Drug-drug Interactions - opportunities for improved standardization and interoperability of data

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Potential drug-drug interactions (PDDIs)

• Exposure two or more drugs that are known to interact
  – “potential” because exposure does not necessarily mean a clinically meaningful effect
Clues about the frequency of harm

- Clinically important events attributable to drug-drug interactions [1]:
  - 5.3% - 14.3% of inpatients
  - 231,000 US emergency department visits

- Hospital admissions associated with an adverse drug event attributable to drug-drug interactions [2]:
  - 22.2% (interquartile range 16.6 - 36.0%)

Key point

No broadly accepted standards exist on how to organize and present PDDI knowledge
PDDI clinical decision support (CDS) information needs

- Review and synthesis of:
  - 77 journal articles
  - 4 white papers from AHRQ-funded PDDI Working Groups
  - 6 semi-structured interviews

"there may be 3 or 4 pharmacokinetic case studies... there may be a bunch of case reports. So then we add up all that information together."

**Topic Definition**
Selection of PDDIs to review is motivated either by the availability of new information or by requests/workflow from clients or constituents.

**Demand-driven**: constituent queries/work assignment
**Data-driven**: new information from literature, drug announcements

**Unmet/PDI Information Needs**
- Challenges: Too many PDDIs to consider. Can efforts be prioritized based on level of interest, prevalence, risk?

**Information search**

**Sources**
- PubMed: trials, case reports
- Medwatch: FDA Event reports
- Google: gray literature
- Compendia
- Drugs@FDA/New Drug Applications
- Product labels
- Manufacturers

**Evidence Item Review**
- Drug/Interaction Information
- Study Design
- Quality and content of report
- Clinical Evidence

**Evidence to be summarized**

**Completion of review**
Subjective, heuristic process
- Challenges: Hard to know when to stop. Possibly when evidence is sufficient for presenting a recommendation.

**Information Management**
ad hoc charts and reports: Information placed in clipboard, emailed, possibly filed (paper or electronic).

**Challenges**
- Revisiting papers can be difficult
- Minimal tracking of information that has been reviewed and rejected

**Synthesis and recommendation**

**Reviewing information**: Look at “whole situation” use plausibility to resolve conflict

**Reaching a conclusion**: Balance safety and evidence, avoid excessive caution.

**Reports and recommendations**: Prose or templates, often with scales

- Challenges: Hard to find evidence of absence - look at tertiary articles
- Consult outside experts if details are unfamiliar
- Manage tradeoffs: false positive vs false negative

**Fig. 2** Potential Drug-Drug Interaction information evaluation and synthesis workflow
PDDI CDS Information needs…

**Mechanism of action**
- Pharmacology
- Formulation
- Timing
- …

**Context**
- Modifying and mitigating factors
- Time of onset
- Manageability
- Frequency
- …

**Evidence**
- Study design
- Reporting information (e.g., funding agency)
- Causality assessment (case reports)
- …

**Clinical Consequences**
- Adverse effect(s)
- Seriousness
- Severity
- …

**Recommended actions**
- Monitor, change drugs, modify strength, adjust timing, etc
- Strength of recommendation
What have we done to address this gap?
The PDDI Minimum Information Model Task Force:

- volunteer-based – ~40 participants
  - W3C, AMIA Pharmacoinformatics, WorldVista, academics

- broad stakeholder involvement
  - NLM, industry, academic institutions, individuals

- Open public participation
  - formed within the Health Care and Life Sciences Interest Group that operates publicly through the World Wide Web Consortium (W3C)
Task force objective and deliverables

• **Objective**: Develop a minimal information model for drug interaction evidence and knowledge as part of an HIT standard like HL7

• **Deliverables**: using an interesting and non-trivial set of potential drug-drug interactions:
  – A minimum information model for potential drug interaction knowledge and evidence
  – A precise vocabulary describing/defining the information model
  – Demonstration of how the information model can support medication reconciliation
The deliverables as a W3C Community Group Report

• Available here: [https://w3id.org/hclscg/pddi](https://w3id.org/hclscg/pddi)
• 10 core information items
• 8 detailed best practice recommendations related to the 10 core information items
• 2 exemplar PDDIs (narrative and prototype JSON artifacts using the information model)
• 12 User stories with related goals
The minimum information model and related vocabulary
**R1** - Explicitly state the drugs involved, ideally using value sets

**R2** – Report a mechanism if known (or state “not known”)

**R3** – State the frequency of harm relative to frequency of exposure if known
**R4** - Explicitly state clinical consequences, ideally using value sets

**R5** - Note if a clinical consequence is **serious**

**R6** - Include an operational classification statement
**R7** - State each known risk modifying factor or patient context

**R8** - State a recommended action if one is known
The envisioned role for a PDDI minimum information model

1. Pre-clinical \rightarrow Expert evidence
2. Clinical \rightarrow Expert evidence
3. Observation \rightarrow Expert evidence

- Annotation of evidence sources according to the minimal information model

- Canonical representation of PDDI information \rightarrow Sharing in knowledgebase

- Domain-specific transformation

- Decision Support Systems
- Structured Product Labeling extensions
- Cohort descriptions for evidence generation
• Link to the report: https://w3id.org/hclscg/pddi
• There are multiple ways to provide feedback:
  – Anonymously provide feedback via this qualtrics survey: https://pitt.co1.qualtrics.com/jfe/form/SV_brNsZtD8vHwPoLX
  – email your comments to Rich Boyce at rdb20@pitt.edu
  – add an issue on the Note's github site:
    • https://github.com/w3c/hcls-drug-drug-interaction/issues
  – reply to the forums.dikb.org topic:
    • https://forums.dikb.org/t/final-comment-periods-for-the-pddi-information-model-community-group-note/211
The information model as part of PDDI CDS as a service

- An HL7 project within the CDS workgroup
  - Create an *implementation guide that* shows how to do PDDI CDS as a service:
    - The minimum information model, FHIR, CDS Hooks, and CQL
  - Join us!
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Discussion