MedDRA Coding, Analysis, and Mappings with Other Terminologies
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MedDRA Coding, Analysis, and Mappings with Other Terminologies

Topics

• MedDRA terminology introduction
• Coding with MedDRA
• Analyzing and presenting MedDRA-coded data
• Mapping of MedDRA and other terminologies

MedDRA Terminology Introduction
MedDRA Definition

MedDRA is a clinically-validated international medical terminology used by regulatory authorities and the regulated biopharmaceutical industry. The terminology is used through the entire regulatory process, from pre-marketing to post-marketing, and for data entry, retrieval, evaluation, and presentation.

MedDRA Scope

IN
- Diseases
- Diagnoses
- Signs
- Symptoms
- Therapeutic indications
- Investigation names & qualitative results
- Medical & surgical procedures
- Medical, social, family history
- Medication errors
- Product quality, device issues
- Terms from other terminologies

OUT
- Frequency qualifiers
- Numerical values for results
- Severity descriptors
- Not an equipment, device, diagnostic product dictionary
- Not a drug dictionary
- Patient demographic terms
- Clinical trial study design terms
- Terms from other terminologies
Which of these concepts can be coded using MedDRA?

<table>
<thead>
<tr>
<th>Concept</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contraception</td>
</tr>
<tr>
<td>Quadruple bypass</td>
</tr>
<tr>
<td>Grade 3</td>
</tr>
<tr>
<td>Social drinking</td>
</tr>
<tr>
<td>High potassium</td>
</tr>
<tr>
<td>Flutter valve device</td>
</tr>
<tr>
<td>Injection site pain</td>
</tr>
<tr>
<td>Off-label use</td>
</tr>
<tr>
<td>Abnormal MRI</td>
</tr>
<tr>
<td>Pharmacist dispensed wrong medication</td>
</tr>
<tr>
<td>Amoxicillin</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Hyperactive reflexes</td>
</tr>
<tr>
<td>Amoxicillin</td>
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</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Hyperactive reflexes</td>
</tr>
</tbody>
</table>
MedDRA Structure

- **Five-level hierarchy**

  - 系统器官分类 (SOC) (26)
  - 高位组语 (HLGT) (335)
  - 高位语 (HLT) (1,713)
  - 首选语 (PT) (19,737)
  - 低位语 (LLT) (70,634)

  **Version 15.1**

  - **SOC** = 心脏器官疾病
  - **HLGT** = 心律失常类疾病
  - **HLT** = 心率和节律异常（不另分类）
  - **PT** = 心律不齐
  - **LLT** = 心脏节律障碍

Non-current Terms

- Non-current terms are flagged at the LLT level within MedDRA
- Not recommended for continued use
- Retained within the terminology to preserve historical data for retrieval and analysis
- Terms that are vague, ambiguous, out-dated, truncated, or misspelled
- Terms derived from other terminologies that do not fit MedDRA rules
MedDRA SOCs

- 26 System Organ Classes (SOCs)

  - 血液及淋巴系统疾病
  - 心脏器官疾病
  - 各种先天性家族性遗传性疾病
  - 耳及迷路类疾病
  - 内分泌系统疾病
  - 眼器官疾病
  - 胃肠系统疾病
  - 全身性疾病及给药部位各种反应
  - 肝胆系统疾病
  - 免疫系统疾病
  - 感染及侵染类疾病
  - 各类损伤、中毒及手术并发症
  - 各类检查
  - 代谢及营养类疾病
  - 各种肌肉骨骼及结缔组织疾病
  - 良性、恶性及性质不明的肿瘤（包括囊状和息肉状）
  - 各类神经系统疾病
  - 妊娠期、产褥期及围产期状况
  - 精神病类
  - 肾脏及泌尿系统疾病
  - 生殖系统及乳腺疾病
  - 呼吸系统、胸及纵隔疾病
  - 皮肤及皮下组织类疾病
  - 社会环境
  - 各种手术及医疗操作
  - 血管与淋巴管疾病

MedDRA Code

- MedDRA code: 8-digit non-expressive numeric code

![Diagram of MedDRA Code](image)
Coding with MedDRA

Why Do We Code?

