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Tackling Polypharmacy: A Multi-Source Decision Support System

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Abstract. Managing the use of multiple medicines, also known as polypharmacy, is a challenge for physicians, pharmacists and patients alike, and is a particular concern for patients with multiple chronic conditions (aka multimorbidity). Patients with multimorbidity are often required to take a considerable number of medications for their different ongoing conditions, and managing/revising these medications effectively is a challenge. There is a need to periodically rearrange drugs taking into account patient's preferences and avoiding adverse drug reactions. We present an incremental, constraint solver based framework for a clinical decision support system that makes it possible to check drug prescriptions using information from multiple sources, including a constraint database and patient records. We illustrate how it can be used to manage clinical conditions while reducing polypharmacy problems and undesired side effects in a patient-centric approach.

Keywords. Polypharmacy, multimorbidity, constraint solvers, clinical decision support systems

1. Introduction

Polypharmacy can be defined as the concomitant use of multiple medications by a patient [1] [2], and is commonly linked to the treatment of multiple chronic diseases, also known as *multimorbidity*, which occurs with the highest prevalence in the elderly [3]. In addition, the use of many drugs simultaneously to treat different diseases is not always clear and may not match patient expectations and preferences [3] [4]. It is important that the use of various medications is safe and effective [5], and this may become questionable when the risks of medication combinations outweigh the benefits.

Studies have indicated that there are risks associated with the use of multiple medications, which include drug interactions and adverse drug reactions [6] [7]. Drug interactions have a negative outcome when the reaction between drugs has, for instance, a toxic effect or decreases the effect of one drug [6]. An adverse drug reaction is defined as any undesirable medical occurrence caused by a pharmaceutical product but not necessarily related to treatment [8] and may occur for different reasons, such as the wrong dose, drug or route [9]. Studies have shown that over half of the hospital admissions and between 25% to 50% of outpatient care arise from adverse drug reactions which could have been mitigated [10].

The complexity of taking decisions when treating patients can be a significant challenge, especially in the presence of polypharmacy which invariably combine many

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factors/variables. Additionally, treatments should be personalised and the patient's individual preferences included in the decision process. The position we take is that, specially in the case of complex decision making, automated tool support is essential. Our approach combines medical knowledge with formal methods techniques to search for and compute optimal solutions for managing the treatment of patients with complex needs. This paper is structured as follows: we describe the proposed framework in Section 2 and illustrate how our approach works in Section 3. We conclude the paper with some overall comments and future work in Section 4.

2. Proposed Framework

To support physicians in making appropriate decisions, we propose a clinical decision system framework to check and manage constraints between drugs, exams, and diseases and take into account patient preferences. The solution consists of five parts: the Electronic Medical Record (EMR) interface, the Knowledge interface, the Knowledge database, the Inference engine and the Decision maker

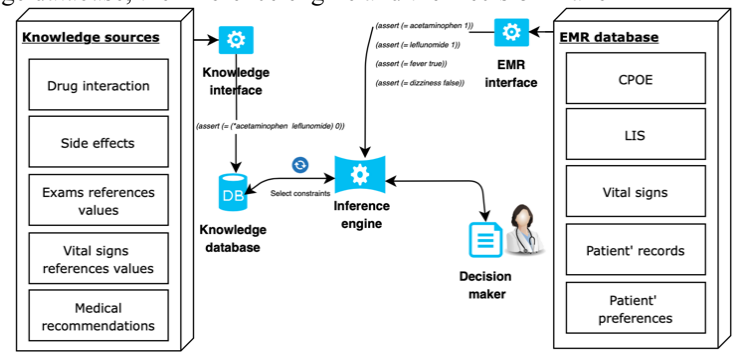

Figure 1. Multi-Source Decision Support System Framework.

The framework shown in Figure 1 takes constraint data from the knowledge sources and patient data from the EMR which are processed independently. The information from both sources is used in the Inference engine, which is responsible for merging both patient and constraint data. The Inference engine checks in the knowledge database if there are constraints that need to be solved according to the patient information then automatically searches for alternative solutions without constraints and displays them for the doctor to decide the appropriate prescription.

2.1. Knowledge interface and database

There are different sources of constraints in knowledge sources which can be used in the Inference engine. To standardize the link between the Inference engine and its sources, we propose a generic knowledge interface. This interface enables the retrieval of data about different constraint types such as drug interactions, side effects, alternative drugs, exam and vital sign reference values. Developing a generic interface will allow users to connect new and different types of constraint sources.

The knowledge interface operates in three steps: receive, process/convert and deliver. The data can be *received* from different channels. Each channel is for a specific type of constraint (e.g., for drug interaction data) and has a custom layout. The data

received by the hub is *converted* into a formal model illustrated in Figure 1 on the *assert* text between the knowledge interface and database, which is compatible with the Z3 [11] solver. *Delivery* is divided into *checking* (searching the knowledge database to see if a specific constraint is already recorded) and *inserting*. If a constraint is already recorded it is discarded, otherwise the system inserts it in the knowledge database to be used by the Inference engine.

2.2. EMR interface

The EMR interface deals with different types of patient data to link the information between the EMR database and Inference engine. Initially, the EMR interface was developed to receive all available information from the patient such as Computerized Physician Order Entry (CPOE) which includes drug prescriptions, laboratory results from the Laboratory Information System (LIS), Vital Signs and Patient Records. The EMR interface also has a channel to receive information on patient preferences. For example, there are medications with side effects such as headache, dizziness or drowsiness, that patients may want to avoid. In these situations, physicians should select drugs which avoid particular side effects.

