Processing Healthcare Data

Guest Lecture

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Disclaimer

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Outline

• Introduction to the Lister Hill National Center for Biomedical Communications
• Interoperability and biomedical terminologies
• Analyzing Opioid Prescriptions in Medicare
Introduction to the Lister Hill National Center for Biomedical Communications
National Library of Medicine

• Largest biomedical library in the world
• Started in 1836 as a small collection of medical books and journals in the office of the United States Army Surgeon General
• Part of the National Institutes of Health since 1962
• Flagship products and services (among many others)
  • PubMed/MEDLINE
  • ClinicalTrials.gov
  • Unified Medical Language System (UMLS)
National Library of Medicine

• Curating data, not just (dusty) books
  • Biomedical literature
  • Gene sequences
  • Clinical trials
  • Information for lay public
  • [...]

• Research, not just products and services
  • NLM Intramural Research program
    • Computational Biology – National Center for Biotechnology Information (NCBI)
    • Computational Health – Lister Hill National Center for Biomedical Communications
  • NLM Intramural Training program

• Extramural programs (grants)
Lister Hill National Center for Biomedical Communications (LHC)

• With NCBI, one of the two research & development centers of NLM
• Established in 1968
• Initially focused on biomedical communications
  • Communication networks applied to health
  • Audiovisual technologies in health applications
  • Use of new technologies for health education
• Current reorganization around health informatics
  • Clinical data science: Interoperable data, scalable methods and translation of discovery into operations
LHC within NLM and NIH (FY2020)

- **NIH**
  - $41.46 billion
  - 20,000 employees

- **NLM**
  - $456 million
  - 1700 employees

- **LHC**
  - $19 million (estimated)
  - 100 employees
4 research areas

- Health Data-Powered Discovery
- Health Information Standards
- Text Processing
- Image Processing
LHC research and development activities

• Natural Language Processing
  • Identifying biomedical concepts and relations in clinical text / literature
  • Clinical question answering

• Image processing
  • Application of machine learning/deep learning techniques to imaging datasets to support diagnostics

• Health information standards
  • Terminology standards (UMLS, SNOMED CT, MeSH, RxNorm, LOINC, …)
  • Information model standards (common data models, FHIR – Fast Healthcare Interoperability Resource)

• Health data-powered discovery
  • Getting insights from large observational databases (EHR and claims data)
LHC Postdoctoral Fellows

• N=86 (over the past 10 years)

• Demographics
  • 40% women, 60% men

• Career after leaving NLM
  • Academia (50%)
  • Industry (34%)
  • Other (16%)
Interoperability among biomedical terminologies
Many biomedical terminologies

• Different purposes
  • Clinical documentation – fine grained
  • Morbidity and mortality statistics – classification (avoid double-counting)
  • Indexing/retrieval – abstraction
  • Text mining – lexical variation

• Developed independently
  • Standard Development Organizations
  • No standard for developing standards
  • Different funding mechanisms
  • Different legacy products
Internal Classification of Diseases

IV Endocrine, nutritional and metabolic diseases
- E00-E07 Disorders of thyroid gland
- E10-E14 Diabetes mellitus
- E15-E16 Other disorders of glucose regulation and pancreatic internal secretion
- E20-E35 Disorders of other endocrine glands
  - E20 Hypoparathyroidism
  - E21 Hyperparathyroidism and other disorders of parathyroid gland
  - E22 Hyperfunction of pituitary gland
  - E23 Hypofunction and other disorders of pituitary gland
- E24 Cushing syndrome
- E25 Adrenogenital disorders
- E26 Hyperaldosteronism
- E27 Other disorders of adrenal gland
  - E27.1 Primary adrenocortical insulin deficiency
  - E27.2 Addisonian crisis
  - E27.3 Drug-induced adrenocortical insufficiency
  - E27.4 Other and unspecified adrenocortical insufficiency
  - E27.5 Adrenomedullary hyperfunction
  - E27.8 Other specified disorders of adrenal gland
  - E27.9 Disorder of adrenal gland, unspecified
- E28 Ovarian dysfunction
- E29 Testicular dysfunction
- E30 Disorders of puberty, not elsewhere classified
- E31 Polyglandular dysfunction
- E32 Diseases of thymus
- E34 Other endocrine disorders
- E35 Disorders of endocrine glands in diseases classified elsewhere

