Drug-Drug Interaction Extraction from Structured Drug Labels

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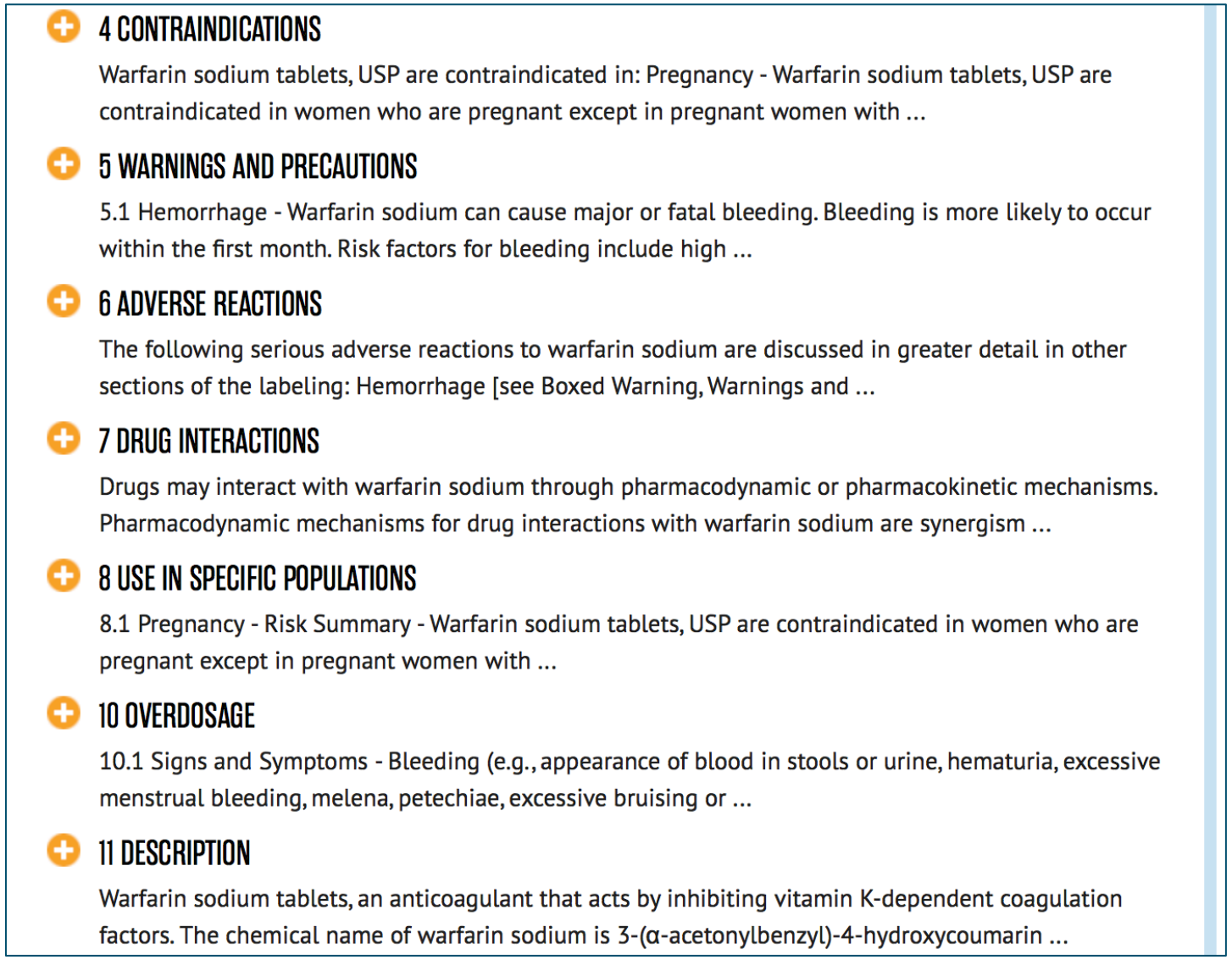
Mechanisms of Drug-Drug Interaction

http://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/drug-interaction

- A drug interaction results when the effects of a drug are altered in some way by the presence of another drug, by food, or by environmental exposure.
- The risk of developing an adverse drug reaction (ADR) secondary to a drug–drug interaction increases significantly with the number of medications a patient is receiving.
- Mechanisms of drug interactions:
  - A pharmacodynamic interaction results when a drug interferes with a second drug at its target site, or changes in some way its anticipated pharmacologic response. The consequence of this interaction results in additivity, synergy, or antagonism of the intended effect. An example of a pharmacodynamic interaction is the synergism that results from combining two or more anti-infectives in the treatment of a resistant pathogen.
  - Pharmacokinetic interactions occur when one drug alters the absorption, distribution, metabolism, or elimination of another drug, thereby changing its concentration in plasma and, consequently, at the targeted site of action. Clinically significant drug interactions are most often due to alterations in pharmacokinetics, secondary to modulation of drug metabolism.

