



MedDRA

What Makes a High-quality Report of Adverse Event: *from MedDRA Coding Perspective*

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MedDRA MSSO





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MedDRA

Overview

- Importance of good quality data
- How clinical data are coded
- MedDRA overview
- Company-specific conventions
- Benefits of good quality data
- How to improve data entry quality?





MedDRA

Importance of good quality data





What is Meant by Good Quality Data?

- Complete
- Accurate
- Diagnosis supported by appropriate investigations
- Causality assessment for adverse events





MedDRA

Quality of Input = Quality of Output

IN



OUT





Quality of Serious Adverse Event (SAE) Reporting in Clinical Trials

- Study finds frequent errors in SAE reports to academic trial sponsors
 - Event verbatim inconsistent with report: 15%
 - Patient outcome not reported: 12.1%
 - Investigational product not identified: 11.2%
 - No causality assessment reported: 9.3%
 - Event seriousness unknown: 3.6%
- Study authors: Knowledge of MedDRA basics and coding practices key to data accuracy and completeness

Crepin S, Villeneuve C, Merle L. Quality of serious adverse events reporting to academic sponsors of clinical trials: far from optimal. Poster at 18th Annual Meeting of French Society of Pharmacology and Therapeutics; 2014 April 22-24, Poitiers, France.



How clinical data are coded





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What is Coding?

