



COLLEGE OF PHARMACY
UNIVERSITY OF MICHIGAN

Department of Clinical Pharmacy and Translational Sciences
March 22, 2021

Drug analytics from claims data
Resources, methods and applications

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National Library of Medicine

Lister Hill National Center for Biomedical Communications

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Outline

◆ Resources

- Drug terminologies
- RxNorm

◆ Methods

- Mapping NDCs to RxNorm
- Linking RxNorm entities to ATC

◆ Applications

- OHDSI – Characterizing treatment pathways



Resources

Interoperability among drug vocabularies

- ◆ Exchange of information requires standardized names
 - Ordering drugs
 - Checking interactions
 - Inventory management
- ◆ No standard naming conventions for drugs
- ◆ Integrating drug vocabularies
- ◆ Unique identifiers for drugs
- ◆ Specify relations among drug entities



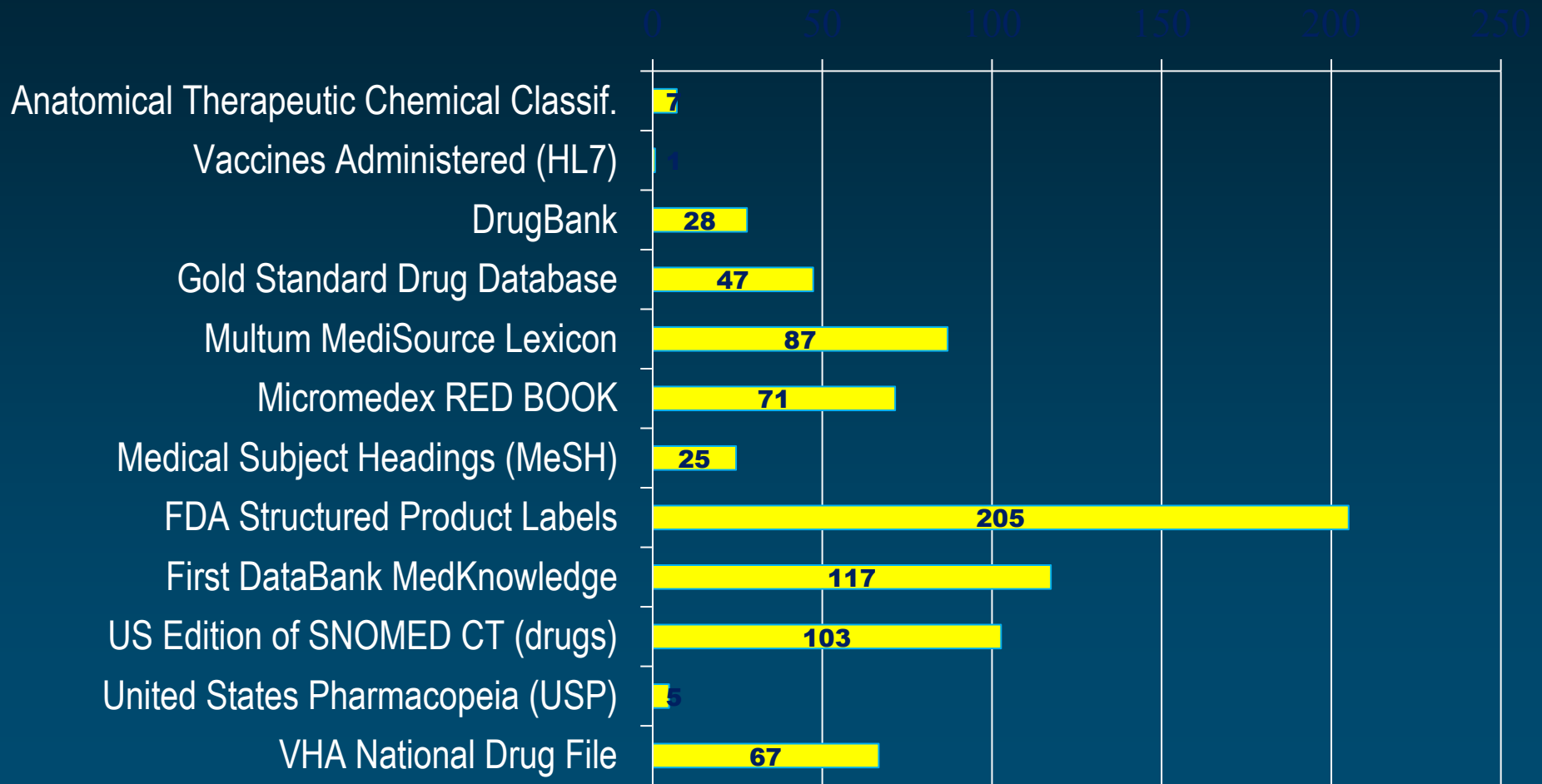
RxNorm

<https://www.nlm.nih.gov/research/umls/rxnorm/>

- ◆ Standard drug terminology
- ◆ Developed by the National Library of Medicine
- ◆ Integrates 13 drug vocabularies (interoperability)
- ◆ Scope
 - Prescription drugs (U.S. market)
 - Only terminology (not a drug knowledge base)
- ◆ Updated monthly
- ◆ Use cases
 - E-prescribing
 - Information exchange
 - Formulary development
 - Reference value sets
 - *Analytics*



