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A Preference-based framework for medical decision making

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Abstract. Medical decision making, such as choosing which drugs to prescribe, requires to consider mandatory constraints, *e.g.* absolute contraindications, but also preferences that may not be satisfiable, e.g. guideline recommendations or patient preferences. The major problem is that these preferences are complex, numerous and come from various sources. The considered criteria are often conflicting and the number of decisions is too large to be explicitly handled. In this paper, we propose a framework for encoding medical preferences using a new connective, called ordered disjunction symbolized by ~×. Intuitively, the preference "*Diuretic~×Betablocker* means: "Prescribe a *Diuretic* if possible, but if this is not possible, then prescribe a *Betablocker*". We give an inference method for reasoning about the preferences and we show how this framework can be applied to a part of a guideline for hypertension.

Keywords. Medical decision making, preferences, preferred solutions, inference, aggregation

Introduction

Medical decision making, such as choosing which drugs to prescribe, requires to consider various pieces of knowledge. Some of them are mandatory, *e.g.* indications and absolute contraindications, while others only express preferences that may not be satisfiable, *e.g.* recommendations from clinical practice guidelines (CPG) and relative contraindications. The integration of preferences in medicine is discussed in different works [1,2,3,4], and *preference* was defined as the desirability of a health-related outcome, process, or treatment choice [4]. Two approaches have been developed in the literature: 1) a quantitative approach [5,6] where preferences are expressed by means of a utility function, the option with the maximal utility is considered the best one, 2) a qualitative approach [7,8,9] where relative preferences are expressed by ordering the options. However, quantitative approaches are more complex because they require to express preferences with numerical values, which is often difficult in medicine. Our aim is to propose a qualitative framework that allows encoding medical knowledge including preferences and a method to select the best solution. This framework contains two types of formulas: 1) integrity constraints representing mandatory knowledge with usual connectives ($\Leftrightarrow$, $\Rightarrow$, $\wedge$, $\vee$, $\neg$) and 2) preferences, using usual connectives and a new connective called *ordered disjunction* ~×

where $A{\sim}{\times}B$ means: "if possible A, but if A is impossible, then at least B". Once integrity constraints and preferences are encoded, an inference relation method is given to rank order the options and determine which is the best one. In section 1 we present the proposed framework and in section 2 we show how this framework can be applied to a subset of a CPG mixing recommendations with absolute and relative contraindications and patient history. Section 3 concludes the paper.

1. Methods

Table 1 provides a simple example concerning the prescription of antihypertensive drugs, inspired by hypertension CPG [10]. In this example, three antihypertensive drugs are considered, and several pieces of knowledge must be taken into account, depending on comorbidities associated with hypertension and patient history. In the rest of this section, we propose a language for encoding these knowledge and reasoning about them.

Table 1. Some recommendations and contra-indications in hypertension CPG [10]. *LVH*: Left Ventricular Hypertrophy, ACI: Angiotensin Converting enzyme Inhibitor, CA: Calcium Antagonist, ARB: Angiotensin II Receptor Blocker, ADE: Adverse Drug Event.

Comorbidity / patient history	Recommendations and contraindications
LVH	Recommendation : ACI, CA, ARB
Heart failure	Relative contraindication: CA
Hyperkalemia	Absolute contraindication: ACI, ARB
History of ADE with ACI	Absolute contraindication: ACI

1.1. The proposed language

The language of the proposed framework is composed of two types of formulas: 1) Propositional formulas expressing integrity constraints and 2) Preference formulas offering a simple way to rank the various options.

Definition 1 *Let O be a set of propositional atoms that represent a set of options. If a_i are propositional atoms in O then each formula φ that is built using classical logical connectives ($\Leftrightarrow$, $\Rightarrow$ $\wedge$, $\vee$, $\neg$) over a_i is a propositional formula. If φ, ψ are propositional formulas then ($\varphi{\sim}{\times}\psi$) is a preference formula.*

Table 2 gives information of Table 1 encoded using the proposed language.

Table 2. Knowledge of Table 1 encoded using the proposed language.

Comorbidity	Preference formulas	Propositional formulas
LVH	$\varphi_1 = ACI{\sim}{\times}CA{\sim}{\times}ARB$	
Heart failure	$\varphi_2 = \neg CA{\sim}{\times}CA$	
Hyperkalemia		$\varphi_3 = \neg\, ACI \wedge \neg\, ARB$
History of ADE with ACI		$\varphi_4 = \neg\, ACI$

1.2. The inference relation

The semantics of formulas represented using our logic is based on the degree of satisfaction of each formula in a particular interpretation *I* (or solution). An interpretation *I* is an assignment of a truth value T (True) or F (False) to each atom. *I* will be represented by the set of its satisfied (True) atoms. An interpretation which satisfies a given formula is called a model. In Table 2, we have three options, thus there is 2^3=8 interpretations or possible solutions. For example, the interpretation *I*={*ARB*, *CA*} represents the solution where both *ARB* and *CA* are prescribed. The inference relation (symbolized by |=) is defined as follows:

Definition 2

1. *Let* $\varphi = a_1 \vec{\times} a_2 \vec{\times} \ldots \vec{\times} a_n$ *be a preference formula. Then* $I \models_k \varphi$ *iff* $I \models a_1 \lor a_2 \lor \ldots \lor a_n$, *and* $k = min(j \mid I \models a_j)$.

2. *Let* ψ *a propositional formula.* $I \models_1 \psi$ *iff* $I \models \psi$.