• Because we want to sort AE data in order to
  o Retrieve
  o Present
  o Analyze
  o Communicate
Role of MedDRA In Coding

• To provide a structured sorting system

Patient information related to drug use: “贫血”, “腹泻”, “肝硬化”, “急性肾炎”

编码

不良反应报告

MedDRA Coding, Analysis, and Mappings with Other Terminologies

Role of MedDRA In Coding (cont)

• Size and specificity ("granularity")
  ○ PT “心脏疾病”, PT “三尖瓣狭窄”

• Hierarchy/grouping terms

• “Support” SOCs widen data collection/analysis options

• Up-to-date and medically rigorous

• User-responsive

• STANDARDIZATION
Why Do We Need Coding Conventions?

• Differences in medical aptitude of coders
• Consistency concerns (many more “choices” to manually code terms in MedDRA compared to older terminologies)
• Even with an autoencoder, will still need manual coding

Why Do We Need Coding Conventions?

• Do you know:

<table>
<thead>
<tr>
<th>Reported</th>
<th>LLT Selected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lip sore</td>
<td>Lip sore (PT Lip pain)</td>
</tr>
<tr>
<td>Lip sores</td>
<td>Sores lip (PT Cheilitis)</td>
</tr>
<tr>
<td>Sore gums</td>
<td>Sore gums (PT Gingival pain)</td>
</tr>
<tr>
<td>Sores gum</td>
<td>Sores gum (PT Gingival inflammation)</td>
</tr>
</tbody>
</table>

From “MedDRA Term Selection: Points to Consider Document” Release 4.4
ICH-Endorsed Guides for Users

• Developed and maintained by an ICH Expert Working Group
  - Updated with each release of MedDRA

• Current versions available on
  - MSSO web site: http://www.meddrasso.com/subscriber_library_ptc.asp
  - ICH: http://www.icc.org/products/meddra/meddraptc.html

• To promote the standard use of MedDRA: two Points to Consider (PTC) documents
  - MedDRA Term Selection: PTC
  - MedDRA Data Retrieval and Presentation: PTC

ICH-Endorsed Guides for Users (cont)

• Both PTC documents emphasize
  - Quality of Source Data
    - Quality of reporting data
      - Report – “Congestion”, but where? Nasal, pulmonary, or intestine?
    - Quality of data converted from a legacy database
  - Do Not Alter MedDRA
    - MedDRA is a standardized terminology with a pre-defined term hierarchy
    - Users must not make ad hoc structural alterations, including changing the primary SOC allocation
    - If terms are incorrectly placed, submit a change request to the MSSO
MedDRA Term Selection: PTC

- An ICH-endorsed MedDRA coding guide
  - Section 4.1 – Versioning (Appendix)
    - 4.1.1 Versioning methodologies
    - 4.1.2 Timing of version implementation

- CDISC Analysis Data Model (ADaM) Data Structure for Adverse Event Analysis (May 2012)
  - Recommended that coding rules and guidelines be developed when using coding dictionaries for AEs
  - The metadata for each coding variable should include both the name and version of the dictionary

MedDRA Term Selection: PTC

- **Always Select a Lowest Level Term**
  - Lowest Level Term that most accurately reflects the reported verbatim information should be selected
  - Degree of specificity may be challenging
    - Example: “Abscess on face” → select “Facial abscess” (面部脓肿), not simply “Abscess” (脓肿)
MedDRA Term Selection: PTC

• Term Selection Points
  o Diagnoses and Provisional Diagnoses with or without Signs and Symptoms
  o Death and Other Patient Outcomes
  o Suicide and Self-Harm
  o Conflicting/Ambiguous/Vague Information
  o Combination Terms
  o Age vs. Event Specificity
  o Body Site vs. Event Specificity
  o Location Specific vs. Microorganism Specific Information
  o Modification of Pre-existing Conditions
  o Exposures During Pregnancy and Breast Feeding
  o Congenital Terms
  o Neoplasms
  o Medical and Surgical Procedures

• Term Selection Points
  o Investigations
  o Medication/Administration Errors and Accidental Exposures
  o Transmission of Infectious Agent via Medicinal Product
  o Overdose, Toxicity and Poisoning
  o Device-related Terms
  o Drug Interactions
  o No Adverse Effect and “Normal” Terms
  o Unexpected Therapeutic Effect
  o Modification of Effect
  o Social Circumstances
  o Medical and Social History
  o Indication for Product Use
  o Off Label Use
  o Product Quality Issues
FDA-Defined Coding Errors