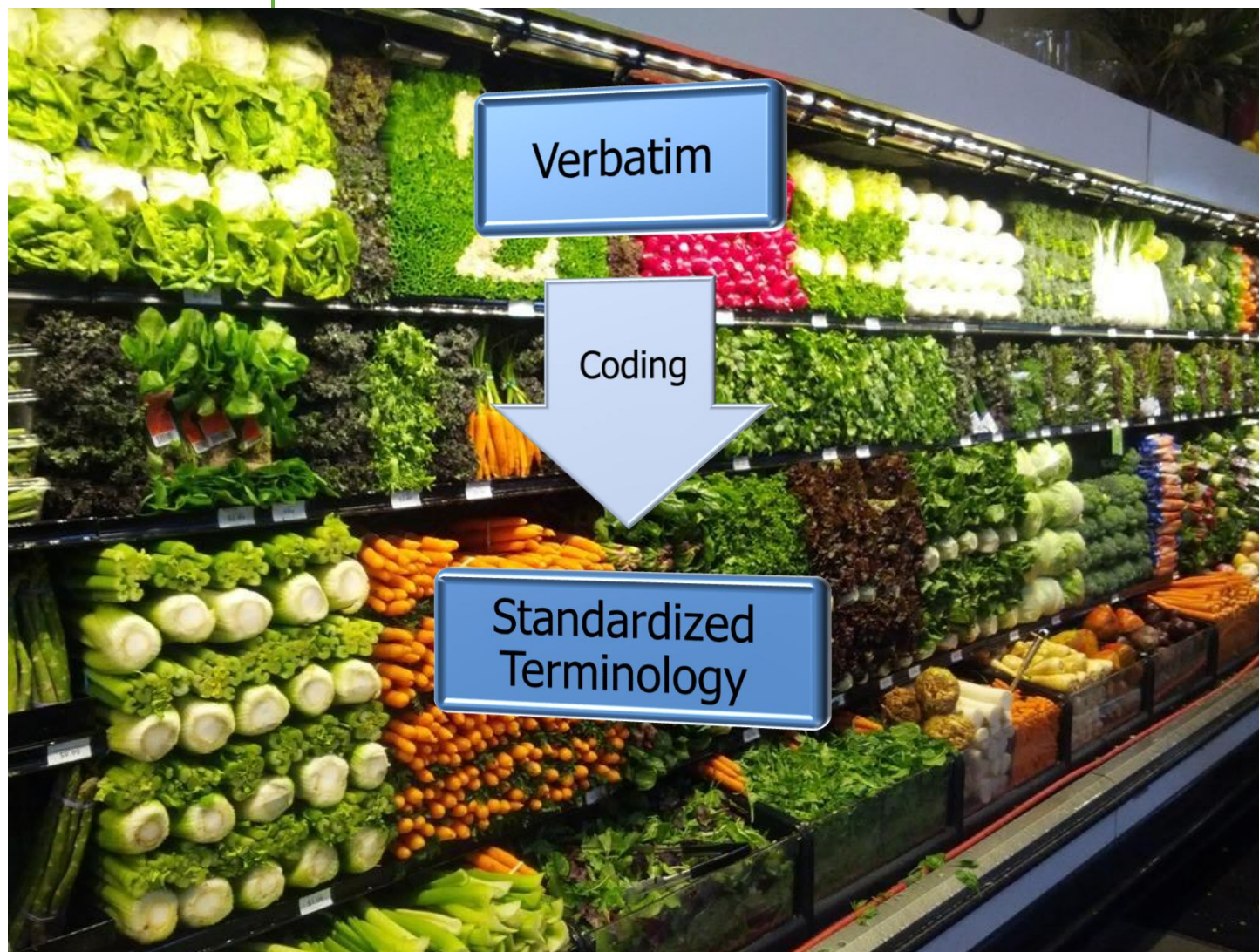


表2.AURA^a研究期间报告的不良反应

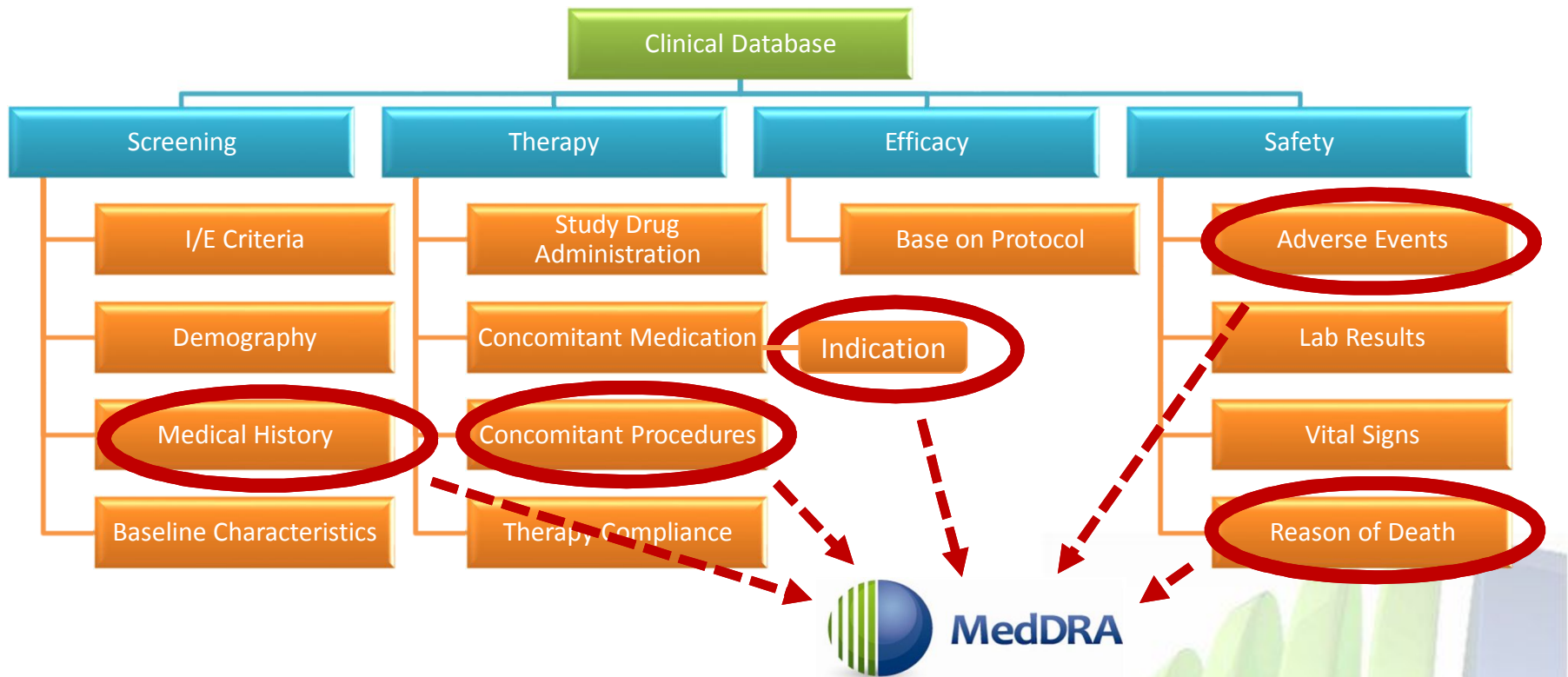
MedDRA SOC	MedDRA术语	CIOMS分类/总体频率 (所有CTCAE分级) ^b	3级或3级以上的 CTCAE的频率
呼吸、胸部及纵膈 系统疾病	间质性肺病 ^c	常见 (3.2%) ^d	1.3%
胃肠道疾病	腹泻	极常见 (44%)	1.0%
	口腔炎	极常见 (15%)	0%
眼部疾病	角膜炎 ^e	少见 (0.9%)	0%
皮肤及皮下组 织疾病	皮疹 ^f	极常见 (41%)	0.7%
	皮肤干燥 ^g	极常见 (29%)	0%
	甲沟炎 ^h	极常见 (27%)	0%
	瘙痒 ⁱ	极常见 (15%)	0%
辅助检查	QTc间期延长 ^j	少见(0.7%)	
(依据检验结 果确定,并按 CTCAE级别的变 化情况给出)	血小板计数下降 ^k	极常见 (54%)	2.1%
	白细胞减少 ^k	极常见 (66%)	2.4%
	中性粒细胞减少 ^k	极常见 (32%)	4.3%

