

MedDRA Literature Commentary

Subject of commentary:

Schroeder, JR, Schmittner, JP, Epstein, DH, and Preston, KL. Adverse events among patients in a behavioral treatment trial for heroin and cocaine dependence: effects of age, race, and gender. *Drug and Alcohol Dependence* 80: 45 – 51, 2005

Commentary:

This article describes adverse events (AEs) in a large (N=286) outpatient study of behavioral interventions for heroin and cocaine dependence in methadone treated patients. The objectives of the study were: 1) to describe the nature and frequency of AEs reported by study participants; and 2) to determine if any segment of the studied population experienced a disproportionate number of events.

MedDRA was used to code the AEs reported in this study. The authors do not state which version of MedDRA was used; the date range of the study was also not stated, so it is not possible to guess what version of MedDRA might have been available to the authors at the time of their data collection. Since some Preferred Terms (PTs) are listed as “NOS” terms in their paper, it is assumed the version of MedDRA used was before Version 6.1 (after Version 6.1, “NOS” terms no longer existed at the PT level). AEs experienced by study participants were collected at weekly visits. Coding of adverse events was done by assigning the collected AE verbatim term to a MedDRA PT.

The 884 AEs reported had the following distribution: infections 26.8%; gastrointestinal disorders 20.5%; musculoskeletal disorders 12.3%; and general disorders 10%. The authors noted a specific issue concerning dental AEs. In their study, dental events were relatively common (over 11% of AEs), located in two SOCs, and consisted of tooth abscess (listed as an infection) and toothache (listed as a gastrointestinal disorder). A higher frequency of toothache was noted in female study subjects.

The authors state that “the MedDRA reporting system may have obscured some events of interest” because MedDRA has been developed for pharmaceutical purposes and not for behavior intervention trials. They specifically note that the scope of AEs collected in such interventional trials may need to be broadened to include behavioral side effects such as suicidal ideation and victimization. They also note that one of the more frequent types of AEs in this study – namely dental conditions – do not have a single specific category in MedDRA but are located within SOC *Infections and infestations* and SOC *Gastrointestinal disorders*.

Summary and Recommendations:

The MSSO believes that the current version of MedDRA (Version 8.1) quite adequately groups dental conditions which were a particular concern to the authors. The attached table indicates that many groupings for dental conditions have existed since the first implementable version of MedDRA (MedDRA Version 2.1). It should be remembered that – by MedDRA term placement rules – all infection terms (e.g., tooth abscess), regardless of their location, have as their primary SOC allocation SOC *Infections and infestations* and have as their secondary SOC allocation their “site of manifestation” (e.g., SOC *Gastrointestinal disorders* in the case of dental conditions). Therefore, the authors could have displayed their data concerning dental conditions using a secondary SOC view to exploit the flexible structure of MedDRA.

There are several important pieces of information that are not stated by the authors – e.g., although they indicate that the collected data from the weekly visits were reviewed by physicians for appropriateness and completeness, there is no description of the QA process applied to the MedDRA coding (i.e., the assignment of verbatim AE terms to MedDRA terms) or a description of the level of medical expertise of the coding personnel. Thus, there is no way of knowing if some of the analytical results are inaccurate due to misclassifications during coding. Additionally, the authors do not describe if any specific coding guidelines – such as the ICH-endorsed “*MedDRA Term Selection: Points to Consider*” were used for this study; thus, an assessment of the degree of coding consistency cannot be made. Finally, the authors indicate that the coding was done to the PT level. This is not the recommended level to code terms using MedDRA as there may not be enough synonym richness to accommodate certain reported AEs (e.g., colloquial expressions). Coding (term assignment) should be done by linking a verbatim term to a Lowest Level Term (LLT), per the “*MedDRA Term Selection: Points to Consider*” document.

The authors could have used a number of alternate presentations of their data to better illustrate their findings as described in the draft “*Data Retrieval and Presentation: Points to Consider*” document. Besides a secondary SOC analysis, the authors could have aggregated dental condition terms into *ad hoc* groupings akin to Standardised MedDRA Queries (SMQ).

The authors also note that it would be helpful to collect more behavior-related AEs in future behavioral intervention studies. MedDRA appears to be well-equipped with such terms (see SOC *Psychiatric disorders*).

Data analysis in MedDRA can be challenging until one is well-trained and knowledgeable about the structure, term placement rules, and analysis tools (e.g., SMQs) available to users. MedDRA users are encouraged to explore and exploit the structure of MedDRA when performing AE analysis including use of groupings (*ad hoc* and standardized) and primary and secondary SOC data

displays. The newly developed ICH-endorsed document – “*Data Retrieval and Presentation: Points to Consider*” – specifically recommends these types of approaches to data analysis. Finally, all MedDRA core subscribers are encouraged to submit Change Requests to the MSSO to not only add terms needed for specific areas of interest but to recommend revisions of groupings to improve data analysis of MedDRA-coded data.

Available Grouping Terms for Dental Conditions		HLGT
MedDRA Version	HLT	
2.1, 2.2, 2.3, 2.4, 3.0, 3.1, 3.2, 3.3	Tooth disorders congenital; Tooth disorders NOS; Tooth missing; Tooth pain and sensation disorders; Tooth pulp disorder; Dental and gingival surgery; Dental developmental disorders and anomalies; Dental infections; Dental infections - pathogen class unspecified; Dental surface disorder; Gum discolouration (all forms); Gum disorders NOS; Gum haemorrhage; Gum infections; Gum pain (all forms)	Tooth and gum conditions
4.0, 4.1, 5.0, 5.1, 6.0, 6.1	Tooth missing; Dental and gingival therapeutic procedures; Dental and periodontal infections and inflammations; Dental developmental disorders and anomalies; Dental disorders congenital; Dental disorders NEC; Dental infections - pathogen class unspecified; Dental pain and sensation disorders; Dental pulp disorders; Dental surface disorders; Gingival discolourations; Gingival disorders NEC; Gingival haemorrhages; Gingival infections; Gingival pains	Dental and gingival conditions
7.0, 7.1, 8.0, 8.1	Tooth missing; Dental and gingival therapeutic procedures; Dental and oral soft tissue infections; Dental and periodontal infections and inflammations; Dental developmental disorders and anomalies; Dental disorders congenital; Dental disorders NEC; Dental pain and sensation disorders; Dental pulp disorders; Dental surface disorders; Gingival discolourations; Gingival disorders NEC; Gingival haemorrhages; Gingival infections; Gingival pains	Dental and gingival conditions