Source vocabularies in RxNorm



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(terms in thousands, as of March 2021)

Normalization Lexical level

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



Warfarin Sodium 1 MG Oral Tablet (855288)



Normalized form

Strength

1 MG

Ingredient

Warfarin Sodium

Dose form

Oral Tablet

Strength

Warfarin Sodium 1 MG (855287)

Ingredient

Clinical drug form

Clinical drug component

Ingredient

Dose form

Warfarin Oral Tablet (374319)

Strength

Warfarin Sodium 1 MG Oral Tablet (855288)

Ingredient

Dose form

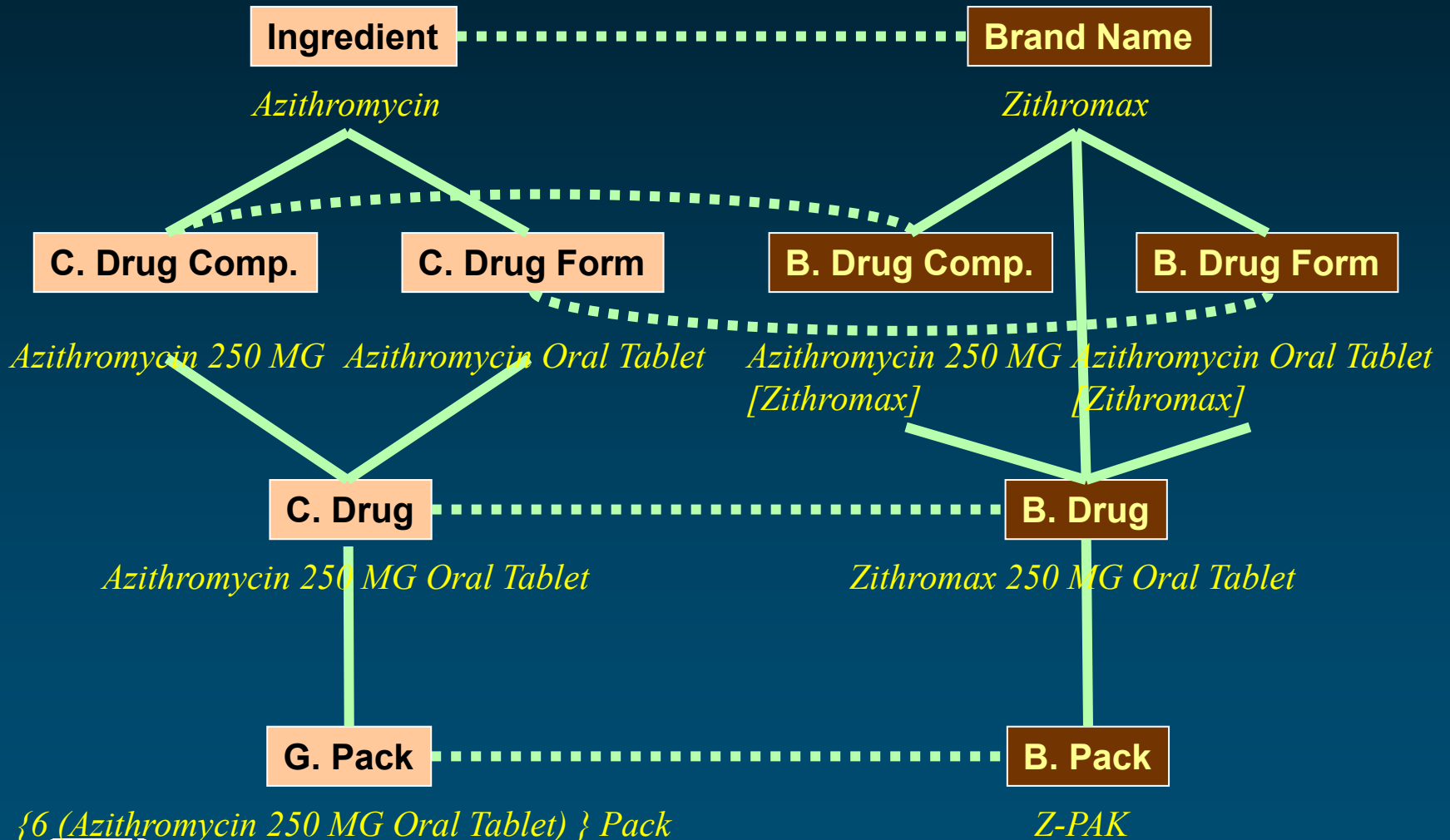
Clinical drug



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Relations among drug entities



{6 (Azithromycin 250 MG Oral Tablet) } Pack

Z-PAK



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RxNorm Example



String azithromycin



azithromycin [RxCUI = 18631]

- RxNorm Graph
- RxNorm Properties
- NDC
- RxTerms
- Pill Images
- Class View
- Interaction View
- Status