^a 表中所列的数据均为III期(AURA3)和II期(AURAex和AURA 2)研究中累积获得的数据;仅对至少服用了1次本品的患者所发生的不良事件进行统计。



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Data to be Coded in a Case Report Form





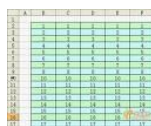
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Coding in Clinical Trials

Study Design



Protocol



Case Report Form



Technical Designer



Database

Study Conduct



Query



Query



Coder



Data Manager

SAE Reconciliation



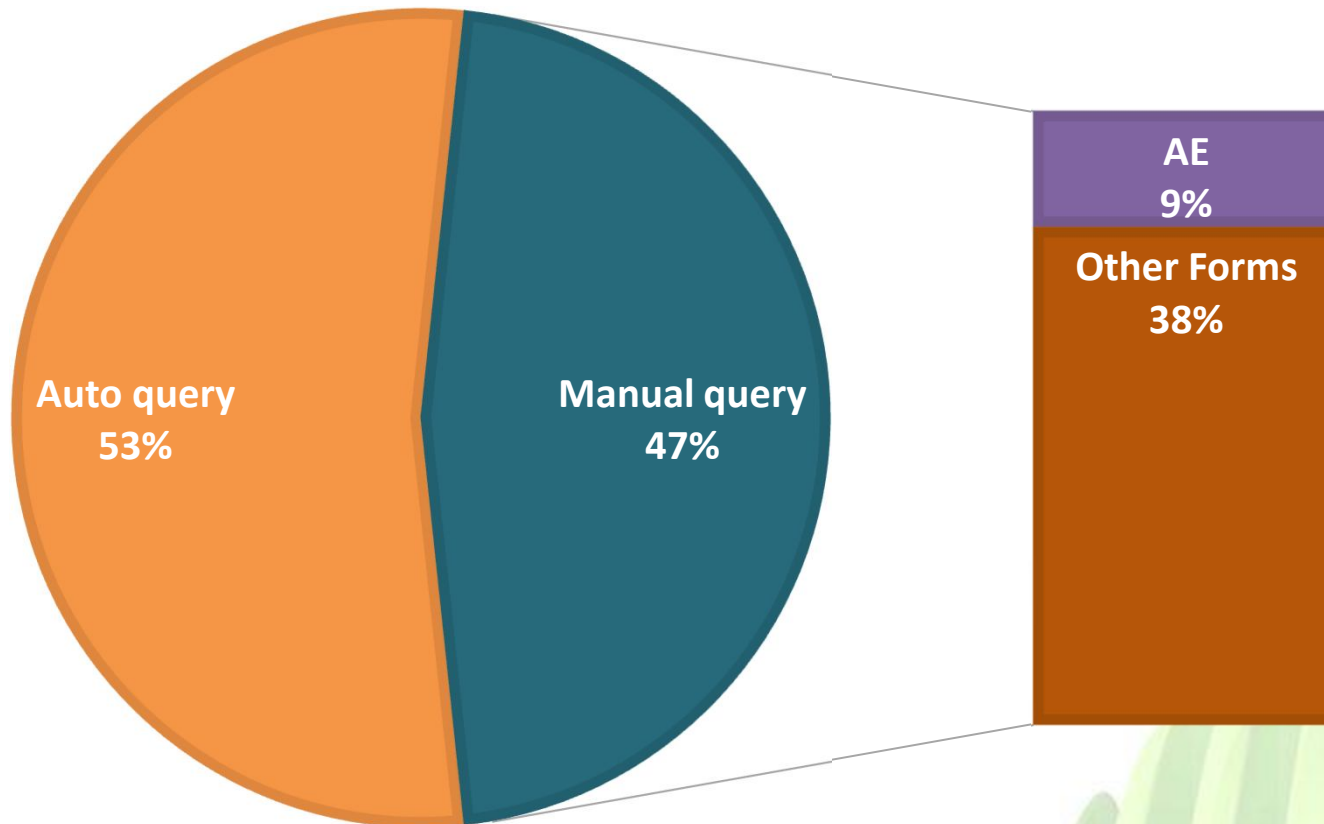
Pharmacovigilance



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How many queries on AE form?

