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# MedDRA – Beyond that basic AE report. How SMQs and MedDRA structure can enhance reporting.

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## ABSTRACT

The basic AE (Adverse Events) table, organized by MedDRA SOC (System Organ Class) is common across clinical reporting. Yet there is a whole structure of MedDRA that allows for more targeted reporting. In addition, MedDRA includes SMQs (Standard Medical Queries) whereby events (or histories) can be summarized across SOCs. SMQs can be especially helpful in pharmacovigilance, late phase, and health outcome analysis.

This paper will describe the basic structure of MedDRA, the relationship of SMQs and SOCs, and examples of how these can be helpful.

## INTRODUCTION

Since patient safety is always of paramount concern, accurate reporting of adverse events is critical and MedDRA, the Medical Dictionary for Regulatory Activities, is the universal standard for identifying and classifying adverse events. Developed by the ICH (International Conference on Harmonization) and implemented first in 1999, it is currently in use by most regulatory bodies and its use is required in the USA, Europe, and Japan. An adverse event is any untoward event that happens to a patient during the course of a clinical trial. During the clinical trial, all information on adverse events is collected and later coded to the MedDRA standard term by specialist medical coders. This standard MedDRA term and its subsequent terms in the MedDRA terminology hierarchy are used in later reporting and in analysis.

AE (adverse event) reports typically only use two levels of the MedDRA hierarchy in reporting (usually Preferred Term and Primary SOC). However, there are times when using more or other levels of the MedDRA hierarchy can present a more robust and meaningful picture of adverse events. By understanding the hierarchy, programmers and analysts can make use of these features. Similarly, in the analysis of AEs, it may be useful to use MedDRA SMQ (Standardized Medical Queries) to group data. SMQs group events by medical condition rather than the System Organ Class . We will look at these options later in this paper.

The focus of this paper is more data structure than coding. Individual companies may internally store their MedDRA data differently. For example, some may provide formats while others have large flat operational datasets, and still others store MedDRA as relational entities. Regardless of the local structure, the concepts are universal.

## MEDDRA AND ITS STRUCTURE

### MEDDRA IN THE CLINICAL STUDY LIFECYCLE

Before discussing structure, it is useful to present the role of MedDRA in the lifecycle of the clinical study. MedDRA codes are dynamic and change and grow with the needs of the MedDRA user community. Currently MedDRA is updated every six months. At the deployment of the study, the most recently available MedDRA version is used. During the course of the study new versions of MedDRA are released. The project team decides whether or when to update the version of MedDRA being used during the course of the study. In a long study where many adverse events are anticipated, the MedDRA version might be updated several times during the course of the study.

The first use of MedDRA is in medical coding of any adverse events that occur in the study. This can be done by automatic systems with specialist review or directly by the medical specialist coders. The coding activity is usually part of the data management team. The coder takes the original verbatim describing the adverse event, such as “patient complained about having a headache” and translates it (or codes it) into a standard term, such as simply “headache”. This tetm then is coded to the MedDRA LLT (Low Level Term), such as 10019211 for headache. The safety or pharmacovigilance team review terms and can run queries across all patients based on MedDRA terms or SMQs. At the end of the study, the MedDRA terms are used in the clinical study report to summarize and classify adverse events.

After successful clinical trials, the individual trials are brought together into a pool for later processing for ISS/ISE[1] or for other pooled analysis. At this point, each clinical trial may have used a different original MedDRA version. It is necessary to recode/update the individual trial MedDRA versions so that all AEs are coded to a common version. This is enabled in MedDRA structure because the LLT code for the AE term does not change across versions; it is the relationships and higher entities that may change.

## MEDDRA STRUCTURE

Most SAS statistical programmers learn about MedDRA via programming tables to report adverse events.

