Representing Drug Classes for Mitigating Concurrently Applied CPGs

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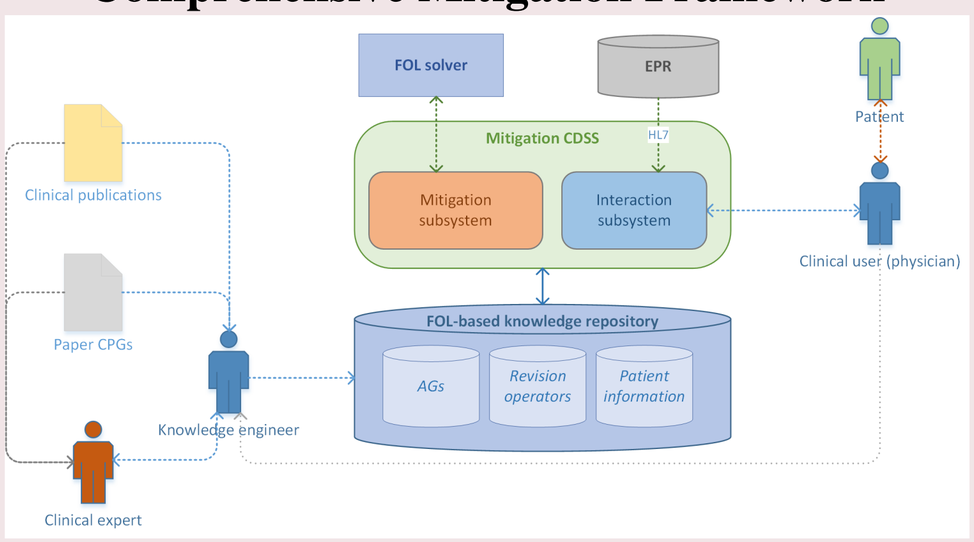
Introduction

- We developed a comprehensive framework for identifying and mitigating adverse interactions in multi-morbid patients managed according to multiple clinical practice guidelines (CPGs)[1],
- The framework relies on first-order logic (FOL) to represent CPGs and secondary medical knowledge and FOL theorem proving to establish valid patient management scenarios,
- It handles many complexities of CPGs (e.g. time-based interactions) and also considers patient preferences[2]. However, it is unable to capture hierarchical dependencies between concepts and thus requires detailed specification of secondary knowledge,
- In this work we address the above shortcoming by expanding the FOL-based knowledge representation to handle hierarchical representations of drug classes.

Comprehensive Mitigation Framework



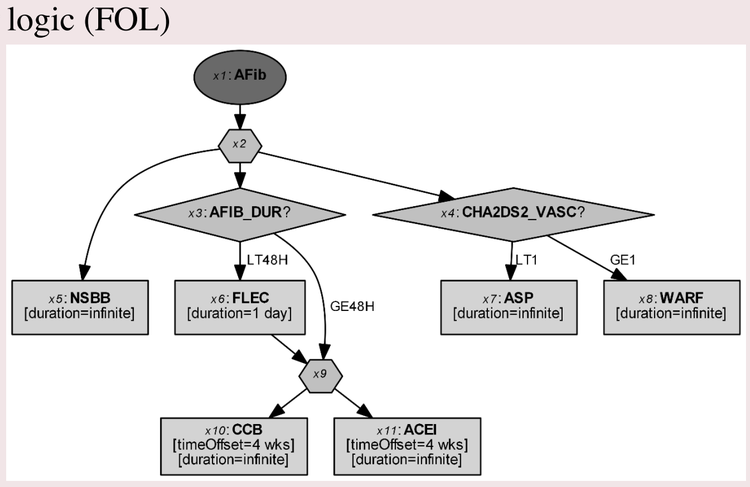
High-level design of the mitigation framework (EPR = electronic patient record).[1]

Mitigation clinical decision support system (CDSS)

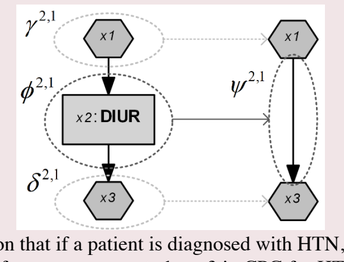
- Responsible for computations, i.e., processing of combined mitigation theories,
- Interfaces clinical users (physicians) and an EPR,
- Executes a mitigation algorithm and invokes an external FOL solver (Z3) for theorem proving and model finding,
- Data capture facility for entering patient information and for importing it from the EPR through standardized protocols like HL7,
- Reports detailed mitigation results (management scenario, applied revision operators) translated into a narrative, textual format, so the clinical user is fully insulated from the underlying FOL-based representation.