NUMBER OF QUERIES IN A CLINICAL STUDY

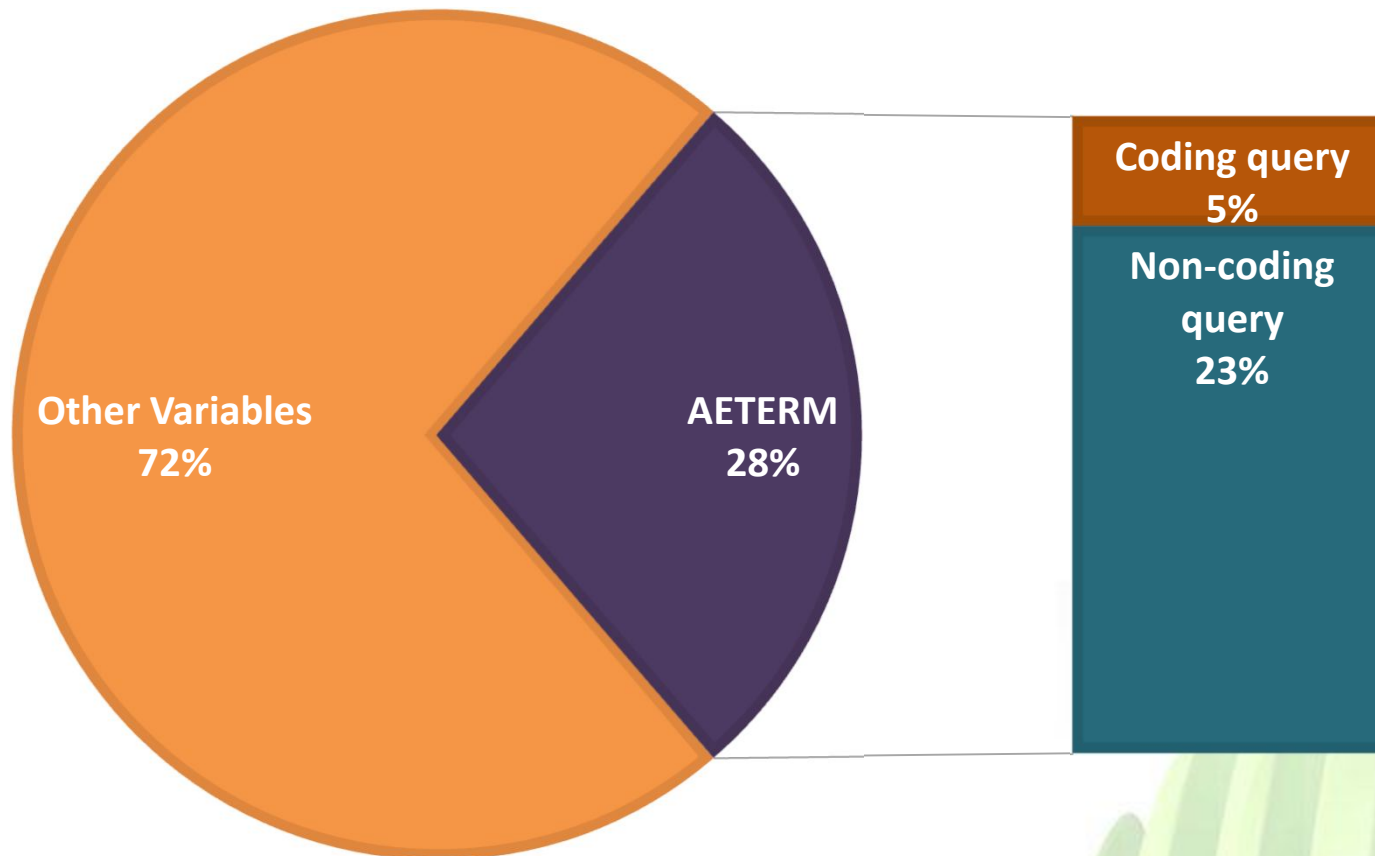




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How many coding queries for AE Term?

NUMBER OF QUERIES IN AN ADVERSE EVENT FORM





MedDRA overview





MedDRA

What is MedDRA?

Med = Medical

D = Dictionary for

R = Regulatory

A = Activities




《监管活动医学词典》





MedDRA

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 of MedDRA

OUT
IN

Not a drug dictionary

Frequency qualifiers

Patient demographic terms

Medical conditions
Indications
Investigations (tests, results)
Medical and surgical procedures
Medical, social, family history
Medication errors
Product quality issues
Device-related issues
Product use issues
Pharmacogenetic terms
Toxicologic issues
Standardized queries