- Missed Concepts
  - All medical concepts described after the product is taken should be coded
  - Example: “The patient took drug X and developed alopecia, increased LFTs and pancreatitis”. Manufacturer only codes alopecia and increased LFTs (missed concept of pancreatitis)
  - Example: “The patient took drug X and developed interstitial nephritis which later deteriorated into renal failure”. Manufacturer only codes interstitial nephritis (missed renal failure concept)

Acknowledgement: Dr. Toni Piazza-Hepp, Office of Surveillance and Epidemiology, CDER, FDA

FDA-Defined Coding Errors (cont)

- “Soft Coding”
  - Selecting a term which is both less specific and less severe than another MedDRA term is “soft coding”
  - Example: “Liver failure” coded as hepatotoxicity or increased LFTs
  - Example: “Aplastic anemia” coded as unspecified anemia
  - Example: “Rash subsequently diagnosed as Stevens Johnson syndrome” coded as rash

Acknowledgement: Dr. Toni Piazza-Hepp, Office of Surveillance and Epidemiology, CDER, FDA
Analyzing and presenting MedDRA-coded data

MedDRA Analysis Features

• Multi-axial (多轴性) = the representation of a medical concept in multiple SOCs
  o Allows grouping by different classifications
  o Allows retrieval and presentation via different data sets

• One of the associations is primary (主); all others are secondary (次)
MedDRA Analysis Features (cont)

• **Multi-axial (多轴性)**

  SOC = 呼吸系统，胸及纵隔疾病
  
  HLT = 各种病毒性呼吸道感染
  
  HLT = 流行性病毒感染
  
  PT = 流行性感冒

  SOC = 感染及侵染类疾病
  
  HLT = 流行性病毒感染

MedDRA Analysis Features (cont)

• 主 SOC Allocation Priority

  1st: 各种先天性家族性遗传性疾病
  
  2nd: 良性、恶性及性质不明的肿瘤（包括囊状和息肉状）
  
  3rd: 感染及侵染类疾病
  
  4th: 主要发病部位
MedDRA Analysis Features (cont)

• 多轴性和 主SOC – an example

不良反应报告


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不良反应报告


MedDRA Coding, Analysis, and Mappings with Other Terminologies

不良反应报告
MedDRA Granularity

<table>
<thead>
<tr>
<th>Other Terminology Preferred Terms</th>
<th>No. of Events</th>
<th>MedDRA Version 15.0 Preferred Terms</th>
<th>No. of Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>INFECTION</td>
<td>15</td>
<td>Upper respiratory tract infection (上呼吸道感染)</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nasopharyngitis (鼻咽炎)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infection (感染)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower respiratory tract infection (下呼吸道感染)</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Skin infection (皮肤感染)</td>
<td>1</td>
</tr>
</tbody>
</table>

MedDRA Hierarchy

- Five levels
  - 系统器官分类 (SOC) (26)
  - 高位组语 (HLGT) (335)
  - 高位语 (HLT) (1,713)
  - 首选语 (PT) (19,737)
  - 低位语 (LLT) (70,634)

Version 15.1
Use of MedDRA at FDA

Acknowledgement: Dr. Chuck Cooper, Office of Translational Sciences, CDER, FDA

Use of MedDRA at FDA (cont)

Acknowledgement: Dr. Chuck Cooper, Office of Translational Sciences, CDER, FDA
Definition of SMQ

- SMQs – MedDRA Analytical tools
- Groupings of terms from one or more MedDRA System Organ Classes (SOCs) related to defined medical condition or area of interest
- Included terms may relate to signs, symptoms, diagnoses, syndromes, physical findings, laboratory and other physiologic test data, etc., related to medical condition or area of interest
- Intended to aid in case identification
SMQ in Production – Examples

- As of Version 15.1, a total of 87 in production
  - 粒细胞缺乏症
  - 过敏性反应
  - 脑血管疾病
  - 惊厥
  - 抑郁症和自杀/自伤
  - 肝脏疾病
  - 缺血性心脏病
  - 缺乏疗效/效果
  - 周围神经病变
  - 妊娠和新生儿主题
  - 伪膜性结肠炎
  - 横纹肌溶解症/肌病
  - 严重的皮肤不良反应
  - 系统性红斑狼疮

