Adverse events following immunization: reporting standardization, automatic case classification and signal detection

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1 BACKGROUND

Analysis of spontaneous reports of Adverse Events Following Immunization (AEFIs) is an important way to identify potential problems in vaccine safety and efficacy and summarize experience for dissemination to health care authorities. However, current reporting methods are not sufficiently controlled. While there is general adoption of Medical Dictionary of Regulatory Activities (MedDRA) in the reporting systems we consider, definitions are not provided for MedDRA terms, reports are not annotated in a consistent manner, differing in experience of annotator, and annotation is done either at entry time, or post-hoc. Sometimes, only the final adverse event code is saved, discarding evidence supporting the diagnosis. Because of these practices, interpretation of such spontaneous reports is tedious, costly and time consuming. The Adverse Event Reporting Ontology (AERO) we are building plays a role in increasing accuracy and quality of reporting, ultimately enhancing response time to adverse event signals.

2 METHODS

In order to address these deficiencies, we work with the Brighton Collaboration who has done extensive work towards standardization of case definitions and diagnostic criteria for vaccine adverse events. Based on our initial results with AERO, a working group has been established within the Brighton network, including representation from the Public Health Agency of Canada (PHAC) and the US Food and Drug Administration (FDA), to incorporate logical representations of Brighton case definitions into AERO, with the aim of increasing quality and accuracy of AEFI reporting. As an example, only 9% of the Vaccine Adverse Event Reporting System (VAERS) anaphylaxis reports post-H1N1vaccination early 2010 were correctly annotated with the MedDRA anaphylaxis term.

Working within the framework being established by the Open Biological and Biomedical Ontologies (OBO) Foundry, the Adverse Events Reporting Ontology (AERO) first documents assessments of relevant signs and symptoms textually. These elements of AEFI reports are then logically defined by being positioned into a hierarchy and related to each other in a way that supports computing an overall diagnosis. Our system allows automatic inference of a diagnosis according to the Brighton criteria based on the evidence encoded in the MedDRA annotations.

3 RESULTS

Our approach allows us to unambiguously refer to a specific set of carefully defined signs and symptoms at the time of data entry, as well as an overall diagnosis that remains linked to its associated signs and symptoms. The adverse event diagnosis is formally expressed, making it amenable to further querying for example for statistical analysis (“what percentage of patients presented with motor manifestations?”) and at different levels of granularity. Finally, by enabling automatic processing of adverse events reports, we will decrease time and money needed for their evaluation. This may allow earlier detection of adverse events signal in the datasets, and trigger a warning for experts to further investigate.