| Primary System Organ Class<br>MedDRA Preferred Term; | Treatment A<br>N=4393 (100%) | Treatment B<br>N=4766 (100%) | Treatment C<br>N=5118 (100%) |
|---|---|---|---|
| Infections and infestations | 538 ( 12.25%) | 551 ( 11.56%) | 638 ( 12.47%) |
| Abdominal sepsis | 1 ( 0.02%) | 1 ( 0.02%) | 2 ( 0.04%) |
| Abdominal wall abscess | 0 | 1 ( 0.02%) | 0 |
| Abscess | 1 ( 0.02%) | 0 | 2 ( 0.04%) |
| Abscess limb | 1 ( 0.02%) | 2 ( 0.04%) | 2 ( 0.04%) |
| Abscess oral | 1 ( 0.02%) | 0 | 0 |
| Acarodermatitis | 2 ( 0.05%) | 1 ( 0.02%) | 0 |
| Acute sinusitis | 0 | 1 ( 0.02%) | 1 ( 0.02%) |
| Acute tonsillitis | 0 | 0 | 2 ( 0.04%) |
| Adenoiditis | 0 | 0 | 1 ( 0.02%) |
| Alveolar osteitis | 2 ( 0.05%) | 0 | 0 |
| Anal abscess | 1 ( 0.02%) | 2 ( 0.04%) | 1 ( 0.02%) |
| Anal fungal infection | 1 ( 0.02%) | 0 | 0 |
| Appendicitis | 2 ( 0.05%) | 1 ( 0.02%) | 2 ( 0.04%) |
| Appendicitis perforated | 1 ( 0.02%) | 1 ( 0.02%) | 0 |
| Arthritis infective | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Bacteraemia | 2 ( 0.05%) | 0 | 2 ( 0.04%) |
| Bacterial disease carrier | 0 | 1 ( 0.02%) | 2 ( 0.04%) |
| Body tinea | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Borrelia infection | 0 | 1 ( 0.02%) | 0 |
| Breast abscess | 1 ( 0.02%) | 1 ( 0.02%) | 0 |
| Bronchiolitis | 1 ( 0.02%) | 1 ( 0.02%) | 0 |

**Output 1 Sample AE report**

The AE table in Output 1 uses only two levels of the MedDRA hierarchy – the Preferred Term (PT) and the Primary SOC. Because this use is so common, some programmers don't realize that there are two intermediate entities between the Preferred Term and the SOC. The LLT or Low Level Term is also known as the coded term. This is the MedDRA code that the medical coding specialist assigns to the original verbatim describing the AE in the CRF. Figure 1 shows a simple version of the path from the LLT to PT to the SOC. This is the structure stored in the Adverse Events domain within the CDISC SDTM model.

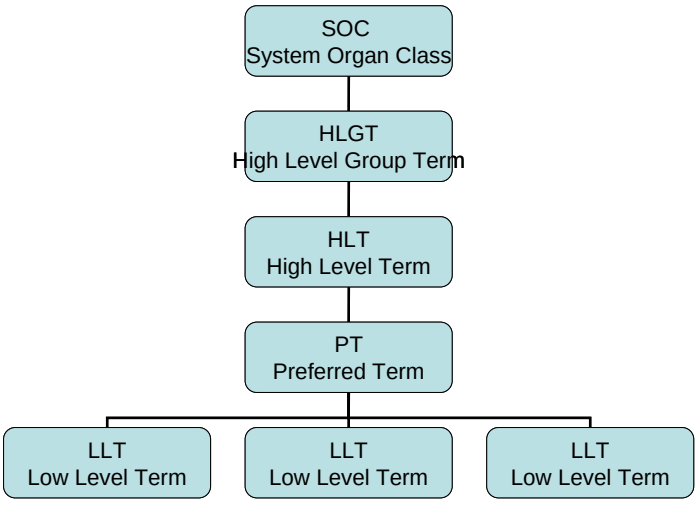


**Figure 1 Path of PT to SOC**

[1] ISS is Integrated Studies - Safety and ISE is Integrated Studies – Efficacy.

It is important to know that within the rules governing MedDRA, the name, code, and definition of the LLT doesn't change. As versions are updated, the PT, HLT, HLGT, and SOC may change. The relationship or association of a PT to a LLT or a PT to HLT or HLT to HLGT or HLGT to SOC may change. But the LLT definition itself is constant.

Figure 1 is the way most programmers think about MedDRA. This makes sense since it is the way we approach it for the AE reports and listings. But in fact, the structure is more complicated. The path from PT to SOC is really multi-axial. The clue is in the term "Primary" SOC, as shown in the heading of an AE report. Since there is a "primary" SOC, one can assume that there are non-primary or "secondary" SOC codes related to the PT. This is shown in Figure 2. Not all PTs are related to multiple SOCs. Many have only one path. Others have two. Still others have three.

