Augmenting Guideline Knowledge with Non-Compliant Clinical Decisions: Experience-Based Decision Support

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Abstract. Guideline-based clinical decision support systems (CDSSs) are expected to improve the quality of care by providing best evidence-based recommendations. However, because clinical practice guidelines (CPGs) may be incomplete and often lag behind the publication time of very last scientific results, CDSSs may not provide up-to-date treatments. It happens that clinical decisions made for specific patients do not comply with CDSS recommendations, whereas they comply with the state of the art. They may also be non-compliant because they rely on some implicit knowledge not covered by CPGs. We propose to capitalize the clinical know-how built from such non-compliant decisions and allow physicians to use it in future similar cases by the development of a decisional event structure that allows the modelling, storage, processing, and reuse of all the information related to a decision-making process. This structure allows the analysis of non-compliant decisions, which generates new experience-based rules. These new rules augment the knowledge embedded in CPGs supporting clinician decision for specific patients poorly covered by CPGs. This work is applied to the management of breast cancer within the EU Horizon 2020 project DESIREE.

Keywords: Experience-based Clinical Decision Support System, Data Mining Techniques, Clinical Guidelines Evolution, Breast Cancer, DESIREE

1 Introduction

Clinical practice guidelines (CPGs) are proposed as a source of information and treatment recommendations that rely on the rigorous evaluation of scientific publications to provide best health care practices [1]. However, CPGs have some weakness-

es. The identification and synthesis of the evidence (e.g. deciding what type of evidence and outcomes should be included in guidelines), the determination of which values should be representative to be integrated in the guideline definition and how to update and implement these guidelines are some of them [2].

Most current clinical decision support systems (CDSSs) facilitate the implementation of CPGs [3], but they still do not overcome the weak points reflected above. For example, current CDSSs do not model implicit clinical knowledge not reflected in CPGs. Consequently, when clinical professionals perform the reasoning process that uses this implicit knowledge, and do not follow CPGs recommendations, i.e. when they make *non-compliant* decisions, the context and the reasoning process in which the implicit knowledge has been used are lost [4]. Over a 9-year period and more than 1000 breast cancer cases, Lin et al. [5] showed that actual chemotherapy decisions deviated from international guidelines in approximately 50% of the cases. This shows that CDSSs may end up useless for clinicians, since they use such systems to support them specially in the decision for special cases not addressed in CPGs.

Therefore, the main objective of our work is to store and process all the relevant information involved in the decision-making process of non-compliant decisions, to enrich the current CPG-based knowledge base formalized in the CDSS. The paper is organized as follows: section 2 presents the state of the art about the main technologies used as basis of our work; section 3 presents a new decision centered structure that will allow the exploitation of the information for each decisional event; section 4 presents the methodology for generating new knowledge and a use case to illustrate it. Finally, section 5 concludes the paper and proposes some future work.

2 Background concepts

2.1 Clinical Practice Guidelines (CPGs)[1]

CPGs are defined as explicit and structured statements that model the current Evidence-Based Medicine (EBM) and the clinical judgment for best patient care at the decision making level [6], [7]. Good quality CPGs must present some characteristics including validity, reproducibility, reliability, representative development, clinical applicability, clinical flexibility and clarity [8]. Implementing CPGs has several benefits among which supporting clinicians in their decision making process, providing educational help for practitioners, improving quality assurance and assessment of the recommended treatment, and avoiding negligent medical practice [9].

Nevertheless, there are some barriers to the implementation and dissemination of CPGs that must be overcome to guarantee they are followed up in clinical practices. One of the main problems is the maintenance and update of CPGs, since because CPGs are not usually expressed in flexible and evolutive platforms, it often happens that CPG contents lag behind actual knowledge [10]. Furthermore, CPGs do not cover all possible clinical cases and recommendations for the specific patients that do not completely fit guideline contents, mainly due to these CPG knowledge gaps [11].

[1] In this paper, we refer to CPGs when talking about CPGs and local (validated) protocols.

