Acquiring and representing drug-drug interaction knowledge as claims and evidence

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Problem
Potential drug-drug interactions are a significant source of preventable drug-related harm. The drug information sources clinicians use are dissonant: Most drug information sources disagree substantially in their content (e.g. Abarca et al. 2003, West et al. 2010, Saverio et al. 2011). This problem has persisted for more than a decade (e.g. Ayaz et al. 2015, Elstein et al. 2015) despite extensive editorial work on the part of each drug information source. This is in part because:
(1) There is no standard, agreed upon method for assessing evidence about drug-drug interactions.
(2) Knowledge claims and evidence about drug-drug interactions are distributed across multiple sources: pre-market studies, post-market studies, and clinical experience.

Disagreement leads to an additional:
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2. Knowledge claims and evidence about drug-drug interactions are distributed across multiple sources: pre-market studies, post-market studies, and clinical experience.

Aim
In this work, we address the distributed nature of drug-drug interaction knowledge, by developing a computable representation for claims and evidence about drug-drug interactions. Our goal is to support:
(a) Knowledge acquisition from full-text natural language (b) Search and retrieval of all evidence.

We are applying this representation to acquire claims and evidence about pharmacokinetic interactions for 65 drugs. This will help us design a search portal, to test whether computerized representations of knowledge claims and evidence can improve search and retrieval of potential drug-drug interactions. This will help us design a search portal, to test whether computerized representations of knowledge claims and evidence can improve search and retrieval of potential drug-drug interactions.

We model knowledge as claims supported by evidence.

Approach
Designing a data model for representing claims and evidence

1. Identify key ontologies relevant for claims and evidence.
   - Nanopublication Ontology represents settled science: Each formalized claim (assertion) is wrapped in provenance and publication info.
   - Micropublications Ontology represents claims and evidence. It views a scientific paper as a network of claims supported by data, methods and materials. Claims, data, methods, and materials can be text, images, or multimedia: anything the Open Annotation Ontology can reference.
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2. Identify key domain ontologies to reuse.
   - Ontology of Biomedical Investigations
   - Chemical Entities of Biological Interest
   - Drug Ontology

3. Conceptualize 3 layers and determine what belongs in each layer:
   - Data
   - Method
   - Claim

4. Formalize key terms about drug-drug interactions in a new ontology, DIDEO.
   - For instance, “potential drug-drug interaction” gets obo:DIDEO_0000000

5. Human curators annotate full-text documents.
   - (a) The curator highlights the claim.
   - (b) The curator enters the claim and scientific method.

Acquiring claims and evidence

1. Formulate claims of interest.
   - “Clarithromycin interacts with simvastatin”

2. Identify relevant source documents.
   - Source documents include FDA-approved drug product labels and full-text research papers (clinical trials and case reports).

   - Experts check that documents meet inclusion criteria.

4. Pre-anonymize by computer text mining.
   - Source documents are pre-processed to find drug mentions, using named entity recognition algorithms.

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Future Work
• Build an information portal that supports clinical pharmacists and drug information professionals in retrieving the claims and evidence.
• Test the information portal in a task-based, within-subject, user study. Measure the completeness of the information experts retrieve with our information portal compared to current state-of-the-art retrieval tools.
• Test the feasibility of authors annotating their own claims and evidence.
• Enable annotation beyond PubMed Central open access HTML.
• Use rule sets of “belief criteria” to transform evidence to a knowledge base.

Ontologies, Data, and Websites
https://github.com/DIDEO/DIDEO
Drug Interaction Knowledge Base website & discussion forums

Publications and Presentations

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