How to “Run” SMQs

- How to use the SMQ to identify case of interest
Use of SMQ at FDA

Acknowledgement: Dr. Chuck Cooper, Office of Translational Sciences, CDER, FDA
Use of SMQ at FDA (cont)

Mapping of MedDRA and Other Terminologies

Acknowledgement: Dr. Chuck Cooper, Office of Translational Sciences, CDER, FDA
Interoperability For Communication

• To improve the quality of patient care requires
  o Communication between the government agency and regulated industry (insurance industry, pharmaceutical industry…)
  o Communication among government agencies

• 2007, HL-7 Interoperability Work Group defined the types of interoperability
  o Technical interoperability
  o Semantic interoperability
    - Use of controlled terminology
    - Defined metadata
  o Process interoperability

Interoperability For Communication (cont)

• Terminologies used in healthcare
  o MedDRA
  o WHOART
  o CTCAE
  o ICD
  o SNOMED

• Mapping – connects one terminology to another
MedDRA and CTCAE

- National Cancer Institute (NCI) - Common Terminology Criteria for Adverse Events (CTCAE)
  - List of AE terms with grading scale
  - Widely used in oncology and HIV clinical research
    - Protocol design
    - Comparative analysis
- CTCAEv3.0 to MedDRA (LLT) mapping
  - Last update in MedDRA v11.0
    (http://meddramsso.com/subscriber_download.asp)
- CTCAEv4.0 uses MedDRA LLTs as its AE terms
  - No need for mapping between CTCAE and MedDRA

MedDRA and WHO-ART

- As of March 2008, MedDRA has been implemented in WHO’s Global Safety Database (Vigibase)
  - WHO National Centres can review data and conduct analyses in both WHO-ART and MedDRA
    - Data can be sent/entered in either MedDRA or WHO-ART
    - Reports generated in either MedDRA or WHO-ART
- With Vigibase containing >7 million ICSRs, it now provides a global repository of MedDRA-coded safety data:
  - Substantial tool for pharmacovigilance
  - Of significant benefit to global patient safety
MedDRA and WHO-ART (cont)

- WHO Uppsala Monitoring Centre (UMC) has developed with ICH/MSSO a “bridge” for mapping from WHO-ART to MedDRA:
  - Allows conversion of legacy data from WHO-ART to MedDRA
  - Maintained current with every version release of WHO-ART and MedDRA
  - Does not work in the other direction since MedDRA is more granular than WHO-ART
  - Updated annually
  - Most recent update – WHO-ART121 to MedDRA v15.0
    - 2178 WHO-ART PTs
    - 92% string match with MedDRA LLT

- WHO UMC receives most of ICSRs coded in MedDRA

MedDRA and ICD

- The ICH MedDRA Management Board considers interest from MedDRA users for mappings with other terminologies, such as ICD, SNOMED CT...

- The ICH MedDRA Management Board has tasked the MSSO to identify the business case for an ICD-10 to MedDRA mapping and investigate the feasibility of such a mapping
MedDRA and ICD (cont)

- ICD-10 to MedDRA mapping
  - Identification of use case
    - Drug safety analysis using Electronic Health Record (EHR) data
    - Epidemiology study
  - Feasibility study of the mapping scope
    - ICD-10 core
      - US modification: ICD-10-CM
      - German modification: ICD-10-GM
      - Australia modification: ICD-10-AM
      - Canadian modification
      - Thailand modification
    - ICD level
      - 3-character
      - 4 character

MedDRA and ICD (cont)

- ICD-10 and MedDRA mapping
  - Feasibility study of the mapping method
    - Existing ICD-9-CM to MedDRA mapping in OMOP database
    - ICD-9-CM to ICD-10 crosswalks
    - Manual mapping
    - Quality assurance
MedDRA and SNOMED CT

- In the UK, SNOMED is used for Electronic Health Records (EHRs)
- A mapping helps to convert EHR to MedDRA-coded data
- The UK Regulator, MHRA - a member of the ICH MedDRA Management Board, is developing a SNOMED CT to MedDRA mapping (*MSSO providing support*)
  - Will be limited to subset = SNOMED CT concept types:
    - Events
    - Findings
    - Procedures
    - Observable entities
    - Situations
- ICH acknowledges that the experience of the UK MHRA will be of benefit to the broader MedDRA user community in the future

Acknowledgement: Mr. Mick Foy, MHRA

谢谢!