E27.0 Other adrenocortical overactivity
- Overproduction of ACTH, not associated with Cushing disease
- Premature adrenalectomy
  - Excl.: Cushing syndrome (E24-)

E27.1 Primary adrenocortical insufficiency
- Addison disease
- Autoimmune adrenals
  - Excl.: amyloidosis (E85-)
  - Tuberculous Addison disease (A18.7)
  - Waterhouse-Friderichen syndrome (A39.1)

E27.2 Addisonian crisis
- Adrenal crisis
- Adrenocortical crisis

E27.3 Drug-induced adrenocortical insufficiency
- Use additional external cause code (Chapter XX), if desired, to identify drug.

E27.4 Other and unspecified adrenocortical insufficiency
  - Adrenal:
    - haemorrhage
    - infarction
  - Adrenocortical insufficiency NOS
  - Hypoaldosteronism
  - Excl.: adenoleukodystrophy [Addison-Schilder] (E71.3)
    - Waterhouse-Friderichen syndrome (A39.1)

E27.5 Adrenomedullary hyperfunction
- Adrenomedullary hyperplasia
- Catecholamine hypersecretion

E27.8 Other specified disorders of adrenal gland
- Abnormality of cortisol-binding globulin

E27.9 Disorder of adrenal gland, unspecified
Medical Subject Headings

MeSH Tree Structures

**Endocrine System Diseases [C19]**
- Adrenal Gland Diseases [C19.053]
  - Adrenal Insufficiency [C19.053.500]
  - Addison Disease [C19.053.500.263]
  - Adrenoleukodystrophy [C19.053.500.270]
  - Hypoaldosteronism [C19.053.500.480]
  - Waterhouse-Friderichsen Syndrome [C19.053.500.740]

**Immune System Diseases [C20]**
- Autoimmune Diseases [C20.111]
  - Addison Disease [C20.111.163]
  - Anemia, Hemolytic, Autoimmune [C20.111.175]
  - Anti-Glomerular Basement Membrane Disease [C20.111.190]
  - Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis [C20.111.193]
  - Antiphospholipid Syndrome [C20.111.197]
  - Arthritis, Juvenile [C20.111.198]
  - Arthritis, Rheumatoid [C20.111.199]
  - Autoimmune Diseases of the Nervous System [C20.111.258] + [...]

15
Practical interoperability issues

• Data integration
  • Analyze datasets coded with different terminologies
    • Biomedical literature indexed with MeSH
      • Pancreatic neoplasm (D010190)
    • Healthcare utilization data (e.g., HCUP – Healthcare Cost and Utilization Project) coded with Clinical Classifications Software (CCS)
      • Cancer of pancreas (17)
  • Using a specific terminology to aggregate data
    • Drugs coded with [A]NDA ([Abbreviated] New Drug Application) or NDC (National Drug Code)
    • Analysis based on the ATC (Anatomical-Therapeutic-Chemical) drug classification
Degrees of semantic interoperability

- **Synonymy**
  - Equivalence between terms (or concepts)
  - Myocardial infarction ↔ Heart attack

- **Mapping**
  - Closest term for the source term in the target terminology
  - Lipitor → Atorvastatin

- **Closest ancestor**
  - Closest term in the target terminology among the ancestors in the source
  - Pancreatic cancer → Pancreatic neoplasm

- **Post-coordination**
  - One term equivalent to the combination of several terms in the target terminology
  - Diabetic nephropathy → Nephropathy + Diabetes mellitus
Integrating datasets

Clinical repositories

Genetic knowledge bases

Other subdomains

UMLS

Biomedical literature

Model organisms

SNOMED CT

Genome annotations

OMIM

MeSH

FMA

GO

NCBI Taxonomy

Anatomy
Point-to-point mappings are impractical
Integration through a reference (e.g., UMLS)