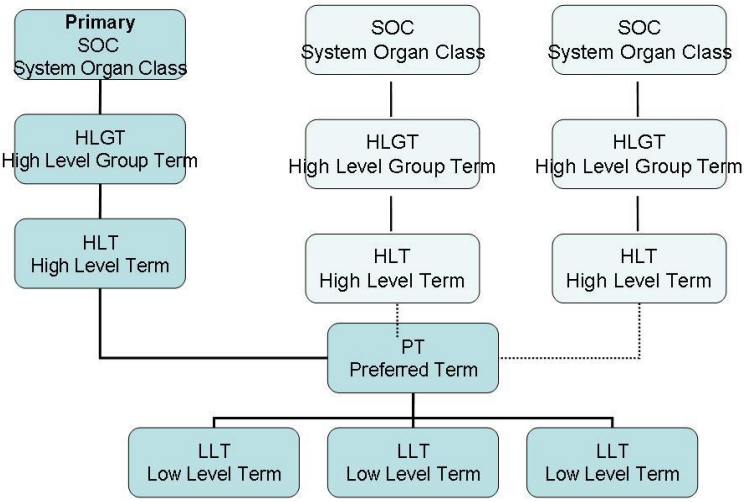


**Figure 2 Multi-axial view of MedDRA**

Let's look at an example of a term and its place in MedDRA. Gestational Diabetes is a form of diabetes that occurs during pregnancy. But how does the PT of Gestational Diabetes map to the Primary SOC, since it is both an endocrine disorder (since it is a type of diabetes) and it is a disease of pregnancy, Figure 3 shows how this term maps to the SOC.

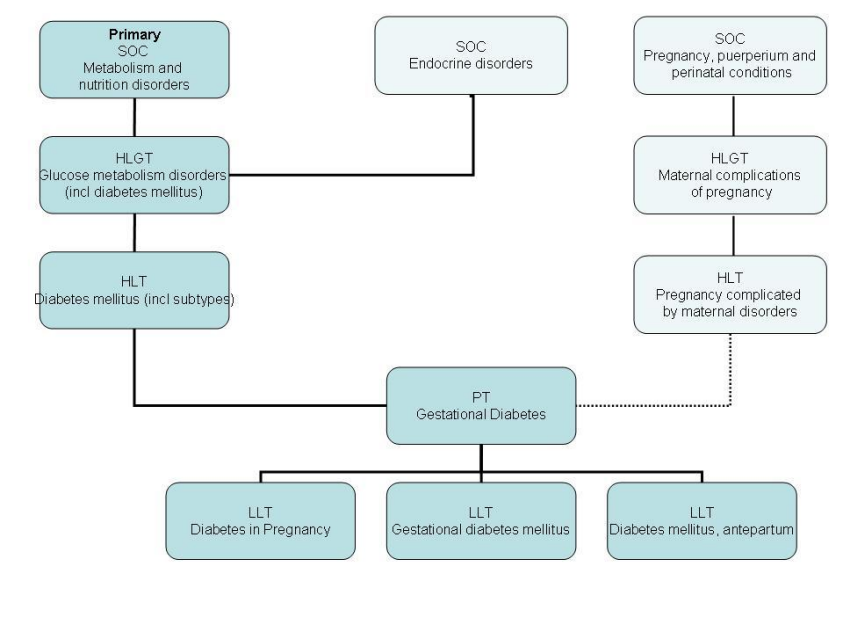


**Figure 3 Example of multi-axial relationships: Gestational Diabetes**

We've been looking at MedDRA structure from the specific to general path of the PT to SOC. From this perspective, every HLT links to only one HLGT, that HLGT links to only one SOC. However, the direction from SOC to HLT is many to one: a SOC can link to multiple HLGTs; each HLGT can link to multiple HLTs which in turn link to multiple PTs. HLGTs can be thought of as a subset of the SOC and the HLT is a subset of the HLGT. The relationship of HLT to PT is many-to-many. A LLT is a subset of a PT.

## USING OTHER LEVELS WITHIN THE AE REPORT

With the full MedDRA report in mind, let's return to the subject of the AE report. AE reports can get very long and unwieldy. This is especially true in large studies or populations that are frail or infirmed. Validation is tedious and time-consuming, so automated checking is often employed. A more serious problem can occur during interim reviews such as Data Monitoring Committees or Institutional Review Boards, where clients or medical specialists are pouring over these reports, looking for the serious or unexpected. This is an example where using HGLT and/or HLT can help capsulize the PT terms into more manageable components. Let's look at an example in Output 2:

| Primary System Organ Class<br>MedDRA Preferred Term; | Treatment A<br>N=4393 (100%) | Treatment B<br>N=4766 (100%) | Treatment C<br>N=5118 (100%) |
|---|---|---|---|
| Blood and lymphatic system disorders | 127 ( 2.89%) | 117 ( 2.45%) | 150 ( 2.93%) |
| Anaemia | 52 ( 1.18%) | 50 ( 1.05%) | 64 ( 1.25%) |
| Anaemia megaloblastic | 0 | 1 ( 0.02%) | 1 ( 0.02%) |
| Anaemia of chronic disease | 0 | 4 ( 0.08%) | 1 ( 0.02%) |
| Anaemia of malignant disease | 2 ( 0.05%) | 0 | 1 ( 0.02%) |
| Anaemia vitamin B12 deficiency | 0 | 0 | 2 ( 0.04%) |
| Aplastic anaemia | 0 | 0 | 1 ( 0.02%) |
| Bone marrow failure | 0 | 2 ( 0.04%) | 1 ( 0.02%) |
| Bone marrow oedema | 0 | 1 ( 0.02%) | 0 |
| Coagulopathy | 2 ( 0.05%) | 0 | 3 ( 0.06%) |
| Disseminated intravascular coagulation | 3 ( 0.07%) | 1 ( 0.02%) | 1 ( 0.02%) |
| Eosinophilia | 2 ( 0.05%) | 0 | 2 ( 0.04%) |
| Febrile neutropenia | 3 ( 0.07%) | 4 ( 0.08%) | 2 ( 0.04%) |
| Haemorrhagic anaemia | 3 ( 0.07%) | 0 | 2 ( 0.04%) |
| Haemorrhagic diathesis | 8 ( 0.18%) | 5 ( 0.10%) | 9 ( 0.18%) |
| Haemorrhagic disorder | 0 | 1 ( 0.02%) | 1 ( 0.02%) |
| Heparin-induced thrombocytopenia | 0 | 0 | 1 ( 0.02%) |
| Hypercoagulation | 0 | 1 ( 0.02%) | 0 |
| Hyperfibrinogenaemia | 0 | 0 | 1 ( 0.02%) |
| Hypochromic anaemia | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Hypothrombinaemia | 1 ( 0.02%) | 0 | 0 |
| Iron deficiency anaemia | 9 ( 0.20%) | 9 ( 0.19%) | 10 ( 0.20%) |
| Leukocytosis | 7 ( 0.16%) | 12 ( 0.25%) | 10 ( 0.20%) |
| Leukopenia | 2 ( 0.05%) | 3 ( 0.06%) | 5 ( 0.10%) |
| Lymph node calcification | 1 ( 0.02%) | 0 | 0 |
| Lymphadenitis | 1 ( 0.02%) | 0 | 0 |

**Output 2 AE Table excerpt showing SOC and PT**

The SOC "Blood and lymphatic system disorders" contains a large number of disparate preferred terms. In a large study (or a study with a high number of adverse events), this SOC group can be unwieldy. In most AE tables, the PTs are sorted either alphabetically or by frequency of occurrence –neither of which gets at the intrinsic meaning of the terms. By further classifying the PTs terms into High Level Group Term (HLGT) the report become more readable, and hopefully more usable. The use of the High Level Group Term is found in Output 3.

Sample AE Tables with SOC and High Level Group Term and Preferred Term

| Primary System Organ Class<br>High Level Group Term<br>Preferred Term; | Treatment A<br>N=4393 (100%) | Treatment B<br>N=4766 (100%) | Treatment C<br>N=5118 (100%) |
|---|---|---|---|
| Blood and lymphatic system disorders | 127 ( 2.89%) | 117 ( 2.45%) | 150 ( 2.93%) |
| Anaemias nonhaemolytic and marrow depression | 67 ( 1.53%) | 70 ( 1.47%) | 92 ( 1.80%) |
| Anaemia | 52 ( 1.18%) | 50 ( 1.05%) | 64 ( 1.25%) |
| Anaemia megaloblastic | 0 | 1 ( 0.02%) | 1 ( 0.02%) |
| Anaemia of chronic disease | 0 | 4 ( 0.08%) | 1 ( 0.02%) |
| Anaemia of malignant disease | 2 ( 0.05%) | 0 | 1 ( 0.02%) |
| Anaemia vitamin B12 deficiency | 0 | 0 | 2 ( 0.04%) |
| Aplastic anaemia | 0 | 0 | 1 ( 0.02%) |
| Bone marrow failure | 0 | 2 ( 0.04%) | 1 ( 0.02%) |
| Haemorrhagic anaemia | 3 ( 0.07%) | 0 | 2 ( 0.04%) |
| Hypochromic anaemia | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Iron deficiency anaemia | 9 ( 0.20%) | 9 ( 0.19%) | 10 ( 0.20%) |
| Microcytic anaemia | 0 | 3 ( 0.06%) | 2 ( 0.04%) |
| Nephrogenic anaemia | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Normochromic normocytic anaemia | 0 | 1 ( 0.02%) | 7 ( 0.14%) |
| Pancytopenia | 0 | 3 ( 0.06%) | 2 ( 0.04%) |