Views

- Classic
- Simple
- Table

Filters

- H
- V
- Rx
- S
- Group
- Form

Links



Legend

- MIN
- Pack
- Multi

Download

| IN/MIN | (1) |
|--------|--------------|
| H Rx S | azithromycin |

| PIN | (3) |
|------|--------------------------|
| Rx S | azithromycin anhydrous |
| Rx S | azithromycin dihydrate |
| Rx S | azithromycin monohydrate |

| BN | (3) |
|--------|-----------|
| H Rx S | AzaSite |
| H Rx S | Zithromax |
| H Rx S | Zmax |

| SCDC | (8) |
|--------|-------------------------------------|
| H Rx S | azithromycin 10 MG/ML |
| H Rx S | azithromycin 1000 MG |
| H Rx S | azithromycin 20 MG/ML |
| H Rx S | azithromycin 250 MG |
| H Rx S | azithromycin 250 MG Oral Capsule |
| H Rx S | azithromycin 250 MG Oral Tablet |
| H Rx S | azithromycin 250 MG Oral Suspension |



| SBDC | (8) |
|--------|-----------------------------------|
| H Rx S | azithromycin 10 MG/ML [AzaSite] |
| H Rx S | azithromycin 1000 MG [Zithromax] |
| H Rx S | azithromycin 20 MG/ML [Zithromax] |
| H Rx S | azithromycin 250 MG [Zithromax] |
| H Rx S | azithromycin 250 MG [Zmax] |
| H Rx S | azithromycin 250 MG [Zmax] |
| H Rx S | azithromycin 250 MG [Zmax] |
| H Rx S | azithromycin 250 MG [Zmax] |

| SCD/GPCK | (13) |
|----------|---|
| H Rx S | azithromycin 10 MG/ML Ophthalmic Solution |
| H Rx S | azithromycin 1000 MG Powder for Oral Suspension |
| H Rx S | azithromycin 20 MG/ML Oral Suspension |
| S | azithromycin 250 MG Oral Capsule |
| H Rx S | azithromycin 250 MG Oral Tablet |
| H Rx S | azithromycin 250 MG Oral Suspension |
| H Rx S | azithromycin 250 MG Oral Suspension |
| H Rx S | azithromycin 250 MG Oral Suspension |
| H Rx S | azithromycin 250 MG Oral Suspension |
| H Rx S | azithromycin 250 MG Oral Suspension |
| H Rx S | azithromycin 250 MG Oral Suspension |
| H Rx S | azithromycin 250 MG Oral Suspension |
| H Rx S | azithromycin 250 MG Oral Suspension |

| SBD/BPCK | (11) |
|----------|---|
| H Rx S | AzaSite 1 % Ophthalmic Solution |
| P H Rx S | TRI-PAK |
| P H Rx S | Z-PAK |
| H Rx S | Zithromax 1 GM Powder for Oral Suspension |
| H Rx S | Zithromax 1 GM Powder for Oral Suspension |
| H Rx S | Zithromax 1 GM Powder for Oral Suspension |
| H Rx S | Zithromax 1 GM Powder for Oral Suspension |
| H Rx S | Zithromax 1 GM Powder for Oral Suspension |
| H Rx S | Zithromax 1 GM Powder for Oral Suspension |
| H Rx S | Zithromax 1 GM Powder for Oral Suspension |
| H Rx S | Zithromax 1 GM Powder for Oral Suspension |

| SCDG | (6) |
|--------|----------------------------------|
| H Rx S | azithromycin Injectable Product |
| H Rx S | azithromycin Ophthalmic Product |
| H Rx S | azithromycin Oral Liquid Product |
| H Rx S | azithromycin Oral Powder Product |
| H Rx S | azithromycin Oral Product |
| H Rx S | azithromycin Oral Product |

| DFG | (6) |
|---------|---------------------|
| HV Rx S | Injectable Product |
| HV Rx S | Ophthalmic Product |
| HV Rx S | Oral Liquid Product |
| HV Rx S | Oral Powder Product |
| HV Rx S | Oral Product |
| HV Rx S | Oral Product |

| SBDG | (8) |
|--------|-------------------------------|
| H Rx S | AzaSite Ophthalmic Product |
| H Rx S | Zithromax Injectable Product |
| H Rx S | Zithromax Oral Liquid Product |
| H Rx S | Zithromax Oral Powder Product |
| H Rx S | Zithromax Oral Product |
| H Rx S | Zithromax Oral Product |
| H Rx S | Zithromax Oral Product |
| H Rx S | Zithromax Oral Product |

What RxNorm does NOT contain

- ◆ Non-prescription drugs (limited coverage of OTC drugs)
- ◆ Non-drug entities (e.g., supplies)
- ◆ Drug classes / drug-class membership
- ◆ Indications, adverse events
- ◆ Drug-drug interactions
- ◆ Pricing information
- ◆ Dosing information

Available through services (APIs)



