • https://github.com/lhncbc/r-snippets-bmi/blob/master/rxnorm/api-use-examples/callingAPI.R

• https://github.com/lhncbc/r-snippets-bmi/
# there are many JSON packages in R, we will pick one of them
library(jsonlite)

# some examples
example='atenolol'
exmaple='bicycle'

# wrapping a call to API into R function
findRxCuibyString <- function(input) {
  url <- sprintf('https://rxnav.nlm.nih.gov/REST/rxciu.json?search=2&allsrc=0&name=%s', input)
  url2 <- URLencode(url)
  j <- jsonlite::fromJSON(url2)

  # result in in variable j, we can traverse JSON as traversing a list in R as in the line below
  out = data.frame(rxnormId=as.integer(j$idGroup.rxnormId))

  # output is just a list of strings, we will extend it with more info
  if (nrow(out) > 0) {
    output$input = input; output$match = 1:nrow(out)
  } else {
    out = data.frame(rxnormId=NA, input=input, match=NA)
  }

  out
}

findRxCuibyString(example)
R demo

• [Live demo]
Part 3 – Experience with OHDSI

Olivier Bodenreider, MD, PhD, NLM
Vojtech Huser, MD, PhD, NLM
Christian Reich, MD, PhD, QuintilesIMS
Part 3 overview

• Clinical data models
• Handling international drugs
Part 3 – Experience with OHDSI

CLINICAL DATA MODELS
FDA Regulatory Action over Time

Number of FDA-caused Withdrawals

- 1960ies
- 1970ies
- 1980ies
- 1990ies
- 2000ies
FDAAA calls for establishing Risk Identification and Analysis System

SEC. 905. ACTIVE POSTMARKET RISK IDENTIFICATION AND ANALYSIS.

(a) IN GENERAL.—Subsection (k) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) is amended by adding at the end the following:

“(3) ACTIVE POSTMARKET RISK IDENTIFICATION.—

“(A) DEFINITION.—In this paragraph, the term ‘data’ refers to information with respect to a drug approved under this section or under section 351 of the Public Health Service Act, including claims data, patient survey data, standardized analytic files that allow for the pooling and analysis of data from disparate data environments, and any other data deemed appropriate by the Secretary.

“(B) DEVELOPMENT OF POSTMARKET RISK IDENTIFICATION AND ANALYSIS METHODS.—The Secretary shall, not later than 2 years after the date of the enactment of the Food and Drug Administration Amendments Act of 2007, in collaboration with public, academic, and private entities—

“(i) develop methods to obtain access to disparate data sources including the data sources specified in subparagraph (C);

“(ii) develop validated methods for the establishment of a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with the goals of including, in aggregate—

“(I) at least 25,000,000 patients by July 1, 2010; and

“(II) at least 100,000,000 patients by July 1, 2012; and

“(iii) convene a committee of experts, including individuals who are recognized in the field of protecting data privacy and security, to make recommendations to the Secretary on the development of tools and methods for the ethical and scientific uses for, and communication of, postmarketing data specified under subparagraph (C), including recommendations on the development of effective research methods for the study of drug safety questions.

“(C) ESTABLISHMENT OF THE POSTMARKET RISK IDENTIFICATION AND ANALYSIS SYSTEM.—
OMOP Experiment 1 (2009-2010)

- 10 data sources
- Claims and EHRs
- 200M+ lives

OMOP Methods Library
- Inception cohort
- Case control
- Logistic regression

Common Data Model
- Open-source
- Standards-based

Drug

Outcome

ACE Inhibitors
Amphotericin B
Antibiotics: erythromycins,
sulfonamides, tetracyclines
Antiepileptics: carbamazepine, phenytoin
Benzodiazepines
Beta blockers
Bisphosphonates: alendronate
Tricyclic antidepressants
Typical antipsychotics
Warfarin

- Angioedema
- Aplastic Anemia
- Acute Liver Injury
- Bleeding
- Hip Fracture
- Hospitalization
- Myocardial Infarction
- Mortality after MI
- Renal Failure
- GI Ulcer Hospitalization
OMOP Experiment 2 (2011-2012)

Drug-outcome pairs

<table>
<thead>
<tr>
<th></th>
<th>Positives</th>
<th>Negatives</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>165</td>
<td>234</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>36</td>
<td>66</td>
</tr>
<tr>
<td>Upper GI Bleed</td>
<td>24</td>
<td>67</td>
</tr>
<tr>
<td>Acute Liver Injury</td>
<td>81</td>
<td>37</td>
</tr>
<tr>
<td>Acute Renal Failure</td>
<td>24</td>
<td>64</td>
</tr>
</tbody>
</table>