Sample AE Tables with SOC and High Level Group Term and Preferred Term

| Primary System Organ Class<br>High Level Group Term<br>Preferred Term; | Treatment A<br>N=4393 (100%) | Treatment B<br>N=4766 (100%) | Treatment C<br>N=5118 (100%) |
|---|---|---|---|
| Coagulopathies and bleeding diatheses (excl thrombocytopenic) | 15 ( 0.34%) | 8 ( 0.17%) | 19 ( 0.37%) |
| Coagulopathy | 2 ( 0.05%) | 0 | 3 ( 0.06%) |
| Disseminated intravascular coagulation | 3 ( 0.07%) | 1 ( 0.02%) | 1 ( 0.02%) |
| Haemorrhagic diathesis | 8 ( 0.18%) | 5 ( 0.10%) | 9 ( 0.18%) |
| Haemorrhagic disorder | 0 | 1 ( 0.02%) | 1 ( 0.02%) |
| Hypercoagulation | 0 | 1 ( 0.02%) | 0 |
| Hyperfibrinogenaemia | 0 | 0 | 1 ( 0.02%) |
| Hypothrombinaemia | 1 ( 0.02%) | 0 | 0 |
| Spontaneous haematoma | 1 ( 0.02%) | 0 | 4 ( 0.08%) |
| Haematological disorders NEC | 0 | 1 ( 0.02%) | 0 |
| Bone marrow oedema | 0 | 1 ( 0.02%) | 0 |
| Platelet disorders | 15 ( 0.34%) | 24 ( 0.50%) | 17 ( 0.33%) |
| Heparin-induced thrombocytopenia | 0 | 0 | 1 ( 0.02%) |
| Thrombocytopenia | 14 ( 0.32%) | 20 ( 0.42%) | 16 ( 0.31%) |
| Thrombocytosis | 1 ( 0.02%) | 4 ( 0.08%) | 0 |

**Output 3 AE Table with addition of HLGT**

As the High Level Term (HLT) is more granular than the HGLT, using the HLT, AEs are classified into more smaller categories. This is shown in Output 4.

Sample AE Tables with SOC High Level Term and Preferred Term

| Primary System Organ Class<br>High Level Term<br>Preferred Term; | Treatment A<br>N=4393 (100%) | Treatment B<br>N=4766 (100%) | Treatment C<br>N=5118 (100%) |
|---|---|---|---|
| Blood and lymphatic system disorders | 127 ( 2.89%) | 117 ( 2.45%) | 150 ( 2.93%) |
| Anaemia deficiencies | 9 ( 0.20%) | 9 ( 0.19%) | 11 ( 0.21%) |
| Anaemia vitamin B12 deficiency | 0 | 0 | 2 ( 0.04%) |
| Iron deficiency anaemia | 9 ( 0.20%) | 9 ( 0.19%) | 10 ( 0.20%) |
| Anaemias NEC | 55 ( 1.25%) | 54 ( 1.13%) | 76 ( 1.48%) |
| Anaemia | 52 ( 1.18%) | 50 ( 1.05%) | 64 ( 1.25%) |
| Anaemia megaloblastic | 0 | 1 ( 0.02%) | 1 ( 0.02%) |
| Haemorrhagic anaemia | 3 ( 0.07%) | 0 | 2 ( 0.04%) |
| Hypochromic anaemia | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Microcytic anaemia | 0 | 3 ( 0.06%) | 2 ( 0.04%) |
| Normochromic normocytic anaemia | 0 | 1 ( 0.02%) | 7 ( 0.14%) |
| Anaemias due to chronic disorders | 3 ( 0.07%) | 4 ( 0.08%) | 3 ( 0.06%) |
| Anaemia of chronic disease | 0 | 4 ( 0.08%) | 1 ( 0.02%) |
| Anaemia of malignant disease | 2 ( 0.05%) | 0 | 1 ( 0.02%) |
| Nephrogenic anaemia | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Bleeding tendencies | 9 ( 0.20%) | 6 ( 0.13%) | 14 ( 0.27%) |
| Haemorrhagic diathesis | 8 ( 0.18%) | 5 ( 0.10%) | 9 ( 0.18%) |
| Haemorrhagic disorder | 0 | 1 ( 0.02%) | 1 ( 0.02%) |
| Spontaneous haematoma | 1 ( 0.02%) | 0 | 4 ( 0.08%) |
| Coagulation factor deficiencies | 1 ( 0.02%) | 0 | 0 |
| Hypothrombinaemia | 1 ( 0.02%) | 0 | 0 |
| Coagulopathies | 5 ( 0.11%) | 2 ( 0.04%) | 5 ( 0.10%) |
| Coagulopathy | 2 ( 0.05%) | 0 | 3 ( 0.06%) |
| Disseminated intravascular coagulation | 3 ( 0.07%) | 1 ( 0.02%) | 1 ( 0.02%) |
| Hypercoagulation | 0 | 1 ( 0.02%) | 0 |
| Hyperfibrinogenaemia | 0 | 0 | 1 ( 0.02%) |
| Eosinophilic disorders | 2 ( 0.05%) | 0 | 2 ( 0.04%) |
| Eosinophilia | 2 ( 0.05%) | 0 | 2 ( 0.04%) |
| Haematological disorders | 0 | 1 ( 0.02%) | 0 |
| Bone marrow oedema | 0 | 1 ( 0.02%) | 0 |
| Leukocytoses NEC | 7 ( 0.16%) | 15 ( 0.31%) | 11 ( 0.21%) |
| Leukocytosis | 7 ( 0.16%) | 12 ( 0.25%) | 10 ( 0.20%) |
| Lymphocytosis | 0 | 0 | 1 ( 0.02%) |
| Neutrophilia | 0 | 3 ( 0.06%) | 0 |