Methods

Example: Analyzing opioid prescriptions in the Medicare dataset

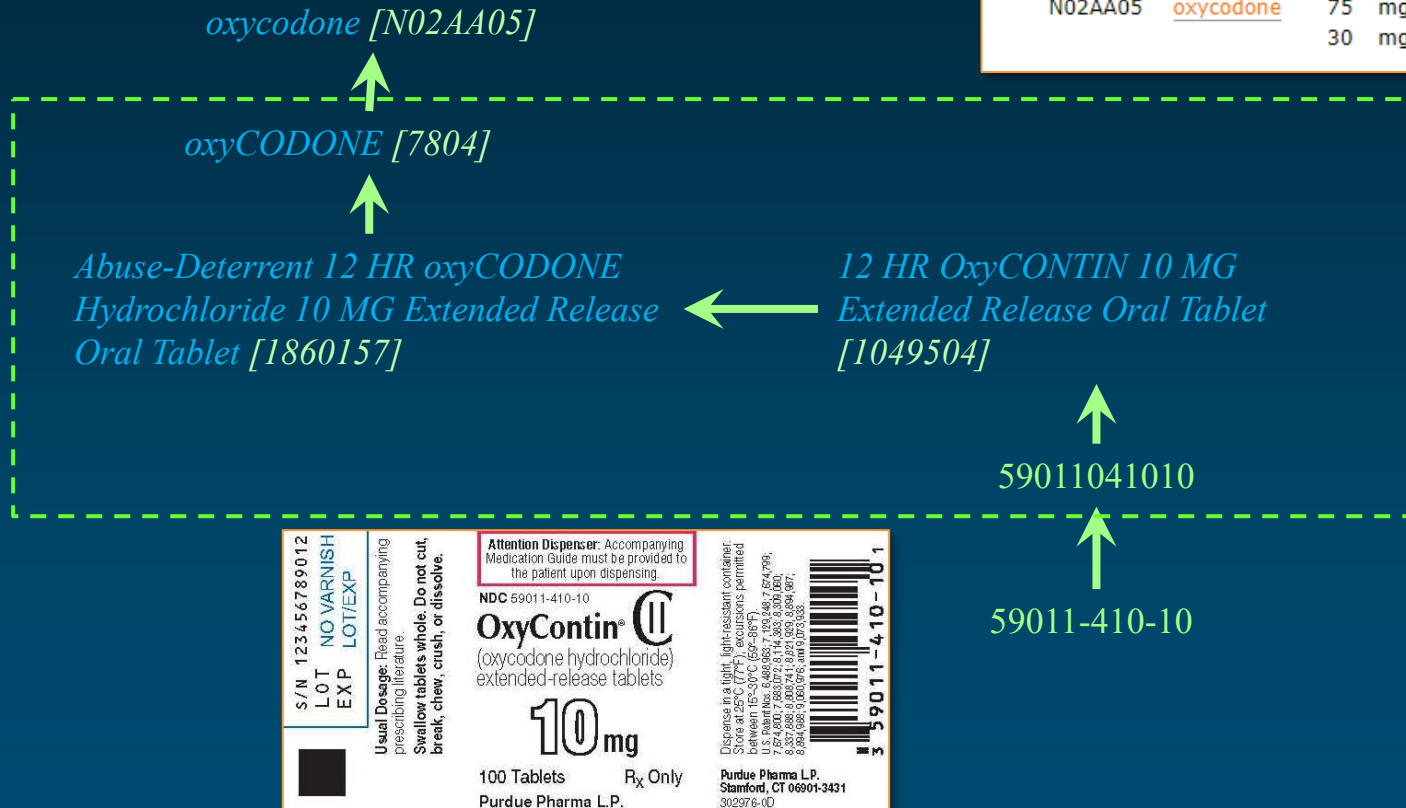
- ◆ NDCs are used to identify medications in claims data
- ◆ Drug classification systems are used to define drug classes, such as opioids
- ◆ RxNorm can be used to bridge between NDCs and popular drug classification systems (e.g., ATC)

Mapping NDCs to ATC drug classes

- ◆ NDCs are attached to a clinical drug (SCD) or a branded (drug)
- ◆ Branded drugs are mapped to clinical drugs
- ◆ Clinical drugs are linked to their ingredient
- ◆ Many drug classification systems link classes to ingredient-level drugs (e.g., ATC, MED-RT, EPC, MeSH pharmacologic actions, SNOMED CT)


Linkages among drug entities

| | | | | | |
|--------------------------------------|------------------|-----|----|-------|------|
| N NERVOUS SYSTEM | | | | | |
| N02 ANALGESICS | | | | | |
| N02A OPIOIDS | | | | | |
| N02AA Natural opium alkaloids | | | | | |
| ATC code | Name | DDD | U | Adm.R | Note |
| N02AA05 | <u>oxycodone</u> | 75 | mg | O | |
| | | 30 | mg | P | |



Identifying opioid drugs from a drug class

◆ ATC – Anatomical Therapeutic Chemical drug classification system



WHO Collaborating Centre for Drug Statistics Methodology

| | |
|---------------------------------------|--|
| News | |
| ATC/DDD Index | |
| Updates included in the ATC/DDD Index | |
| ATC/DDD methodology | |
| ATC | |
| DDD | |
| ATC/DDD alterations, cumulative lists | |
| ATC/DDD Index and Guidelines | |
| Use of ATC/DDD | |
| Courses | |

