Categorization and classification of drugs

Olivier Bodenreider
Lister Hill National Center for Biomedical Communications
Bethesda, Maryland - USA
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Outline

- Drug classification systems in action
  - RxClass demo
- Desiderata for drug classification systems
- Opioid drugs in drug classification systems
  - ATC
  - ICD-10
- Classifying illicit drugs
Drug classification systems in action

**RxClass**

- Developed by the National Library of Medicine
- Linked to RxNorm drugs
- Integrates multiple drug classification systems
  - Anatomical Therapeutic Chemical (ATC) drug classification – WHO
  - Established Pharmacological Classes (EPC) – VA/FDA (MED-RT)
  - Pharmacological Actions – NLM (MeSH)
  - Chemical structure – FDA (MED-RT)
  - Mechanism of action – FDA (MED-RT)
  - Physiologic effect – FDA (MED-RT)
  - Therapeutic use & contraindications – VA (MED-RT)
  - VA Formulary classes – VA (VANDF)

https://mor.nlm.nih.gov/RxClass/
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### Opioid anesthetics

#### 6 RxNorm generic drugs in ATC / similar classes

<table>
<thead>
<tr>
<th>Type</th>
<th>RXCUI</th>
<th>RxNorm Name</th>
<th>Source Id</th>
<th>Source Name</th>
<th>Relation</th>
<th>All classes</th>
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</tr>
</tbody>
</table>
Desiderata for drug classification systems

- From the perspective of drug analytics in large clinical datasets
  - May not be directly applicable to opioids in death certificates

Desiderata for drug classification systems

◆ Administrative desiderata
  • Authoritative source
  • Regular updates
  • License?

◆ Hierarchical structure
  • Support for aggregation (vs. flat list)
  • Avoid double counting (single vs. multiple parents)
  • Number of levels (fixed vs. variable)
  • Drugs at the lowest level?
Desiderata for drug classification systems

- **Coverage**
  - All/most drugs of interest need to be covered

- **Granularity**
  - Necessary to support fined-grained analyses

- **Non-ambiguity**
  - Does the classification provide enough information for automatic classification?

- **Dispersion**
  - Cases analyzed should be distributed among as many classes as meaningfully possible
Application to Medicare data

Figure 2. Desideratum F: Dispersion. Proportion of Medicare Part D claims from 2006 to 2014 covered by a given proportion of classes.*
Opioids in ATC

- 3 main ATC classes for opioids
  - N01AH Opioid anesthetics
  - N02A OPIOIDS
  - N07BC Drugs used in opioid dependence

[ATC classes and examples]

https://www.whocc.no/atc_ddd_index/
N02A subclasses

Nervous System
N02 Analgesics
N02A Opioids
N02AA Natural opioid alkaloids
  - morphine
  - opium
  - hydromorphone
  - nicomorphine
  - oxycodone
  - dihydrocodeine
  - papaveretum
  - morphine, combinations
  - oxycodone and naloxone
  - dihydrocodeine, combinations
codeine, combinations excl. psycholeptics
codeine, combinations with psycholeptics

N02AB Phenylpiperidine derivatives
  - ketobemidone
  - pethidine
  - fentanyl
  - pethidine, combinations excl. psycholeptics
  - pethidine, combinations with psycholeptics

N02AC Diphenylpropylamine derivatives
  - dextromoramide
  - pintramide
dextropropoxyphene
  - beztramide
  - methadone, combinations excl. psycholeptics
dextropropoxyphene, combinations excl. psycholeptics
dextropropoxyphene, combinations with psycholeptics

N02AF Morphinan derivatives
  - buprenorphine
  - nalbuphine
  - butorphanol

N02AD Benzomorphan derivatives
  - pentazocine
  - phenazocine

N02AE ORIPAVINE derivatives
  - buprenorphine
  - nalbuphine

N02AX Other opioids
  - buprenorphine
  - nalbuphine
  - butorphanol

N02AX01 buprenorphine
N02AX02 tramadol
N02AX03 dezocine
N02AX04 meptazinol
N02AX06 tapentadol

DDD values:
- buprenorphine: 12
- nalbuphine: 80
- butorphanol: 12
- tramadol: 6.2
- dezocine: 1.2
- meptazinol: 1.2
- tapentadol: 0.4
Where is codeine?

- Codeine is not listed (as a single-ingredient drug) under the main class N02A OPIOIDS.
Opioids in ICD-10

- Insufficient granularity for analyzing individual drugs (e.g., Fentanyl)
Illicit drugs

- Not covered by the clinical drug classification systems
- Alternative sources
  - National Forensic Laboratory Information System (NFLIS)
## NFLIS classification

<table>
<thead>
<tr>
<th>Categories/Subcategories</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analogesics</strong></td>
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<tr>
<td>Narcotic Analogesics</td>
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<tr>
<td>Antidepressants</td>
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<tr>
<td>Benzodiazepines</td>
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<td><strong>Cocaine Alkaloids</strong></td>
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<tr>
<td>Cocaine Alkaloids</td>
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<tr>
<td><strong>Depressants and Tranquilizers</strong></td>
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<td>Piperazines (Hallucinogen)</td>
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<td>Psychedelic</td>
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<tr>
<td>Synthetic Cannabinoids</td>
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<td>Synthetic Cathinones</td>
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<td>Synthetic Cathinones (Hallucinogen)</td>
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<tr>
<td>Tryptamines</td>
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<td>Heroin</td>
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</tbody>
</table>

**Grand Total:** 3867
Requirements and use cases

- If drug classification systems are the solution, what is the problem?

- **Use cases**
  - Drug-related mortality statistics
  - Others?

- **Requirements**
  - Drugs vs. substances
  - Granularity (coarse vs. fine-grained classes)
  - National vs. international
  - …
Medical Ontology Research

Contact: olivier@nlm.nih.gov
Web: https://mor.nlm.nih.gov

Olivier Bodenreider
Lister Hill National Center for Biomedical Communications
Bethesda, Maryland - USA