Knowledge representation in Health Research: the modeling of Adverse Events Following Immunization

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Aims and Objectives of the Research

The overall goal of my thesis is to improve safety signal detection in vaccine adverse events reports within the Canadian healthcare system. A system that would provide an easy and fast way to isolate reports of potential interest for human experts to focus their attention on would significantly decrease time and resources currently needed for signal detection.

Justification for the Research Topic

Free-text reporting of Adverse Events Following Immunization (AEFIs) leads to inaccurate and incomplete data. Accurate representation of adverse event is a crucial part of clinical research: it may initiate further investigation of potential problems in vaccine safety or efficacy, and facilitate subsequent dissemination of safety-related information to the scientific community and the public [1,2]. However, current methods used for adverse events reporting are not sufficient, mitigating their usefulness. There is no standardization of the terminology used in the current Electronic Data Capture System used by Public Health Agency of Canada – at best a Medical Dictionary of Regulatory Activities (MedDRA [3]) code is assigned after parsing the clinician's input, but this code is not linked to any definition. Several studies highlight the potential issues in using MedDRA for adverse event reporting, ranging from inaccurate reporting (as several terms are non-exact synonyms) to lack of semantic grouping features impairing processing in pharmacovigilance [4-8]. Additionally, only the final adverse event code as determined by the system is saved, and information about sub-parts are lost, therefore restricting ability of the physician to go back to the set of symptoms observed to establish the diagnostic, and limiting the ability to query the resulting datasets.

Research Questions

Is it possible to automate the diagnosis of adverse events for safety signal detection?

(1) Can the logic of a clinical guideline be encoded as an ontology to allow for semantic querying, i.e., be complex enough to encode all logical aspects while maintaining reasoning capabilities?

(2) Can a mapping between the ontology and another resource used to annotate existing AE reports datasets be established, and allow for ontologically-supported diagnosis to be inferred from the current reports?

(3) Is it possible to apply known algorithms to classified datasets to detect statistically significant patterns?

(4) Is the detection of those patterns more efficient in terms of time and cost than performed by human review?

Research Methodology

Regarding vaccine adverse events, the Brighton Collaboration [9] has done extensive work towards standardization. This global network of world-renowned experts aims to provide high quality vaccine safety information. They create methodological standards for accurate risk assessment, including standardized case definitions of AEFIs. While they do not provide a causal assessment between a given adverse event and the immunization process, the case definitions are designed to define the levels of diagnostic certainty of reported AEFIs.

Aim 1. To develop an ontology to logically represent Brighton definitions, resulting in increased quality and accuracy of AEFIs reporting. In collaboration with the Brighton Collaboration, I will create an application ontology, the Adverse Events Reporting Ontology (AERO). AERO defines individual signs and symptoms textually. They will then be logically defined by being positioned into a hierarchy, and linked between them and an overall diagnosis.

Aim 2. Establish a mapping between MedDRA and the AERO. MedDRA - the Medical Dictionary for Regulatory Activities - is currently being used to encode adverse events reports into reporting systems such as the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) or the Vaccine Adverse Event Reporting System (VAERS) in the US. Each term in AERO will be linked to the corresponding term(s) in MedDRA.

Aim 3. Perform automatic case classification on structured datasets. Using the mapping built in aim 2, we will be able to process automatically the existing MedDRA annotations on the data, to infer if a Brighton criteria has been met or not. For example, the tool would be able to suggest anaphylaxis diagnosis based on a set of MedDRA annotations.

Aim 4. Detect safety signals. Using the classified datasets, known statistical methods can be applied to determine if the proportion of reported cases according to the Brighton is statistically significant.

Research Results to Date

The AERO project is available at http://purl.obolibrary.org/obo/aero. AERO is listed on the OBO library at http://obofoundry.org/cgi-bin/detail.cgi?id=AERO and under BioPortal at http://bioportal.bioontology.org/visualize/45521. The initial effort has been described in [10]. Based on preliminary results of the AERO work, the Brighton Collaboration expressed interest in partnering. As of November 2011, I am leading a Brighton working group which goal is to support further development of the AERO and work towards using it to perform automatic case classification of adverse event reports, as described above.

References

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