Relevant SPL sections

Boxed Warning, Contraindications, Dosage and Administration, Drug and/or laboratory test interaction, Drug Interactions, Precautions, Warnings and Precautions, Warnings



4 CONTRAINDICATIONS

Warfarin sodium tablets, USP are contraindicated in: Pregnancy - Warfarin sodium tablets, USP are contraindicated in women who are pregnant except in pregnant women with ...

5 WARNINGS AND PRECAUTIONS

5.1 Hemorrhage - Warfarin sodium can cause major or fatal bleeding. Bleeding is more likely to occur within the first month. Risk factors for bleeding include high ...

6 ADVERSE REACTIONS

The following serious adverse reactions to warfarin sodium are discussed in greater detail in other sections of the labeling: Hemorrhage [see Boxed Warning, Warnings and ...

7 DRUG INTERACTIONS

Drugs may interact with warfarin sodium through pharmacodynamic or pharmacokinetic mechanisms. Pharmacodynamic mechanisms for drug interactions with warfarin sodium are synergism ...

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy - Risk Summary - Warfarin sodium tablets, USP are contraindicated in women who are pregnant except in pregnant women with ...

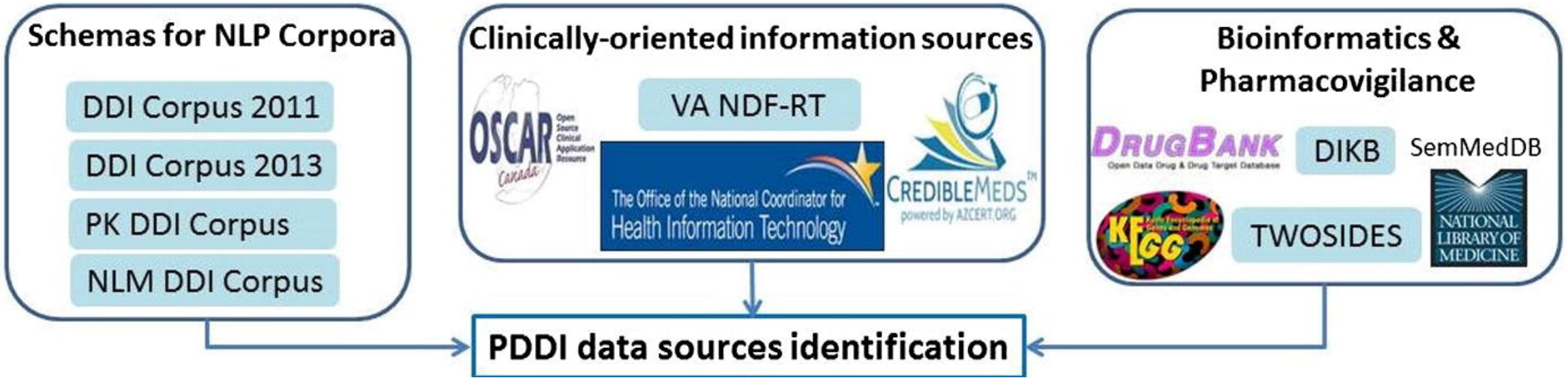
10 OVERDOSAGE

10.1 Signs and Symptoms - Bleeding (e.g., appearance of blood in stools or urine, hematuria, excessive menstrual bleeding, melena, petechiae, excessive bruising or ...

11 DESCRIPTION

Warfarin sodium tablets, an anticoagulant that acts by inhibiting vitamin K-dependent coagulation factors. The chemical name of warfarin sodium is 3-(α-acetonylbenzyl)-4-hydroxycoumarin ...

