

TOWARDS AN ADVERSE EVENT REPORTING ONTOLOGY

INTERNATIONAL CONFERENCE ON BIOMEDICAL ONTOLOGY
REPRESENTING ADVERSE EVENTS WORKSHOP

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Importance of adverse event reporting (AE reporting)



- Important to decrease morbidity and mortality
- Safety alerts, recalls, prescription revisions, SOPs revisions...
- A shared, standard reporting system for AE would improve patient safety

PCIRN mission

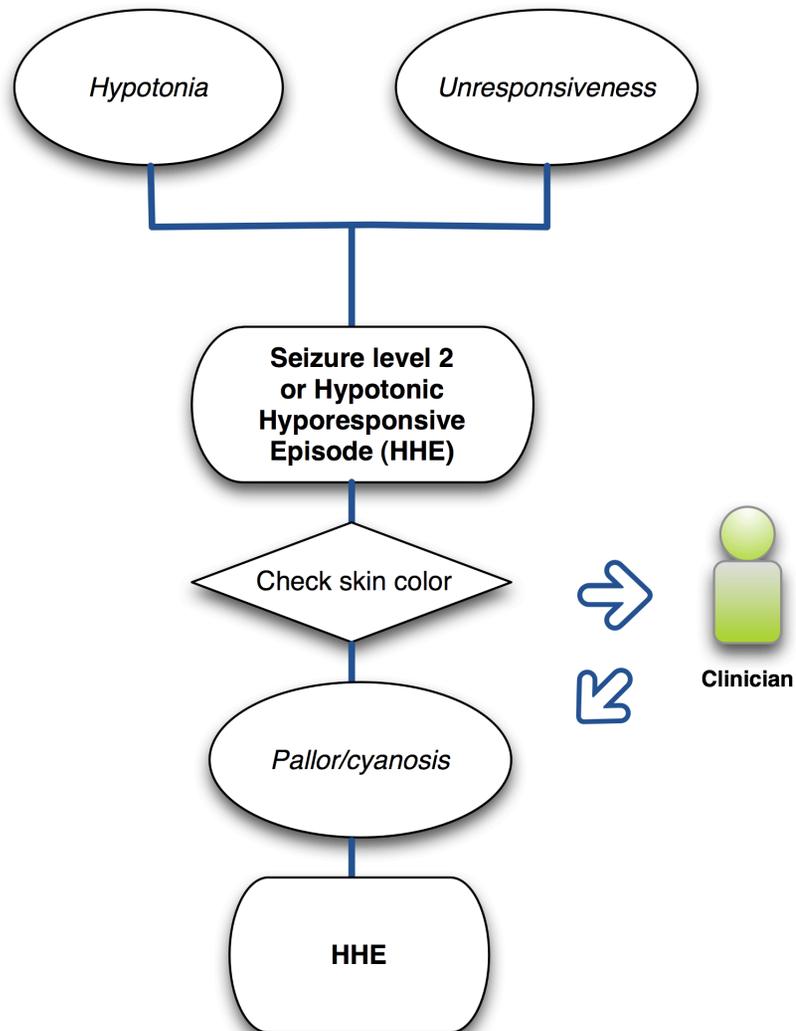


- PCIRN: Public Health Agency Canada/Canadian Institutes of Health Research Influenza Research Network
- Canadian national network of key influenza vaccine researchers.
- Develops and tests methodologies/methods related to the evaluation of pandemic influenza vaccines as they pertain to safety, immunogenicity and effectiveness, and program implementation and evaluation.
- <http://www.pcirn.ca/>

PCIRN AE reporting: current problem

- Forms use *Medical Dictionary of Regulatory Activities (MedDRA)* at best
 - ▣ No definitions
 - ▣ Ambiguous terms
- But often only “description” text input field offered to record result of diagnosis
- PCIRN wants a tool to help confirm that the diagnosis follows the guidelines, and the ability to perform more complex queries on reports