**Output 4 AE Term with addition of HLT**

By using both HLT and HLGT within even further classification is displayed. This is shown in Output 5.

| Primary System Organ Class<br>High Level Group Term<br>High Level Term<br>Preferred Term; | Treatment A<br>N=4393 (100%) | Treatment B<br>N=4766 (100%) | Treatment C<br>N=5118 (100%) |
|---|---|---|---|
| Blood and lymphatic system disorders | 127 ( 2.89%) | 117 ( 2.45%) | 150 ( 2.93%) |
| Anaemias nonhaemolytic and marrow depression | 67 ( 1.53%) | 70 ( 1.47%) | 92 ( 1.80%) |
| Anaemia deficiencies | 9 ( 0.20%) | 9 ( 0.19%) | 11 ( 0.21%) |
| Anaemia vitamin B12 deficiency | 0 | 0 | 2 ( 0.04%) |
| Iron deficiency anaemia | 9 ( 0.20%) | 9 ( 0.19%) | 10 ( 0.20%) |
| Anaemias NEC | 55 ( 1.25%) | 54 ( 1.13%) | 76 ( 1.48%) |
| Anaemia | 52 ( 1.18%) | 50 ( 1.05%) | 64 ( 1.25%) |
| Anaemia megaloblastic | 0 | 1 ( 0.02%) | 1 ( 0.02%) |
| Haemorrhagic anaemia | 3 ( 0.07%) | 0 | 2 ( 0.04%) |
| Hypochromic anaemia | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Microcytic anaemia | 0 | 3 ( 0.06%) | 2 ( 0.04%) |
| Normochromic normocytic anaemia | 0 | 1 ( 0.02%) | 7 ( 0.14%) |
| Anaemias due to chronic disorders | 3 ( 0.07%) | 4 ( 0.08%) | 3 ( 0.06%) |
| Anaemia of chronic disease | 0 | 4 ( 0.08%) | 1 ( 0.02%) |
| Anaemia of malignant disease | 2 ( 0.05%) | 0 | 1 ( 0.02%) |
| Nephrogenic anaemia | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Marrow depression and hypoplastic anaemias | 0 | 5 ( 0.10%) | 4 ( 0.08%) |
| Aplastic anaemia | 0 | 0 | 1 ( 0.02%) |
| Bone marrow failure | 0 | 2 ( 0.04%) | 1 ( 0.02%) |
| Pancytopenia | 0 | 3 ( 0.06%) | 2 ( 0.04%) |
| Coagulopathies and bleeding diatheses (excl thrombocytopenic) | 15 ( 0.34%) | 8 ( 0.17%) | 19 ( 0.37%) |
| Bleeding tendencies | 9 ( 0.20%) | 6 ( 0.13%) | 14 ( 0.27%) |
| Haemorrhagic diathesis | 8 ( 0.18%) | 5 ( 0.10%) | 9 ( 0.18%) |
| Haemorrhagic disorder | 0 | 1 ( 0.02%) | 1 ( 0.02%) |
| Spontaneous haematoma | 1 ( 0.02%) | 0 | 4 ( 0.08%) |
| Coagulation factor deficiencies | 1 ( 0.02%) | 0 | 0 |
| Hypothrombinaemia | 1 ( 0.02%) | 0 | 0 |
| Coagulopathies | 5 ( 0.11%) | 2 ( 0.04%) | 5 ( 0.10%) |
| Coagulopathy | 2 ( 0.05%) | 0 | 3 ( 0.06%) |
| Disseminated intravascular coagulation | 3 ( 0.07%) | 1 ( 0.02%) | 1 ( 0.02%) |
| Hypercoagulation | 0 | 1 ( 0.02%) | 0 |
| Hyperfibrinogenaemia | 0 | 0 | 1 ( 0.02%) |