Similar to the knowledge interface, after receiving information from the EMR, the EMR interface processes the data in three steps: identify, process/convert and deliver. In the first step, the hub *identifies* the type of data (e.g., exam results, drug prescriptions, vital signs or patient records). In the next step, the hub *converts* the data into a formal showed in Figure model to be compatible with the Z3 [11] solver, showed in Figure 1 between the EMR database and interface. Finally, the information is *delivered* to the Inference engine.

2.3. Inference engine and decision maker

The Inference engine was proposed to create links between the knowledge database and patient data, so that it is possible for example to search for drugs that do not have undesired side effects. The compiler receives patients' clinical information and selects the related constraints on the knowledge database to define solutions using the constraint solver Z3 [11].

Firstly, the compiler receives the data from the EMR interface and checks if there are constraints that need to be solved. Secondly, after receiving patient data, a query is executed in the knowledge database based on the received data (e.g., Acetaminophen and Leflunomide drug prescription), to find the linked constraint (in this example, the drug-drug interaction, drug-adverse reaction, drug-disease interaction and drug-food interaction). Finally, if constraints are found for the patient data, the compiler is executed to solve or manage them. As a result, the compiler returns advice to physicians, the decision maker, which takes into account a number of important variables and allows the physician to choose the most appropriate treatment plan to be adopted for a given patient.

3. Practical example

To illustrate how our approach works, we present an extended hypothetical example taken from [5] about a 69 years old man. The patient arrives in hospital after a fainting

and seizures episode and complaining about arm pain and dizziness. The physician checks the patient's previous data on the EMR as shown on the first row of Table 1. Thereafter the physician requests a blood glucose test, verifies the blood pressure and prescribes Dextrose 10% and Electrolyte 500 ml and Codeine phosphate (7,5 mg) + Acetaminophen (300 mg) as shown in the second row of Table 1.

During the consultation, the patient data (previous and new records) is sent from the EMR to the EMR interface and sent to the Inference engine.

Table 1. Patient data

Current medical history	Result exams	Drugs	Patient' preferences
(Previous) Frequent falls Dementia – mixed Alzheimer's disease /alcohol abuse	**(Previous)** BP 120/74 mmHg Blood glucose test 90 mg/dL	**(Continuous use)** Trazodone 150 mg Thiamine 50 mg Bendroflumethiazide 2.5 mg	**(Previous)** Patient reports: feeling tired and short of breath
(New records) Fainting episode, seizures	**(New records)** BP 132/74 mmHg Blood glucose test 125 mg/dL	**(New records)** Codeine phosphate (7,5 mg) + Acetaminophen (300 mg) Dextrose 10% and Electrolyte 500 ml	**(New records)** Patient reports: Feeling arm pain and dizziness

Given the drug interactions and medical recommendations from the knowledge source, the Inference engine checks the constraints from the knowledge database against the patient data and highlights the relevant constraints as in the three tables below.

Table 2. Constraint drug interaction data

Drug	Drug	Interaction	Severity
Trazodone	Codeine phosphate	risk of a rare but serious condition called the serotonin syndrome, which may include symptoms such as confusion, hallucinations, seizures, blurred vision	Moderate
Trazodone	Bendroflumethiazide	lowering blood pressure	Moderate

Table 3. Medical recommendations

Drug	Condition	Recommendation
Dextrose 10%	blood glucose test 125 mg/dL	May cause hyperglycemia

Table 4. Side effects

Drug	Side effects	Used for the following conditions (associated conditions)
Trazodone 10%	dizziness	Alcohol Dependence, Alzheimer's Disease (AD), Dementias
Bendroflumethiazide	dizziness	High Blood Pressure
Codeine	dizziness	Pain, Acute, Severe Pain, Moderate Pain

Thereafter, the physician interactively manages these constraints with the Inference engine. To solve the first interaction in Table 2 between Trazodone and Codeine phosphate, the system shows to the physician the drug interaction and lists alternative drugs to manage the problem. The alternative drugs are selected from the knowledge database according to the associated conditions shown in Table 4. For all listed drugs, the system shows all the possible constraints, for example, interactions with other drugs or side effects that should be avoided according to patient preferences. The alternative drugs are sorted from the best to the more intricate options, that is, from the smallest to the biggest number of related constraints. The physician can also decide

to exclude a drug from the prescription or prescribe a drug that is not listed, for example, to minimise a side effect.

Moreover, if the physician decides to change/include/exclude a drug, the system reloads in real-time the constraints based on this decision. Otherwise, the system keeps the existing constraints and flags the chosen drugs in order to avoid repeated alerts in case of reloading. The same process is repeated to solve the medical recommendations in Table 3 and the side effects in Table 4. The process ends when there are no constraints to be solved, which does not mean that all restrictions have been solved, but that all decisions regarding the constraints have been made.

4. Conclusion

In this paper, we presented the vision of a framework to support physicians to make the appropriate decisions considering different types of drug constraints and interactions, and respecting patient preferences. The framework is enabled to receive multiple data sources combining patient and constraint records. As a clinical decision support system, our proposed automated solution only offers advice and the final decision remains with the physician. We demonstrated how the system can give advice to manage drug conflicts for a realistic but hypothetical example, highlighting the importance of gathering medical evidence and knowledge in decision making. In future work, we intend to fully develop, implement and evaluate the proposed solution.

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