2.2 Clinical Decision Support Systems (CDSSs)

In the last decade, CDSSs have proven to be potential tools to promote the implementation of CPGs [12]–[15] and give assistance to the clinicians in a decision-making process. They are often designed to help the implementation, integration, and application of CPGs, i.e. guideline-based CDSSs support clinicians in making CPG-compliant decisions [16]. Studies have reported that CDSSs do improve care quality and decrease medical errors [17]. Although guideline-based CDSS have a positive impact on the quality of medical practice they are quite constraining, as they depend on the *a priori* defined domain knowledge.

2.3 Techniques for knowledge discovery

Large biomedical databases contain unexploited knowledge that can give relevant information in the decision-making process.

Data mining techniques aim to discover this knowledge using classification, clustering and association algorithms [18]. In breast cancer domain for example data mining techniques are used mainly to predict the best result from a treatment for a patient [19] or to perform its survivability [20].

On the other hand, machine learning techniques, such as Case-Based reasoning (CBR) provides a recommendation for a new patient based on the decision previously made for similar patients [21]. Four steps are followed to get the recommendation: (i) case retrieval within the knowledge base built from previously solved cases, (ii) reuse of the most similar case(s), (iii) solution testing to see how the prior decision(s) fit(s) to the new case, and (iv) record of the newly acquired knowledge [22].

Current studies describe CPG implementation though different applications, such as rule based CDSS [2] or CBR [23], [24], along with data mining techniques to cover clinical "grey areas" that CPGs are not able to manage or for which their definition is relatively fuzzy [25].

3 Methods for Experience Modelling

Considering all the above mentioned constrains of current CDSS, we propose a new paradigm of decision support named "experience-based" as a hybrid CDSS following the principle of augmenting CPGs knowledge from data mining techniques and the study of CPG non-compliant cases.

This section describes the method we proposed to augment the current guideline-based CDSSs with experience, which results in an experience-based CDSS. For that, we first describe the decisional events structure that allows us to retrieve, model, and exploit all the information related to the decision-making process (Section 3.1). Thereafter we present the method to enrich CPGs by adding experience-based rules based on the decisional events information (Section 3.2).

3.1 Decisional event structure

A decisional event structure has been proposed in [26] to model all the information regarding the decision-making process. This decisional event structure is defined by a set of components:

1. $\boldsymbol{P = \{P_i\}}$:Set of patient clinical parameters
2. $\boldsymbol{R = \{R_j\}}$: Set of clinical statements expressed in a computer-interpretable way (IF-THEN rules). These clinical statements represent the knowledge coming from different sources (e.g. CPGs, local guidelines, experience-based rules generated by the system) and are itemized in the following components:
   (a) . $\boldsymbol{A = \{A_m\}}$: Set of the antecedents that compose the *conditional part* of rules, i.e. the IF-part. These antecedents evaluate patient clinical parameters with *a priori* defined conditions by CPGs with relational mathematic operators.
   (b) . $\boldsymbol{W}$: A recommendation coming from the accomplishment of the conditions defined in the antecedents, which is the *consequence part* of the rule, i.e. the THEN-part. In some cases, the provided recommendation could be an aggrupation of various treatments (i.e. a set of recommendations), expressed as $W = \{S_1, S_2, \dots S_l\}\ with\ l > 1$ where $\boldsymbol{S}$ is an atomic treatment.
3. $\boldsymbol{FD:}$ Final decision taken by clinicians which could be compliant with the recommendation provided by the guideline $\boldsymbol{W}$ or not.
4. $\boldsymbol{E}$: Actual treatment administrated at time t_1 after the decision is made, which could be compliant with $\boldsymbol{FD}$ or not.
5. $\boldsymbol{C = \{C_k\}}$: Set of criteria followed by clinicians to reach an agreement about a final decision. These criteria will be sorted in different groups that will have a closed list of Boolean possible values $\boldsymbol{J_n}$. So, we can define a single criterion as a set of justifications $C_1 = \{J_1, J_2, \dots J_n\}\ with\ n \geq 1$. For example, *Tumor Size* could be a criterion of non-compliance which justification is the difficult follow-up, which could be either *true* or *false* (i.e. Boolean value).
6. $\boldsymbol{O(t)}$: Set of outcomes of a studied patient after a time *t* to be able to assess the success or failure of the given treatment.