N NERVOUS SYSTEM

N02 **ANALGESICS**

N02A **OPIOIDS**

N02AA **Natural opium alkaloids**

N02AB **Phenylpiperidine derivatives**

N02AC **Diphenylpropylamine derivatives**

N02AD **Benzomorphan derivatives**

N02AE **Oripavine derivatives**

N02AF **Morphinan derivatives**

N02AG **Opioids in combination with antispasmodics**

N02AJ **Opioids in combination with non-opioid analgesics**

N02AX **Other opioids**

N02AA **Natural opium alkaloids**

| ATC code | Name |
|----------|---|
| N02AA01 | morphine |
| N02AA02 | opium |
| N02AA03 | hydromorphone |
| N02AA04 | nicomorphine |
| N02AA05 | oxycodone |
| N02AA08 | dihydrocodeine |
| N02AA10 | papaveretum |
| N02AA51 | morphine, combinations |
| N02AA53 | hydromorphone and naloxone |
| N02AA55 | oxycodone and naloxone |
| N02AA56 | oxycodone and naltrexone |
| N02AA58 | dihydrocodeine, combinations |
| N02AA59 | codeine, combinations excl. psycholeptics |
| N02AA79 | codeine, combinations with psycholeptics |



Issues: Obsolete NDCs

| | | | | | |
|--------------------------------------|------------------|-----|----|-------|------|
| N NERVOUS SYSTEM | | | | | |
| N02 ANALGESICS | | | | | |
| N02A OPIOIDS | | | | | |
| N02AA Natural opium alkaloids | | | | | |
| ATC code | Name | DDD | U | Adm.R | Note |
| N02AA05 | <u>oxycodone</u> | 75 | mg | O | |
| | | 30 | mg | P | |

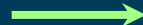
oxycodone [N02AA05]



oxyCODONE [7804]



*Abuse-Deterrent 12 HR oxyCODONE
Hydrochloride 10 MG Extended Release
Oral Tablet [1860157]*



*12 HR OxyCONTIN 10 MG
Extended Release Oral Tablet
[1049504]*



*Obsolete NDCs can be queried
under Historical NDCs in RxNav*

2 Current NDCs

59011041010
59011041020

129 Obsolete NDCs

10544059120
10544059130
16590067710
16590067715
16590067720
[...]





ⓘ

✕
🔍
↺



12 HR OxyCONTIN 10 MG Extended Release Oral Tablet [RxCUI = 1049504]

- RxNorm Graph
- RxNorm Properties
- NDC
- RxTerms
- Pill Images
- Class View
- Interaction View
- Status

Views

- Current NDC
- Historical NDC

Download

| RxCUI | Relationship | Manufacturer NDC | Manufacturer | Product NDC | Product |
|---------|--------------|------------------|--------------|-------------|---------|
| 1049504 | direct | 48692088010 | 201101 | 201206 | No |
| 1049504 | direct | 48692088025 | 201101 | 201206 | No |
| 1049504 | direct | 54868381300 | 201101 | 201607 | No |
| 1049504 | direct | 54868381301 | 201101 | 201607 | No |
| 1049504 | direct | 54868381302 | 201101 | 201402 | No |
| 1049504 | direct | 54868381303 | 201101 | 201607 | No |
| 1049504 | direct | 54868381304 | 201101 | 201607 | No |
| 1049504 | direct | 54868381305 | 201101 | 201607 | No |
| 1049504 | direct | 59011010010 | 201101 | 201306 | No |
| 1049504 | direct | 59011010020 | 201101 | 201306 | No |
| 1049504 | direct | 59011010025 | 201101 | 201309 | No |
| 1049504 | direct | 59011041010 | 201101 | 202103 | Yes |
| 1049504 | direct | 59011041020 | 201101 | 202103 | Yes |
| 1049504 | direct | 63629377501 | 201101 | 201709 | No |
| 1049504 | direct | 63629377502 | 201101 | 201709 | No |
| 1049504 | direct | 63629377503 | 201102 | 201709 | No |
| 1049504 | direct | 63629377504 | 201102 | 201709 | No |
| 1049504 | direct | 63629377505 | 201102 | 201709 | No |
| 1049504 | direct | 63629386101 | 201409 | 201708 | No |
| 1049504 | direct | 63629386102 | 201409 | 201708 | No |

Applications

Characterizing treatment pathways at scale using the OHDSI network



COLLOQUIUM
PAPER

Characterizing treatment pathways at scale using the OHDSI network

George Hripcsak^{a,b,c,1}, Patrick B. Ryan^{c,d}, Jon D. Duke^{c,e}, Nigam H. Shah^{c,f}, Rae Woong Park^{c,g}, Vojtech Huser^{c,h}, Marc A. Suchard^{c,i,j,k}, Martijn J. Schuemie^{c,d}, Frank J. DeFalco^{c,d}, Adler Perotte^{a,c}, Juan M. Banda^{c,f}, Christian G. Reich^{c,l}, Lisa M. Schilling^{c,m}, Michael E. Matheny^{c,n,o}, Daniella Meeker^{c,p,q}, Nicole Pratt^{c,r}, and David Madigan^{c,s}

www.pnas.org/cgi/doi/10.1073/pnas.1510502113

PNAS | July 5, 2016 | vol. 113 | no. 27 | 7329–7336

Observational Health Data Sciences and Informatics (OHDSI)
<https://ohdsi.org/>



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Characterizing treatment pathways at scale using the OHDSI network

