Ontology-based Knowledge Management for Personalized Adverse Drug Events Detection

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Adverse Drug Event

- The 4th leading cause of death
- Cause 1 out of 5 injuries or deaths to hospitalized patients
- Yearly cost $136 Billion in US in 2000
Problems

- **Doctor aspect**
  - Doctor prescribes based on his prior, experienced knowledge on drugs.
  - He/she does not check ADE information on the system since it is time consuming task.
  - Doctor recommends drug based on general condition, rather than the personal, specific recommendations.

- **Patient aspect**
  - Patient hard to find reliable web portal for his personalized drug safety questions
Challenges

- How to build a general system to uniformly manage ADE knowledge
- The integration of patients’ record system with ADE knowledge base
- How to apply relationships among clinical terms to match knowledge and patients’ records
Architecture

- Takes ADE knowledge and patients’ data as input
- Uses standard vocabulary (such as SNOMED-CT) to manipulate these data
- Provide service of personalized ADE detection by semantic query and reasoning
Semantic Query for ADE Detection

- **SPARQL Query**
  - Given a patient's prescription (i.e., a list of drugs), we issue semantic queries to find the adverse reactions caused by each drug $d_i$, and the drug interactions for each pair of drugs $(d_i, d_j)$, together with their consequences and conditions.

- **D2R Mapping**
  - integrate ontology reasoning with the semantic query
  - adds the independency between the ADE query logic and the physical storage
Semantic Reasoning over SNOMED

- **SNOMED CT (Systematized Nomenclature of Medicine - Clinical Terms)**
  - Concepts: over 365,000, organized in 19 hierarchies, such as Drug, Substance, Symptom, etc.
  - Descriptions: over 993,420, including synonyms
  - Relationships: Approximately 1.46 million

- **Why SNOMED**
  - Systematically organized computer processable collection of medical terminology
  - Comprehensive and widely used, easy for information exchange and integration

- **Enrich ADE knowledge**

- **Enable the semantic matching between ADE conditions and patient’s records**
## Enrich ADE knowledge

<table>
<thead>
<tr>
<th>Type</th>
<th>ADE knowledge</th>
<th>SNOMED relationship(s)</th>
<th>Inferred Knowledge</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>drug_B -&gt; disorder_D</td>
<td>drug_A sct:subClassOf drug_B</td>
<td>drug_A-&gt; disorder_D</td>
</tr>
<tr>
<td>II</td>
<td>ingredient_I -&gt; disorder_D</td>
<td>drug_A sct:hasActiveIngredient ingredient_J AND ingredient_J sct:subClassOf ingredient_I</td>
<td>drug_A-&gt; disorder_D</td>
</tr>
<tr>
<td>III</td>
<td>Nil (no ADE information for a given drug A)</td>
<td>drug_A sct:hasActiveIngredient ingredient_J AND ingredient_J sct:subClassOf ingredient_I AND disorder_D sct:hasCausitiveAgent ingredient_I</td>
<td>drug_A-&gt; disorder_D</td>
</tr>
</tbody>
</table>
Enable the semantic matching between ADE conditions and patient’s records

- A fragment of CDA document

```xml
<Observation>
  <code code="ASSERTION" codeSystem="2.16.840.1.113883.5.4"/>
  <value xsi:type="CD" code="126707007" codeSystem="2.16.840.1.113883.6.96" codeSystemName="SNOMED CT" displayName="Neoplasm of hilus of lung"/>
</Observation>
```

- Relevant ADE knowledge

  “for patient who has disorder on lung, Drug A leads to adverse reaction R”

- The query for clinical condition matching is to check if the patient has the observation of disorder with finding site at lung.

  \[
  Q(x) \leftarrow \text{emr:patient}(x), \text{emr:hasObservation}(x, y), \text{sct:Disorder}(y), \text{sct:findingSite}(y, z), \text{sct:Lung}(z).
  \]

- From SNOMED

  1. \( \text{sct:Neoplasm of hilus of lung} \sqsubseteq \text{sct:Neoplasm of lung} \cap \text{sct:findingSite} \cap \text{sct:hilus of lung} \)
  2. \( \text{sct:Neoplasm of lung} \sqsubseteq \text{sct:Disorder} \)
  3. \( \text{sct:hilus of lung} \sqsubseteq \text{sct:Lung} \)

By referencing SNOMED, we know the above patient meets the ADE condition specified by the query.

Implementation

- **J2EE environments with DB2 V9 and Web Sphere V7**

- **ADE knowledge enrichment and enhancement**
  - Seek for more ADE-relevant information from various data sources,
  - Extract ADE knowledge from multiple sources,
  - Encode ADE, knowledge using standardized codes and terms,
  - Incorporate different knowledge and keep semantic consistency.

- **Knowledge Sources**
  - Customer data from Korean Gil Hospital
  - Structured Product Labeling (SPL) from US FDA
  - Linked Open Drug Data (LODD)
Summary

- Two kinds of ontologies are introduced into the system
  - define the ADE ontology to uniformly manage the ADE knowledge from multiple sources

- Semantic query on RDF view and semantic reasoning over clinical ontology
  - take advantage of the rich semantics from the terminology SNOMED-CT

- A general ADE knowledge management system that can load, store, and query ADE data from heterogeneous sources with different formats.
Thanks!

Q & A