Ideally, clinicians' decisions are compliant with CPGs, thus choosing one of the recommendation provided by the guideline-based CDSS as their final decision FD. But in certain cases, when clinicians do not comply with CPGs (e.g. BU considers the patient preferences in their decision), FD is different from CPG-based recommendation(s) for that patient. In both cases, the administrated treatment E is expected to be equal to the final decision FD, but due to deviations in the treatment plan, E could differ from FD.

The modelling of all the contextual information of a decision-making process into a decisional event structure makes possible to understand, process, and reuse the implicit clinical knowledge.

3.2 Experience-based rules

The data modeled within the decisional event structure is used to identify relevant information in the decision-making process and to retrieve implicit clinical knowledge [6]. In cases where clinicians do not follow CPGs-based recommendation(s), thus being non-compliant with the CPGs, there is an implicit clinical knowledge that we seek to exploit to enrich the knowledge base of the CDSS.

Below we present the method to analyse a decisional event and build the experience-based rules from non-compliant decisions:

- The starting point of the method is to retrieve the set of CPG rules that were executed in the decisional event $\boldsymbol{RS} = \{R_1, R_2, \dots R_j\}\ with\ j > 0$. The antecedents (i.e. IF-part) of these rules are defined as $\boldsymbol{CR} = \{A_1, A_2, \dots A_k\}\ with\ k > 0$. The evaluated patient parameters accomplished all of them.
- Thereafter, we identify and retrieve the rule set $\boldsymbol{RS'} = \{R'_1, R'_2, \dots R'_u\}\ with\ u > 0$ whose recommendation $\boldsymbol{W}$ match with the final decision $\boldsymbol{FD}$ made by clinicians. The antecedents of this secondary rule set $\boldsymbol{RS'}$ are defined as $\boldsymbol{CR'} = \{A'_1, A'_2, \dots A'_m\}\ with\ m > 0$ and the evaluated patient parameters did not accomplish at least one from each rule $\boldsymbol{R}$'.
- From both sets of antecedents, $\boldsymbol{CR}$ and $\boldsymbol{CR'}$, we look for *'conflictive antecedents'*, i.e. incompatible antecedents (e.g. *Tumor Size >20* ϵ $\boldsymbol{CR}$ and *Tumor Size ≤20* ϵ $\boldsymbol{CR'}$), or antecedents that are complementary, i.e. *'complementary antecedents'* (See example in the Use Case explained below).
  - We keep the complementary antecedents in the experience-based rule generated from the non-compliant decision.
    - In some cases, one or more antecedent could be defined in the non-compliant antecedent set $\boldsymbol{CR'}$ but not in the compliant one $\boldsymbol{CR}$, i.e. antecedents defined in the relative complement of $\boldsymbol{CR}$ formally noted as: $\boldsymbol{CR'\backslash CR}$. For this scenario, this new antecedent will be included in the new rule with the patient's clinical parameter as constraint value.
  - When the identified $\boldsymbol{CR}$ and $\boldsymbol{CR'}$ sets contain conflictive antecedents, the following steps must be adopted, depending on the reasons of the conflict:
    - If the antecedent is defined in both $\boldsymbol{CR}$ and $\boldsymbol{CR'}$ (i.e. when it is defined in $\boldsymbol{CR} \cap \boldsymbol{CR'}$) but with different value constraints, in the new experience-based rule, this antecedent will be defined with the patient's clinical parameter value as constraint (e.g. the tumor size in $\boldsymbol{CR}$ is characterized by *Tumor Size >20* whereas for $\boldsymbol{CR'}$ is measured as *Tumor Size ≤20* $\boldsymbol{CR'}$. In the experience based rule it will take the patient value: *Tumor Size* = P_i). In this case, we will be adjusting the value of a constraint.
- Lastly, the set of criteria $\boldsymbol{C_k}$ (e.g. clinical preferences, patient preferences) defined by clinicians in the decision-making process composed by one or more Boolean justifications $\boldsymbol{J_n}$ give us hints about new relevant clinical parameters to include (e.g. because they were not defined in the CPGs) or study.