Numerical values for results

Clinical trial study design terms

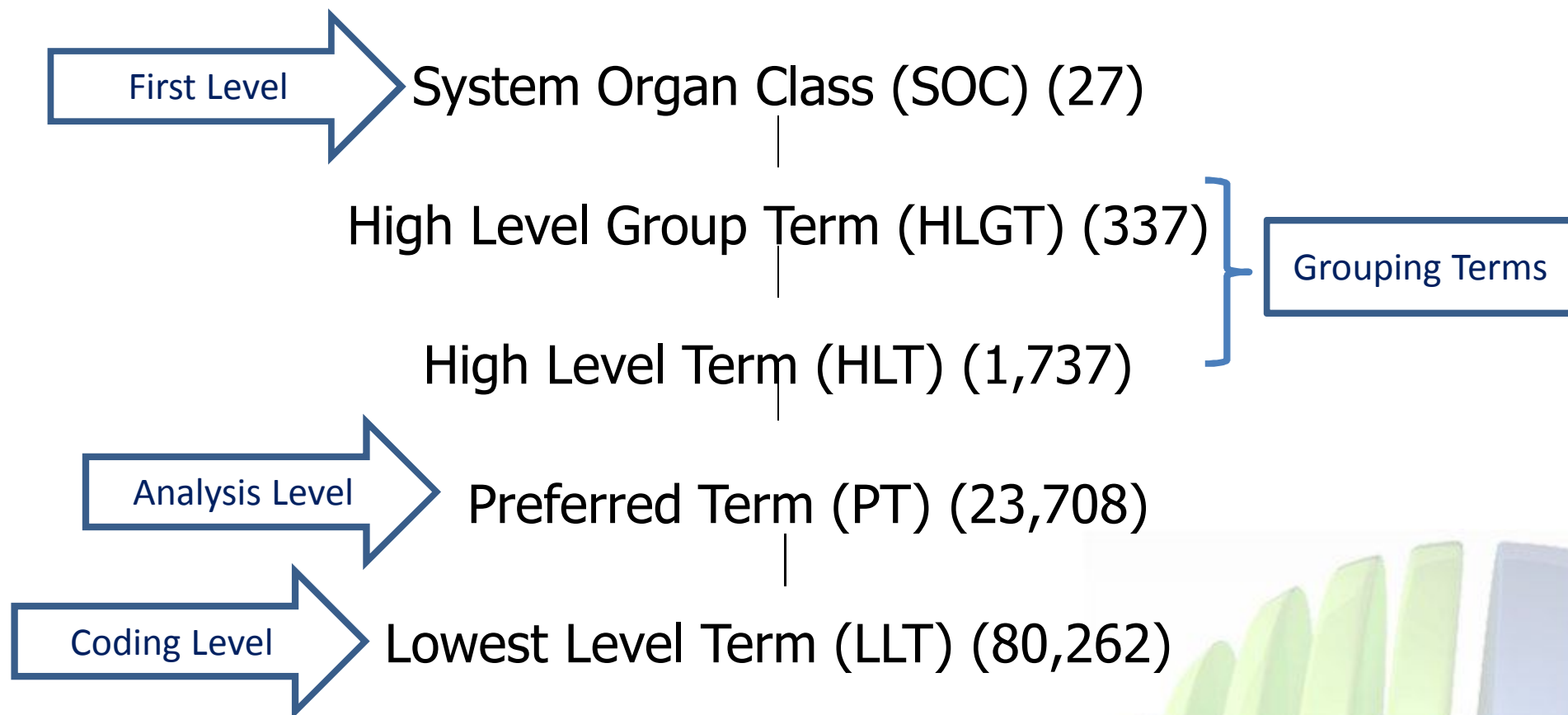
Severity descriptors

Not an equipment, device, diagnostic product dictionary



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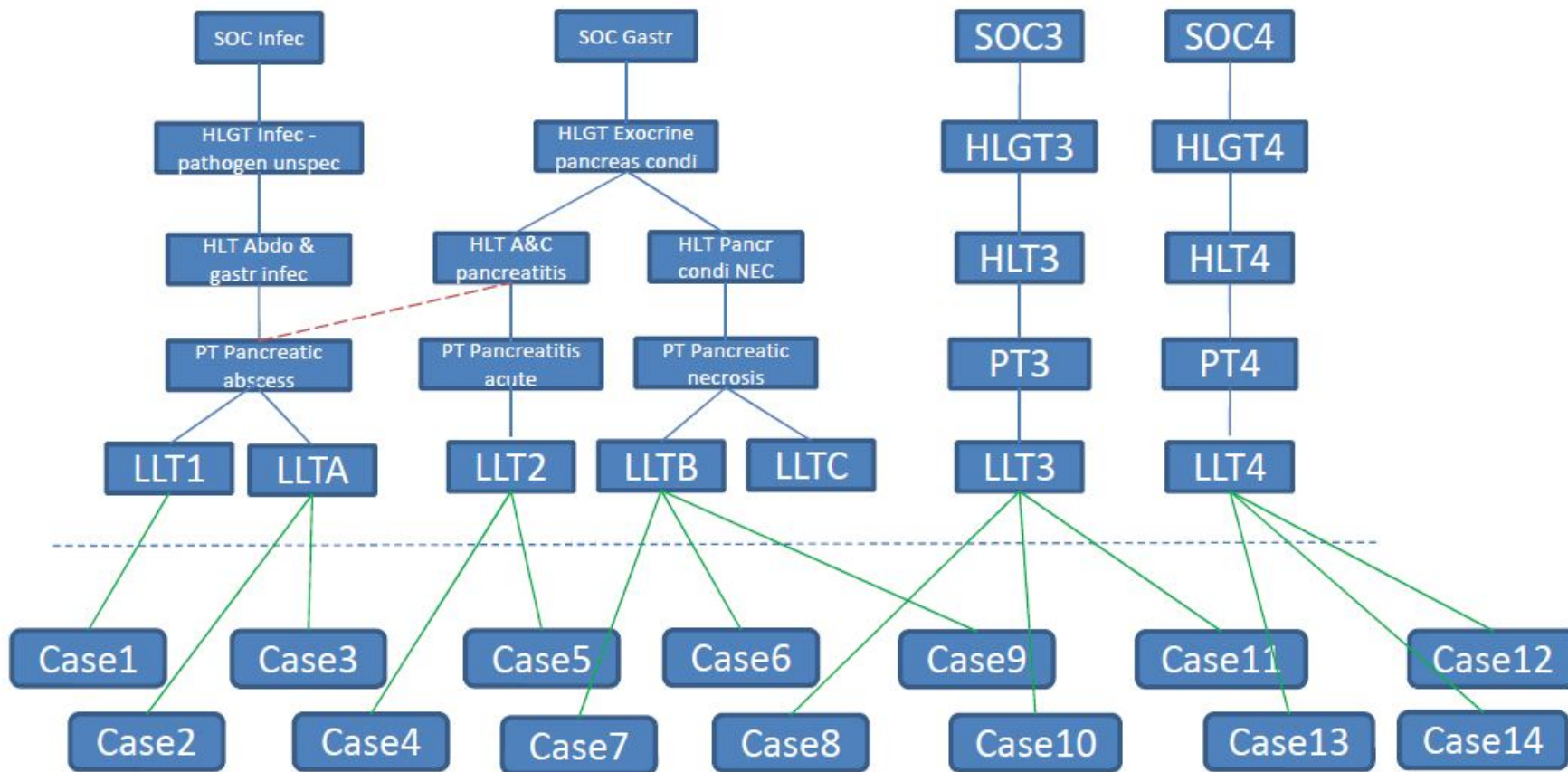
MedDRA Structure