Addison's disease (363732003)

Clinical repositories

SNOMED CT

OMIM

Genetic knowledge bases

Biomedical literature

Addison Disease (D000224)

Other subdomains

NCBI Taxonomy

Model organisms

FMA

GO

Anatomy

Genome annotations

Addison's disease (363732003)
Semantic interoperability through UMLS

• Synonymy
  • *Synonymous terms clustered into the same ULMS concept*
  • Myocardial infarction ↔ Heart attack

• Mapping
  • *Existing mapping tables integrated into UMLS (e.g., ICD10 to SNOMED CT)*
  • Lipitor → Atorvastatin

• Closest ancestor
  • *Hierarchical relations are recorded in UMLS and can be navigated*
  • Pancreatic cancer → Pancreatic neoplasm

• Post-coordination
  • *Logical definitions for concepts re recorded in UMLS (whenever available)*
  • Diabetic nephropathy → Nephropathy + Diabetes mellitus
Pancreatic cancer → Pancreatic neoplasm

Legend
- UMLS
- MeSH
- SNOMED CT
- CCS

C030297
- Pancreatic Neoplasms [D010190]
- Neoplasm of pancreas [126859007]

C0346647
- Malignant tumor of pancreas [363418001]
- Pancreatic cancer [17]
Analyzing Opioid Prescriptions in Medicare
Medicare Part D dataset

• Main variables in the Drug Event File
  • Beneficiary information (ID and demographics)
  • Date on which the prescription was filled
  • Drug: identified by NDC (11-digit format)
  • Quantity Dispensed
  • Days Supply
  • Cost information

• Related information for the NDC (provided by First Databank)
  • Brand name, generic name, strength, dosage form code, and dosage form description
Use case: Analysis of opioid prescriptions

- Identify prescriptions corresponding to opioids in the Medicare part D dataset
- For each opioid drug, calculate the trend of dispensation over time ("number of prescriptions")
- For all opioids, calculate the trend of total (or daily) dose dispensed in oral morphine milligram equivalents
Analysis of opioid prescriptions – How to?

• Identify prescriptions corresponding to opioids in the Medicare part D dataset
  • Use ATC classes to identify opioid drugs
  • Link NDC codes (Medicare) to ATC codes through RxNorm
• For each opioid drug, calculate the trend of dispensation over time ("number of prescriptions")
• For all opioids, calculate the trend of total (or daily) dose dispensed in oral morphine milligram equivalents
Identifying opioid drugs from a drug class

• ATC – Anatomical Therapeutic Chemical drug classification system

<table>
<thead>
<tr>
<th>ATC code</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>N02AA01</td>
<td>morphine</td>
</tr>
<tr>
<td>N02AA02</td>
<td>opium</td>
</tr>
<tr>
<td>N02AA03</td>
<td>hydromorphone</td>
</tr>
<tr>
<td>N02AA04</td>
<td>nicomorphine</td>
</tr>
<tr>
<td>N02AA05</td>
<td>oxycodone</td>
</tr>
<tr>
<td>N02AA08</td>
<td>dihydrocodeine</td>
</tr>
<tr>
<td>N02AA10</td>
<td>papaveretum</td>
</tr>
<tr>
<td>N02AA51</td>
<td>morphine, combinations</td>
</tr>
<tr>
<td>N02AA53</td>
<td>hydromorphone and naloxone</td>
</tr>
<tr>
<td>N02AA55</td>
<td>oxycodone and naloxone</td>
</tr>
<tr>
<td>N02AA56</td>
<td>oxycodone and naltrexone</td>
</tr>
<tr>
<td>N02AA58</td>
<td>dihydrocodeine, combinations</td>
</tr>
<tr>
<td>N02AA59</td>
<td>codeine, combinations excl. psycholeptics</td>
</tr>
<tr>
<td>N02AA79</td>
<td>codeine, combinations with psycholeptics</td>
</tr>
</tbody>
</table>
Linkages among drug entities

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]

59011041010

59011-410-10
Why converting to MME?

