Building a time-saving and adaptable tool to report adverse drug events

Yves Parès, Gunnar Declerck, Sajjad Hussain, Romain Ng, Marie-Christine Jaulent

Context of the work

Material: the SALUS project & platform

The ICSR Reporting System

Specifications
Semantic interoperability
Functional architecture

Results

Discussion & Conclusion

INSERM UMRS 872, Eq.20: E-Health Knowledge Engineering, Paris, France.
Pharmacovigilance

- Detect and prevent Adverse Drug Events (ADEs)
- Postmarketing surveillance
- Need: Individual Case Safety Reports (reports of occurrences of suspected ADEs)

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1 Bates DW et al, Detecting adverse events using information technology: JAMIA 10(2), 2003; pp. 115-128.
Pharmacovigilance

- Detect and prevent Adverse Drug Events (ADEs)
- Postmarketing surveillance
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Currently

- Only 5% of cases reported to health authorities\(^1\):
  - Underreporting
- However, cases frequently described in EHRs\(^2\)

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\(^1\) Bates DW et al, Detecting adverse events using information technology: JAMIA 10(2), 2003; pp. 115-128.

Individual Case Safety Report

Reasons of underreporting

- Detection: complex cognitive process
- Filling the report (ICSR): time-consuming & error-prone
- Submission: sometimes cumbersome (paper-based for some regulatory authorities)
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Individual Case Safety Report

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Semi-automatic reporting

Earlier attempt, ASTER project:

- Automatic detection of ADEs
- ICSR prepopulation with EHR data
- ICSR submission to the FDA
Semi-automatic reporting: room for enhancements

ASTER interest confirmed by physicians, but:

- Tied to specific content models (EHR)
- Still needs manual processing of ICSR before submitting
- Can be improved w.r.t automation & interoperability
SALUS: General objectives

Add interoperability to the state of the art

- Syntactic (EHR / ICSR content models) and semantic (terminologies) interoperability
- Detection and prepopulation tools independent of the EHR system in use
- Automated pseudonymisation/anonymisation of ICSRs using different content models
- Report generation following standards and adaptable to local requirements
SALUS: General objectives
Add interoperability to the state of the art

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Gather and mine data to support clinical studies

- Post-market safety studies
- Clinical research studies
- Clinical trial studies
ICH E2B(R2)

- A standard used by the WHO Uppsala Monitoring Centre
- Relies on web standards:
  - XML for serialization
  - Web services for protocol
- Uses terminological standards (MedDRA)
- Must be extended/cut down to support national/local authorities’ requirements (e.g. AIFA in Italy)
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A tool for the heath practitioner

- Support the reporting of Adverse Drug Events occurrences
- Make that task easier thanks to the prepopulation of:
  - patient data (from EHR)
  - constant data (local configuration)
- Reduce time and error risk while filling ICSRs
- Send ICSRs to a local regulatory body
- Save a partial ICSR for later completion
- View already sent and pending ICSRs
- Update and nullify an already sent ICSR
Salus Core Ontology

Defining an ontology out of the Common Data Elements

- Need to make mapping between content models
- Mapping each model with each other: $N^*(N-1)$ mappings
- Solution: use a systematic approach to identify Common Data Elements
- Formalize the CDEs in an ontology: SCO
- SCO: common denominator between standards for clinical care (HL7 CCD, EN 13606 EHR Extracts or proprietary models)
- SCO used by all the semantic components of SALUS platform (for queries)

(??? After that, maybe a slide showing some mappings from MIXHS paper ????)
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System components

Figure: ICSR Reporting System components, in yellow
Scenario completion

Potential Adverse Drug Event detected

- Patient comes back for a monitoring visit, with a new symptom
- HP adapts the prescription
- HP, as usual, inputs these new pieces of info into the EHR
- ADE Notification Manager, through a subscription mechanism, receives the new data
- It pops a notification in the EHR GUI
- HP agrees with the ADE, and chooses to create an ICSR now
- Our ICSR Reporting System is triggered
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Scenario completion

ADE Notification Manager detects a possible ADE and issues a notification.
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Scenario completion

HP agrees, patient ID sent to Reporting Manager. Web browser launched, waiting for Reporting Tool to send form.
Scenario completion

Reporting Manager queries for the patient medical summary, needed for prepopulation.
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Scenario completion

Scenario completion

Patient summary (RDF/N3 file) routed to the Reporting Tool. Uses SparQL queries on it to prepare the ICSR HTML form.
Local Triplestore queried for constant data (mundane administrative fields).
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Scenario completion

Prepared form sent to the HP, through the Web browser that was kept awaiting.
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Figure: Excerpt from the GUI, with the corresponding E2B that will be generated
Reporting Tool receives the completed form, transforms it into RDF data and validates it.
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Scenario completion

Report Generator creates the E2B/XML report from the RDF representation of the ICSR.
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Scenario completion

Personal information fields in the ICSR are mangled. Matchings are kept within the hospital information system.
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Scenario completion

Report Generator receives the final ICSR and sends it to the regulatory authority.
Results

Content Models harmonization

- Salus Core Ontology (ontology of Common Data Elements) built
- E2B, HL7 CCD templates, ISO/CEN 13606 templates & OMOP Common Data Model mapped to SCO
Results

Capacities of the reporting system

- Handles prepopulation by extracting data from patient summaries thanks to SparQL queries targeting CDEs
- Provides support to HP to complete remaining fields:
  - Provides close choice list mechanism (through terminologies)
  - Doesn’t encumber HP with fields not required by the authority
  - Folds/expands form to show only necessary fields (e.g. additional fields about seriousness showed only if HP deems ADE serious)
  - Deduces content of fields from content of others
- Generates E2B/XML file to be submitted to the UMC
Comparison with existing reporting systems

- FDA MedWatch or UMC Vigiflow more complex and cumbersome
- Require several steps and pages to complete a form
- Not integrated with hospital’s EHR
- ICSR Reporting Tool provides unique & terse view, with only necessary fields
Method for future evaluation

Three test phases:

- Robustness of prepopulation & conversion between content models with real EHR data
- Functional and non-functional software quality evaluation (e.g. time taken by prepopulation, fault cases and crashes tolerance). Follows evaluation reference model ISO/IEC CD 25040
- End user evaluation in pilote sites (TU Dresden and Lombardy Region SISS) with real implementation of the tool. Criteria will be:
  - User satisfaction and time to complete ICSRs
  - Regulatory authorities satisfaction (amount of relevant information provided)
Limitations encountered

- Lots of data in EHR still in free-text: limited amount of data queriable for prepopulation
- Alignments between content models and terminologies are still partial: impossible to always have 1-to-1 mappings, various levels of granularity are present
- Prepopulation of patient history not fully automatic: must be guided by HP’s experience
Conclusion

Research Contributions:

- **Clinical Standardization**: Utilizing the standard clinical terminologies and information models to query medical summaries from EHRs.

- **Semantic Harmonization**: Establishing mapping between the standard clinical terminologies/information models and local schemas of EHRs.

- **Querying Heterogeneous Medical Data**: Based on the supported semantic harmonization, querying heterogeneous EHRs allows reporting systems to retrieve relevant information from different EHRs.

- **Pre-populating ICSR Forms using Patient Data**: Pre-populating EHR data for ADE reporting. Our population techniques is scalable to incorporate other clinical use-cases, e.g. generating and sharing lab reports to other health institutions.