Namely, given a preference formula $a_1 \vec{\times} a_2 \vec{\times} \ldots \vec{\times} a_n$, an interpretation *I* satisfies φ to a degree *k* (formally, we write $I \models_k \varphi$), if it satisfies the k^{th} proposition of φ (i.e. a_k) and does not satisfy the preceding ones ($a_1, a_2, \ldots, a_{k-1}$). If no proposition a_k of φ is satisfied by *I*, the satisfaction degree is equal to 0. For propositional formulas, the satisfaction degree is 1 if they are satisfied, and 0 otherwise. For example, if we consider the interpretation *I*={*CA*, *ARB*}, then φ_1 is satisfied to degree 2 (we write $I \models_2 \varphi_1$). If *I*={Ø} (*i.e.* no drug prescription), then φ_1 is not satisfied.

1.3. Preferred solutions

If there is only one formula, best solutions are the ones which satisfy the formula with the smallest non-zero degree. However, in general many formulas should be considered (*e.g.* in case where the patient have several comorbidities). So, it is important to consider the different cases in order to give the best solution(s). In our framework, we use a lexicographic order, which is based on the number of formulas satisfied to a particular degree. To define the preferred solutions, let us consider *T* be a set of preference formulas, *K* a set of propositional formulas. The set of propositional and preference formulas is represented by $K \cup T$.

Definition 3 Let $I^k(T)$ denote the subset of formulas of T satisfied by an interpretation I to a degree k with respect to the patient cases. The cardinality of a set is denoted by |.|. An interpretation I_1 is $K \cup T$-preferred over an interpretation I_2 if there is k such that $|I_1^k(T)| > |I_2^k(T)|$ and for all $j < k$: $|I_1^j(T)| = |I_2^j(T)|$. I is a preferred solution of $K \cup T$ if:

1. *I satisfies each formula of K, and satisfies each formula in T to some degree,*
2. *I is maximally preferred with respect to* $K \cup T$.

Intuitively, a preferred solution of $K \cup T$ is an interpretation which satisfies each formula in K and satisfies the maximal number of formulas in T with a non-zero smallest degree.

2. Results

In this section, we present reasoning example using the proposed framework and the knowledge pieces from Table 1. To do that, we apply the following algorithm: 1) determine the patient comorbidities, 2) for each comorbidity, represent the associated absolute contra-indications as propositional formulas and relative contradictions and recommendation as preference formulas, 3) compute the set of all possible interpretations, 4) compute the satisfaction degree of each formula for each interpretation, 5) compute the preferred solutions.

Table 3 shows the 8 possible interpretations for the example of Table 1, and for each, the satisfaction degrees for the 4 formulas we defined in Table 2. Using Table 3, the preferred solutions for various clinical situations can be determined (by applying Definition 3). For example, for a patient with hypertension and LVH, the best solutions are I_5 to I_8, *i.e.* ACI or any drug association including an ACI (with satisfaction degree 1). For a patient with two comorbidities, LVH and hyperkaliemia, the best solution is I_2, *i.e.* CA.

Table 3. The 8 possible interpretations for the example of Table 1, the corresponding drug prescriptions (ACI, ARB and/or CA) and the satisfaction degrees for the 4 formulas defined in Table 2. HF: heart failure, HK:hyperkaliemia, ADE-ACI: history of Adverse Drug Event with ACI.

Interpretations	***ACI***	***ARB***	***CA***	**has(*LVH*)** $\rightarrow \varphi_1$	**has(HF)** $\rightarrow \varphi_2$	**has(HK)** $\rightarrow \varphi_3$	**has(ADE-ACI)** $\rightarrow \varphi_4$
I_1	F	F	F	0	1	1	1
I_2	F	F	T	2	2	1	1
I_3	F	T	F	3	1	0	1
I_4	F	T	T	2	2	0	1
I_5	T	F	F	1	1	0	0
I_6	T	F	T	1	2	0	0
I_7	T	T	F	1	1	0	0
I_8	T	T	T	1	2	0	0

3. Discussion and conclusion

In this article, we have presented a qualitative framework for encoding medical knowledge including mandatory statements but also preferences, and for reasoning about them.

This framework is interesting since it can integrate preferences of different sources such as drug properties (*e.g.* contraindications), CPGs (*e.g.* recommendations) and patient history (*e.g.* history of adverse event with a given drug). In a previous work [7], we already successfully used a similar ordered disjunction on non-medical domain, particularly in alert correlation. We applied our framework to a limited example on the hypertensive drugs where the formulas are manually formulated, we plan to extend this example by formalizing the hole CPG and implementing it in the ASTI clinical decision support system [11]. In addition, frequently, several preference formulas are available, based on different criteria, such as efficiency, tolerance or cost (*e.g.* ACI should be preferred to ARB due to their lower cost). In these situations, it would be interesting to define rules for combining several preference formulas into a single one. This would require to take into account the specificities of the criteria. For example, costs are additive, thus we can deduce from the previous cost-based preference that a bitherapy Diuretics+ACI should be preferred to Diuretics+ARB; this may not be true for other non-additive criteria. In our example (Table 1), we considered an order of preference between the 3 recommended drug class for LVH, although this is not clearly stated in the CPG. The order does exist between ACI and ARB (due to cost), but is less obvious for CA. Preferences elicitation is a difficult problem and we need to study how one can encode evidence and results obtained from reviews, meta-analyses or reports on clinical trials with respect to some factors.

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