Methods
- Case-Control
- New User Cohort
- Disproportionality methods
- ICTPD
- LGPS
- Self-Controlled Cohort
- SCCS

Observational data
- 4 claims databases
- 1 ambulatory EMR
European OMOP Experiment

Methods
- Case-Control
- New User Cohort
- Disproportionality methods
- ICTPD
- LGPS
- Self-Controlled Cohort
- SCCS

Drug-outcome pairs

<table>
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### Ground Truth for OMOP Experiment

<table>
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<tr>
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<td>91</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>165</strong></td>
<td><strong>234</strong></td>
<td><strong>399</strong></td>
</tr>
</tbody>
</table>

**Criteria for positive controls:**
- Event listed in Boxed Warning or Warnings/Precautions section of active FDA structured product label
- Drug listed as ‘causative agent’ in Tisdale et al, 2010: Drug-Induced Diseases
- Literature review identified no powered studies with refuting evidence of effect

**Criteria for negative controls:**
- Event not listed anywhere in any section of active FDA structured product label
- Drug not listed as ‘causative agent’ in Tisdale et al, 2010: Drug-Induced Diseases
- Literature review identified no powered studies with evidence of potential positive association
## Data Used in European Experiment

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<th>Name</th>
<th>Description</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aarhus</td>
<td>Danish national health registry, covering the Aarhus region. Includes inhabitant registry, drug dispensations, hospital claims, lab values, and death registry.</td>
<td>2 M</td>
</tr>
<tr>
<td>ARS</td>
<td>Italian record linkage system covering the Tuscany region, including inhabitant registry, drug dispensations, hospital claims, and death registry</td>
<td>4 M</td>
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<tr>
<td>Health-Search</td>
<td>Italian general practice database (no children)</td>
<td>1 M</td>
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<tr>
<td>IPCI</td>
<td>Dutch general practice database</td>
<td>0.75 M</td>
</tr>
<tr>
<td>Pedianet</td>
<td>Italian general practice pediatric database</td>
<td>0.14 M</td>
</tr>
<tr>
<td>PHARMO</td>
<td>Dutch record linkage system. Includes inhabitant registry, drug dispensations, hospital claims, and lab values.</td>
<td>1.28 M</td>
</tr>
</tbody>
</table>
OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP Results
Main findings in OMOP experiment

- Heterogeneity in estimates due to choice of database
- Heterogeneity in estimates due to analysis choices
- Except little heterogeneity due to outcome definitions
- Good performance ($AUC > 0.7$) in distinguishing positive from negative controls for optimal methods when stratifying by outcome and restricting to powered test cases
- Self controlled methods perform best for all outcomes
Observational Health Data Sciences and Informatics (OHDSI)
Plans and Ambitions
Letter Soup

- **OMOP**: ended in 2013 with Symposium
- **IMEDS**: Program at Reagan-Udall Foundation of the FDA
  - Methodological research to inform Industry and Agency
  - Research Lab
- **OHDSI**: Open Research Collaborative started by OMOP PIs and coordinated through Columbia University
  - Multiple stakeholders: academia, government, industry
  - Multiple geographies: US, Europe, Asia-Pacific
  - Multiple disciplines: Statistics, epidemiology, informatics, clinical sciences
  - Maintains OMOP CDM and Vocabularies
OHDSI’s vision

OHDSI collaborators access a network of 1 billion patients to generate evidence about all aspects of healthcare. Patients and clinicians and other decision-makers around the world use OHDSI tools and evidence every day.

Join us on the journey

http://ohdsi.org
A caricature of the patient journey
Questions asked across the patient journey

Which treatment did patients choose after diagnosis?

Which patients chose which treatments?

How many patients experienced the outcome after treatment?

What is the probability I will develop the disease?

Does one treatment cause the outcome more than an alternative?

Does treatment cause outcome?

What is the probability I will experience the outcome?
Classifying questions across the patient journey

• **Clinical characterization**: What happened to them?
  – What treatment did they choose after diagnosis?
  – Which patients chose which treatments?
  – How many patients experienced the outcome after treatment?

• **Patient-level prediction**: What will happen to me?
  – What is the probability that I will develop the disease?
  – What is the probability that I will experience the outcome?