To sum up, when a new clinical parameter has to be added in the generation of the experience based rule from one of the studied rule sets CR or CR' (i.e. complementary antecedents) it must always be equal to the patient's value.

To illustrate the applicability of this method, a use case is presented next.

3.3 Use case: Breast Cancer

We present a simplified use case based on the local protocol from Onkologikoa Foundation, where we apply the previously presented method. We consider two patients, Patient 1 and Patient 2 suffering from an Invasive Ductal Carcinoma (IDC).

		PATIENT 1	PATIENT 2
P_1	Age	65	73
P_2	Sex	Woman	Woman
P_3	Number of Pregnancies	0	4
P_4	Number of Lesions	2	2
P_5	Location	Right, Lower outer quadrant	Right, Upper outer quadrant
P_6	Size (mm)	21	22
P_7	BIRADS	5	-
P_8	Ulceration	NO	NO
P_9	Skin metastasis	NO	NO
P_{10}	cT (size)	T2	T2
P_{11}	cN (number)	0	0
P_{12}	cM (metastasis)	0	0
P_{13}	Stage	2a	2a
P_{14}	Histological type	Invasive	Invasive
P_{15}	Grade	GII	GI
P_{16}	Carcinoma in situ type	Ductal carcinoma	Ductal carcinoma
P_{17}	Estrogen receptor	Positive	Positive
P_{18}	Progesterone receptor	Positive	Positive
P_{19}	HER-2 receptor	Negative	Negative
P_{20}	Ki67 (%)	14	16
P_{21}	Clinical criterion: Tumor Size	-	Follow-up difficulty

Table 1. Set of clinical parameters and values defining Patient 1 and Patient 2.

The highlighted parameters (in grey) are those considered by Onkologikoa's protocols. In Figure 1 we illustrate one of the rules from which the antecedents of its conditional statement are met for patient 1.

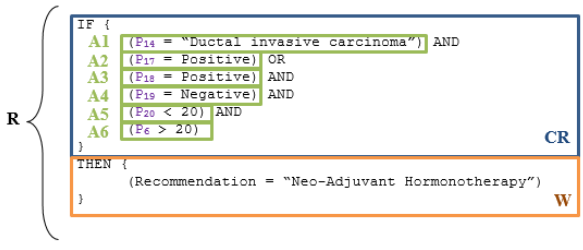

Fig. 1. Local protocol derived rule for non-metastatic breast cancer with infiltrating tumor.

In Figure 1 we identify the conditional statement (in blue) named CR. This conditional statement is composed by a set of antecedents (i.e. $CR = A_1 \cup A_2 \cup A_3 \cup A_4 \cup A_5 \cup A_6$, highlighted in green). The consequence statement (in orange) provides protocol-based recommendation *W*= "Neo-Adjuvant Hormonotherapy".

The BU decided not to comply with the provided recommendation and decided ***FD***= "surgery". The reason behind this final decision was the criteria ***C***= "Tumor Size" with the justification $\boldsymbol{J_1}$= "Follow-up difficulty".

In Figure 2 we summarize the data related to this decisional event. The criteria ***C*** and justification ***J*** that explained the decision of the different treatment and the non-compliant ***FD*** are highlighted because their source was not protocol-based, but relied on clinicians' know-how.

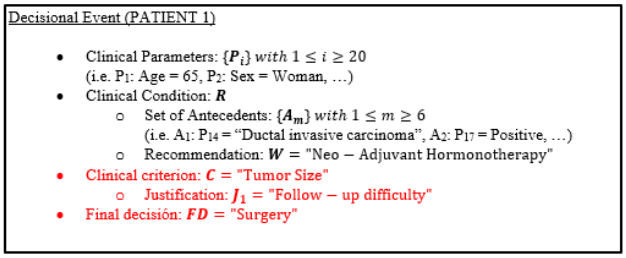

Fig. 2. Summary of the data that composes the decisional event for Patient 1.