- Opioids have widely different potency levels
  - Fentanyl is about 100 times more potent than morphine

- Difficult to
  - Compare doses across drugs
  - Compare doses over time for multiple drugs
  - Aggregate results

- Reference: 1 mg of morphine administered orally

- Use case: How do these two drugs compare?
  - 12 HR OxyCONTIN 10 MG Extended Release Oral Tablet (twice a day)
  - 72 HR fentaNYL 0.012 MG/HR Transdermal System
MME conversion factor

- Conversion factor for each drug
  - Available from CMS
  - Compiled from CDC data

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### Opioid Oral Morphine Milligram Equivalent (MME) Conversion Factors

<table>
<thead>
<tr>
<th>Type of Opioid (strength units)</th>
<th>MME Conversion Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine film/tablet (mg)</td>
<td>30</td>
</tr>
<tr>
<td>Buprenorphine patch (mcg/hr)</td>
<td>12.6</td>
</tr>
<tr>
<td>Buprenorphine film (mcg)</td>
<td>0.03</td>
</tr>
<tr>
<td>Butorphanol (mg)</td>
<td>7</td>
</tr>
<tr>
<td>Codeine (mg)</td>
<td>0.15</td>
</tr>
<tr>
<td>Dihydrocodeine (mg)</td>
<td>0.25</td>
</tr>
<tr>
<td>Fentanyl buccal or SL tablets, or lozenge/troche (mcg)</td>
<td>0.13</td>
</tr>
<tr>
<td>Fentanyl film or oral spray (mcg)</td>
<td>0.18</td>
</tr>
<tr>
<td>Fentanyl nasal spray (mcg)</td>
<td>0.16</td>
</tr>
<tr>
<td>Fentanyl patch (mcg)</td>
<td>7.2</td>
</tr>
<tr>
<td>Hydrocodone (mg)</td>
<td>1</td>
</tr>
<tr>
<td>Hydromorphone (mg)</td>
<td>4</td>
</tr>
</tbody>
</table>

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### Opioid Conversion Factors

<table>
<thead>
<tr>
<th>Opioid</th>
<th>MME Conversion Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levorphanol tartrate (mg)</td>
<td>11</td>
</tr>
<tr>
<td>Meperidine hydrochloride (mg)</td>
<td>0.1</td>
</tr>
<tr>
<td>Methadone (mg)</td>
<td>3</td>
</tr>
<tr>
<td>&gt;0, &lt;= 20</td>
<td>4</td>
</tr>
<tr>
<td>&gt;20, &lt;=40</td>
<td>8</td>
</tr>
<tr>
<td>&gt;40, &lt;=60</td>
<td>10</td>
</tr>
<tr>
<td>&gt;60</td>
<td>12</td>
</tr>
<tr>
<td>Morphine (mg)</td>
<td>1</td>
</tr>
<tr>
<td>Opium (mg)</td>
<td>1</td>
</tr>
<tr>
<td>Oxycodone (mg)</td>
<td>1.5</td>
</tr>
<tr>
<td>Oxymorphone (mg)</td>
<td>3</td>
</tr>
<tr>
<td>Pentazocine (mg)</td>
<td>0.37</td>
</tr>
<tr>
<td>Tapentadol (mg)</td>
<td>0.4</td>
</tr>
<tr>
<td>Tramadol (mg)</td>
<td>0.1</td>
</tr>
</tbody>
</table>

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Example #1

• Drug: NDC = 59011041010
  • 12 HR OxyCONTIN 10 MG Extended Release Oral Tablet [1049504]
  • Ingredient: Oxycodone
  • Strength: 10 MG

• Dispensation information
  • Quantity Dispensed: 20
  • Days Supply: 10

• MME conversion factor: 1.5

\[
MME(mg) = 10 \times \frac{20}{10} \times 1.5 = 30 \, mg
\]

• MME/day:
Medicare data

Annual prescribing rate
[among opioid patients]