- ◆ Objectives: analyze the variability of pharmacological treatment interventions over three years across three diseases (type-2 diabetes mellitus, hypertension, or depression)
- ◆ Inclusion criteria: exposure to an antidiabetic, antihypertensive, or antidepressant medication for 3 years, as well as presence of at least one diagnostic code for the corresponding disease
- ◆ Exclusion criteria: based on diagnostic data (e.g., exclusion of schizophrenia patients from the depression cohort)

Characterizing treatment pathways at scale using the OHDSI network

- ◆ Materials: 11 datasets representing a total of 255 million patients
 - EHR data (South Korea, U.K., U.S.) 67M
 - Claims data (U.S., Japan) 188M
- ◆ Methods: Analyze the sequences of medications that patients were placed on during those 3 years, to reveal patterns and variation in treatment among data sources and diseases

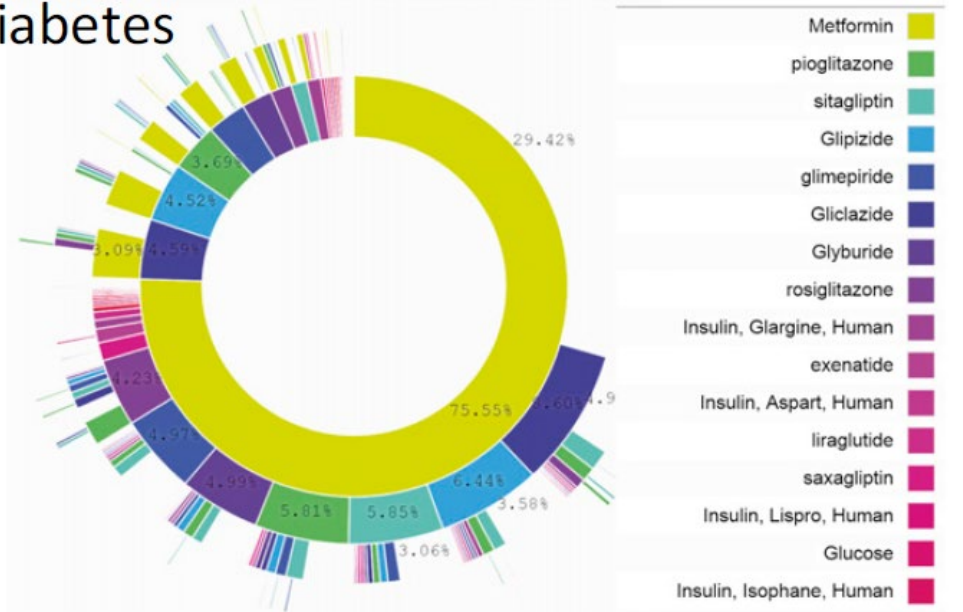
Characterizing treatment pathways at scale using the OHDSI network