Related work

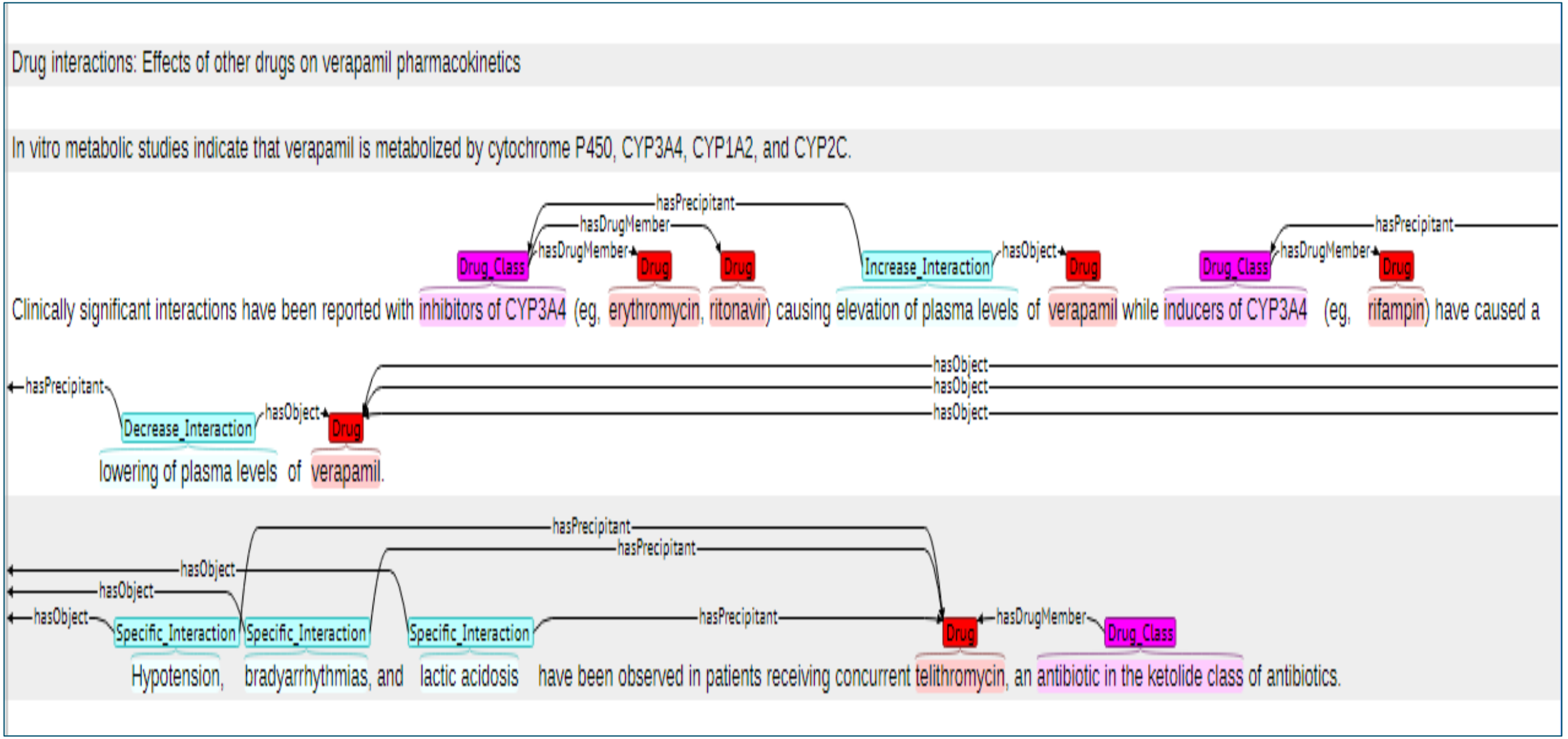


- **An attempt to combine all publically available PDDIs sources.**
- **The merged dataset consists of fourteen different sources of PDDIs information.**
- Ayvaz S, Horn J, Hassanzadeh O, Zhu Q, Stan J, Tatonetti NP, Vilar S, Brochhausen M, Samwald M, Rastegar-Mojarad M, Dumontier M. Toward a complete dataset of drug–drug interaction information from publicly available sources. Journal of biomedical informatics. 2015 Jun 30;55:206-17.

Annotation

- **Entities**
  - Drug
  - Drug class
  - Substance
  - Span / Expression
- **Interaction events**
  - Caution (*Unspecified)*
  - Increase / Decrease (*Pharmacokinetic)*
  - Specific (*Pharmacodynamic)*

Training set



Objective

- Identify substances interacting with the label drug
- Identify interaction type
- Provide justification (sentence containing the interaction)
- Produce output for FDA review:
  - Sentences from the designated SPL sections
  - Section name
  - The type of interaction – pharmacokinetic, pharmacodynamic or unspecified
  - The labeled drug and generic ingredient(s) identified by the SPL set id
  - The interacting substance encoded in UNII, or in NDF-RT NUI if it is a drug class
  - The consequence of the interaction encoded in SNOMED CT if it is a medical condition, or in National Cancer Institute Thesaurus codes if it is a pharmacokinetic effect

Tasks

- Task 1
- Extract Interacting Drugs/Substances and the sentences that contain interactions.

- Task 2
- Identify the interacting drugs and the specific interaction types: pharmacokinetic, pharmacodynamic or unspecified.

- Task 3
- Normalize the interacting substance to UNII, and the drug classes to NDF-RT NUI. Normalize the consequence of the interaction to SNOMED CT if it is a medical condition. Normalize pharmacokinetic effects to National Cancer Institute Thesaurus codes.

Data

- Training
  - NLM-DDI CD corpus https://lhce-brat.nlm.nih.gov/NLMDDICorpus.htm
- Test
  - A: Automatically annotated sentences reviewed and corrected by FDA
  - B: Fully manually annotated sections (simplified annotations)