

Representing Drug Classes for Mitigating Concurrently Applied CPGs

Martin Michalowski¹, Szymon Wilk², Wojtek Michalowski³, Marc Carrier⁴

¹University of Minnesota, Minneapolis MN, USA; ²Poznan University of Technology, Poznan, Poland; ³University of Ottawa, Ottawa, Canada; ⁴The Ottawa Hospital Research Institute, Ottawa, Canada

Introduction

We developed a 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 preferences². One limitation is its inability to capture hierarchical dependencies between concepts at different levels of granularity. This limitation results in a very detailed specification of secondary knowledge. In this work we address this shortcoming by expanding the FOL-based knowledge representation to handle hierarchical representations of drug classes.

Hierarchical Representation of Drug Classes

Our expanded representation describes hierarchical relationships between drug classes using a logical biconditional $a \leftrightarrow b$, where a is a single predicate $drugClass(c)$, and the consequent b is a disjunction of several such predicates corresponding to more specific drug classes. A biconditional is powerful because it is transitive and can be infinitely nested. To identify drugs from a given class we use an implication $a \rightarrow b$, where a is also a single $drugClass(c)$, and b is a set of terms corresponding to specific drugs. Consider the class of anticoagulants consisting of vitamin-k antagonists and novel oral anticoagulants (NOACs), and specific drugs for each class:

$drugClass(anticoag) \leftrightarrow drugClass(vitamin_k) \vee drugClass(NOAC)$

$drugClass(vitamin_k) \rightarrow \{warfarin, atromentin, phenindione\}$

$drugClass(NOAC) \rightarrow \{dabigatran, rivaroxaban, apixaban, edoxaban, betrixaban\}$

In our framework a predicate $action(x, dc)$ represents administering the drug dc where dc can indicate a specific drug or a class of drugs. For any $action$ predicate where dc is a $drugClass(c)$ consisting of more specific classes, we assert $(action(x, c_1) \vee action(x, c_2) \vee \dots)$ for all classes c_i in that specific drug class c . Otherwise, we assert $(action(x, d_1) \vee action(x, d_2) \vee \dots)$ is in the set of grounded terms d_i in that drug class. When representing the combined FOL theory for a specific patient, we expand all $drugClass$ predicates as described above so the combined theory is using the grounded terms for specific drugs in its representation.

In our example the mitigation framework asserts that the administered anticoagulant is either a vitamin-k antagonist or NOAC by expanding the predicate $action(x, drugClass(anticoag))$ to $(action(x, drugClass(vitamin_k)) \vee action(x, drugClass(NOAC)))$. Further expanding these formulas asserts that a vitamin-k antagonist is in the set of drugs (grounded terms) by replacing $drugClass(vitamin_k)$ with the sentence $(action(x, warfarin) \vee action(x, atromentin) \vee action(x, phenindione))$. A similar expansion is applied to the NOACs.

Conclusions

In our previous work we designed a physician aid that integrates CPGs, best-in-class mitigation strategies, and secondary medical knowledge from evidence-based repositories to propose personalized treatment for specific multi-morbid patient encounters at the point of care. Our initial results were very promising and one of the next steps is to move our research into practice. Towards this end, we designed a richer mitigation framework that supports hierarchical relationships of drug classes. This expanded support simplifies the process of representing and applying revisions that represent mitigation strategies for adverse interactions at the level of drug classes. The mitigation and customization algorithms do not need to be changed. At the structural level our representation of drug class hierarchies is similar to what is used in existing terminologies³ but integration with our framework allows for more advanced processing of such knowledge as FOL has more sophisticated reasoning capabilities (e.g., entailment) than description logics.

References

1. Wilk S, Michalowski M, Michalowski W, Rosu D, Carrier M, Kezadri-Hamiaz M. "Comprehensive mitigation framework for concurrent application of multiple clinical practice guidelines." J Biomed Inform, 66:52-71, 2017.
2. Michalowski M, Wilk S, Rosu D, Kezadri M, Michalowski W, Carrier M. "Expanding a first-order logic mitigation framework to handle multimorbid patient preferences." AMIA Annu Symp Proc, 895-904, 2015.
3. Sharp, Mark E. "Toward a comprehensive drug ontology: extraction of drug-indication relations from diverse information sources." J Biomed Semantics, 8:2, 2017.