◆ Results

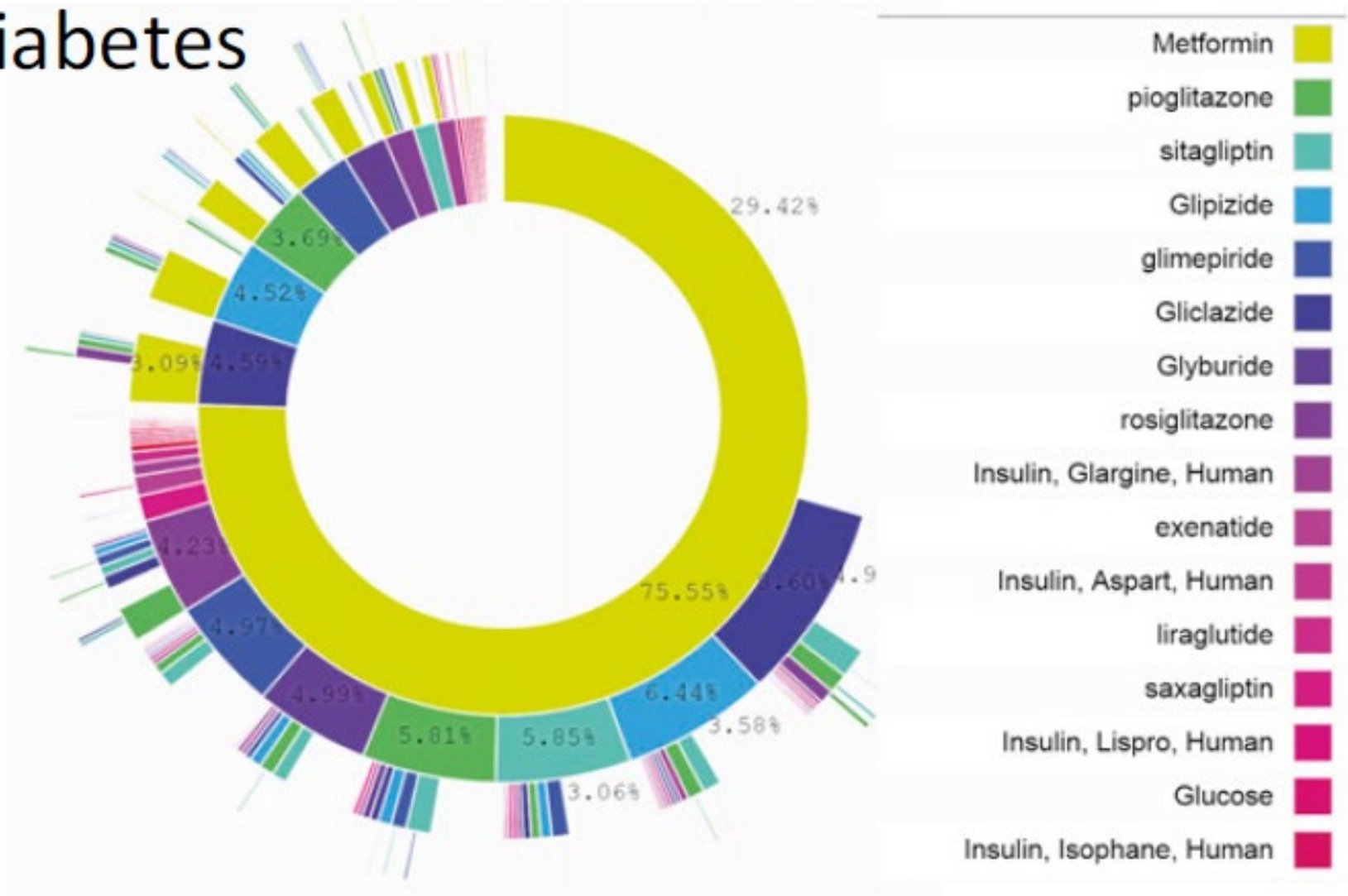
- Patients with 3 years of uninterrupted therapy
 - 327,110 diabetes patients
 - 1,182,792 hypertension patients
 - 264,841 depression patients

● Treatment pathways

A Diabetes



A Diabetes



Differences across diseases

◆ Diabetes

- Metformin is the first line of treatment and often the only treatment

◆ Hypertension

- Slight predominance of HCTZ, frequently paired with other medications

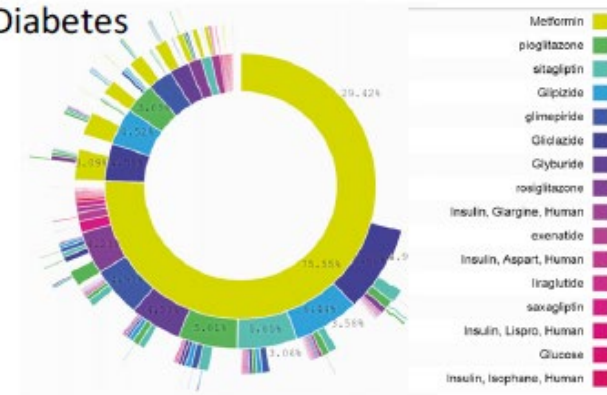
◆ Depression

- Even spread of medications

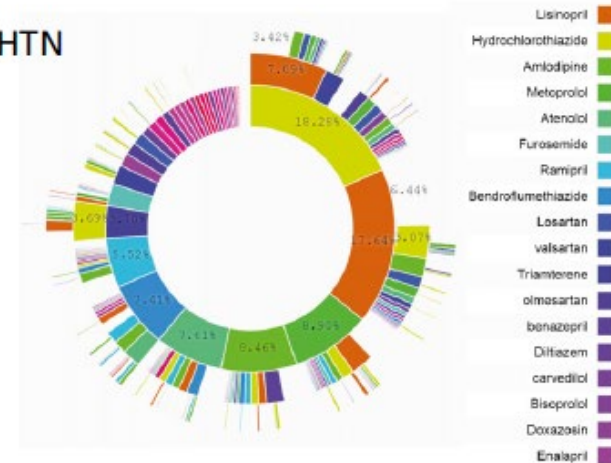
◆ Unique treatment pathways (within a cohort)