Once the decision-making process is completed, and since the decision was not compliant, data is processed to retrieve the implicit knowledge used and consequently augment the knowledge base. The set of rules which recommendation ***W*** matches with ***FD*****=** "surgery" is retrieved. Figure 3 shows a protocol rule that does not match Patient 1 clinical parameter "size" (highlighted in red in the figure), but provides the desired recommendation "surgery".

```
IF {
    (P14 = "Ductal invasive carcinoma") AND
    (P17 = Positive) OR
    (P18 = Positive) AND
    (P19 = Negative) AND
    (P6 < 20) AND
    (P11 = 0)
}
THEN {
    (Recommendation = "Surgery")
}
```

Fig. 3. Example of a protocol rule that provides the desired recommendation despite it does not apply to Patient 1.

The new experience-based rule (Figure 4) will contain **(i)** the antecedents checked by both rules, i.e. *'complementary antecedents'* $\in \boldsymbol{CR} \cap \boldsymbol{CR'}(same\ P_i\ equal\ value)$ (in black), **(ii)** the adjustment of the parameter that was not compliant in one of them characterized by the most restrictive value, i.e. *'conflictive antecedents'* $\in \boldsymbol{CR} \cap \boldsymbol{CR'}$ $(same\ P_i\ different\ value)$ (in blue), **(iii)** the inclusion of a clinical parameter

that was only measured in one of the rules, i.e. inclusion of $\boldsymbol{P_i \in CR \backslash CR' \cup CR' \backslash CR}$ (in green) and (**iv**) the inclusion of clinical criteria that justifies the non-compliancy from the BU (in orange):

```
IF {
    (P14 = "Ductal invasive carcinoma") AND
    (P17 = Positive) OR
    (P18 = Positive) AND
    (P19 = Negative) AND
    (P20 <20) AND
    (P6 = 21) AND
    (P11 = 0)
}
THEN {
    (Recommendation = "Surgery"
     Justification= "Tumor Size: Follow-up difficulty")
}
```

Fig. 4. The experience-base rule generated from the non-compliant decision for Patient 1

Once the experience-based rule is generated, it will be stored in the knowledge base and could be fired for any patient whose clinical parameters checked the conditional statement. To illustrate such case, we present Patient 2 (Table 1). Notice that Patient 2 has parameters similar as those defined for Patient 1 (Table 1), but some additional information concerning clinical parameters (P_{21}: *Tumor size = Follow-up difficulty*).

For Patient 2, protocol- and experience-based rules are executed and provide the two recommendations displayed in Figure 5.

```
CPG Recommendation: Neo-Adjuvant Hormonotherapy
Experience Recommendation: Surgery
(Justification = Tumor Size: Follow-up difficulty)
```

Fig. 5. Recommendations generated by both protocol- and experience based rule sets for Patient 2.

4 Conclusions and Future Work

This work presents a methodology to augment the knowledge of CPGs with clinician experience. First, a decisional event structure is described. This structure formalizes all the decision-related parameters in a computer-interpretable way, allowing its interpretation and reuse. The decisional event structure includes data that plays an important role in the decision-making process (e.g. patients preferences, clinician preferences…), but is not explicitly considered in current CPGs and often explains the reason of non-compliance with CPGs. Hence, this decisional event structure can be a source of knowledge discovery and a starting point for the study of CPG update to cover uncovered specific clinical cases (e.g. onco-geriatric cases).

Second, based on the decisional event structure, we presented the exploitation of the events related to cases where clinicians do not comply with CPGs. For that, we analyzed and processed the implicit clinical knowledge, often omitted in current clinical daily practices, that affects the decision-making process. This process allows the creation of new experience-based rules, which are part of CPGs evolvement.

Nevertheless, the generated experience-based rules, generated from non-compliant cases, must be validated by clinicians to include them in the CPGs-based rule set. This way, we avoid polluting the CPG knowledge base when adding new rules, without clinical supervision and acceptance.

As future work, we will build a quality assessment algorithm that will provide information about the success or failure of the treatments recommended by experience-based rules based on different parameters defined by the outcomes of the patient, such as quality of life or life expectancy.

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