• **Population-level effect estimation**: What are the causal effects?
  – Does treatment cause outcome?
  – Does one treatment cause the outcome more than an alternative?
OBSERVATIONAL MEDICAL OUTCOMES PARTNERSHIP

OMOP Common Data Model
OMOP Common Data Model

Standardized clinical data
- Person
  - Observation_period
  - Specimen
  - Death
  - Visit_occurrence
  - Procedure_occurrence
  - Drug_exposure
  - Device_exposure
  - Condition_occurrence
  - Measurement
  - Note
  - Observation
  - Fact_relationship

Standardized health system data
- Location
- Care_site
- Provider
- Payer_plan_period
- Visit_cost
- Procedure_cost
- Drug_cost
- Device_cost

Standardized derived elements
- Cohort
- Drug_era
- Dose_era
- Condition_era

Standardized meta-data
- CDM_source

Standardized vocabulary
- Concept
- Vocabulary
- Concept_relationship
- Relationship
- Concept_synonym
- Concept_ancestor
- Source_to_concept_map
- Drug_strength
- Cohort_definition

Standardized health economics
Simple Use Case

Give me all patients who take

Plavix 75 mg Tablets
OMOP Vocabulary

Branded Drug

clopidogrel 75 MG Oral Tablet [Plavix]
OMOP Vocabulary

Clinical Drug

clopidogrel 75 MG Oral Tablet

clopidogrel 75 MG Oral Tablet [Plavix]
OMOP Vocabulary Relationships

Drug Component

- clopidogrel 75 MG
- clopidogrel 75 MG Oral Tablet
- clopidogrel 75 MG Oral Tablet [Plavix]
- 75 MG

www.amia.org
OMOP Vocabulary

Ingredient

clopidogrel

clopidogrel 75 MG

clopidogrel Tablet

clopidogrel Tablet [Plavix]

clopidogrel 75 MG [Plavix]

clopidogrel 75 MG Oral Tablet

clopidogrel 75 MG Oral Tablet [Plavix]
OMOP Vocabulary

Ingredient

clopidogrel

clopidogrel 75 MG

clopidogrel Tablet

clopidogrel Tablet [Plavix]

clopidogrel 75 MG [Plavix]

clopidogrel 75 MG Oral Tablet

clopidogrel 75 MG Oral Tablet [Plavix]

RxNorm
Relationships
OMOP Vocabulary Common Data Model

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`
4. Local codes mapped to concepts through `source_to_concept_map`
CONCEPT –
Single standardized Reference Table

All vocabularies stacked up in one table

Vocabulary ID
All Content in CDM is Coded as Concepts

- Concepts are referred to by concept_id
- All details are in the CONCEPT table:

```sql
SELECT *
FROM concept
WHERE concept_id = 1322185;
```

<table>
<thead>
<tr>
<th>concept_id</th>
<th>concept_name</th>
<th>domain_id</th>
<th>vocabulary_id</th>
<th>concept_class_id</th>
<th>standard_concept</th>
<th>concept_code</th>
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</thead>
<tbody>
<tr>
<td>1322185</td>
<td>clopidogrel 75 MG Oral Tablet [Plavix]</td>
<td>Drug</td>
<td>RxNorm</td>
<td>Branded Drug</td>
<td>S</td>
<td>213169</td>
</tr>
</tbody>
</table>
### Drugs by Ingredients

3. Check Descendants (other drug products containing Warfarin and Dabigatran)

```sql
SELECT max_levels_of_separation, descendant.*
FROM concept_ancestor a, concept descendant
WHERE a.ancestor_concept_id = 1310149 /* Warfarin */
  AND a.descendant_concept_id = descendant.concept_id
ORDER BY max_levels_of_separation;
```