A diagnosis confirmation tool

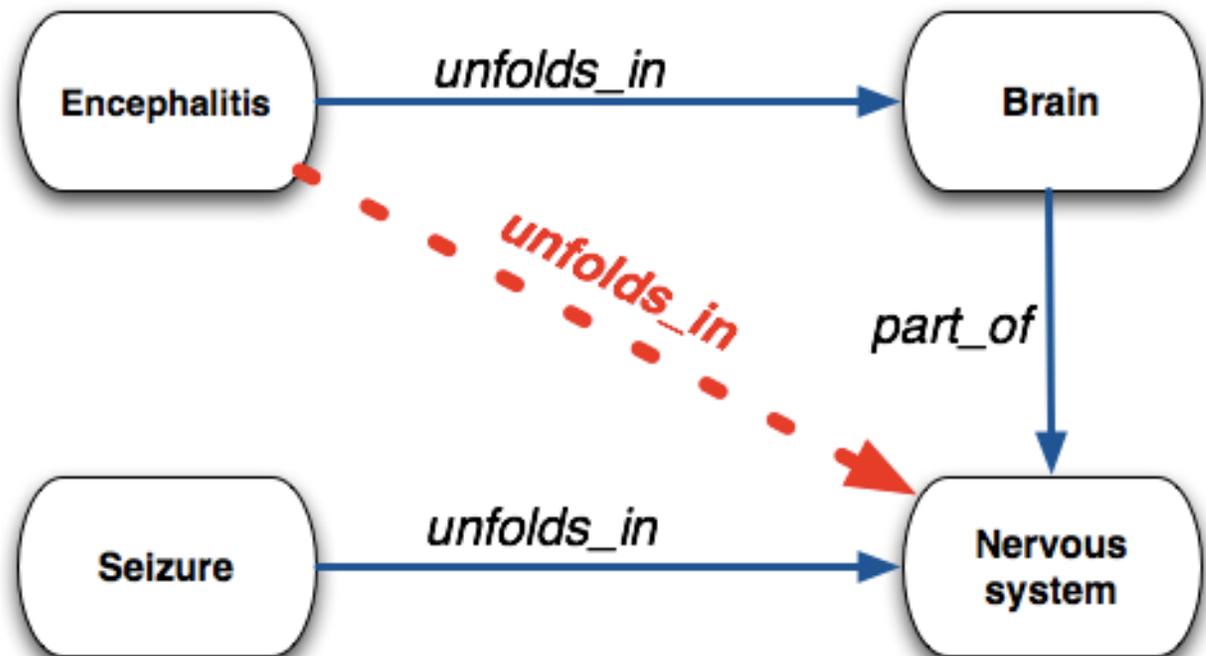


- Given diagnosis, retrieves appropriate parts of guidelines and prompts for additional information needed to reach diagnosis according to them
- Example: Clinician records *Seizure level 2*. System prompts for associated symptoms. Clinician records *hypotonia* and *unresponsiveness*. System asks about skin color to help clinician make final determination of *Seizure level 2 or Hypotonic-Hyporesponsive Episode (HHE)*

Enabling more complex queries

- Current system can't ask for AE reports related to nervous system
- By making relations explicit and adding general knowledge we can infer new things

- Computer can infer link such as **“Encephalitis unfolds_in Nervous system”**



A 3 step approach to improving adverse event reporting

- ① Use standard definitions for terms used in AE reporting
 - ❑ Ensure that *AE Following Immunization* (AEFI) is reported in accordance to a PCIRN selected guideline
 - ❑ Specify evidence that confirms AEFI diagnosis
- ② Convert the guideline into a computer manipulable form
 - ❑ Use automatic reasoning to support diagnosis confirmation and enhance query results
- ③ Make diagnosis confirmation tool part of reporting workflow
 - ❑ Enable annotation at data entry time by clinicians

① Standard definitions: the Brighton artifacts

- Brighton collaboration provides diagnosis guidelines to help standardize reporting

- Built by 300 contributors from patient care, public health, scientific, pharmaceutical, regulatory and professional organizations

Bonhoeffer et al. Vaccine, 2002.

- Good applicability, sensitivity, and specificity

Kohl et al. Vaccine, 2007.

- Performs well against other standards

Erlewyn-Lajeunesse et al. Drug safety, 2010.