MedDRA

MedDRA 和编码病例



- 使用 MedDRA 结构来检索病例





MedDRA

Making the Most of MedDRA

- To take advantage of MedDRA's richness and specificity, the source data should be
 - Clear
 - Concise
 - Complete
 - Accurate
- General principles apply to all clinical data



Problems With Coding Data

- Appropriate coding requires clear initial data
- What is clear to the investigator at the point of data entry may be unclear to the sponsor at the point of data coding
- Sponsor must only code reported verbatim term; not permitted to interpret or draw information from other sources
- Example: Ambiguous information
 - Congestion (nasal, liver, sinus, pulmonary?)
 - Cramp (muscle, menstrual, abdominal?)
 - Pain (pain where?)



MedDRA

Problems With Coding Data (cont)

- Example: Ambiguous abbreviations
 - MI (myocardial infarction or mitral incompetence?)
 - GU pain (gastric ulcer pain or genito-urinary pain?)
 - Decreased BS (breath sounds, bowel sounds or blood sugar?)
- Exercise caution with abbreviations that could be misinterpreted
- ECG, COPD, HIV are examples of standard abbreviations



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Problems With Coding Data (cont)

- Example: Vague information
 - Patient felt “fuzzy”, “weird”, “experienced every adverse event”

Try to use accepted medical terminology

- Example: Non-specific information
 - “Left wrist edema” (coded as *Peripheral edema*)
 - More specific - “Injection site edema left wrist” (coded as *Injection site edema*)





Problems With Coding Data (cont)

- Death, hospitalization, and disability are outcomes and are not usually considered to be adverse events
- Provide details of the underlying event, if known
- Examples:
 - “Death due to myocardial infarction” (Coded as *Myocardial infarction* with death captured as the outcome)
 - “Hospitalization due to congestive heart failure” (Coded as *Congestive heart failure* with hospitalization captured as the outcome)



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Problems With Coding Data (cont)

- Example: Ambiguous laboratory data
 - “Glucose of 40”
 - (Source of specimen - blood, urine, CSF? What units?)
 - Would have to code as *Glucose abnormal* if additional clarification is not obtained
- Example: Conflicting laboratory data
 - “Hyperkalemia with serum potassium of 1.6 mEq/L”
 - Would have to code as *Serum potassium abnormal*

If using numeric values, provide units and reference range. Be specific about specimen source and diagnostic result/clinical diagnosis.



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Problems With Coding Data (cont)

- Example: Combination terms
 - Diarrhea, nausea, and vomiting

Try to avoid combination terms - these will have to be split into three individual terms:

- Diarrhea
- Nausea
- Vomiting





Reporting a Specific Diagnosis

- Where possible, report the most important medical event or specific diagnosis rather than individual signs and symptoms
- Can provide provisional diagnosis e.g. “possible”, “presumed”, “rule out”
- Accuracy is important in preventing dilution of safety signals or generating false signals

SIGNS and SYMPTOMS	DIAGNOSIS
Chest pain, dyspnea, diaphoresis, ECG changes	Myocardial infarction



MedDRA

Generating Quality Data

- Clear
- Concise
- Complete
- Accurate
- Be specific if necessary - MedDRA can handle multiple specific medical concepts:
 - Headache - more than 50 types, including cluster, sinus, migraine, lumbar puncture headache
 - Organisms - down to species level e.g. *Staphylococcus aureus*