**Output 5 AE Table using HLGT and HLT**

These examples show how using HLGT and HLT can increase the readability of AE reports. Having more readable reports can make improve the ability for reviews to check the data. This technique can also help identify AEs of special interest because of frequency or treatment.

## SMQ IN REPORTING

The basic AE report is designed to show what AEs are occurring within the study. It can be inadequate when trying to identify medical conditions that are occurring within the study. An AE could possibly fall under several different types of medical conditions. This is where SMQs are useful. SMQs or standard medical queries are queries that associate PTs with medical conditions. Developed by the MedDRA community, SMQs allow for a standard way of identifying possible conditions based on PTs. SMQs pull PTs from across SOC classifications. Some SOC groups, such as “Investigations” (lab tests and other procedures) contain PTs that are associated with a wide number of medical problems.

To get a feeling for the relationship of SMQs to SOC, it is helpful to look at some examples. Table 1 shows an excerpt of a cross tabulation of the number of PTs for a given SMQ and their associated Primary SOC. In MedDRA version 14.1, the SMQ “Abdominal arterial occlusion, thrombosis and embolism” contained 8 PT codes which pulled from the SOC areas of “Blood and lymphatic system disorders”, “Gastrointestinal disorders”,” Hepatobiliary disorders”, and “Vascular disorders”.

**Table 1 Sample relationship of SMQ to SOC per count of PTs**

| SMQ Name | SOC Name | Count | Percent |
|---|---|---|---|
| Abdominal arterial occlusion, thrombosis and embolism | Blood and lymphatic system disorders | 1 | 12.50% |
| Abdominal arterial occlusion, thrombosis and embolism | Gastrointestinal disorders | 3 | 37.50% |
| Abdominal arterial occlusion, thrombosis and embolism | Hepatobiliary disorders | 3 | 37.50% |
| Abdominal arterial occlusion, thrombosis and embolism | Vascular disorders | 1 | 12.50% |
| Abdominal cavity hemorrhage | Gastrointestinal disorders | 6 | 66.67% |
| Abdominal cavity hemorrhage | Investigations | 1 | 11.11% |
| Abdominal cavity hemorrhage | Vascular disorders | 2 | 22.22% |
| Abdominal infarction | Blood and lymphatic system disorders | 1 | 20.00% |
| Abdominal infarction | Gastrointestinal disorders | 3 | 60.00% |
| Abdominal infarction | Hepatobiliary disorders | 1 | 20.00% |
| Abdominal vascular occlusion and thrombosis not specified as arterial or venous | Gastrointestinal disorders | 2 | 100.00% |
| Abdominal venous occlusion and thrombosis | Blood and lymphatic system disorders | 2 | 22.22% |
| Abdominal venous occlusion and thrombosis | Gastrointestinal disorders | 1 | 11.11% |
| Abdominal venous occlusion and thrombosis | Hepatobiliary disorders | 6 | 66.67% |
| Abnormal INR (International normalized ratio) | Investigations | 4 | 100.00% |
| Abnormal dreams | Psychiatric disorders | 2 | 100.00% |

Let's look at an example of an AE report using SOC to one using SMQ (Output 6). Preferred Terms related to "Liver Infections" are found in the SOC areas of "Investigations" and "Infections and Infestations". These are large SOCs and can be several pages long. So, if these are AEs of interest, they are often identified in the hard copy output by highlights, Post-its, or paper clips.

