MedDRA Literature Commentary

Subject of commentary:

Bousquet, C, Lagier, G, Lillo-Le Louet, A, Le Beller, C, Venot, A and Jaulent, M-C. Appraisal of the MedDRA Conceptual Structure for Describing and Grouping Adverse Drug Reactions. Drug Safety 2005; 28(1), 19 – 34.

Commentary:

This article reviews the structural and terminological properties of MedDRA and its ability to group semantically linked adverse events in order to improve the performance of safety reporting systems, including automated signal detection methods.

The article begins by describing terminological systems and then shows the hierarchical structure of MedDRA with the numbers of terms based on version 5.1. The concept of multi-axiality is demonstrated using the example of the PT Diabetic nephropathy NOS. However, only one secondary SOC (Metabolism and nutrition disorders) is shown in this example; the authors do not mention the other secondary SOC (Endocrine). There then follows a brief description of other terminological systems including UMLS and SNOMED.

In the next section, the authors examine maintenance, data retrieval and software requirements for three “generations” of terminological systems. The first-generation terminologies are those such as ICD that are based on textual descriptions of concepts with no categorical structure. These systems may be paper-based or electronically based, installed as a flat file. Second-generation systems are those such as SNOMED that are built with a categorical structure and a cross thesaurus. Third-generation systems like GALEN are those use logical language to compute relationships. Such systems can help to automate the addition of new terms and aid data retrieval but they require highly specialized software.

The authors then describe the “desiderata” proposed by Cimino for an ideal standardized terminology and apply the criteria to MedDRA. MedDRA is rated as excellent in for several factors such as vocabulary content, the use of non-semantic codes and the retention of non-current terms. The authors rate MedDRA poorly for its lack of formal definitions (it is not a dictionary) and its lack of polyhierarchy (a PT maps only to one HLT within a SOC). They state that there is no automated mechanism for users to check that terms with the same meaning are represented in other parts of the terminology; however, various autoencoder tools and search tools such as SSCs and SMQs do have the capability to check for semantically related terms across the terminology.
MedDRA is described as a first-generation system with term use limited to the MSSO’s predefined expressions and data retrieval limited by predefined classes (HLT, HLGT and SOC). The authors refer to tools that are being proposed to navigate the MedDRA structure but do not seem to be aware that such browser tools already exist and are in widespread use. The MSSO provides a browser free of charge and there are also commercially available browsers. Browser tools are embedded in almost all applications that MedDRA users have on their systems.

The authors then discuss what they see as the current limitations of MedDRA. They note that MedDRA is a specialized terminology for regulatory activities and that it cannot represent all information in patient records or in product labeling where natural language is used to convey non-terminological concepts such as “child under twelve”. They also note that other multi-purpose terminologies are available, including UMLS which links these terminologies. The limitations of using HLTs and HLGTs and SSCs for the purposes of signal detection are discussed; however, there is only a brief mention that SMQs are under development. It is noted that SSCs and SMQs are created manually by experts rather than having them generated automatically from the MedDRA files.

The authors conclude that MedDRA does not have the attributes of a third-generation system and is not a clinical nomenclature. As such, it does not allow the automated positioning of new terms or the automated generation of SSCs or SMQs. The authors suggest linking MedDRA to a third generation system to add computational capabilities while preserving the MedDRA structure.
While it might be technically feasible to link MedDRA to another system, it would make the overall system more complicated for users. In addition, there are significant limitations of automated systems for the positioning of terms. An automated tool would simply not be able to handle issues of medical interpretation, common usage or colloquial expressions. The MSSO believes that the current manual maintenance process, which involves a thorough review with a consensus opinion on term placement, is the process that best satisfies the needs of the user community. It is particularly difficult to see how automated tools could aid in the generation of SMQs. The tool might be successful in identifying the closely related terms that may be included as “narrow” search terms in an SMQ e.g. PTs “Electrocardiogram QT prolonged” and “Long QT syndrome” in the SMQ Torsade de Pointes/QT prolongation. However, it is unlikely that a tool could identify the non semantically related terms that are nonetheless clinically associated with the condition and that need to be included in a broad search. Broad search terms in the SMQ Torsade de Pointes/QT prolongation include sudden and cardiac death terms such as “Sudden death” and “ Cardiac death” because of their frequent association with torsade de pointes. Syncope was also included as a broad search term as a result of testing by the user community when it was found that this term, albeit a very non-specific one, did aid in the identification of potential cases.

Summary:

This is a rather technical article written from a medical informatics perspective. It evaluates MedDRA against a set of criteria for the ideal terminology but neglects to do the same comparison for other terminologies. It inappropriately compares MedDRA to a standard that is not relevant to the purpose for which MedDRA was developed. The article is somewhat outdated and does not adequately address the browser tools and SMQs that have been developed and are now in use. The authors propose linking MedDRA to third generation systems to increase its computational abilities but they do not discuss the limitations of automated tools and how they would not obviate the need for careful medical review and user community involvement in the terminology maintenance process.