Unqualified Test Name Term List

- MSSO developed and maintains list of unqualified test name terms
 - These terms (e.g., PT *Blood glucose*) should never be reported as AEs
 - Intended for use in E2B test name field only
- List can be used to check data quality
 - Identifies inappropriate terms in data fields other than test name data element
 - Intended as recommendation only





MedDRA

List Available for Download

Medical Dictionary for Regulatory Activities

Home About MedDRA How to Use Training Subscription News & Events RSS +

Unqualified Test Name Term List / Support Documentation / How to Use / Home

Description
Unqualified test name terms, e.g., PT Blood glucose, are intended for use only in the test name data element in data transmission standards and are not meant for use in other data fields capturing information such as adverse events/adverse reactions, medical history, or indications. The Unqualified Test Name Term List could be helpful to users in regulatory authorities and industry as a standardised query to check data quality by identifying the inappropriate use of unqualified test name terms in data fields other than the test name data element.

Supporting Documentation
[Unqualified Test Name Term List \(pdf\)](#)

Term List
[Unqualified Test Name Term List \(MedDRA Version 19.1\) \(xlsx\)](#)

- Link on Support Documentation page on MedDRA website
- Spreadsheet of LLT/PT names and codes from SOC *Investigations*
 - >3,800 terms in v22.0
- Explanatory document
 - Purpose, uses, development of list



MedDRA

List v21.0

◇	A	B	C
1	Term	Code	Level
2	17 ketosteroids urine	10000005	PT
3	17-hydroxycorticosteroid activity	10051618	LLT
4	2',5'-oligoadenylate synthetase test	10058945	PT
5	24 hour electrocardiogram	10073349	LLT
6	5-HIAA urine	10060014	LLT
7	5-hydroxyindolacetic acid	10050342	PT
8	5-hydroxyindolacetic acid in urine	10059972	PT
9	5'nucleotidase	10059898	PT
10	A/G ratio	10000037	LLT
11	Abdomen CT	10077423	LLT
12	Abdomen scan	10061936	PT
13	Abdominal CAT	10057791	LLT
14	Abdominal scan NOS	10000091	LLT
15	Abdominal wall biopsy	10000102	LLT
16	Abdominal X-ray	10061612	PT
17	Abdominal X-ray NOS	10050402	LLT
18	Absolute lymphocyte count	10073552	LLT
19	Absolute neutrophil count	10052033	LLT



Company-specific conventions





General Coding Guidelines - Example

- Coding will be carried out in adherence with MedDRA Term Selection: Points to Consider.
- General Points:
 - Misspelling
 - Translations
 - Abbreviations and Acronyms
 - Combination Terms





MedDRA Term Selection: Points to Consider (MTS:PTC)

MedDRA® TERM SELECTION: POINTS TO CONSIDER ICH-Endorsed Guide for MedDRA Users

Release 4.17
Based on MedDRA Version 22.0

1 March 2019

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- Provides term selection advice for industry and regulatory purposes
- Objective is to promote accurate and consistent term selection to facilitate a common understanding of shared data
- Recommended to be used as basis for individual organization's own coding conventions



Do Not Add Information

- Do not make diagnosis if only signs/symptoms reported

Reported	LLT Selected	Comment
Abdominal pain, increased serum amylase, and increased serum lipase	Abdominal pain	It is inappropriate to assign an LLT for diagnosis of “pancreatitis”
	Serum amylase increased	
	Lipase increased	



- Grouped investigation result terms

Reported	LLT Selected	Comment
Increased alkaline phosphatase, increased SGPT, increased SGOT and elevated LDH	Alkaline phosphatase increased SGPT increased SGOT increased LDH increased	Select four individual terms. A single term such as LLT <i>Liver function tests abnormal</i> should not be selected.