- Adopted by PHAC and used within PCIRN

Gagnon et al., Journal of allergy and clinical immunology, 2010.

② Build an OWL ontology to represent the guidelines



- Domain is modeled using an ontology
- Each entity is defined textually
 - Human readable definition, label
- Each entity is defined logically
 - Relations to other entities

③ Implement in reporting systems: Dacima EDC (commercial system)

- Assist in confirming a reported clinical entity (e.g., seizure)
 - ▣ Diagnosis support at data entry time
- Prompt for disambiguating information to narrow diagnosis
- Enable interoperability and advanced querying of AE reports
- Current status: discussion with Dacima about implementing these improvements to their Electronic Data Capture system (Daciforms)

The Adverse Event Reporting Ontology - AERO

AERO is an OWL ontology that represents the Brighton guidelines

The screenshot displays the AERO ontology viewer interface. The browser address bar shows the URL `http://purl.obolibrary.org/obo/aero.owl`. The main navigation tabs include 'Active Ontology', 'Entities', 'Classes', 'Object Properties', 'Data Properties', 'Individuals', 'OWLviz', 'DL Query', and 'OntoGraf'. The 'Classes' tab is active, showing a class hierarchy for 'adverse event'. The hierarchy is as follows:

- Thing
 - ObsoleteClass
 - 'adverse event'
 - 'AEFI generalized convulsive seizure according to Brighton guidelines'
 - 'AEFI seizure level 1 of certainty according to Brighton guidelines'
 - 'adverse event following immunization'
 - 'adverse side effect'
 - entity
 - continuant
 - dependent_continuant
 - independent_continuant
 - spatial_region
 - occurrent
 - processual_entity
 - _manifestations
 - 'adverse event process'
 - behavior
 - 'device malfunction'
 - 'etiological process'
 - fever
 - fiat_process_part
 - 'inflammatory response'
 - 'planned process'
 - process
 - process_aggregate
 - process_boundary
 - processual_context
 - seizure
 - spatiotemporal_region
 - temporal_region
 - sign
 - symptom

The right-hand pane shows the 'Annotations' for 'adverse event', including:

- definition source:** "ICH Topic E 2 A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting"
- editor note:** "MC, 20110719: we don't currently cover cases where the adverse event is a quality of the patient, such as pallor."@en
- comment:** "I initially made adverse event a defined class: is_a sign and preceded by administration. However, by doing so, and as the range of preceded by is processual entities, I was implicitly making adverse event a subclass of processual entity, therefore making adverse event rash (a continuant) inconsistent."@en
- definition:** "An adverse event is an undesirable, unfavorable and unintended medical occurrence presenting in a predetermined time frame following administration of a compound or usage of a device"@en
- label:** "adverse event"@en

The bottom pane shows the 'Description' for 'adverse event', including:

- Equivalent classes:** 'disorder resulting from an adverse event process' or 'adverse event process'
- Superclasses:** entity

AERO – elements and issues



- What is an adverse event?
- Processes and continuants
- Adverse event report
- Use of guidelines: case definitions

Adverse event definition



- An adverse event is an undesirable, unfavorable and unintended medical occurrence presenting in a predetermined time frame following administration of a compound or usage of a device
 - ▣ No causality assessment
 - ▣ Compliant with U.S. Food and Drug Administration (FDA) and International Conference on Harmonization guideline (ICH E2A)

AERO:adverse event



- Occurrents:
 - ▣ motor manifestations, seizures, inflammatory responses...
- Continuants:
 - ▣ sensorineural deafness reported after measles, mumps, and rubella immunization, rash...
- Logical definition:
 - ▣ 'disorder resulting from an adverse event process' or 'adverse event process'

AERO:adverse event report



- Subclass of IAO: report
- In most cases, an adverse event *is_about* an adverse event
- Medical device reporting: also reports about device malfunction
- Logical definition:
 - ▣ 'is about' some ('adverse event' or 'device malfunction')

Call for contributions



- Help develop the prototype
 - Ontological issues to solve
 - Describe severity, expectedness
 - Add more AEFIs
 - Cover drugs and device related AEs
- Review AERO. AERO is available at <http://purl.obolibrary.org/obo/aero>

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