- 10% TDM
- 25% HTN

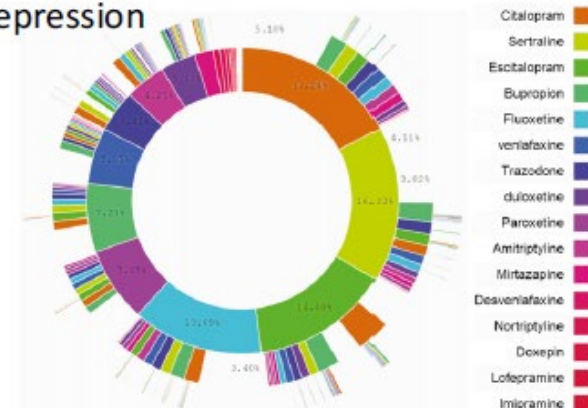
A Diabetes



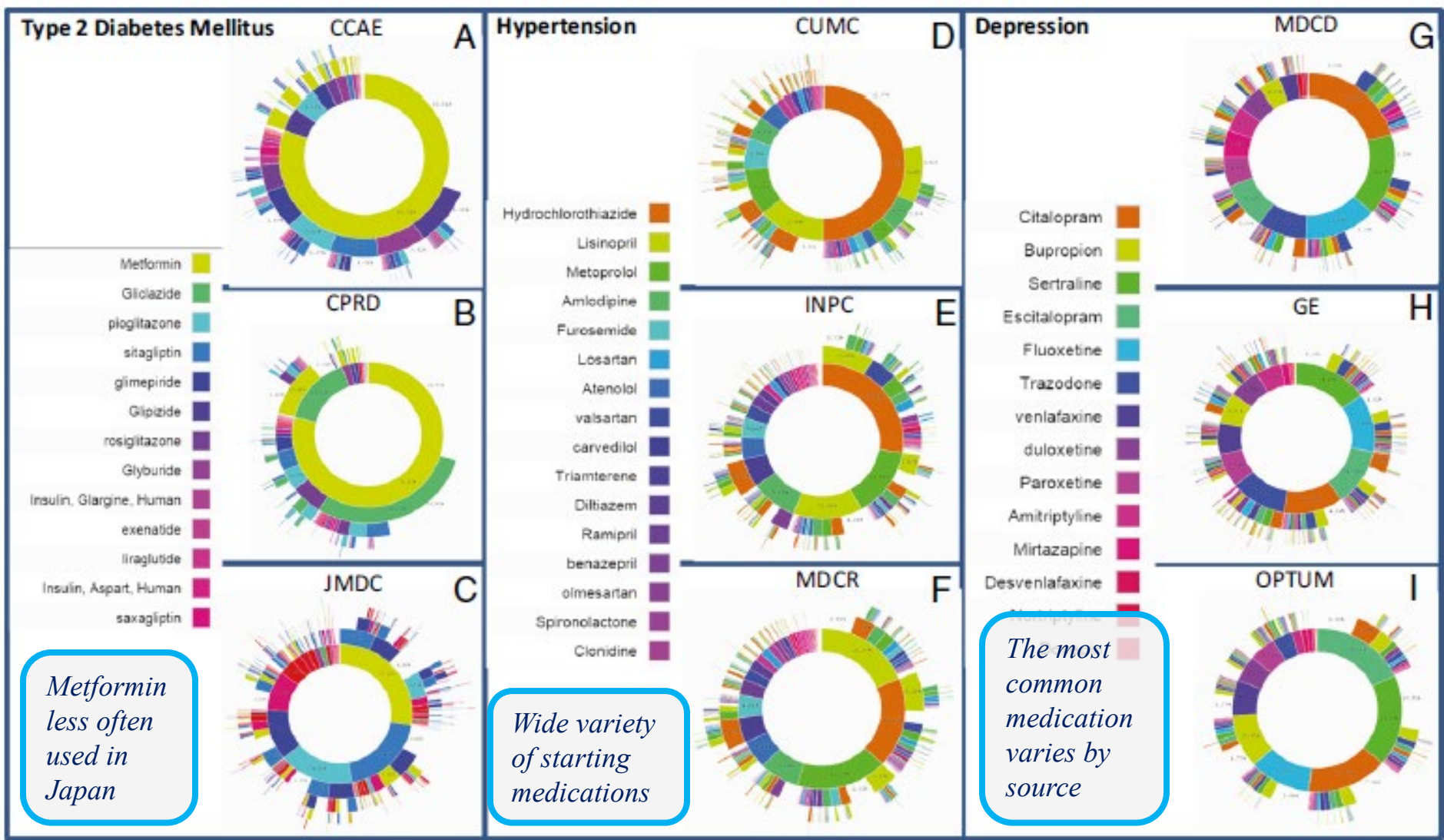
B HTN

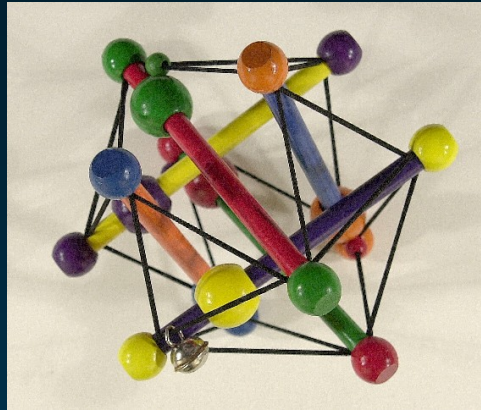


C Depression



Differences across countries





Medical Ontology Research

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Web: mor.nlm.nih.gov

Olivier Bodenreider



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