| Primary System Organ Class<br>Preferred Term; | Treatment A<br>N=4393 (100%) | Treatment B<br>N=4766 (100%) | Treatment C<br>N=5118 (100%) |
|---|---|---|---|
| Infections and infestations | | | |
| Genitourinary tract infection | 1 ( 0.02%) | 0 | 0 |
| Giardiasis | 0 | 0 | 1 ( 0.02%) |
| Gingival abscess | 0 | 1 ( 0.02%) | 0 |
| Gingival infection | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Graft infection | 2 ( 0.05%) | 1 ( 0.02%) | 0 |
| Groin abscess | 0 | 0 | 1 ( 0.02%) |
| Groin infection | 1 ( 0.02%) | 1 ( 0.02%) | 2 ( 0.04%) |
| H1N1 influenza | 0 | 2 ( 0.04%) | 2 ( 0.04%) |
| Helicobacter gastritis | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Helicobacter infection | 1 ( 0.02%) | 0 | 3 ( 0.06%) |
| Hepatitis B | 0 | 1 ( 0.02%) | 0 |
| Hepatitis C | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Hepatitis E | 0 | 0 | 1 ( 0.02%) |
| Herpes dermatitis | 0 | 1 ( 0.02%) | 0 |
| Herpes simplex | 4 ( 0.09%) | 1 ( 0.02%) | 3 ( 0.06%) |
| Herpes virus infection | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Herpes zoster | 8 ( 0.18%) | 9 ( 0.19%) | 10 ( 0.20%) |
| Herpes zoster infection neurological | 0 | 1 ( 0.02%) | 0 |
| Hordeolum | 0 | 0 | 1 ( 0.02%) |
| Impetigo | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Infected bites | 0 | 0 | 2 ( 0.04%) |
| Infected cyst | 0 | 1 ( 0.02%) | 0 |
| Infected dermal cyst | 0 | 1 ( 0.02%) | 1 ( 0.02%) |
| Infected skin ulcer | 0 | 1 ( 0.02%) | 1 ( 0.02%) |
| Infection | 3 ( 0.07%) | 6 ( 0.13%) | 3 ( 0.06%) |
| Infectious peritonitis | 3 ( 0.07%) | 0 | 0 |
| Infectious pleural effusion | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Infective exacerbation of bronchiectasis | 0 | 0 | 1 ( 0.02%) |
| Infective exacerbation of chronic obstructive airways disease | 5 ( 0.11%) | 2 ( 0.04%) | 9 ( 0.18%) |
| Infective glossitis | 0 | 1 ( 0.02%) | 0 |
| Infective spondylitis | 0 | 0 | 2 ( 0.04%) |
| Influenza | 24 ( 0.55%) | 26 ( 0.55%) | 19 ( 0.37%) |
| Infusion site cellulitis | 0 | 1 ( 0.02%) | 0 |
| Infusion site infection | 1 ( 0.02%) | 0 | 1 ( 0.02%) |

**Output 6 PTs of intested within SOC**

When the SMQ is identified as an event of interest, adapting the classic AE report to select based on the SMQ is fairly straight-forward. The result , shown in Output 7, is a table that is more targeted for analysis.

AE terms found in SMQ Liver Infections

| SMQ<br>Preferred Term; | Treatment A<br>N=4393 (100%) | Treatment B<br>N=4766 (100%) | Treatment C<br>N=5118<br>(100%) |
|---|---|---|---|
| ANY EVENT | 1 ( 0.02%) | 2 ( 0.04%) | 4 ( 0.08%) |
| Liver infections (SMQ) | 1 ( 0.02%) | 2 ( 0.04%) | 4 ( 0.08%) |
| Hepatitis B | 0 | 1 ( 0.02%) | 0 |
| Hepatitis B core antibody positive | 0 | 1 ( 0.02%) | 0 |
| Hepatitis B virus test positive | 0 | 0 | 1 ( 0.02%) |
| Hepatitis C | 1 ( 0.02%) | 0 | 1 ( 0.02%) |
| Hepatitis E | 0 | 0 | 1 ( 0.02%) |
| Liver abscess | 0 | 0 | 1 ( 0.02%) |

End of table

**Output 7 SMQ display of PTs**

Because a PT can be associated with more than one SMQ (or may not be associated with any SMQ!) programmers need to be mindful that presenting multiple SMQs within the same tables can create double-counting of events. It is

usually better to present each SMQ in a separate table. When used in a clinical study report, SMQs must be documented in CDISC model AdAM as part of the submission package.

## CONCLUSION

The various levels of MedDRA and use of SMQs provide a useful and standard method for exploring AE data. With little additional programming, the intermediate levels of HLT and HLGT can make review of AE reports more user-friendly. The use of SMQs can provide a way of grouping AE data to not only facilitate review but also to improve analysis of AEs by grouping data in a more meaningful way.

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