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Investigations

- Medical condition vs. investigation result

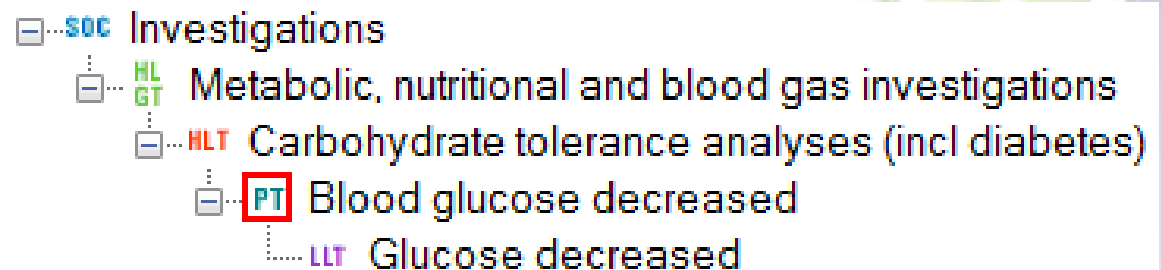
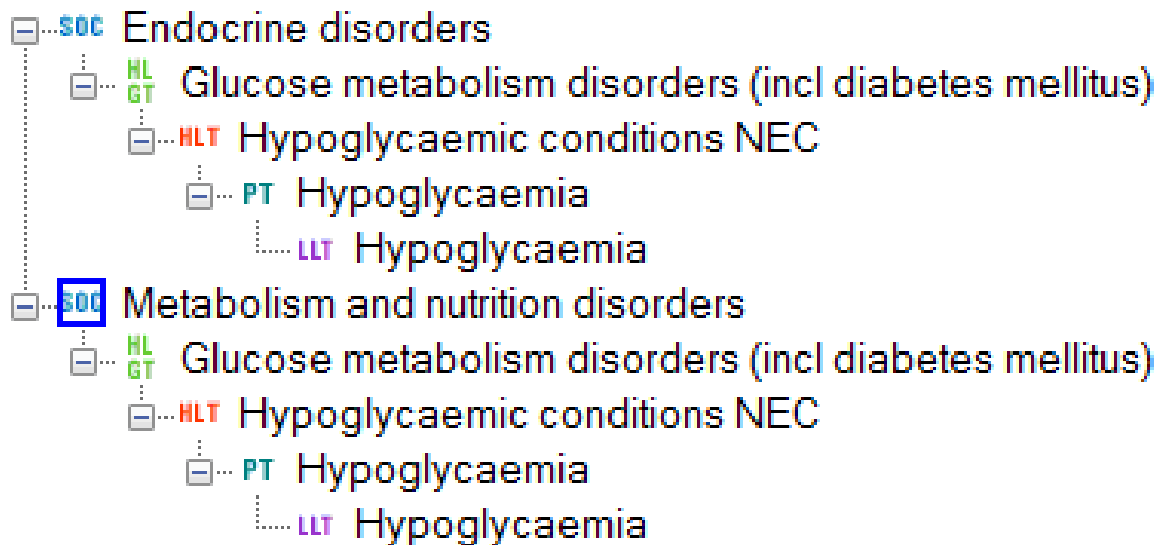
Reported	LLT Selected	Comment
Hypoglycaemia	Hypoglycaemia	LLT <i>Hypoglycaemia</i> links to SOC <i>Metabolism and nutrition disorders</i>
Decreased glucose	Glucose decreased	LLT <i>Glucose decreased</i> links to SOC <i>Investigations</i>



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Investigations

- Medical condition vs. investigation result





Sponsor or Project Specific Conventions - Example

Chest Pain

- Code to Chest pain?
- Query to specify the type?
 - Cardiac chest pain
 - Non-cardiac chest pain
 - Musculoskeletal Chest Pain
- Depend on the panel / form?
 - Adverse event – query
 - Medical history – not query





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Benefits of good quality data





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Benefits of Quality Data

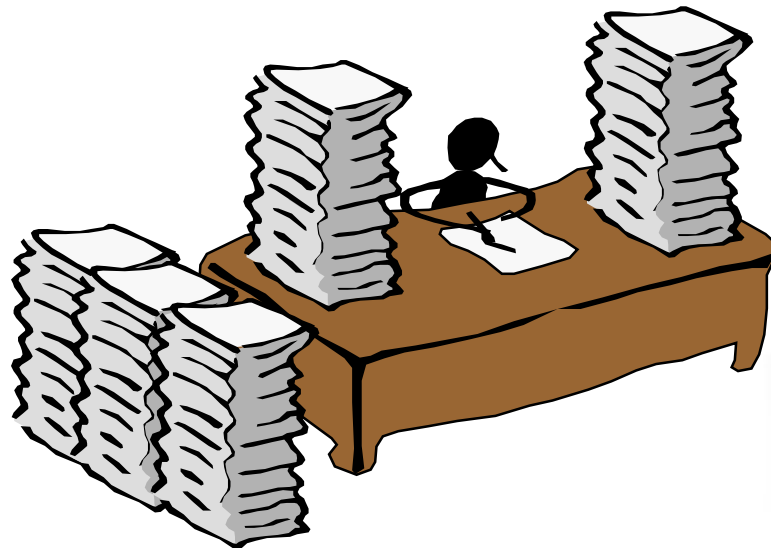
- Accurate and timely information on issues that affect conduct of clinical trial and affect patient safety
- Improved communication among sponsors, investigators, and regulatory agencies about medicinal products
 - Aids in safety signal detection and evaluation
 - Ensures accuracy of information about the product including investigators' brochures and prescribing information
 - Benefits medical professionals
 - Benefits patients



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Benefits of Quality Data (cont)

- Fewer queries for investigator and sponsor





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Quality Data

IN



OUT





MedDRA

How to improve data entry quality?
How to avoid coding queries?





How to avoid coding queries?

- Data Completion Guidelines



CCG Example

- CRF Design



ADR System.PNG



CRF Example.PNG

- CRC/Investigator Training
- CRA Coordination
- Communication with Coders





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MSSO Contacts

- Website
 - www.meddra.org
- Email
 - mssohelp@meddra.org
- Frequently Asked Question
 - www.meddra.org/faq



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