<table>
<thead>
<tr>
<th>concept_id</th>
<th>concept_name</th>
<th>vocabulary_id</th>
<th>concept_class_id</th>
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</thead>
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<td>Warfarin</td>
<td>RxNorm</td>
<td>Ingredient</td>
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<tr>
<td>36221229</td>
<td>Jantoven Pill</td>
<td>RxNorm</td>
<td>Branded Dose Group</td>
</tr>
<tr>
<td>40163559</td>
<td>Warfarin Sodium 6 MG</td>
<td>RxNorm</td>
<td>Clinical Drug Comp</td>
</tr>
<tr>
<td>40163544</td>
<td>Warfarin Sodium 3 MG [Jantoven]</td>
<td>RxNorm</td>
<td>Clinical Drug Comp</td>
</tr>
<tr>
<td>21134746</td>
<td>Warfarin 0.2 MG/ML</td>
<td>RxNorm Ext</td>
<td>Clinical Drug Comp</td>
</tr>
<tr>
<td>21105414</td>
<td>Warfarin 5 MG/ML</td>
<td>RxNorm Ext</td>
<td>Clinical Drug Comp</td>
</tr>
<tr>
<td>36221228</td>
<td>Jantoven Oral Product</td>
<td>RxNorm</td>
<td>Clinical Drug Comp</td>
</tr>
<tr>
<td>40163565</td>
<td>Warfarin Sodium 7.5 MG</td>
<td>RxNorm</td>
<td>Clinical Drug Comp</td>
</tr>
<tr>
<td>21115236</td>
<td>Warfarin 0.3 MG/ML</td>
<td>RxNorm Ext</td>
<td>Clinical Drug Comp</td>
</tr>
<tr>
<td>40163509</td>
<td>Warfarin Sodium 1 MG</td>
<td>RxNorm</td>
<td>Clinical Drug Comp</td>
</tr>
<tr>
<td>21156284</td>
<td>1 ML Warfarin 0.02 MG/ML Oral Solution</td>
<td>RxNorm Ext</td>
<td>Quant Clinical Drug</td>
</tr>
<tr>
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<td>RxNorm Ext</td>
<td>Clinical Drug</td>
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</tr>
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<td>RxNorm Ext</td>
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<tr>
<td>40093133</td>
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<td>Branded Drug Form</td>
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<td>Warfarin Sodium 2 MG/ML Injectable Solution</td>
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<table>
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<tr>
<th>concept_id</th>
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<td>36229332</td>
<td>Plavix Pill</td>
<td>RxNorm</td>
<td>Branded Dose Group</td>
</tr>
<tr>
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<td>RxNorm Ext</td>
<td>Quant Clinical Drug</td>
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</table>
### Members of our Drug Classes

Check Ingredient Descendants of Drug Class Anticoagulants

```sql
SELECT max_levels_of_separation, descendant.*
FROM concept_ancestor a, concept descendant
WHERE a.ancestor_concept_id = 21600961 /* ATC Antithromboic Agent */
AND a.descendant_concept_id = descendant.concept_id
AND descendant.concept_class = 'Ingredient'
ORDER BY max_levels_of_separation;
```

<table>
<thead>
<tr>
<th>concept_id</th>
<th>concept_name</th>
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<td>Drug</td>
<td>RxNorm</td>
<td>Ingredient</td>
</tr>
</tbody>
</table>
Fulfilling the Use Case

Example queries for the Drug Era table

```sql
/*
Find all periods of exposure for patients exposed to warfarin
*/

CREATE TEMPORARY TABLE warfarin_all_exposures AS
SELECT
  person_id,
  drug_concept_id,
  drug_era_start_date,
  drug_era_end_date
FROM
drug_era
WHERE
  drug_concept_id IN (1310149 /* warfarin */)
```

WHERE
```
drug_concept_id IN (1310149 /* warfarin */)
```
Fulfilling Another Use Case

Example queries for the Drug Era table

```sql
/*
Find all periods of exposure for patients exposed to warfarin
*/

CREATE TEMPORARY TABLE warfarin_all_exposures AS
SELECT
    person_id,
    drug_concept_id,
    drug_era_start_date,
    drug_era_end_date
FROM
    drug_era
WHERE
    drug_concept_id IN (1310149 /* warfarin */)

WHERE
    drug_concept_id IN (1310149 /* warfarin */)
```

```sql
WHERE
    drug_concept_id IN (1310149 /* warfarin */)
    SELECT descendant.concept_id
    FROM concept_ancestor a, concept descendant
    WHERE a.ancestor_concept_id = 21500803 /* ETC Anticoagulants */
    AND a.descendant_concept_id = descendant.concept_id
```
Many Other Use Cases

OMOP Vocabulary Queries

Drug Queries

The following drug domain queries are available:

- D01: Find drug concept by concept ID
- D02: Find drug or class by keyword
- D03: Find ingredients of a drug
- D04: Find drugs by ingredient
- D05: Find generic drugs by ingredient
- D06: Find branded drugs by ingredient
- D07: Find single ingredient drugs by ingredient
- D08: Find drug classes for a drug or ingredient
- D09: Find drugs by drug class
- D10: Find ingredient by drug class
- D11: Find source codes by drug class
- D12: Find indications for a drug
- D13: Find indications as condition concepts for a drug
- D14: Find drugs for an indication
- D15: Find drugs for an indication provided as condition concepts
- D16: Find drugs for an indication by indication type
- D17: Find ingredients for an indication

http://vocabqueries.omop.org/
Part 3 – Experience with OHDSI

HANDLING INTERNATIONAL DRUGS ("RXNORM EXTENSION")
Germany: AMIS

### Ergebnisse

**Suchschnitt**

Sortierte Suchschritte sind mit einem * markiert

» alle Suchschritte anzeigen

1. **Arzneimittelname: clopidogrel?**
   - 2. **AJ29**
   - Stand: 11.11.2016 07:32:00

### Arzneimittel

**Suchschnitt: Arzneimittelname: clopidogrel?**

Ergebnis 1-10 von 338

<table>
<thead>
<tr>
<th>AM-Name</th>
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<th>Anmelder</th>
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France

BASE DE DONNÉES PUBLIQUE DES MÉDICAMENTS

Visiter [medicaments.gouv.fr]

Téléchargement

Termes du contrat de licence

Conformément à l'article L. 161-40-1 du code de la sécurité sociale dans sa rédaction issue de l'article 8 de la loi n° 2011-2012 du 29/12/2011, l'information contenue dans la base de données publique des médicaments (BDPM) est mise à disposition des usagers au moyen des fichiers offerts au téléchargement libre et gratuit.

Format de données et lien entre les différents fichiers

Le lien suivant vous permettra d'accéder à un fichier décrivant le contenu, le format et les liens existants entre les fichiers mis à disposition ci-dessous.

- Télécharger le fichier descriptif (pdf, 28 Ko)

Liste des fichiers disponibles au téléchargement

La base de données est actualisée tous les mois. La date de mise à jour de la base figure en haut et à droite dans le bandeau de navigation.

Attention : le fichier des informations importantes est généré au moment où vous cliquez, contrairement aux autres fichiers qui sont mis à jour en même temps que l'ensemble des données de la base. Cela est dû au fait que les informations importantes sont sujéttes à des mises à jour potentiellement plus fréquentes.

- Fichier des spécialités (date de mise à jour : 28/10/2016, 2688 Ko)
- Fichier des présentations (date de mise à jour : 12/11/2016, 3800 Ko)
- Fichier des compositions (date de mise à jour : 28/10/2016, 2068 Ko)
- Fichier des avis SMR de la HAS (date de mise à jour : 28/10/2016, 2985 Ko)
- Fichier des avis ASMR de la HAS (date de mise à jour : 28/10/2016, 1561 Ko)
- Fichier des liens vers les avis de la commission de la transparence de la HAS (date de mise à jour : 28/10/2016, 347 Ko)
- Fichier des groupes génériques (date de mise à jour : 28/10/2016, 937 Ko)
- Fichier des conditions de prescription et de délivrance (date de mise à jour : 28/10/2016, 716 Ko)
- Fichier des informations importantes (génération en direct)
Drug Product Database - All Files

The Drug Product Database (DPD) system captures information on Canadian human, veterinary and disinfectant products approved for use by Health Canada. This extract contains both marketed (active) and discontinued (inactivated) products in separate files. This data extract contains information about Drug Product - All Files.

Publisher - Current Organization Name: Health Canada

Licence: Open Government Licence - Canada

Resources

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UK – dm+d

TRUD > All downloads

NHSBSA dm+d releases

You are subscribed to this item. Your subscription request was accepted on Friday 16th May 2014 at 3:53pm.

NHSBSA_11.0.0_201611070000001
Released on Monday 7th November 2016
NHSBSA Release Week 45
Download this release (11.0 MB)
Checksum | Signature | Public key #6
About checksums | About signatures and public keys

NHSBSA_10.4.0_201610310000001
Released on Monday 31st October 2016
NHSBSA Release Week 44
Download this release (10.9 MB)
Checksum | Signature | Public key #6
About checksums | About signatures and public keys
Plavix Prepackaged Product
Part 3 – Experience with OHDSI

RESOURCES
Resources

1. Download
   http://athena.ohdsi.org

2. Rebuild (not for the faint of heart)
   https://github.com/OHDSI/Vocabulary-v5.0

3. Documentation (incomplete still)
Questions

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