FOL-based knowledge repository

- Stores the knowledge used by the mitigation framework using first-order logic (FOL)

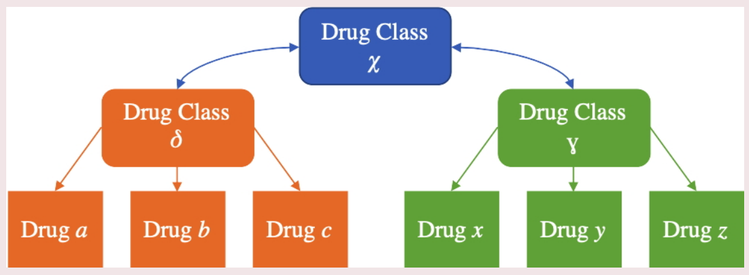


Actionable graph representing CPG for AFib (AFIB_DUR = duration of AFib episode, *LT48H* = <48 h, *GE48H* = ≥ 48 h, *CHA2DS2_VASC* = CHA2DS2-VASc score, *LT1* = <1, *GE1* = ≥ 1, *NSBB* = non-selective beta blocker, *FLEC* = flecainide, *CCB* = calcium channel blocker, *ACEI* = ACE inhibitor, *ASP* = aspirin, *WARF* = warfarin).[1]



Revision operator representing the revision that if a patient is diagnosed with HTN, CKD and AFib, and prescribed diuretics for HTN, then remove diuretics from management phase 3 in CPG for HTN.[1]

Hierarchical Representation of Drug Classes



- Hierarchical relationships between drug classes described using a logical biconditional a ↔ b
  - a is a single predicate drugClass(c),
  - consequent b is a disjunction of several such predicates corresponding to more specific drug classes.
- Drugs from a given class identified using an implication a → b
  - a is a single drugClass(c),
  - b is a set of terms corresponding to specific drugs.
- Predicate action(x, dc) represents administering the drug dc
  - dc indicates a specific drug or a class of drugs.
- For any action predicate where dc is a drugClass(c) consisting of more specific classes:
  - Assert (action(x, c_1) ∨ action(x, c_2) ∨ ...) for all classes c_i in that specific drug class *c*,
  - Otherwise, assert (action(x, d_1) ∨ action(x, d_2) ∨ ...) is in the set of grounded terms d_i in that drug class.
- Representing the combined FOL theory for a specific patient, expand all drugClass predicates so the combined theory is using the grounded terms for specific drugs in its representation.

Anticoagulation example

- Class of anticoagulants consisting of vitamin-k antagonists and novel oral anticoagulants (NOACs), and specific drugs for each class:

  drugClass(anticoag) ↔ drugClass(vitamin-k) ∨ drugClass(NOAC)

  drugClass(vitamin-k) → {warfarin, atromentin, phenindione}

  drugClass(NOAC) → {dabigatran, rivaroxaban, apixaban, edoxaban, betrixaban}
- Assert that the administered anticoagulant is either a vitamin-k antagonist or NOAC
  - Expand the predicate action(x, drugClass(anticoag)) to (action(x, drugClass(vitamin k))∨ action(x, drugClass(NOAC)),
  - Expand these formulas to assert that a vitamin-k antagonist is in the set of drugs (grounded terms)
    - Replace drugClass(vitamin-k) with the sentence (action(x, warfarin) ∨ action(x, atromentin) ∨ action(x, phenindione)),
    - Replace drugClass(NOAC) with the sentence (action(x, dabigatran) ∨ action(x, rivaroxaban) ∨ action(x, apixaban) ∨ action(x, edoxaban) ∨ action(x, betrixaban)).

Conclusions

- Designed a richer mitigation framework that supports hierarchal relationships of drug classes
  - Simplified process of representing and applying revisions at the level of drug classes.
- Mitigation and customization algorithms do not need to be changed,
- Structurally similar to existing terminologies[3], but allows for more advanced processing of such knowledge as FOL offers more sophisticated reasoning capabilities (e.g., entailment) than description logics.

References

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